STAR-IDAZ
International Research
Consortium on Animal Health

Annual state-of-the-art report on animal health research on IRC priorities

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Contents

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SIRCAH has been supported by a European H2020 contract, "Secretariat for the International Research Consortium on Animal Health" since 2016, which schedules the annual publication of a report on the state-of-the art on animal health research on STAR-IDAZ IRC priorities. The report aims to inform stakeholders at large about developments in the field of the STAR-IDAZ IRC priority diseases and support decisions by policy makers and research funders.

More information on STAR-IDAZ IRC can be found at **www.star-idaz.net**

Disclaimer:

The report is a presentation of the current initiatives and recent scientific literature, organised to identify and highlight trends and advances in research on animal health, with a focus on priority animal diseases at a global level. The report does not target initiatives aimed at implementing animal disease control strategies (e.g., roadmaps for the control or eradication of infectious diseases) or at improving animal health control infrastructures.

Since the information relating to advances in animal health research is based on published articles, a time lapse between scientific breakthroughs and their publication is inevitable and so the report may not fully capture information on ongoing, or recently concluded, studies.

The findings and conclusions in this report are those of the contributors, who are responsible for the contents, and do not necessarily represent the views of the European Commission. Therefore, no statement in this report should be construed as an official position of the European Commission or of any of STAR-IDAZ IRC and SIRCAH members.

Executive summary

Introduction

The STAR-IDAZ International Research Consortium (STAR-IDAZ IRC) was established in 2016 to coordinate research activities at the international level, to speed up the development of new and improved animal health strategies for priority diseases/infections/issues of animals. The goal of the initiative is to deliver improved control tools and strategies, including candidate vaccines, diagnostics, therapeutics and other animal health products and procedures and/or key scientific information and tools to support risk analysis and disease control for at least 30 priority diseases by 2022.

The aim of this report is to provide STAR-IDAZ IRC Members, as well as other animal health stakeholders, with an overview of the existing opportunities to speed up research, to boost collaboration in the sector, and to provide an overview of the latest discoveries on priority animal health diseases. Overall, this will support the decisions of policy makers and research funders, to accelerate coordinated development of control methods at the international level.

Methods

The first two Chapters of this report target initiatives taken to speed up research and development (R&D), to facilitate transnational R&D collaborations, and recent infrastructures and databases to facilitate R&D respectively. Information was collected by scanning the web with relevant keywords or collecting information from the IRC partners.

The third Chapter reports on recent research developments on IRC priority diseases. For each disease, information about existing global research coordination networks is provided, and a collection of the main information on identified research gaps was derived from the DISCONTOOLS database. A selection of promising innovations or major research outcomes published in scientific journals between January and September 2021 were identified through a scan of the scientific literature in the CAB Abstracts database, using specific keywords for each of the priority diseases/issues. Trends in published research, associated with the keywords exploited have been reported to show, whenever possible, main statistics on each priority disease/issue for topics such as diagnostic, epidemiology, vaccination/vaccine development and therapeutics. A graphical analysis of the estimated distribution of articles, based on country of first author, among the four STAR-IDAZ Regional Networks (Americas, Africa and Middle East, Asia and Australasia, and Europe), has been also reported. This has been supplemented with information on current research initiatives on the priority diseases and issues, collected from experts and research funders during STAR-IDAZ IRC Executive Committee, Scientific Committee, and Regional Networks meetings and roadmap workshops.

This report does not necessarily reflect the opinion of the STAR-IDAZ IRC members, but is the result of an analysis, by the Scientific Secretariat of the STAR-IDAZ IRC (SIRCAH), based on the collection of information from selected sources, including literature surveys.

Main acronyms

ACDP	Australian Centre for Disease Preparedness
AfVANET	African Vaccinology Network
AFENET	African Field Epidemiology Network
AI	Avian Influenza
AMR	AntiMicrobial Resistance
ANIHWA ERA-NET	European Research Area Network on Animal Health and Welfare
ASF	African swine fever
ATA	Alternatives To Antibiotics
AU	African Union
AU-IBAR	African Bureau of Animal Resources
AvCoV	Avian Coronavirus
BBSRC	Biotechnology and Biological Sciences Research Council
BMGF	Bill and Melinda Gates Foundation
BSL	BioSafety Level
bTB	Bovine Tuberculosis
CA	Contagious Agalactia
CABI	Centre for Agriculture and Bioscience International
CBPP	Contagious Bovine Pleuropneumonia
CCHF	Crimean-Congo Hemorrhagic Fever
CDP	Continuing Professional Development
CEPI	Coalition for Epidemic Preparedness Innovations
CIRAD	French Agricultural Research Centre for International Development
COMBAR	COMBatting Anthelmintic resistance in Ruminants
COPA COGECA	Committee of Professional Agricultural Organisations-General Confederation of Agricultural Cooperatives
COST	EU Cooperation in Science and Technology
CoVs	Coronaviruses
CRWAD	Conference of Research Workers in Animal Disease
CSIC	Spanish National Research Council
CWG AHW	Collaborative Working Group on European Animal Health and Welfare Research
DEFRA	Department for Environment, Food & Rural Affairs (UK)
DISCONTOOLS	Disease Control Tools
DIVA	Differentiating Infected from Vaccinated Animals
ECTAD	Emergency Centre for Transboundary Animal Diseases
EDCTP	European-Developing Countries Clinical Trial Partnership
EFSA	European Food Safety Authority
EJP One Health	European Joint Programme Co-fund on One Health
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMIDA ERA-NET	European Research Area Network on Emerging and Major Infectious Diseases of Livestock
ERA-NET	European Research Area Network
ERRAZE	Early Recognition and Rapid Action in Zoonotic Disease Preparedness
EVA	European Virus Archive
FAO	Food and Agriculture Organization of the United Nations
FLI	Friedrich-Loeffler-Institut - German Federal Research Institute for Animal Health
FMD	Foot-and-Mouth Disease

FP	Framework Programme
GALVmed	Global Alliance for Livestock Veterinary Medicines
GAMRIF	Global AMR Innovation Fund GAMRIF
GARA	Global ASF Research Alliance
GAVI	Global Alliance for Vaccine and Immunisation
GCRF	Global Challenges Research Fund
GFRA	Global FMD Research Alliance
Global AMR R&D Hub	Global Antimicrobial Resistance Research and Development Hub
GloPID-R	Global Research Collaboration for Infectious Disease Preparedness
GMP	Good Manufacturing Practices
GOARN	Global Outbreak Alert and Response Network
GRAbTB	Global Research Alliance for Bovine Tuberculosis
HPAI	Highly Pathogenic Avian Influenza
IAEA	International Atomic Energy Agency
IBS	International Brucellosis Society
IBV	Infectious Bronchitis Virus
ICRAD	International Coordination of Research on Infectious Animal Diseases
IDRC	International Development Research Centre
IHI	Innovative Health Initiative
IMI	Innovative Medicines Initiative
InnoVet- AMR	Innovative Veterinary Solutions for Antimicrobial Resistance
INIA	Spanish National Institute for Agricultural Research
INRAE	French National Research Institute for Agriculture, Food and Environment
IOM	International Organisation for Mycoplasmology
IRC	International Research Consortium
IRD	French National Research Institute for Sustainable Development
IRPCM	International Research Program of Comparative Mycoplasmology
IRTA	Institute for Research and Agrofood Technology
IZS	Italian Experimantal Zooprofilactic Institute
IVVN	International Veterinary Vaccinology Network
JRAs	Joint Research Activities
KVI	Kimron Veterinary Institute
LiHRA	Livestock Helminth Research Alliance
LMICs	Low- and Middle-Income Countries
LPAI	Low Pathogenic Avian influenza
LVIF	Livestock Vaccine Innovation Fund
MERS-CoV	Middle East Respiratory Syndrome CoV
MINSAL	Italian Ministry of Health
NAK	Hungary's National Agricultural Chamber
NVRI	Nigerian National Veterinary Research Institute
OFFLU	OIE/FAO Network of Expertise on Avian influenza
OIE	World Organisation for Animal Health
PANDORA	Pan-African Network for Rapid Research, Response and Preparedness for Infectious Diseases
PEAV	Porcine Enteric Alphacoronavirus
PED	Porcine Epidemic Diarrhoea virus
PHEIC	Public Health Emergency of International Concern
PRDC	Porcine Respiratory Disease Complex
PRRS	Porcine Reproductive and Respiratory Syndrome
R&D	Research and Development
REA	Research Executive Agency

RVF	Rift Valley Fever
SADC	South African Development Community
SADS	Swine Acute Diarrhea Syndrome
SARS-CoV-2	Severe Acute Respiratory Syndrome CoV2
SCAR	Standing Committee on Agricultural Research
SDG	Sustainable Development Goals
SERIDA	Asturias Regional Service for Agri-Food Research and Development
SIRCAH	Secretariat of the International Research Consortium on Animal Health
SIV	Swine Influenza Virus
SRIA	Strategic Research & Innovation Agenda
STAR IDAZ Global Net	Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses
TGEv	Transmissible gastroenteritis virus
TNA	Transnational Access
TPPs	Target Product Profiles
TRANSVAC	European Network of Vaccine Research and Development
TSE	Transmissible Spongiform Encephalopathy
UNDP	United Nations Development Programme
UKCDR	United Kingdom Collaborative on Development Research
UK DFID	United Kingdom Department for International Development
USAID	United States Agency for International Development
VBD	Vector Borne Disease
VetBioNet	Veterinary Biocontained research facility Network
WG	Working Group
WHO	World Health Organisation
WUR	Wageningen University & Research
ZAPI	Zoonoses Anticipation and Preparedness Initiative
ZODIAC	Zoonotic Disease Integrated Action

I. INTERNATIONAL INITIATIVES TO SPEED UP R&D

Research and development (R&D) are fundamental to ensure the development of adequate disease prevention and control tools, as well as to make better use of knowledge that is currently available, and for modelling disease impact. Several initiatives have been started, at a regional or at a global level, to speed up research so as to deliver timely solutions to emerging issues.

The aim of this chapter is to provide a list of the main funding and regulatory easing initiatives, and of the fast-track development pathways, which are designed to accelerate the delivery of R&D relevant to the animal health sector.

Global research networks on specific diseases

The sharing of information and scientific knowledge is of paramount importance to ensure disease preparedness. To this end, global research networks and alliances have been established on a number of infectious diseases to exchange and generate knowledge that would support the development of tools to successfully prevent, control or eradicate such diseases.

Although these networks present slightly different objectives, the identification of research needs and the coordination of research on priority issues are common activities.

Further details on the specific networks for the other STAR-IDAZ IRC priority diseases are provided in Chapter III.

AfVANET - African Vaccinology Network

Website: http://afvanet.org/

AFRICAN VACCINOLOGY NETWORK

Partners ca.	Budget	Start date:
NA	NA	2019

Overview

The African Vaccinology Network (AfVANET) is a network of African scientists, researchers, scholars and policymakers involved in vaccine research and development. AfVANET provides a forum for African scientists to take a greater part in establishing priorities for vaccine development for emerging and re-emerging human and veterinary diseases affecting the continent.

The concept of AfVANET was born during the Keystone Symposium "New Approaches to Vaccines for Human and Veterinary Tropical Diseases" held in Cape Town, South Africa in May 2016. It was noted in the symposium that while African countries suffer the most from the infectious diseases discussed during the conference, the research and innovation used to tackle these diseases mostly come from outside the continent. The need for a better involvement of African scientists in finding solutions to infectious diseases that affect the health and wellbeing of people on the African continent was stressed. The network will collaborate with experts from the World Health Organisation (WHO), the World Organisation for Animal Health (OIE), the African Union Centre for Disease Control (AU CDC), the African Field Epidemiology Network (AFENET), the Global Alliance for Vaccine and Immunisation (GAVI) and the Global Alliance for Livestock Veterinary Medicine (GALVmed).

Aim and priorities

Aim: to promote and retain Africa's potential by fostering collaboration, innovation, training, and trust between vaccine Research & Development organisations and facilities for human and animal health in Africa.

Priorities: Vaccines, Genomics and transmission, Clinical Research, Health Systems Research Ethics, Population Health.

Objectives

- Bring together all stakeholders in vaccinology and related sciences in Africa;
- Identify and prioritise vaccine gaps in Africa;
- Promote vaccine research and development in Africa; and
- Promote sound ethics, biosafety and biosecurity in Africa.

News

The kick-off meeting of the AfVANET took place on 19-20 March 2019 in Nairobi, Kenya. Around 30 speakers, from both the human and animal health sectors, attended the meeting, coming from Africa, Asia, Australia, and Europe.

The AfVANET committee is working toward making AfVANET recognized by African governments and the African Union (AU).

AgResults Brucellosis vaccine prize

Website: https://brucellosisvaccine.org/

Partners ca.	Budget	Start date:
6	US$ 30 million prize	2016-2026

Overview

The Brucellosis Vaccine Prize is a US$ 30 million prize competition that invites vaccine developers ('solvers') to submit their proposals for developing a suitable vaccine that is efficacious, safe and viable for use against *Brucella melitensis* in small ruminants in developing countries. This global competition is funded by AgResults (a collaborative initiative between the governments of Australia, Canada, the UK and the USA, as well as the Bill & Melinda Gates Foundation), and implemented by the Global Alliance for Livestock Veterinary Medicines (GALVmed).

'Pull mechanisms' such as this prize, reward research output rather than research input.

Aim and priorities

Aim: developing a suitable vaccine that is efficacious, safe and viable for use against *Brucella melitensis* in small ruminants.

Objectives

The competition is open to any animal health, biotechnology, or pharmaceutical company, and other organisations. It is structured in three phases:

- Phase 1 ('Application Phase'): solvers were invited to submit their initial application to participate in the Competition (deadline 18 November, 2017). The first Milestone Payment was a one-off payment of US$ 100,000, which could be awarded to a maximum of ten participants.
- Phase 2 ('Solving Phase'): solvers work towards the production of a proof-of-concept together with other deliverables (which are outlined in the official Competition Rules document). This phase can start for each Solver upon successful application and leading up to the potential award of Milestone Payment 2 (US$ 1,000,000; up to a max of 4 solvers).
- Phase 3 ('Final Phase'): solvers will be required to take their vaccine candidates from their 2nd Milestone Deliverables to a registered product. This phase can start for each solver upon successful application and completion of Phase 2 and leading up to the potential award of the Grand Prize (US$ 20,000,000) or Best in Class Prize (US$ 5,000,000). The competition will close in November 2026.

News

Phase 1 is now concluded, and 10 participants have already been awarded the first Milestone Payment; the competition is now in Phase 2 (15 participants have entered this phase). For organisations that have been accepted into Phase 2 of the competition, the primary focus will be to demonstrate proof of principles of efficacy and safety, and establish a scaled production process, together with other deliverables. The competition will probably be extended until 2022 to complete Phase 2.

AgResults FMD Vaccine Challenge Project

Website: https://www.galvmed.org/foot-and-mouth-project/

Partners ca.
7

Budget
US$ 17.68 million
prize competition

Start date:
2020

Overview

In January 2020, AgResults started a new competition for encouraging the development and uptake of an improved vaccine specifically for the needs of East Africa, called The Foot and Mouth Disease (FMD) Challenge Project. The project is supported by Australia, United Kingdom, Canada, USA, BMGF, and the World Bank, and is led by GALVmed. The FMD Vaccine Challenge Project will encourage pharmaceutical companies around the world to participate. These companies will participate as "competitors" to create vaccines that meet criteria established for the region. Once the vaccines are approved and registered, competitors will become eligible to commence sales.

The project will contribute to the cost-per-dose paid to the competing manufacturers, thereby encouraging government and private sector actors to better combat FMD by consistently purchasing high volumes of vaccines at affordable prices. To build a stable market around FMD control, the project will promote the development of a private sector model for buying and distributing vaccines, while enhancing existing public sector control efforts. As the market develops, the project plans to expand access to effective vaccines among smallholder farmers, yielding improvements in livestock health and increases in net income.

Aim and priorities

Aim: develop, register, and commercialise effective vaccines for the control of FMD in East Africa.

Priorities:

- Development of high-quality FMD vaccines, tailored for the Eastern African strains;
- Increased vaccine production and regional purchases to create greater market stability and a reduction in price; and
- Development of a private sector model for buying and distributing FMD vaccines to complement public sector efforts.

Objectives

The competition has two phases:

- Development Phase: competitors must submit FMD vaccine dossiers (that they believe meets all of the elements of the AgResults Target Product Profile) to the regulatory authorities in at least two target countries, by August 2023. If no dossiers are submitted by this date, AgResults reserves the right to terminate the competition. If a Competitor submits a dossier for assessment by the deadline, they will be eligible to apply to AgResults (via the online portal) upon receipt of full product registration in at least two target countries.
- Cost-Share Phase: will start once the first vaccine is approved by AgResults and the Competitor has received order(s) of at least 150,000 doses. The AgResults-funded portion of the vaccine cost will not exceed a vaccine price of US$ 2.00. Anything above US$ 2.00 will be paid for by the buyer. AgResults provides funding directly to manufacturers.

Once the first vaccine has been approved by AgResults, other Competitors will still be eligible to submit applications (until 3.5 years after the start of the Cost-Share Phase).

News

The Request for Applications document, containing full details of the Competition, was published in July 2020 and can be accessed at **https://www.galvmed.org/wp-content/uploads/2020/09/FMD-Vaccine-Challenge-Project-RFA-FINAL-rev1-010920.pdf**.

GALVmed is conducting a first round of data collection and plans to share a preliminary report in 2021.

CEPI - Coalition for Epidemic Preparedness Innovations

Website: http://cepi.net/

Partners ca.
35

Budget
US$ 3.5 to
4 billion/ 5yrs

Start date:
Cepi 2017-2021
Cepi 2.0 2022-2026

Overview

CEPI's coalition partners include global health organisations, vaccine developers and manufacturers, academic institutions, governments, philanthropies and civil society. It was founded by the governments of Norway and India, the Bill & Melinda Gates Foundation (BMGF), Wellcome, and the World Economic Forum. To date, CEPI has secured financial support from Australia, Austria, Belgium, BMGF, Canada, Denmark, the European Commission, Finland, Germany, Hungary, Italy, Japan, Kuwait, Lithuania, Luxembourg, Malaysia, Mexico, Netherlands, New Zealand, Norway, Panama, Saudi Arabia, Serbia, Singapore, Switzerland, United Kingdom, USAID, Ethiopia, The Republic of Korea, Indonesia, and Wellcome. Additionally, in 2020 CEPI received support from private sector entities as well as public contributions through the UN Foundation COVID-19 Solidarity Response Fund. CEPI Secretariat is based in Oslo, Norway.

Aim and priorities

Aim: to finance and coordinate the development of new vaccines to prevent and contain infectious disease epidemics, also ensuring that the vaccines to be developed will be affordable and available to populations with the most need.

Priorities: CEPI initially focused on vaccines for known epidemic threats, selected on the priority list of pathogens outlined in the WHO R&D Blueprint. In the first years of activity, the targets have been Middle East Respiratory Syndrome coronavirus (MERS-CoV), Lassa virus, Nipah virus, Rift Valley fever, Chikungunya and the so-called "Disease X" (i.e., a serious international epidemic caused by a pathogen currently unknown to cause human disease).

Although CEPI's focus is on human diseases, most of the diseases in the WHO R&D Blueprint are zoonoses, and, in some specific cases, CEPI would consider the development of animal vaccines, as this would represent an effective way for controlling the disease and preventing the development of human cases.

In 2020, CEPI activities mostly shifted toward COVID-19 response, and more specifically toward the development of human vaccines: 9 partnerships to develop vaccines against COVID-19 were initiated. The programme will leverage rapid response platforms already supported by CEPI as well as new partnerships, with the aim of advancing COVID-19 vaccine candidates into clinical testing as quickly as possible.

Objectives

- Stimulate, facilitate and finance the development of new vaccines against infections of epidemic potential, especially where pathways to regulatory approval and commercialisation are highly unpredictable;
- Advance candidate vaccines through the development process, so safety and efficacy are proved in principle through human trials, before epidemics begin. This will enable rapid full trials or emergency deployment in outbreaks;
- Establish the technical capabilities and processes necessary to accelerate research, development, manufacturing and clinical trials in the context of an outbreak;
- Work with industry, regulators and other bodies to ensure any vaccines developed get licensed and reach the people who need them; and
- Support the long-term development of epidemic vaccine preparedness within the countries most at risk from epidemic threats.

News

CEPI's **5-year plan 2022-2026** lays out a US$ 3.5 billion roadmap to reduce vaccine development timelines to 100 days, develop a universal vaccine against COVID-19 and other betacoronaviruses, and create a "library" of vaccine candidates for use against known and unknown pathogens.

A detailed implementation plan for the CEPI strategy for 2022-26 will be developed within 2021, building from an assessment of implications and risks related to the new strategy and will include the updated governance structure, secretariat set-up, and decision-making processes to guide the operation of the strategy starting in 2022.

CWG AHW - Collaborative Working Group on European Animal Health and Welfare Research

Website: http://www.scar-cwg-ahw.org/

Partners ca.	Budget	Start date:
20	NA	2005

Overview

In 2005, in response to an initiative of the EU Standing Committee on Agricultural Research (SCAR), the Collaborative Working Group on European Animal Health and Welfare Research (CWG AHW) was established. The aims of this group, encompassing representatives of funding bodies from over 20 European countries, were the sharing of information, coordination of research activities, and the definition of a common research agenda.

Several actions have been initiated in the EU under the auspices of the CWG AHW, with the aim of improving transnational collaboration in research and to start a European coordination of research to define a coherent European Research Area (ERA). Building on this framework, networks between research funders on animal health were supported through four EU funded initiatives, the EMIDA ERA-NET (European Research Area Network on Emerging and Major Infectious Diseases of Livestock 2008 - 2011), the STAR IDAZ Global Net (Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses, 2011 - 2015), the ANIHWA ERA-NET (European Research Area Network on Animal Health and Welfare, 2011-2015), and the ICRAD ERA-NET (International Coordination of Research on Infectious Animal Diseases, 2019 - 2023). Currently, the CWG also acts as European Regional Network for the STAR-IDAZ IRC.

Aim and priorities

Aim: to establish a durable and focused network of research funders from Member and Associated States of the EU – leading to improved collaboration on research prioritisation and procurement, creating the necessary critical mass and focus on animal health and welfare research needs.

Priorities: health, wellbeing and welfare of farmed production animals including fish and bees. Specifically, it includes welfare, infectious and non-infectious diseases including those conditions which pose a threat to human health, food safety issues relating to livestock products, and diseases of wildlife where they act as reservoirs of infection for humans or production animals.

Objectives

- Share information on research projects;
- Coordinate research activities;
- Work towards a common research agenda;
- Work towards mutual research funding activities, in the field of animal health, fish health and those conditions which pose a threat to human health.

Other activities include mapping the landscape in relation to provisions of research facilities, including expertise and micro-organism collection.

News

The CWG AHW has continued to hold plenary biannual meetings since it was formed, with participation of the subgroups Strategy & Foresight Unit (SFU) and Animal Welfare, and two Management Board meetings. These meetings enable members to share information on ongoing research activities and options for collaboration, as well updates on emerging diseases and current animal health issues.

Additional meetings were held during 2021 as the CWG AHW is part of the core group for the preparation of a candidate European Partnership for Animal Health and Welfare (PAHW) under the cluster 6 of Horizon Europe (Food, bioeconomy, natural resources, agriculture and environment). The partnership aims to deliver key knowledge, services and products to significantly improve the control of animal infectious disease and animal welfare in a coordinated way. The general objectives of the partnership will be to reinforce the preparedness of all actors involved in animal health and welfare against animal disease, to place animal welfare at the foreground of livestock production, to enhance cross-sector collaboration to prevent the spill-over from animals, food and the environment to humans. A new strategic research and innovation agenda is currently being prepared for the partnership and the participatory approach for its design should start by January 2022, in order to be finalised before the beginning of the partnership which is planned to start in 2023. A first draft of the European partnership proposal with more details can be found **here**.

Moreover, the CWG AHW maintained and consolidated interaction with international organisations (EFSA, OIE, COST), industry (COPA & COGECA, AnimalhealthEurope) and with large projects STAR-IDAZ IRC, ICRAD, One Health EJP and DISCONTOOLS.

On the 1 October 2021 the ERA NET ICRAD will open the 2nd transnational call on “One Health Approach to Zoonoses Research and Innovation”. Deadline for the submission of the proposal will be 15 December 2021. A webinar will be held on 8 October 2021 to provide information to interested applicants. Further information can be found **here**.

ECOHEALTH ALLIANCE

Website: https://www.ecohealthalliance.org/programs

Partners ca.
30 countries

Budget
US$ 10 Million

Start date:
2000

Overview

EcoHealth Alliance is a global environmental health non-profit organization dedicated to a 'One Health' approach to protect the health of people, animals and the environment from emerging infectious diseases. The organization formed with the merger of two highly respected organizations, Wildlife Trust and the Consortium for Conservation Medicine. The concern for wildlife conservation and the health of our planet, led EcoHealth Alliance to become an environmental science and public health leader working to prevent pandemics in global hotspot regions across the globe and to promote conservation. It uses a multidisciplinary method to solve health challenges caused by global changes and human-animal interactions. It works with local governments, in-country scientists, and policymakers around the world to make critical on-the-ground-changes for the prediction and prevention of infectious disease.

Aim and priorities

Aim: to protect wildlife and public health from the emergence of disease.

Priorities: Impact on:

- Biosurveillance;
- Deforestation;
- One Health;
- Pandemic Prevention;
- Wildlife Conservation.

Objectives

EcoHealth Alliance's programs are founded on innovations in research, training, global partnerships, and policy initiatives. The strategic focus will be on:

- Pandemic prevention: understanding what causes diseases to emerge, designing better ways to track their origins, and designing pandemic prevention strategies based on good science.
- Policy and Health: influencing national and global policy on pandemic prevention, sustainable development, and conservation; co-design policy initiatives in the USA and globally which promote the linkages between health and the environment and target pandemic prevention through sustainability.
- Conservation tackling:
  - Deforestation: Assessing the economic cost of emerging diseases linked to deforestation and using this to persuade policymakers, consumers, and industry to develop more sustainable approaches to land-use change.
  - Wildlife trade: Tracking the risk of disease emergence from the wildlife trade and the incentives that drive this trade to encourage alternative solutions and reduce species loss, ethical implications, and disease risk.

News

Recent publications from EcoHealth Alliance scientists and its program partners of interest to STAR-IDAZ are related to the link between wildlife and pandemics such as: i) **Wild animal and zoonotic disease risk management and regulation in China: Examining gaps and One Health opportunities in scope, mandates, and monitoring systems**; ii) **Knowledge, Attitude, and Practice Regarding Zoonotic Risk in Wildlife Trade, Southern China**.

Furthermore, an opinion piece was published in the journal philosophical transactions of the Royal Society B on "**The future of zoonotic risk prediction**", summarising the findings of an interdisciplinary workshop on zoonotic risk technologies.

ERFAN - Enhancing Research for Africa Network

Website: https://www.izs.it/IZS/Cooperazione_1/IZSAM_in_Africa/ERFAN_-_Enhancing_Research_For_Africa_Network

ERFAN
Enhancing Research For Africa Network

Partners ca.
34

Budget
€ 1.5 million

Start date:
2018

Overview

ERFAN is an **international scientific network,** funded by the Italian Ministry of Health and supported by OIE, to build fruitful collaborations for both African countries and Italian institutions, allowing a continuous and updated knowledge of animal and human health conditions in relation to the African continent.

IZSAM and the African partners of the SADC (Southern African Development Community) Region, such as Angola, Botswana, Mozambique, Namibia, South Africa, Tanzania, Zambia and Zimbabwe, organized the first ERFAN Meeting in Pretoria in 2017. This was an opportunity to outline a four-year action plan to make the ERFAN Scientific Network operational. The Regional Representatives of the International Organizations such as SADC, European Union, OIE (World Animal Health Organization), FAO (Food and Agriculture Organization of the United Nations), AU-IBAR (African Bureau of Animal Resources), IAEA (International Atomic Energy Agency) and delegates of the Italian Ministry of Foreign Affairs and International Cooperation and the veterinary institutions defined the organizational and operational structure of ERFAN.

Aim and priorities

Aim: to enhance research collaboration for Africa

Priorities: Animal welfare, food hygiene, vector borne diseases, in particular mosquitoes and culicoides; contagious bovine pleuropneumonia and small ruminants mycoplasmosis; brucellosis; anthrax; bovine tuberculosis; TSE; project design for international cooperation

Objectives

- Improve veterinary laboratory performances of all veterinary institutions involved, through training, research and technology transfer;
- Enhance collaborations among the partners of the network by exchanging resources, epidemiological data, technology and knowledge;
- Identify research needs and gaps, in relation to One Health concept; animal-human-ecosystem health, food safety, epidemiological studies, animal welfare, etc.;
- Improve cooperation, in veterinary science, between African and Italian partners.

News

The first ERFAN general meeting was held in Rome on 4 October 2021. The event offered the opportunity for a dialogue and exchange between policy and scientist at international level through an inter- and transdisciplinary approach. ERFAN action plan for 2021/2022 was presented and the network's communication strategy to facilitate processes was discussed.

ERRAZE@WUR - Early Recognition and Rapid Action in Zoonotic Emergencies

Website: https://www.wur.nl/en/Research-Results/Research-programmes/Cross-WUR-programmes/ERRAZE-at-WUR.htm

WAGENINGEN UNIVERSITY & RESEARCH

Partners ca.
NA

Budget
€ 6.5 million

Start date:
2020-2024

Overview

ERRAZE is an initiative for an integrated global multi-stakeholder approach to the prevention and management of (potentially) pandemic diseases, to support policy makers and decision makers and thus society at large in preventing future pandemics and mitigating their impact. WUR brings together expertise in the areas of human, animal, plant and environmental health, the global agro-food system, economic and social developments, food safety and security, ethics and policy to find answers to the questions raised by new pandemic threats.

Aim and priorities

Aim: to help build the knowledge base needed to prevent future pandemics and to limit their impact, developing an integrated global multi-stakeholder approach.
Priorities:

- Pandemic preparedness;
- Pandemic response management;
- Pandemic prevention;
- Recovery and learnings from pandemic.

Objectives

- Develop maps with high-risk areas for pathogen (re-emergence (hotspots);
- Further develop and describe evidence-based sustainable preventive interventions to the agri-food system;
- Develop system models, linked to the risk maps, to simulate the effect of preventive measures in combination with human behavior;
- Continue to develop and use tools to identify stressors to the natural ecosystem and its species that could enhance pathogen shedding by reservoir hosts;
- Surveillance to enable early warning, rapid characterization of novel pathogens, developing plug-and-play vaccines and therapeutics, and developing contingency plans;
- Further develop agile, appropriate and scalable diagnostic and data collection tools;
- Develop new scenarios for biosecurity and models to underpin and evaluate their efficacy and cost-benefit impacts;
- Inform policy and institutional change towards contingency and recovery plan by use of sophisticated models for scenario analyses;
- Develop insights and tools that help combine data-based evidence with expertise-based evidence;
- Ensure that appropriate pandemic crisis feedback and learning mechanisms are completed, improving future pandemic prevention, preparedness and response.

News

The first round of activities of the ERRAZE@WUR programme was launched in July 2021 and focuses on four strategic goals:

- Automation and digitisation in diagnostic capabilities; crisis response;
- Updating existing methods for (novel) pathogen detection, identification and characterisation; crisis preparedness;
- Strengthen the FAIR (findable, accessible, interoperable, reusable) data infrastructure;
- Creating the basis for novel diagnostic reagents and therapeutics for previously undescribed emerging zoonosis with a non-immune library of llama single-domain antibodies.

GALVmed - Global Alliance for Livestock Veterinary Medicines

Website: https://www.galvmed.org/

Partners ca.	**Budget**	**Start date:**
NA	US$ 100 million	2008

Overview

The Global Alliance for Livestock Veterinary Medicines (GALVmed) is a not-for-profit global alliance, registered as a charitable foundation, with headquarters in Edinburgh and offices in Nairobi and New Delhi.

GALVmed was formally established in 2005, with initial funding from the UK Government Department for International Development (DFID). By 2008, funding from BMGF and the UK Government enabled GALVmed to commence programmes of delivery. Since 2008, GALVmed has received over US$ 100 million in donor funding for programmes in pursuit of its mission.

Aim and priorities

Aim: to reduce poverty and make a sustainable difference in access to veterinary medicines for small scale livestock farmers in sub-Saharan Africa and Asia.

Priorities: GALVmed funded programmes have targeted the development of new products (veterinary vaccines, pharmaceuticals, and diagnostics) and various product improvements (such as heat tolerance, production cost reductions, formulations for easy applications), as well as the development of sustainable access to these products.

Objectives

- **Research & Development**: to support R&D for animal health products on specific needs of small-scale livestock producers in Asia and sub-Saharan Africa. Currently, the main projects involve animal African trypanosomiasis, brucellosis, foot-and-mouth disease (FMD), and smaller projects for cysticercosis, Newcastle disease (ND), and other diseases.
- **Commercial Development**: to establish sustainable markets for improving marketing and distribution channels for animal health products to be used by small and medium scale producers in priority regions.
- **Policy & Advocacy**: current activities include advocating regulatory harmonisation in Africa, encouraging establishment of vaccine banks, supporting development of standards for veterinarians and veterinary paraprofessionals to improve access to veterinary services in low- and middle-income countries, and strengthening veterinary products regulatory systems, including improving regulatory controls to help eliminate substandard or falsified products.

News

GALVmed projects currently focus on 17 neglected livestock diseases that have a large economic impact on small-scale livestock producers in Africa and South Asia: African swine fever, animal African trypanosomosis, brucellosis, *Chlamydia abortus*, contagious bovine pleuropneumonia, contagious caprine pleuropneumonia, East Coast fever, and foot-and-mouth disease, fowlpox, Gumboro, lumpy skin disease, Newcastle disease, peste des petits ruminants, porcine cysticercosis, Q fever, Rift Valley fever, sheep and goat pox.

GALVmed is also managing two competitions by offering prizes for successful completion of various milestones rather than offering up-front research grants. The goal is to incentivise development, registration, and commercialisation of new or improved vaccines against brucellosis and FMD

Additional information about the two AgResults competitions can be found in the two dedicated sections in this Chapter.

Recently, GALVmed have established a partnership with the International Livestock Research Institute (ILRI) and Clinglobal. The aim is to launch a platform to transform animal health solutions and services in low- and middle-income countries (TAHSSL). It will be a one-stop shop to conduct research on animal health product technologies that will generate robust proof-of-concept data to de-risk potential private sector entry into product development, registration and use.

GCRF - Global Challenges Research Fund

Website: https://www.ukri.org/research/global-challenges-research-fund/

Partners ca.	Budget	Start date:
400	£ 1.5 billion	2016-2021

Overview

The Global Challenges Research Fund (GCRF) is a 5-year (2016-2021) £ 1.5 billion fund, issued by the UK Government, aiming to support cutting-edge research that addresses the challenges faced by developing countries.

The GCRF funding was awarded to UK researchers and to countries and territories eligible to receive official development assistance, which consist of all low- and middle-income countries based on gross national income per capita as published by the World Bank. A memorandum of understanding was signed with UNDP to ensure closer collaboration between researchers and policymakers across the world by combining collective expertise in driving international development, research and innovation.

Several calls were issued already, starting in 2016, and more than 500 projects have been funded at a global level.

GCRF is also supporting major programmes that address the United Nations Sustainable Development Goals (SDGs) including interdisciplinary research hubs, a partnership programme with African universities, and a programme to grow research capability between institutions in the developing world and the UK.

Particularly, the CGRF has awarded between £ 13-£ 20 million each year over five years to 12 interdisciplinary research hubs working across a range of development challenges

The hubs bring together researchers, governments, international agencies, NGOs and community groups in developing countries and the UK. They share knowledge and expertise on innovative and sustainable solutions to help make the world safer, healthier, and more prosperous.

The hubs include 400 unique partner organisations in 85 countries and 550 researchers from a range of disciplines addressing 16 of the UN SDGs.

Aim and priorities

Aim: to support cutting-edge research that addresses the challenges faced by developing countries.

Priorities: The GCRF developed a list of twelve priority challenge areas, falling under three main themes: 1. Equitable access to sustainable development, 2. Sustainable economies and societies, and 3. Human rights, good governance and social justice.

Research on animal health and zoonoses can be included under several of the priority challenges, mainly those concerned with safe and resilient food systems supported by sustainable marine resources and agriculture, and sustainable health.

Objectives

- Promote challenge-led disciplinary and interdisciplinary research, including the participation of researchers who may not previously have considered the applicability of their work to development issues;
- Strengthen capacity for research, innovation and knowledge exchange in the UK and developing countries through partnership with excellent UK research and researchers;
- Provide an agile response to emergencies where there is an urgent research need.

News

Between 2016 and 2021, funding has been allocated to hundreds of projects which can be viewed **here**.

Furthermore, among the **funded hubs** there is the **One Health Poultry Hub.** The Hub is led by the Royal Veterinary College and comprises partners in Asia, Australia and Europe.

GloPID-R - Global Research Collaboration for Infectious Disease Preparedness

Website: https://www.glopid-r.org/

GLOPID-R

Partners ca.
29

Budget
NA

Start date:
2015-2019
2020-2022

Overview

GloPID-R brings together worldwide funding bodies investing in research related to new or re-emerging infectious diseases. The GloPID-R Secretariat is a project which receives funding from the European Union's Horizon 2020. The World Health Organization, the Coalition for Epidemic Preparedness Innovations (CEPI) and the European & Developing Countries Clinical Trials Partnership (EDCTP) are also actively engaged in the network. The need for the rapid development of essential diagnostics, vaccines and therapeutics at the outset of an emerging infectious disease outbreak was highlighted when Ebola struck in West Africa in 2014 and has been confirmed in the battle against COVID-19.

GloPID-R support readiness for upcoming outbreaks by analyzing the current state of knowledge and preparedness and identifying gaps as possible areas for funding.

It identifies priority areas and creates working groups, develops videos and publications, and hosts workshops on these topics. GloPID-R is also actively involved in systemic preparedness, connecting clinical trial networks, building a framework for data sharing and improving the rapid delivery of research funding.

Aim and priorities

Aim: to ensure that research capacity and capabilities are in place to support the rapid initiation of scientific research in case of an outbreak.

Priorities: GloPID-R has taken action in the following recent outbreaks:

Novel Coronavirus COVID-19, Ebola, Plague, Yellow Fever, ZIKA, Chikungunya.

Objectives

- Facilitate the exchange of information;
- Address scientific, legal, ethical and financial challenges;
- Implement a 'One Health' approach with close cooperation between human and animal health researchers;
- Establish a strategic agenda for research response;
- Connect infectious disease research networks;
- Involve developing countries.

The main activities of GloPID-R focus on:

- Clinical Trial Networks - Creating links between clinical trial networks and addressing challenges in capacity building or trial implementation in the midst of a crisis.
- Data Sharing - Building the first international framework to facilitate data sharing during public health emergencies.
- Social Science Research- Raising awareness about the vital role social science research plays in understanding infectious diseases.
- Long-Term Research- Identifying scientific gaps and addressing research challenges through a Long-Term Research Agenda.
- Funding - Working to improve the rapid delivery of funds to research projects when a crisis strikes.

News

Developed by UKCDR & GloPID-R, the **Covid-19 research project tracker** is a live database mapping funded research projects connected with WHO Research Roadmap. As of 2 June 2021, the tracker has been used nearly 30,000 times and covers: 10,610 research projects taking place across 142 countries; 201 funders from 48 countries, overUS$ 4.7bn in investments.

To make the best use of the data in the Tracker, it has been producing a quarterly **Living Mapping Review of COVID-19 funded research projects**, which analyses globally funded COVID-19 related research. It was also taken a deeper look at three key themes that emerged during the analysis: **Indirect health impacts**; **Research capacity strengthening**; and **Long Covid**.

A collaboration among GloPID-R and STAR-IDAZ IRC is currently being finalised.

GOARN - Global Outbreak Alert and Response Network

Website: https://extranet.who.int/goarn/

GOARN

Partners ca.	**Budget**	**Start date:**
270	NA	2000

Overview

The Global Outbreak Alert and Response Network – also referred to as GOARN – is a global technical partnership, established by the World Health Organization (WHO) as a key mechanism to engage the resources of technical agencies beyond the United Nations for rapid identification, confirmation and response to public health emergencies of international importance.

Aim and priorities

Aim: to provide technical support to WHO Member States experiencing a human health emergency due to various threats including disease outbreaks, food safety, chemical toxins, zoonosis, natural and manmade disasters etc.

Priorities: Public health emergency support and preparedness.

Objectives

At the request of a Ministry of Health, the Network delivers support to augment the overall WHO response to the public health emergency. Based on the varied and evolving needs of an emergency, this support could include:

- the deployment of technical experts to the affected countries, under the leadership of WHO,
- provision of technical advice through expert committees established during the emergency,
- provision of resources for the response efforts, such as laboratory and operational logistics, tools and equipment to reinforce field teams, etc.

Beyond providing this direct assistance to public health emergency response, GOARN Partners may engage in the Network in several additional ways, including:

- Support for GOARN outbreak response training to strengthen the Network's capacity and performance;
- Operational research and development of tools and technologies that support GOARN field teams in improving outbreak response interventions;
- Networking among GOARN Partners to share information and establish opportunities for outbreak response collaboration.

News

Recently GOARN made available a **Covid-19 Knowledge Hub**, curated by GOARN Partners including UN agencies, International and national NGOs, academic institutions and consortiums. It consists in a public platform for access to the best resources available to support engagement in responding to this pandemic.

The Hub offers multidisciplinary information on COVID-19 for several stakeholders from policy makers, to responders, to researchers, to educators, to affected communities and the general public.

IHI - Innovative Health Initiative

Candidates for European Partnerships in health | European Commission (europa.eu)

Currently candidate for EU Partnership

Partners ca.
NA

Budget
Proposed
€ 2.4 billion

Start date:
IHI 2021-2024

Overview

IHI will build on the successes and lessons learnt from IMI. Like IMI, IHI will work by bringing together diverse stakeholders (universities, companies large and small, and other health stakeholders) in collaborative projects that address disease areas where there is a high burden on patients and/or society. However, in IHI there will be a much greater focus on cross-sectoral projects involving the biopharmaceutical, biotechnology and medical technology sectors, including companies active in the digital area.

On governance, it is currently planned that IHI will have a Governing Board (made up of equal numbers of representatives from the European Commission and industry partners) as well as two advisory bodies: the States Representatives Group (SRG) and the Innovation Panel. The SRG will include representatives of the EU Member States and the countries associated to Horizon Europe. The Innovation Panel will tentatively comprise representatives of the European Commission, the industry partners, the SRG, the scientific community, other health stakeholders, and the IHI programme office.

As is the case in IMI, the 'public' partner in the partnership will be the European Union, represented by the European Commission.

The IHI industry partners will be **COCIR**, **EFPIA**, **EuropaBio**, **MedTech Europe** and **Vaccines Europe**.

In addition, organisations that want to support specific areas of research without becoming full members of IHI can apply to become 'contributing partners' (similar to the Associated Partners in IMI).

Aim and priorities

Aim: to help create an EU-wide health research and innovation ecosystem that facilitates the translation of scientific knowledge into tangible innovations.

Priorities: Innovations should be safe, effective, people-centred and cost-effective, and cover prevention, diagnostics, treatment and disease management. IHI will contribute to a number of European policies, most notably **Europe's Beating Cancer Plan**, the **new Industrial Strategy for Europe** and the **Pharmaceutical Strategy for Europe**.

Objectives

- Create an EU-wide health research and innovation ecosystem that facilitates translation of scientific knowledge into innovations;
- Foster the development of safe, effective, people-centred and cost-effective innovations that respond to strategic unmet public health needs currently insufficiently served by industry;
- Drive cross-sectoral health innovation for a globally competitive European health industry.

News

On 23 February 2021, the European Commission published a **proposal** for a Single Basic Act establishing a number of joint undertakings under Horizon Europe, including the Innovative Health Initiative (IHI). The European Commission's proposal is now being discussed by the Council, in consultation with the European Parliament.

A **draft of the SRIA** was prepared jointly by the prospective IHI member industry associations within IMI and the European Commission services and it was published on 21 June 2021. The SRIA will reflect the final views of the European Commission once it becomes a formal document of IHI upon finalisation and adoption by its Governing Board.

All information on IHI is indicative and the details are subject to change during the legislative process, until the regulation has been formally adopted by the Council.

IMI - Innovative Medicines Initiative

Website: http://www.imi.europa.eu/

Partners ca.
5,246

Budget
€ 5.3 billion

Start date:
IMI 2008-2013
IMI2 2014-2020
(IHI 2021-2024)

Overview

The Innovative Medicines Initiative (IMI) is the Europe's largest public-private initiative.

IMI was launched in 2008 and, to date, has an available budget of about € 5.3 billion (€ 2 billion for 2008-2013 and € 3.3 billion for 2014-2024). Almost half of this budget is provided 'in kind' by the EPFIA (European Federation of Pharmaceutical Industries and Associations) companies that are participating in the projects.

In 2020, a few weeks after the first reports of COVID-19 in the European Union, IMI launched a 45 million euros fast-track Call for proposals to develop therapeutics and diagnostics for current and future coronavirus outbreaks.

Overall, IMI has funded 171 projects, currently 110 ongoing. While the main emphasis of these projects is on human health, some focus is on broad challenges in medical products development, such as drug and vaccine safety, the sustainability of chemical drug production, the use of stem cells for drug discovery, and antimicrobial resistance (AMR). One of these projects, Zoonoses Anticipation and Preparedness Initiative (ZAPI), financed in 2015, is specifically directed at zoonotic diseases, and this indicates that other initiatives in this area could be implemented in the future. More information about ZAPI can be found in the dedicated section in this Chapter.

Aim and priorities

Aim: to speed up the development of better and safer medicines.

Priorities: IMI supports collaborative research projects and builds networks of industrial and academic experts to boost pharmaceutical innovation in Europe.

Objectives

- improve the current drug development process by providing support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products;
- develop diagnostic and treatment biomarkers for diseases clearly linked to clinical relevance and approved by regulators;
- where possible, reduce the time to reach clinical proof of concept in medicine development, such as for cancer, immunological, respiratory, neurological and neurodegenerative diseases;
- increase the success rate in clinical trials of priority medicines identified by the World Health Organisation;
- develop new therapies for diseases for which there is a high unmet need, such as Alzheimer's disease and limited market incentives, such as antimicrobial resistance;
- reduce the failure rate of vaccine candidates in phase III clinical trials through new biomarkers for initial efficacy and safety checks.

News

IMI is currently working for the preparation of the future IHI. In 2019, around 100 different stakeholders, including academic institutions, healthcare professionals and patients, responded to a public consultation on the first draft Strategic Research and Innovation Agenda (SRIA).

The consultation paved the way for the development of a **new draft of the SRIA**, which was prepared jointly by the prospective IHI member industry associations and the European Commission services. The new draft was published on 21 June 2021. The SRIA will reflect the final views of the European Commission once it becomes a formal document of IHI upon finalisation and adoption by its Governing Board.

This document does not pre-empt the outcome of the formal decision-making process or the legislative procedure for the establishment of joint undertakings (see IHI).

InnoVet-AMR - Innovative Veterinary Solutions for Antimicrobial Resistance

Website: https://www.idrc.ca/en/initiative/innovet-amr-innovative-veterinary-solutions-antimicrobial-resistance

Partners ca.	Budget	Start date:
2	CA$ 27.9 million	2018-2022

Overview

The Innovative Veterinary Solutions for Antimicrobial Resistance (InnoVet-AMR) is a four-year, CA$ 27.9 million partnership between IDRC and the UK government's Global AMR Innovation Fund (GAMRIF) which is part of the Department of Health and Social Care.

Aim and priorities

Aim: to fund research that will develop innovative veterinary solutions focused on product development to reduce therapeutic and prevent non-therapeutic antimicrobial use in livestock and aquaculture production in low- and middle-income countries (LMICs).

Priorities: The programme specifically focuses on reducing AMR in swine, poultry, and aquaculture animals.

Objectives

- Support research that will identify innovative veterinary solutions, including vaccines and alternative solutions, to reduce the use of antimicrobials in livestock and aquaculture operations in LMICs;
- Build effective partnerships to better coordinate discovery, development, and sustainable delivery of affordable innovative veterinary solutions to reduce the use of antimicrobials in livestock and aquaculture operations in LMICs.

News

12 projects are ongoing from the call "Developing innovative veterinary solutions for the fight against antimicrobial resistance" more information is available at **https://www.idrc.ca/en/research-in-action/new-innovet-amr-projects**

IVVN - International Veterinary Vaccinology Network

Website: http://intvetvaccnet.co.uk/

Partners ca.
1,000

Budget
£ 2.8 million/
4 years

Start date:
2017

Overview

The International Veterinary Vaccinology Network (IVVN) is a multidisciplinary and inter-connected vaccinology research and development community. Built on the basis of the UK Veterinary Vaccinology Network, the IVVN has to date more than 1,000 members.

The IVVN facilitates collaborations between scientists, industrial partners and others from the UK and low-and-middle income countries (LMICs) across the broad range of disciplines that can contribute to vaccine development, by funding scientific meetings, workshops, laboratory exchanges and supporting 'pump-priming' projects. Awards of up to £ 100,000 were available to support pump-priming projects from collaborative teams of IVVN members, which address a key bottleneck preventing the development of a vaccine for livestock and zoonotic diseases of importance in LMICs. The IVVN have awarded funding to 13 projects over four rounds of funding, the last of which was announced in April 2020. Laboratory exchange funding Awards of up to £ 10,000 are available to support transfer of expertise between laboratories within the Network, or to fund a proof-of-concept piece of work.

Aim and priorities

Aim: to address the challenges impeding vaccine discovery, as well as evaluation and delivery of vaccines that will have impact on the control of priority livestock and zoonotic diseases in low-and-middle income countries (LMICs).

Priorities: Vaccinology in the field of Animal health

Objectives

- Establish an interactive and multi-disciplinary Network to facilitate dissemination of knowledge and exchange of 'state-of-the-art' technology between members of the veterinary (and human) vaccinology communities;
- Identify and fund collaborative teams with complementary expertise that through application of novel approaches can effectively address critical 'bottle-necks' in vaccine development for LMICs-relevant pathogens;
- Advance the development of veterinary vaccines for LMICs-relevant diseases;
- Provide the scientific and logistical support for members to secure substantive funding to expand on the preliminary data generated by pump-priming funding; and
- Engage with a variety of industry partners, in both developed and LMICs, to ensure the sustainable delivery of effective vaccines.

News

During the COVID-19 pandemic, IVVN held 4 virtual thematic symposia to give its members the opportunity to exchange experiences with experts in a variety of areas of vaccine research: vaccines for swine on 16 December 2020, vaccines for poultry on 25 February 2021, vaccines for ruminants on 26 April 2021, vaccines for aquaculture on 6th July 2021. Recordings and presentations can be found in the **IVVN Virtual Symposia page**.

In addition, after a long break due to Covid-19, the IVVN's African Schools Outreach Programme resumed its activities in June 2021, with five new team members trained and workshops delivered to 160 students in two Nigerian high schools.

LVIF - Livestock Vaccine Innovation Fund

Website: https://www.idrc.ca/en/initiative/livestock-vaccine-innovation-fund

Partners ca.
3

Budget
CA$ 57 million

Start date:
2015-2020

Overview

The LVIF is a five-and-a-half year (2015-2020), CA$ 57 million, partnership between BMGF, Global Affairs Canada and Canada's International Development Research Centre (IDRC). The initiative supports research into vaccine solutions, through a series of global competitive calls.

Aim and priorities

Aim: to bring together vaccine researchers, manufacturers, and distributors, to accelerate the discovery of new vaccines and the improvement of existing solutions.

Priorities: The initiative concentrates on those animal diseases posing the greatest risk to subsistence livestock farmers/keepers in Sub-Saharan Africa, South and Southeast Asia, and targets transboundary diseases to achieve a lasting regional impact.

Objectives

- To accelerate the development of new vaccines against neglected livestock diseases by supporting innovation and leading-edge research,
- To increase the efficacy, marketability and use of existing livestock vaccines, and
- To foster effective partnerships between vaccine researchers and public and private sector actors to more efficiently develop, register, commercialise, and deploy livestock vaccines.

News

Currently six projects have been completed and 16 are ongoing, more information available at **Search Results | IDRC - International Development Research Centre.**

One Health EJP- European Joint Programme Co-fund on One Health (zoonoses – emerging threats)

Website: https://onehealthejp.eu/

Partners ca.
44

Budget
€ 90 million

Start date:
2018-2023

Overview

The European Joint Programme (EJP) Co-fund on One Health (zoonoses – emerging threats) is an initiative aiming to create a European joint programme to deal with "one health" issues, primarily targeting food-borne zoonoses and antimicrobial resistance, and, to a lesser extent, emerging zoonotic threats. The project Consortium, in order to ensure a One Health approach, includes a balanced number of human/public health and veterinary institutions.

Integration and alignment in research will be improved through funding of research projects. Three research calls have been launched, and a total of 29 projects have been funded. In addition to traditional research projects, the EJP funds integrative projects to develop common protocols or infrastructure that support collaborative processes (e.g., platforms for uploading, sharing, and analysing sequence data, experimental facilities or risk assessment structures), as well as PhD students, Summer Schools, and Short-Term Missions, and implemented numerous integrative activities.

Aim and priorities

Aim: to build a sustainable framework for an integrated community of research groups including reference laboratories in the fields of life sciences, medicine, veterinary medicine, animal sciences, food sciences and environmental sciences.

Priorities: One Health

Objectives

- Harmonise approaches across Europe for the assessment and management of foodborne zoonotic infections, antimicrobial resistance and emerging threats through collaboration between our food, veterinary and medical partners;
- Improve the quality and compatibility of information using an interdisciplinary and integrative approach to One Health challenges;
- Equip risk managers and policy makers with the best tools for intervention measures at the policy level;
- Create a sustainable European One Health Network.

News

In February 2021, the One Health EJP's second CPD Module focusing on Digital Innovation for One Health Practitioners was organized and hosted by BfR in Germany.

It was centered on the use of innovative open-source software solutions to support risk assessment, zoonotic outbreak investigations and data interoperability. Particularly, solutions that support foodborne disease outbreak investigations, efficient surveillance data integration and the re-use of risk assessment models for One Health researchers and professionals were targeted.

On 3rd March 2021, 6 new partners joined to the One Health EJP consortium (National Food and Veterinary Risk Assessment Institute - Lithuania, Institute of Health Carlos III -Spain, Institute of Food Safety, Animal Health and Environment - Latvia, Finnish Food Authority - Finland, Finnish Institute for Health and Welfare - Finland, National Food Chain Safety Office - Hungary).

The 2nd annual scientific meeting of the One Health EJP took place between 9 and 11 June 2021, as a hybrid event, in DGI Byen, Copenhagen, Denmark and on-line. The scientific programme of the event included 6 keynote talks, 30 oral presentations and more than 160 poster presentations. A Satellite Workshop to the meeting, "Online Software Fair and Developer Meetup", was also organised to encourage knowledge sharing and allowed participants to present their digital innovation tools applicable to scenarios of food safety, public health and animal health.

A new project, **COVRIN**, started on 1 March 2021. The aim of the project is to generate and share data of integrative research activities on SARS-CoV2 virus-host interactions, virus evolution and drivers for emergence, risk assessment and risk modelling, in order to increase the preparedness for future Coronavirus outbreaks.

PANDORA - Pan-African Network for Rapid Research, Response and Preparedness for Infectious Diseases

Website: https://www.pando ra-id.net/

Partners ca.	Budget	Start date:
22	€ 10 million	2018

Overview

PANDORA-ID-NET is a multidisciplinary 'One Health' initiative that supports response to emerging infections in Africa. It is underpinned by a € 10 million grant funded by the European and Developing Countries Clinical Trials Partnership (EDCTP). The network supports the development of robust 'ready to go within 48-72 hours' PANDORA-ID-NET trained outbreak rapid response teams that can appraise, evaluate and conduct public health research in each of the four African regions. These response teams will be multidisciplinary, including members from the clinical, veterinary, environmental and operational sides of disease research and linked to other regional and global networks on emerging infections.

Aim and priorities

Aim: to develop and strengthen effective outbreak response capacities across all geographical regions in sub-Saharan Africa, in partnership with national governments and other international stakeholders.

Priorities: Rapid response, capacity developments, Training.

Objectives

- Epidemiological, surveillance, clinical and pathogenesis studies;
- Zoonotic One Health interface studies;
- Specific Clinical trials on existing and sporadic Zoonotic diseases;
- Data collection, analyses, integration, sharing and reporting;
- Engaging with policy makers, communities and overcoming ethical and regulatory obstacles;
- Capacity building and training.

News

The network in the last year focused several **activities on Covid-19,** among them, a BSAC funded project, which is a collaboration between University College London, UK, HerpeZ in Zambia and the Institute of Endemic Diseases in Sudan. It is conducting an innovative study exploring whether changes to infection prevention and control policies that were introduced due to COVID-19 actually make it more likely that patients will catch other, potentially drug-resistant, infections while in hospital. PANDORA members also contributed to the publication of a novel post mortem autopsy study from University Teaching Hospital Zambia. This shows the extensive damage that occurs in the body due to COVID-19. The manuscript can be downloaded **here** and contains color photos of the effects of COVID-19 on the brain, lung, kidneys and liver.

PREZODE - Preventing Zoonotic Disease Emergence

Website: https://prezode.org/

Partners ca.	Budget	Start date:
NA	NA	2022

Overview

PREZODE is an international One Health initiative supporting emergence risk reduction strategies for zoonotic infectious diseases, following the recommendations of the forthcoming High-Level Expert Panel on One Health of the Tripartite. It will integrate research on animal, human and environmental health to better understand zoonotic emergence risks, co-design with stakeholders monitoring and early warning systems, and support science-based policies aiming at risk mitigation of zoonotic diseases emergence.

The Preparatory Committee is currently composed of the three research institutes that started PREZODE: CIRAD, The French Agricultural Research Centre for International Development; INRAE, French National Research Institute for Agriculture, Food and Environment; IRD, French National Research Institute for Sustainable Development.

Aim and priorities

Aim: to support science-based policies aiming at risk mitigation of zoonotic diseases emergence.

Priorities: emergence of zoonotic infectious diseases and implementation of innovative methods to improve prevention and mitigate emergence risks.

Objectives

To develop:

- A scientific and operational framework to coordinate research projects, health networks and operational actions to strengthen the integrated approach and maximize the impact;
- A platform for sharing knowledge acquired through past, current and future projects and capitalizing on success stories and pilot actions in different regions of the world;
- A resource centre available notably for the One Health High Level Expert Panel, to facilitate in particular the development of recommendations for decision makers by the latter.

News

PREZODE was launched in January 2021 during the One Planet Summit on Biodiversity. During 2021, efforts were devoted to building the initiative with all the interested partners, before the operational launch in 2022. This stage comprises a broad consultation of all stakeholders (countries and authorities, national organizations, international organizations, research and development partners, other initiatives). To date, the participatory workshops gathered more than 1,000 participants from around 50 countries. More workshops will be organized before the end of the year.

Furthermore, the initiative started to develop the strategic agenda and the governance, through a co-design process in consultation with all stakeholders (international organizations, countries, national and regional authorities, research and development partners, funders, other initiatives).

STAR-IDAZ IRC – International Research Consortium on Animal Health

Website: http://www.star-idaz.net/

Partners ca.
28
19 members countries
50 associated countries

Budget
US$ 2.5 billion

Start date:
2011-2015
2016-2022

Overview

STAR-IDAZ is an International Research Consortium (IRC) of research funders and programme owners, aiming to maximise funding for coordinated animal health research. The IRC was built on an international forum of R&D programme owners/managers and international organisations established under a four-year (2011-2015) EC FP7 project: "Global Strategic Alliances for the Coordination of Research on the Major Infectious Diseases of Animals and Zoonoses" (STAR-IDAZ). The aim of the global network is to share information, improve collaboration on research activities and work towards common research agendas and coordinated research funding on the major animal diseases affecting livestock production and/or human health.

STAR-IDAZ successfully established, through its global and regional activities, a network of organisations managing research budgets or programmes in approximately 50 countries that are committed to working together. The scope of the project included coordination of research relevant to emerging and major infectious diseases of livestock, including fish and managed bees, and those infections of livestock that carry the risk of disease threat to human health. Diseases of wildlife were also considered where they were identified as reservoirs of infection with emerging and major infectious diseases of humans or production animals.

Since 2015, STAR-IDAZ has moved forward as a self-sustaining network under an agreed Memorandum of Understanding with most partners signing up to a higher level of commitment in STAR-IDAZ International Research Consortium. Since 2016 it is supported by a Secretariat (SIRCAH) funded by the European Commission.

Aim and priorities

Aim: to coordinate research at the international level to contribute to new and improved animal health strategies for at least 30 priority diseases/infections/issues.

Priorities: major animal diseases affecting livestock production and/or human health

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Objectives

- Strengthen the linkages between and reduce the duplication of global research effort on high priority infectious diseases of animals (including zoonoses) maximise the efficient use of expertise and resources and accelerate coordinated development of control methods;
- Identify and co-ordinate the response to gaps in research activities for targeted diseases;
- Create the necessary critical mass and capacity to address emerging infectious disease threats;
- Improve the cost–effectiveness and added value to network partners of current research programmes;
- Develop durable procedures for a better co-ordinated, rapid response to urgent research needs;
- Identify unique regions with localised diseases and improve access to research in those areas; and
- Improve access to and the utility of research results across all partner organisations.

News

In 2021 the IRC Executive Committee, the Scientific Committee and the working groups continued their networking activities delivering outputs mainly in the following domains:

Emerging issues

Sixty-five initiatives, networks and projects were identified through a mapping exercise on emerging issues. This was followed by a workshop bringing together representatives from 20 selected networks and projects. The meeting provided the opportunity to share information on activities and find potential areas for collaborations, while building the basis for a WG to take forward future collaboration on emerging issues.

Influenza

A **review on Animal influenza research** was delivered to help identify knowledge gaps that need to be addressed to deliver improved disease control. The report identified what has been achieved by global research since the previous gap analysis and related activities carried out by USDA in 2013, OFFLU in 2014, by the EC in 2015 and by WHO in 2016 and 2017. The review includes information on avian, swine, equine and other influenza viruses of veterinary interest which will be considered in a gap analysis workshop of experts planned for Spring 2022 in Ames, Iowa, USA, to be jointly organised by USDA ARS and the STAR IDAZ IRC.

Alternative To Antibiotics

Five online workshops are currently being planned to identify and prioritise knowledge gaps for the roadmaps on ATA (12, 15, 18, 22 October and 9 November 2021) focusing on phage technologies, immunomodulators, microbiomes and their manipulation and on the mechanisms behind the functions of antibiotics as growth promoters. The last workshop will cover the issues involved in taking new ATA to market and the associated challenges.

News

ASF

The IRC contributed to the GARA online workshop 'Troubleshooting techniques for full genome sequencing of African swine fever' (September 2021) and to the previous one 'Current efforts in African swine fever vaccines: a virtual seminar and discussion' (May 2021) which covered recent developments and challenges in vaccine development, including licensing, regulation and commercialization.

Vector transmission and control

Lead summaries, considering what STAR-IDAZ is aiming to achieve, major challenges, possible solution routes and what these depend on have been produced based on a starting roadmap grouped into three sections: 1. control through host resistance to the vector, 2. control by modulating how the vector interacts with the pathogen and the host to transmit the disease and 3. control of the vector in the environment.

Vaccinology

A vaccinology survey has been circulated through the International Vaccinology Network. A research review on vaccine platform technology has been commissioned by STAR-IDAZ IRC, and will also cover artificial intelligence, bioinformatics and animal models.

Helminths

Various **roadmaps** for nematodes and liver flukes have been developed and over 60 projects were identified by a mapping exercise of current research activities.

Furthermore, the STAR-IDAZ Regional Networks meet every six months. Four regional virtual meetings took place in the last semester: Africa and Middle East on the 22 March and on 7 September, Americas on the 17 May, Asia and Australasia on the 22 June.

During the meetings, regional members were updated on the current status and activities of the Network, common research priorities on One Health were discussed and agreed, opportunities for sharing resources, including access to samples and strains of organisms, specialised facilities and expertise were explored as well as international funding opportunities.

WHO R&D Blueprint

Website: http://www.who.int/blueprint/en/

Partners ca.
WHO Member States

Budget
NA

Start date:
2016

Overview

A broad global coalition of experts from several medical, scientific, and regulatory backgrounds was convened by the WHO to contribute to the Blueprint. The World Organisation for Animal Health (OIE) serves as an observer in the Scientific Advisory Group of the initiative.

While the R&D Blueprint focuses on human diseases, most of the emerging human diseases are zoonoses, and thus the activity of this action could have positive impact on the control of animal diseases as well.

Aim and priorities

Aim: to accelerate the development and availability of effective tests, vaccines and medicines that can be used to save lives and avert large-scale crises through a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics.

Priorities:

One of the key components of the Blueprint is the delivery of R&D roadmaps to accelerate the development and implementation of effective medical countermeasures for WHO priority pathogens, aimed at reducing morbidity, mortality, and transmission. The current Blueprint priority pathogens are the following:

- Crimean-Congo hemorrhagic fever (CCHF);
- Ebola virus disease and Marburg virus disease;
- Lassa fever;
- Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS);
- Nipah and henipaviral diseases;
- Rift Valley fever (RVF);
- Zika;
- "Disease X".

Disease X represents a hypothetical unknown pathogen that could cause a serious international epidemic, thus the R&D Blueprint explicitly seeks to enable cross-cutting R&D preparedness that is also relevant for an unknown "Disease X" as far as possible. This definition fits COVID-19 well, and it is now one of the priority pathogens for the Blueprint.

Objectives

1. Improve coordination and foster an enabling environment.
2. Accelerate R&D processes.
3. Develop new norms and standards tailored to the epidemic context.
4. Streamline operational R&D response during outbreaks.

Among other activities, the R&D Blueprint will:

- Define and refine a robust and transparent semi-quantitative prioritisation methodology for infectious diseases most likely to create epidemics;
- Annual update, using the prioritisation methodology described above, the list of diseases and pathogens to prioritise for research and development in public health emergency context;
- Develop a decision tree to assess the need for urgent R&D for potential emerging pathogens not yet included on the list; and
- Develop R&D Roadmaps and generic Target Product Profiles (TPPs) for priority diseases, through broad and open consultations with leading experts and other stakeholders.

News

In May 2021 the report **"COVID-19 Research and Innovation Achievements"** was published. It provides a summary of global research initiatives and achievements to tackle COVID-19 agreed at the outset of the pandemic. It shows research progress on knowledge gaps, and identifies key R&D achievements.

Within a few weeks of declaring COVID-19 to be a public health emergency of international concern (PHEIC), WHO published a **coordinated global research roadmap**, identifying the knowledge gaps that the world scientists urgently need to fill to find solutions to tackle the COVID-19 pandemic. Fourteen months later, research on most of the knowledge gaps has been initiated, is progressing and has provided answers to several of the knowledge gaps identified in the roadmap.

ZAPI - Zoonoses Anticipation and Preparedness Initiative

Website: http://zapi-imi.eu/

Partners ca.	**Budget**	**Start date:**
20	€ 22 million	2015-2021

Overview

The Zoonoses Anticipation and Preparedness Initiative (ZAPI) is one of the projects funded within the framework of the IMI public-private partnership.

ZAPI is a 5-year (2015-2020), 22 million euros, collaborative partnership between more than 20 European partners, including leading human and veterinary research institutions, non-governmental organisations, regulatory agencies, expert academic groups, vaccine and biotech manufacturers. Boehringer Ingelheim Animal Health is the lead industry partner for vaccine development projects, and AstraZeneca is the lead industry partner for antibody products.

ZAPI is focused on methods of rapidly delivering products, rather than on their delivery itself. Its aim is full "development by design", applicable to a wide range of pathogens that may emerge in future. The recently emerging target pathogens, RVF virus, Schmallenberg Virus, and the MERS-CoV, were used as 'Proof-of-principle'. This approach which focused on using molecular biology and protein modelling techniques to develop and characterise prototype vaccines and antibody products that employ virus-like particles to serve as carriers for various vaccine antigens.

The prototype ZAPI vaccine production platforms were primarily based on the use of recombinant baculovirus or yeast to produce large quantities of purified protein antigens in serum-free media, which are then 'decorated' onto the surface of a virus-like particle ('multimeric protein scaffold particle') using a proprietary protein-binding technology known as SpyTag/SpyCatcher. ZAPI research has demonstrated that this formulation could significantly enhance the immunogenicity of peptide antigens, and has other advantages, such as markedly improved thermotolerance, and ease of formulation for large scale production of vaccines.

Aim and priorities

Aim: to enable swift responses to major new infectious disease threats at the European and global levels, to be available within a few months after the first cases of the outbreak have occurred.

Priorities: Design of new manufacturing processes (up to large scale) for delivering effective control tools, such as vaccines, antibodies/antibody-like molecules, against (re-)emerging zoonotic diseases with pandemic potential.

Objectives

The ZAPI has three main objectives:

- To identify the best protective subunit vaccines and neutralising antibodies against potential new zoonotic diseases or strains of viruses, such as bunyaviruses or coronaviruses;
- To define optimum manufacturing technologies and processes for these vaccines and antibodies to enable high-volume production capacity; and
- To gain alignment with regulatory authorities and policy makers and secure pre-approval of the new vaccine and antibody manufacturing methodologies for future emerging zoonotic viral diseases.

News

A ZAPI Final Stakeholders Global Meeting was held virtually on 4-5 February 2021 to present an overview of the main findings and key learnings from the ZAPI project partnership's experience for improving One Health preparedness status for future pandemics.

ZODIAC - Zoonotic Disease Integrated Action

Website: https://www.iaea.org/services/zodiac

Partners ca.
IAEA Member States

Budget
NA

Start date:
2020

Overview

Zoonotic Disease Integrated Action (ZODIAC) is an IAEA (International Atomic Energy Agency) initiative established in June 2020 to help countries prevent pandemics caused by bacteria, parasites, fungi or viruses that originate in animals and can be transmitted to humans.

This initiative will benefit from the expertise of the joint laboratories of the IAEA and the Food and Agriculture Organization of the United Nations (FAO) and from cooperation with partners such as the World Health Organization (WHO) and the World Organisation for Animal Health (OIE) under the One Health approach, collaboration between human health and animal health experts. Research, development and innovation will be at the centre of this initiative. The outcomes of the research and development activities undertaken by the IAEA in cooperation with its partners, using immunological, molecular, nuclear and isotopic techniques will be made immediately available to institutions participating in ZODIAC.

Aim and priorities

Aim: to support countries in the use of nuclear and nuclear-derived techniques for the timely detection and control of pathogens at the animal-human interface.

Priorities: It will help tackle a range of zoonotic diseases, such as the ones caused by coronaviruses, the Zika virus, avian influenza viruses as well as other pathogens yet unknown.

Objectives

Under ZODIAC, veterinary and public health officials from Member States can benefit from joint research and development activities and from expert guidance as well as from the technical, scientific and laboratory support of the IAEA and its partners. Particularly for:

- Strengthening detection and diagnostic capabilities;
- Developing and making novel technologies available for the detection of zoonotic diseases;
- Making real-time decision-making support tools available for timely interventions;
- Providing access to data on the impact of zoonotic diseases on human health;
- Providing access to an IAEA coordinated response team in case of an outbreak.

News

On the 22 September 2021, at the side-lines of the IAEA's annual General Conference, representatives of the IAEA's Zoonotic Disease Integrated Action (ZODIAC) initiative and PREZODE underlined their commitment to work together by signing the PREZODE declaration of intent on fighting such diseases that spread from animals to humans. IAEA experts will work closely together with PREZODE counterparts to explore areas of collaboration and foster synergies between the two initiatives, for example in capacity building or through the participation of representatives of both initiatives at each other's events on zoonoses.

II. RECENT INFRASTRUCTURES AND DATABASES TO FACILITATE R&D

Conducting scientific research requires significant research infrastructure, including facilities, resources and related services. The establishment of common databases, allowing the sharing of knowledge and facilitating networking, is of paramount importance to facilitate and accelerate R&D.

The aim of this chapter is to provide a list of the main distributed infrastructure and databases relevant to the animal health sector.

CWG AHW Project Database

http://database.scar-cwg-ahw.org/

The Collaborative Working Group on European Animal Health and Welfare Research (CWG) was established in 2005 to increase information sharing and research coordination in the European area. To meet these objectives, as one of the objectives of the EMIDA project, a database was established under the CWG to capture information on research project funded on animal health. This database was further updated under the ANIHWA project, to also collect projects on animal welfare supported by CWG funding bodies. This was expanded under STAR-IDAZ to include project data from organisations outside of Europe.

To date, details of over 2,340 projects (both national and international) have been uploaded to the project database by the project partners. The projects can be searched according to research area, disease, pathogen, animal species, country, end date and by full text.

This database represents a valuable tool to map current research on animal health, to allow research funders to identify areas where investments in research are lacking and to avoid duplications.

In 2020, the CWG conducted a survey to collect information about research projects being currently funded or planned on CoVs by the members' organisations and funding bodies. The collected information was shared with the STAR-IDAZ IRC and CWG members and is now stored in the STAR-IDAZ IRC website members' area, complementing the information collected by the CWG project database on this area.

DISCONTOOLS - Disease Control Tools

http://www.discontools.eu/

DISCONTOOLS (DISease CONtrol TOOLS) is an open-access database to assist public and private funders of animal health research and researchers in identifying research gaps and planning future research. The database contains research gaps as well as a gap scoring and prioritisation model for more than 50 infectious diseases in animals. The data are provided by disease-specific expert groups, reviewed by a project management board and updated in a 5-year cycle. Users can select their topics of interest, compare the selected topics across diseases and prioritise the diseases according to a range of customisable criteria. By identifying the gaps in knowledge and available control tools, DISCONTOOLS helps to prioritise research and speed up the development of new diagnostics, vaccines and pharmaceuticals.

DISCONTOOLS is funded by a consortium of members from the European Collaborative Working Group on Animal Health and Welfare Research (CWG AHW), with industry providing secretariat support. The website received a facelift in 2018 and has become .an important resource for funders of animal health research and the research community to develop research agendas and evaluate research proposals. Recently, DISCONTOOLS published an **e-book** with one-pagers on the gaps in control tools and research needs for 53 animal diseases. A symposium was organized on 20 October 2021 to highlight the achievements of the various expert groups and discuss how this can help to shape future animal health research priorities. The symposium also marked the start of a new updating cycle of the disease information.

EVAg - European Virus Archive

https://www.european-virus-archive.com/

The European Virus Archive (EVA) project was funded under the European Commission FP7 (2009-2014) to create and mobilise a European network of high calibre centres with the appropriate expertise, to collect, amplify, characterise, standardise, authenticate, distribute, and track, mammalian and other exotic viruses. The network produced associated reagents on demand, to laboratories, mainly throughout Europe. In 2015, a new project was awarded funding under the Horizon 2020 Programme to enlarge the archive and make it global (EVAg, 2015-2019).

Currently, EVAg is a non-profit organisation dedicated to the characterisation, conservation, production, and distribution of biological materials in the field of virology. Its global virus collection is a valuable support tool for the organisation of scientific research, education, and disease control through human and veterinary health programmes, providing both essential resources as well as a platform for the continuation of project-derived products.

The EVAg consortium includes an international group of 26 laboratories, 17 belonging to EU Member States' institutions and 9 to non-EU institutions, and a number of Associated Partners (to date, 14 institutions from 11 non-EU Member States and 3 EU Member States), all sharing the common interest of creating an international virus collection.

In 2020, EVAg joined the struggle against COVID-19, building a new section in its portal dedicated to information concerning preclinical evaluation of molecules with antiviral potential against the SARS-CoV-2, and making available on its catalogue SARS-CoV-2 biological material (full virus, viral proteins, nucleic acids and diagnostics tools).

Global AMR R&D Hub - Global Antimicrobial Resistance Research and Development Hub

https://globalamrhub.org/

The Global Antimicrobial Resistance Research and Development Hub (Global AMR R&D Hub) was established in May 2018, in response to the Joint Statement of Intent of the G20 Focal Points of the G20 Health Working Group. It called for the setting-up of a new, international R&D collaboration hub in the field of antimicrobial research and product development aimed at maximising the impact of new and existing initiatives in basic and clinical antimicrobial research, as well as product development.

The main goal of the Global AMR R&D Hub is to promote high-level coordination among governments and upstream funders from different world regions, to better align national and international efforts in the fight against AMR. Its scope is embedded in a comprehensive One Health approach relating to R&D on AMR, comprising human and animal health as well as environmental aspects.

The central deliverable of the Global AMR R&D Hub is a near real-time Dynamic Dashboard (https://dashboard.globalamrhub.org/) providing information and analysis at a high level on current initiatives, funding flows and activities in the field of AMR R&D. The dashboard presents pre-analysed information, to inform policy makers in their decision making on strategic investments and actions in AMR R&D. While the Dashboard initially covered only bacterial infections for humans, in 2020 it was enlarged to include information on AMR R&D related to animal health too. The OIE and the STAR-IDAZ IRC, along with other international experts, have supported the Hub in identifying animal health-specific categorisation fields for the implementing this new feature of the Dynamic Dashboard. The animal health part of the Hub already contains information on 1084 projects from 89 funders worldwide, for a total budget of over US$ 660 million.

In 2020, the Global AMR R&D Hub entered a formal collaboration partnership with the STAR-IDAZ IRC, with the aim of cooperating on their common interest to strengthen global research efforts and reduce duplication of research on priority infectious diseases of animals relevant to AMR. This joint effort includes the exchange and dissemination of relevant AMR R&D expertise, information and data in animal health and supports more efficient use of international resources through the identification of gaps, overlaps and research coordination.In December 2020, the Hub held a virtual conference titled "Translating AMR R&D mapping into policy and action", which aimed to start translating the AMR R&D information presented in the Global AMR R&D Hub's Dynamic Dashboard into policy and action. Key outcomes, ideas and discussion points raised at the conference will be referred to the Global AMR R&D Hub's Board of Members (which is comprised of policy makers, funders and international organisations) to be considered in their recommendations on where more action is needed. The event was built around three sections, one of which was entirely dedicated to the animal health field (Session 2, "Filling AMR R&D gaps in animal health at country, regional and global level"). A full meeting report is available at **https://globalamrhub.org/wp-content/uploads/2021/01/Conference-report-and-recommendations_v2.pdf**.

In 2021, a Funding Distributor Report was added to the Dynamic Dashboard. It provides the possibility to find information on the amount of funding distributed among different topics. Furthermore the Dashboard, since February 2021, collects information also on R&D investments on human fungal diseases.

On August 2021, two reports were released, one "**Estimating global patient needs and market potential for priority health technologies addressing antimicrobial resistance**", the other produced in collaboration with OIE and Health for Animals on "**Using the Dynamic Dashboard to identify gaps and opportunities for the development of veterinary vaccines in an effort to reduce antibiotic use**".

TRANSVAC

https://www.transvac.org/

To facilitate access to vaccinology skills and capacities and promote collaborations in the European vaccine landscape to accelerate the development of safe, effective, and affordable vaccines, the European Commission has funded TRANSVAC2, a European vaccine R&D infrastructure, under the Horizon 2020 Framework Programme (2017-2022; € 10.6 million).

TRANSVAC2 builds upon the success of TRANSVAC (i.e., the European Network of Vaccine Research and Development) funded under the EC´s previous Framework Programme (FP7). The first TRANSVAC project made significant contributions to the European vaccine development landscape, providing scientific-technical services to more than 29 vaccine projects and developing a roadmap for the establishment of a sustainable European vaccine R&D.

The main goal of TRANSVAC2 is to support innovation for vaccine development. High quality technical services across four different service platforms are offered: i) Technology (for process development and Good Manufacturing Practices (GMP) production), ii) Immunocorrelates and Systems Biology, iii) Animal models, and iv) support for Clinical Trials.

Academic and non-academic research groups, including SMEs, can apply to benefit from the expertise, reagents, and facilities offered by TRANSVAC2 to accelerate the development of their vaccines.

TRANSVAC2 also offers training courses to provide fundamental and advanced knowledge on a wide-range of vaccine development-related topics. Training modules will be harmonised with existing European vaccinology courses, aiming to complement existing infrastructures and activities. TRANSVAC2 will therefore centralise and expand the training opportunities available to the European vaccine community. In 2021 courses were offered on “Key considerations and best practices for viral vaccine process development, scale-up and implementation at manufacturing scale including single use technologies” and “Process development and scale-up of recombinant protein vaccines”.

With this comprehensive approach, TRANSVAC2 functions as a leverage and innovation catalyst between all stakeholders involved in vaccine R&D in Europe and contributes to the development of effective products to address European and global health challenges. This reinforces the European leadership in controlling the burden and spread of diseases, and the economic assets represented by vaccine developers in Europe.

TRANSVAC2 seeks to support vaccine-related projects currently in the preclinical phase of development. It launched two calls in 2020 (June and October) and two in 2021 (March and June). TRANSVAC2’s joint research activities (JRAs) aim to address current major gaps in vaccine development knowledge and are designed to feed directly into and to support the transnational activities. The main focus of such activities is improving adjuvants, predictive assays, systems biology, and animal models.

VetBioNet - Veterinary Biocontained research facility Network

http://www.vetbionet.eu/

VetBioNet (Veterinary Biocontained research facility Network) is a project funded under the European Commission Horizon 2020 Research Framework for large research infrastructures (2017-2021). The project consortium includes 30 academic and industrial partners from 14 countries across Europe, Africa, and Oceania. VetBioNet's principal objective is to strengthen European capacity and competence to meet the challenges of emerging infectious diseases by reinforcing the network of European BSL3 (Biosafety Level 3) infrastructures dedicated to livestock. It will serve as a multidisciplinary network seeking to drive the European R&D agenda related to emerging epizootic and zoonotic diseases. Moreover, it will develop new technologies as well as activities such as standardisation of protocols and best practices and facilitate connecting with similar institutes outside Europe.

To reach its overall objectives, VetBioNet will:

- Promote and facilitate Transnational Access (TNA) to the infrastructure resources of the network, including BSL3 animal experimental facilities and laboratories, technological platforms, and sample collections;
- Promote technological development by involving private partners in the integrating activities of the network and by providing a communication platform for bidirectional exchange with industry stakeholders (Stakeholder Platform);
- Enhance the preparedness of the major European BSL3 research infrastructures to accelerate the response to (re)emerging epizootic and zoonotic threats by sharing capacities beyond the infrastructures;
- Harmonise Best Practices and promote the use of global standards in European BSL3 infrastructures;
- Forge cooperative relationships with non-European BSL3 infrastructures, research institutes, industrial partners, international organisations, and policy makers;
- Ensure high ethical standards and clarify the social impact of VetBioNet research work;
- Develop and implement a Sustainability Plan for the network to continue beyond the five-year term of funding; and
- Carry out Joint Research Activities (JRAs) designed to improve the scientific and technological standards of the integrated services provided by the network infrastructures.

The project is structured around three types of activities: transnational access (TNA), networking activities and joint research activities (JRAs). TNA provides free-of-charge access to the BSL3 facilities, technical resources and sample collections of VetBioNet consortium members, via an ongoing research call process and through a dedicated web portal. The JRAs include programmes optimising the modelling of epizootic and zoonotic diseases in animals, based on in vitro cell, tissue and organ cultures.

Among the results achieved so far on the development and optimisation of livestock infection models, three disease models have been finalised. These involve the standardisation of infection trials with peste-des-petits-ruminants (PPR) virus in sheep, poultry infection trials with both avian influenza virus and with Salmonella, and the development of trout and carp disease models for the study of viral fish diseases.

To support its integrated activities, VetBioNet has developed accredited training courses with the Federation of European Laboratory Animal Science Associations and other organisations. The first training school took place in January 2019.

The project is harmonising protocols and best practices, establishing guidelines to help upgrade high-containment facilities and promoting the use of global standards in all European BSL3 facilities, with a particular focus on animal welfare and alternatives to animal experimentation.

In 2021 VetBioNet opened a transnational call offering free-of-charge access to bio-contained animal facilities, analytical platforms & services of many European Institutes, to perform studies dedicated to advance research on epizootic and zoonotic diseases and to promote technological development.

III. STATE OF THE ART IN IRC PRIORITY DISEASES

In the framework of the STAR-IDAZ project, a list of priority diseases and crosscutting issues for which research coordination is required to make progress and deliver the control tools that are needed was identified. This preliminary list was further discussed during the meetings of the STAR-IDAZ IRC Executive and Scientific Committees' meetings held between 2017 and 2021 and updated accordingly. The full list of the currently identified priorities is reported below.

1. African swine fever (ASF)
2. Animal genomics/genetics for animal health
3. Antimicrobial resistance (AMR) and the development of innovative alternatives to antibiotics
4. Bovine tuberculosis (bTB)
5. Brucellosis
6. Coronaviruses (CoVs)
7. Diagnostics (tools and technologies)
8. Emerging issues
9. Epidemiology
10. Foot-and-mouth disease (FMD)
11. Foresight
12. Helminths
13. Vaccinology
14. Influenza
15. Mastitis
16. Mycoplasmas (including contagious bovine pleuropneumonia – CBPP and contagious caprine pleuropneumonia - CCPP)
17. One Health
18. Porcine reproductive and respiratory syndrome (PRRS)
19. Porcine respiratory disease complex (PRDC)
20. Pox virus infections
21. Vector-borne diseases (VBD)

In the framework of the STAR-IDAZ IRC Executive Committee meeting that was held in Kenya (2017), the first six diseases/issues to be addressed were selected. These were: ASF, bTB, brucellosis, FMD, helminths, and PRRS. During the STAR-IDAZ IRC Executive Committee meeting, held the following year (2018) in Spain, CoVs and VBD were selected as additional topics to be addressed. At the STAR-IDAZ IRC Executive Committee meeting, held in China in 2019, the scope of the work to be performed on VBD was better defined, and it was decided to start working on antimicrobial resistance (AMR) and the development of innovative alternatives to antibiotics. In the Executive Committee meetings held online during 2021, it was decided to address mycoplasma, mastitis and influenza next.

Other priorities discussed during the Executive Committee meetings included vaccinology, diagnostics, emerging diseases and One Health. These issues are currently being addressed by the STAR-IDAZ IRC but will not be covered in this report, which focuses on diseases/syndromes rather than technologies and broad networks coordination plan.

This report provides an overview of the state of the art of research, at a global level, for each of the selected diseases/syndromes, providing information on:

1. existing or planned global networks aiming at guiding future research on the topic, and that are acting as STAR-IDAZ IRC Working Groups (see below);
2. identified research gaps on control tools (diagnostics, vaccines, and pharmaceuticals), extracted from the DISCONTOOLS database;
3. recent research advances, providing an overview of a selection of highly relevant papers on the subject matter[1];
4. trends in published research, showing estimated statistics extracted from the CABI Abstract database on the topics and the STAR-IDAZ regions where relevant papers are published;
5. ongoing research, presenting a non-exhaustive list of ongoing research projects funded by the STAR-IDAZ IRC partners.

For each of its priority diseases/issues, STAR-IDAZ IRC is establishing geographically balanced Working Groups (WGs) of experts to perform gap analyses and to draw research roadmaps on the selected diseases/issues. For diseases/issues where global networks dedicated to gap analyses already exist, these groups were requested to support the STAR-IDAZ IRC and act as WGs. The 'Existing global research networks' sections describe the pre-existing global network or, when this is not present, the STAR-IDAZ IRC newly established WG for each priority disease.

For 'Recent research advances' sections, the selection of articles outlined resulted from a review of the literature published on the priority diseases in the last year and a selection of key articles presenting overviews of the current state of knowledge or providing significant advances in science. Due to the large volume of literature published on the selected diseases/issues, it was not feasible to include a comprehensive list of recent publications, but only a selection of a few highly relevant one, selected by SIRCAH.

"Trends in published research", associated with the keywords exploited in the literature search have been also reported to show, whenever possible, main statistics on each priority disease/issue for topics such as diagnostic, epidemiology, vaccination/vaccine development and therapeutics. Moreover, a graphical analysis of the estimated distribution of articles, based on country of first author, among the four STAR-IDAZ Regional Networks (Americas, Africa and Middle East, Asia & Australasia and Europe), has been reported. This data represents only an estimation of the trend in published research based on data searched by keywords and depend on the keywords attributed by CAB Abstracts. Some articles may be counted under more than one topic when more than one keyword was attributed to the article. Furthermore, for some diseases/issues it was not possible to apply the standard topic search due to the complexity of the issue.

The 'Ongoing research' sections present lists of projects targeting the selected priority diseases, classified based on the country of origin and name of the funding body issuing the project. The lists only focus on projects issued by STAR-IDAZ IRC and STAR-IDAZ Network Members, and are non-exhaustive, being based on information extracted from the reports of the STAR-IDAZ IRC Executive meetings, from Regional Network meetings and working group activities. Nevertheless, in the view of the authors, such lists still provide a valuable tool to support decision making by research funders, providing support in avoiding duplication of efforts and identifying potential synergies and collaborations.

1 Previous editions of the report contained a selection of scientific papers over a 3-years' time (i.e., the year of the report's publication and the two previous ones). Since last report, it was decided to provide focus on most recent finding only (i.e., occurred over the past year), and to delete reference to older papers.

1. African swine fever (ASF)

Global network: Global African Swine Fever Research Alliance (GARA)

Website: https://www.ars.usda.gov/GARA/

Partners ca.
38

Budget
NA

Start date:
2013

Overview

The Global African Swine Fever Research Alliance (GARA) was launched with the aim of establishing and sustaining global research partnerships that will generate scientific knowledge and tools to contribute to the prevention, control and, where feasible, eradication of African swine fever (ASF).

The GARA has, to date, 38 partners coming from all regions of the world and several stakeholders, including STAR-IDAZ. In 2020, Alex Morrow, Chair of SIRCAH, was elected as Finance Director for the GARA (2020-2023) and joined its Advisory Board.

GARA Members conducted research gap analyses on ASF diagnostics, vaccinology, epidemiology and virology, which are now periodically updated during the group biannual meetings. These meetings also provide an opportunity for researchers to network and exchange new knowledge about the disease and the development of control tools.

Aim and priorities

Aim: To establish and sustain global research partnerships that will generate scientific knowledge and tools to contribute to the successful prevention, control and where feasible eradication of African swine fever (ASF).

Objectives

- Identify research opportunities and facilitate collaborations within the Alliance;
- Conduct strategic and multi-disciplinary research to better understand ASF;
- Determine social and economic drivers and impact of ASF;
- Develop novel and improved tools to support the prevention and control of ASF;
- Determine the impact of ASF prevention and control tools; and
- Serve as a communication and technology sharing gateway for the global ASF research community and stakeholders.

News

SIRCAH had agreed with GARA to host a session during the 2020 physical meeting, to be dedicated to the validation of the STAR-IDAZ IRC roadmaps for ASF (disease control, vaccines, and diagnostic tests). Due to the current COVID-19 pandemic, the meeting was postponed, tentatively to 2022, the roadmap workshop session was also postponed to 7-10 June 2022, Galway, Ireland.

Draft versions of the STAR-IDAZ IRC **roadmaps** are available on the STAR-IDAZ IRC website.

On 6 May 2021, GARA ran a virtual seminar on 'Current efforts in African Swine Fever Vaccines'. Speakers from the USA, Europe, Africa and China discussed recent developments in AFS vaccines including licensing, regulation and commercialization. A second webinar was organized in September 2021 on 'Troubleshooting techniques for full genome sequencing of African swine fever'. A third one is planned for December2021.

DISCONTOOLS research need

R&D needs for ASF:

- Elucidation of the immune response to infection for the identification of target proteins and genes for vaccination.
- Characterisation at genome level of ASFV infection with different isolates.
- Characterisation of the different epidemiological scenarios worldwide for ASF and design ASF control and eradication strategies for each of them.
- Diagnostics: i) expansion of field validation for all tests and appropriate specimens; ii) established cell lines that make virus isolation a cost-effective test for its implementation at the National Reference Laboratories; iii) improvements in molecular characterization tests to determine the source of the outbreaks; and iv) develop DIVA test to allow and accurate monitoring of the effectiveness of the potential vaccine.
- Major efforts to provide an effective and sufficiently effective, safe and DIVA vaccine for wild boar and domestic pigs.

Recent developments

A cell culture-adapted vaccine virus against the current African swine fever virus pandemic strain[2]

In this paper, the authors report on a recently developed vaccine candidate, ASFV-G-ΔI177L, made by deleting the I177L gene from the genome of the highly virulent ASFV pandemic strain Georgia (ASFV-G). ASFV-G-ΔI177L is safe and highly efficacious in challenge studies using parental ASFV-G. Large-scale production of ASFV-G-ΔI177L has been limited because it can replicate efficiently only in primary swine macrophages. In the article, the authors present the development of an ASFV-G-ΔI177L derivative strain, ASFV-G-ΔI177L/ΔLVR, that replicates efficiently in a stable porcine cell line. In challenge studies, ASFV-G-ΔI177L/ΔLVR maintained the same level of attenuation, immunogenic characteristics, and protective efficacy as ASFV-G-ΔI177L. The authors conclude that ASFV-G-ΔI177L/ΔLVR is the first rationally designed ASF vaccine candidate that can be used for large-scale commercial vaccine manufacture.

Emergence and prevalence of naturally occurring lower virulent African swine fever viruses in domestic pigs in China in 2020[3]

In this paper, the authors report on their surveillance of ASFVs in seven provinces of China, from June to December 2020. A total of 22 viruses were isolated and characterized as genotype II ASFVs, with mutations, deletions, insertions, or short-fragment replacement occurring in all isolates compared with Pig/HLJ/2018 (HLJ/18), the earliest isolate in China. Eleven isolates had four different types of natural mutations or deletion in the EP402R gene and displayed a non-hemadsorbing (non-HAD) phenotype. Four isolates were tested for virulence in pigs; two were found to be as highly lethal as HLJ/18. However, two non-HAD isolates showed lower virulence but were highly transmissible; infection with 106 TCID50 dose was partially lethal and caused acute or sub-acute disease, whereas 103 TCID50 dose caused non-lethal, sub-acute or chronic disease, and persistent infection. The emergence of lower virulent natural mutants brings greater difficulty to the early diagnosis of ASF and creates new challenges for ASFV control.

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2 Borca, M. V.,Rai, A., Ramirez-Medina, E., Silva, E., Velazquez-Salinas, L., Vuono, E., Pruitt, S., Espinoza, N., Gladue, D. P. (2021). A cell culture-adapted vaccine virus against the current African swine fever virus pandemic strain. American Society for Microbiology (ASM) , Washington, D.C. , USA , Journal of Virology, Vol. 95, No. 14, JVI.00123-21-JVI.00123-21

3 Sun, E., Zhang, Z., Wang, Z., He, X., Zhang, X., Wang, L., Wang, W., Huang, L., Xi, F., Huangfu, H., Tsegay, G., Huo, H., Sun, J., Tian, Z., Xia, W., Yu, X., Li, F., Liu, R., Guan, Y., Zhao, D., Bu Z. Emergence and prevalence of naturally occurring lower virulent African swine fever viruses in domestic pigs in China in 2020 Sci China Life Sci., 64(5):752-765. doi: **10.1007/s11427-021-1904-4. Epub 2021 Feb 26**.

Rapid and sensitive RPA-Cas12a-fluorescence assay for point-of-care detection of African swine fever virus[4]

In this study the authors developed an assay for rapid and visible detection of ASF based on the conserved p72 gene sequence of ASFV. They combined the Cas12a-based assay with recombinase polymerase amplification (RPA) and a fluorophore-quencher (FQ)-labeled reporter assay. Five crRNAs designed for Cas12a-based assay showed specificity with remarkable fluorescence intensity under visual inspection. Within 20 minutes, with an initial concentration of two copies of DNA, the assay produced significant differences between experimental and negative groups, indicating the high sensitivity and rapidity of the method. In conclusion, the developed RPA-Cas12a-fluorescence assay seems to provide a fast and visible tool for point-of-care ASFV detection with high sensitivity and specificity, which can be rapidly performed on-site under isothermal conditions, promising better control and prevention of ASF.

Others from EFSA scientific opinions

The European Commission requested EFSA to provide study designs for the investigation of four research domains according to major gaps in knowledge identified by EFSA in a report published in 2019: (i) the patterns of seasonality of African swine fever (ASF) in wild boar and domestic pigs in the EU; (ii) the epidemiology of ASF in wild boar; (iii) survival of ASF virus (ASFV) in the environment and (iv) transmission of ASFV by vectors. The following four scientific opinions were recently published:

A Research objectives to fill knowledge gaps in African swine fever virus survival in the environment and carcasses, which could improve the control of African swine fever virus in wild boar populations.[5]

B Research priorities to fill knowledge gaps in wild boar management measures that could improve the control of African swine fever in wild boar populations.[6]

C Research priorities to fill knowledge gaps in the control of African swine fever: possible transmission of African swine fever virus by vectors.[7]

D Research priorities to fill knowledge gaps on ASF seasonality that could improve the control of ASF.[8]

4 Fu J, Zhang Y, Cai G, Meng G, Shi S. (2021) Rapid and sensitive RPA-Cas12a-fluorescence assay for point-of-care detection of African swine fever virus. PLoS One. Jul 19;16(7):e0254815. doi: 10.1371/journal.pone.0254815. eCollection 2021.

5 Nielsen, S. S., Alvarez, J., Bicout, D. J., Calistri, P., Depner, K., Drewe, J. A., Garin-Bastuji, B., Rojas, J. L. G., Schmidt, C., Herskin, M., Michel, V., Pasquali, P., Roberts, H. C., Sihvonen, L. H., Spoolder, H., Stahl, K., Velarde, A., Winckler, C., Blome, S., Boklund, A., Bøtner, A., Dhollander, S., Rapagnà, C., Stede, Y. van der, Chueca, M. A. M. (2021) , Wiley , Oxford , UK , EFSA Journal, Vol. 19 , No. 6

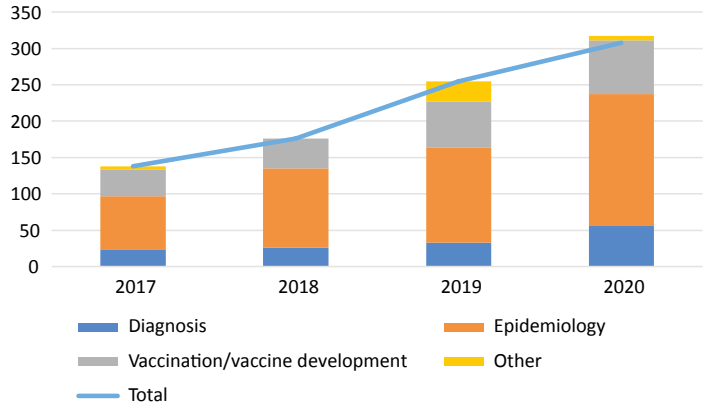
6 Nielsen, S. S., Alvarez, J., Bicout, D. J., Calistri, P., Canali, E., Drewe, J. A., Garin-Bastuji, B., Rojas, J. L. G., Schmidt, C., Herskin, M., Michel, V., Padalino, B., Pasquali, P., Roberts, H. C., Spoolder, H., Stahl, K., Velarde, A., Winckler, C., Blome, S., Boklund, A., Bøtner, A., Dhollander, S., Rapagnà, C., Stede, Y. van der, Chueca, M. A. M. (2021) , Wiley , Oxford , UK , EFSA Journal, Vol. 19 , No. 7

7 Nielsen, S. S., Alvarez, J., Bicout, D. J., Calistri, P., Depner, K., Drewe, J. A., Garin-Bastuji, B., Rojas, J. L. G., Schmidt, C., Herskin, M., Michel, V., Pasquali, P., Roberts, H. C., Sihvonen, L. H., Spoolder, H., Stahl, K., Velarde, A., Winckler, C., Blome, S., Boklund, A., Bøtner, A., Dhollander, S., Rapagnà, C., Stede, Y. van der, Chueca, M. A. M. (2021) , Wiley , Oxford , UK , EFSA Journal, Vol. 19 , No. 6

8 Nielsen, S. S., Alvarez, J., Bicout, D. J., Calistri, P., Depner, K., Drewe, J. A., Garin-Bastuji, B., Rojas, J. L. G., Schmidt, C. G., Herskin, M., Michel, V., Pasquali, P., Roberts, H. C., Sihvonen, L. H., Spoolder, H., Stahl, K., Velarde, A., Winckler, C., Blome, S., Boklund, A., Bøtner, A., Dhollander, S., Stede, Y. van der; Chueca, M. Á. M. (2021) , Wiley , Oxford , UK , EFSA Journal, Vol. 19 , No. 4

Trends in published research

Total records &
Main topics



Country/ Region of
first Author (2017/2020)

Ongoing research

Non-exhaustive list of ongoing projects on ASF funded by STAR-IDAZ IRC and STAR-IDAZ Network Members reported in 2021:

Area	Country/ Organisation	Research projects
Vaccine development	Belgium	• Study of the pathogenesis (role of host receptors) of African swine fever (ASF) and innate immune response in ASF virus infected domestic pigs- RF 20/6351 ASFIMMUNE
	UK (DEFRA)	• Generate reference strains of previous uncharacterised genotypes of ASFV and circulating genotype II isolates – The Pirbright Institute • Establish large scale cultures of macrophage cell lines and prepare frozen stocks – The Pirbright Institute • Test different culture methods for macrophage cell lines for use in ASFV diagnosis – The Pirbright Institute • Investigate other cells for virus growth and diagnosis – The Pirbright Institute • Identify ASFV CD4+CD8+ antigens Immunogenicity and protective efficacy in pigs of pools of recombinant adenoviruses expressing CD4+CD8+ antigens – The Pirbright Institute • Build ASFV interactome map and generate gene deleted viruses to valid interactions – ICRAD • Optimize gene-deleted ASFV live attenuated vaccine candidates and porcine macrophage cell lines – BBRSC
	European Commission (EC)	• VACDIVA project: provide three safe and effective pilot vaccines for wild boars and domestic pigs that are ready for registration **https://vacdiva.eu/** • DEFEND Project: understand drivers of ASFV emergence, and generate research outputs which underpin novel diagnostic tools and vaccines, and authenticate appropriate and rapid responses by decision-makers **https://defend2020.eu/**
	France	• Development and evaluation of potential ASF vaccines • Comparative pathogenic mechanisms of infection by genotype II • ASFV in pigs and wild boars (VetBioNet, VIP unit) • High throughput cartography of ASFV / host interactions • The African swine fever virus Interactome project (ASFVInt) to identify cellular signalling pathways, functional modules, and machineries that are manipulated by the virus to its own benefit or even are essential for ASFV replication • New ASF vaccines for the intramuscular or oral routes (ASF-IMVO, VIP unit) • Vesicles as a vector for new ASFV antigens (ASF-Vec, VIP unit) • Genetic evolution of the different lineages of ASFV (EvolPPA, GVB Unit) • "111" program: expert exchange with Yangzhou University and Yangzhou University (China)
	Italy	• Genetic variants of domestic and wild pig connected with African swine fever - IZS Sardinia
	Nigeria (NVRI)	• Developing innovative and sustainable approaches to prevent the spread of African swine fever in Africa (ASF-RESIST)
	Spain	• African swine fever: from emergency responses to endemicity prevention - Institut de Recerca y Tecnologia Agroalimentaries de catalunya (IRTA) - PID2019-107616rb-i00 • Characterization of relevant genetic determinants for the development of a vaccine against the virus of the of African swine fever - National Institute for Agricultural and Food Research and Technology (INIA) - RTI 2018-097305-R-100 • Modulation of innate immune response to African swine fever (ASF), in view of vaccines development. Spanish National Research Council (CSIC) - PID2020-117300RB-I00

Area	Country/ Organisation	Research projects
Diagnostics	European Commission (EC)	• DEFEND Project: understand drivers of ASFV emergence, and generate research outputs which underpin novel diagnostic tools and vaccines, and authenticate appropriate and rapid responses by decision-makers **https://defend2020.eu/** • VACDIVA project: provide three safe and effective pilot vaccines for wild boars and domestic pigs that are ready for registration. It will also validate DIVA tests and develop cost-benefit and -effective surveillance and control-vaccination strategies
	France	• Validation of molecular, serological and virological assays for ASFV detection
	Italy	• Heterologous system and characterization of recombinant proteins VP72 and/ or VP32 of African swine fever virus - IZS UM • ASFEND- modeling of passive surveillance as key tool for African swine fever Exit Strategy - IZS Sardinia
	Nigeria (NVRI)	• Developing innovative and sustainable approaches to prevent the spread of African swine fever in Africa (ASF-RESIST)
	UK (DEFRA)	• Evaluation of ELISA kits and PCR reagents - The Pirbright Institute • Establish large scale cultures of macrophage cell lines and prepare frozen stocks • Test different culture methods for macrophage cell lines for use in ASFV diagnosis • Surveillance contract – alternative ELUISA to Ingenasa • Investigate other cells for virus growth and diagnosis
Control strategies	Belgium	• Study of the pathogenesis (role of host receptors) of African swine fever (ASF) and innate immune response in ASF virus infected domestic pigs - RF 20/6351 ASFIMMUNE
	France	• Deciphering virus-host molecular interactions opens new perspectives to predict/simulate future emergencies and develop effective countermeasures for disease control, such as novel spectrum anti-ASFV compounds • ASF-Challenge: 1/ predicting the spatio-temporal dynamics of viral dissemination after a fictive outbreak of PPA at the interface between populations of wild boars and pig farms, and 2/ evaluating control measures complementary to regulatory measures - INRAE • ASFV transmission, epidemiological modeling of the swine boar interface (Episabe-Unit) ASFV transmission, epidemiological transmission within wild boar populations (Episabe-Unit) • Study of the thermal inactivation of reference ASFV-containing standard samples
	Italy	• Improvement of strategies, of prevention/control methods of African swine fever
	UK (DEFRA)	• Determine ASFV survival in water at different temperatures over time - The Pirbright Institute • UV inactivation kinetics of ASFV in water of different turbidity's - The Pirbright Institute • Thorough literature review of the effectiveness of disinfectants against ASFV - The Pirbright Institute • Determine survival of ASFV in dried blood, urine and faeces at different temperatures over time - The Pirbright Institute • Determine survival of ASFV in stable flies fed on infected pigs over time. • Integrate results in models of ASFV transmission within and between pig farms in the UK - The Pirbright Institute • Develop a decision support tool to estimate time of introduction of ASFV to a pig herd based on mortality data - The Pirbright Institute
Other	Spain	Sialoma and saliva microtranscriptoma of *Ornithodoros* sp., African swine fever vector ticks. Design and evaluation of anti-ornithodoros multiantigenic vaccine - Spanish National Reserch Council (CSIC) -RTI 2018-098297-B-100

2. Bovine tuberculosis (bTB)

Global network: Global Research Alliance for Bovine Tuberculosis (GRAbTB)

Website: https://www.star-idaz.net/global-research-alliance-for-bovine-tuberculosis-grabtb/

Partners ca.
15

Budget
NA

Start date:
2014

Overview

The Global Research Alliance for Bovine Tuberculosis (GRAbTB) was initiated under the STAR-IDAZ project to facilitate research cooperation and technical exchange on bovine tuberculosis (bTB). The GRAbTB has, to date, 15 partners coming from Asia and Australasia, the Americas and Europe, and is looking to expand the network.

GRAbTB performed research gap analyses on bTB epidemiology and control, diagnostics, vaccinology, and host-pathogen interaction in two workshops since 2014. In 2017, based on these gap analyses, three research roadmaps were drafted by SIRCAH, in collaboration with GRAbTB, on bTB vaccines, diagnostics, and epidemiology. These roadmaps were discussed by GRAbTB and other bTB experts at a workshop in Birmingham, UK in December 2017. After the meeting, SIRCAH and GRAbTB worked on the refining and finalising the roadmaps. The structure of generic roadmaps for diagnostic and disease control strategies were further discussed in a meeting of the GRAbTB Executive Committee, that was held in London, UK in July 2019. The discussion led to improvements to the diagnostics roadmap and on the disease control strategies one.

Aim and priorities

Aim: to establish and sustain global research partnerships that will generate scientific knowledge and tools to contribute to the successful control and eradication of bovine TB.

Objectives

- Identify research opportunities and facilitate collaborations within the Alliance
- Conduct strategic and multi-disciplinary research to better understand TB
- Develop and share novel and improved tools to control TB
- Serve as a communication and technology sharing gateway for the global bovine TB research community and stakeholders
- Promote collaboration with the human TB research community

News

GRAbTB will organise subgroups to produce lead summaries for the revised roadmaps for diagnostics and disease control strategies, and to provide a final validation of the vaccine development roadmap, that is published on the STAR-IDAZ IRC website.

The next meeting of the GRAbTB was planned to be held on the side of the 7th International Conference on Mycobacterium bovis, that should have been held in Galway, Ireland in June 2020. Due to the COVID-19 situation, the meeting was postponed as well as the GRAbTB meeting was also postponed, tentatively to June 2022.

A draft version of the STAR-IDAZ IRC **roadmap** for the development of bTB vaccines is available on the STAR-IDAZ IRC website.

DISCONTOOLS research needs

R&D needs for bTB:

- The development of defined **skin test reagents** based on specific *M. bovis* antigens to overcome the limitations of largely undefined and difficult to produce and standardize tuberculins.
- Rapid, specific and simple **diagnostic tests for live animals**, particularly for cattle in developing countries, and for wildlife species.
- Improved delivery systems for the application of **vaccines in wildlife**.
- Further investigations into the **host pathogen interactions** and the immune response to support the development of new vaccines and better diagnostic tools.
- A better understanding of the **epidemiology of *M. bovis*** infections in cattle and cattle herds to enable strategies for the use of new vaccines when available.
- Information on infection by and pathogenesis of *M. bovis, M. caprae, M. pinnipedii* and even *M. tuberculosis* in other animal species.

Recent developments

Macrophage-specific responses to human- and animal-adapted tubercle bacilli reveal pathogen and host factors driving multinucleated cell formation.[9]

To identify factors that contribute to host tropism of *Mycobacterium bovis* (Mbv) and *M. tuberculosis* (Mtb), the authors analysed blood-derived primary human and bovine macrophages (hMφ or bMφ), respectively infected with Mbv and Mtb. The study shows that Mbv and Mtb reside in different cellular compartments and differentially replicate in hMφ whereas both Mbv and Mtb efficiently replicate in bMφ. Particularly, only the infection of bMφ with Mbv promoted the formation of multinucleated giant cells (MNGCs), a hallmark of tuberculous granulomas. These findings implicate MNGC formation in the contrasting pathology between Mtb and Mbv for the bovine host and identify MPB70 from Mbv and extracellular vesicles from bMφ as mediators of this process.

Field evaluation of specific mycobacterial protein-based skin test for the differentiation of *Mycobacterium bovis*-infected and Bacillus Calmette Guerin-vaccinated crossbred cattle in Ethiopia.[10]

In this articles the authors describe an evaluation of a DIVA skin test (DST) that is based on a cocktail (DSTc) or fusion (DSTf) of specific (ESAT-6, CFP-10 and Rv3615c) *M. bovis* proteins in Zebu-Holstein-Friesians crossbred cattle in Ethiopia. 74 calves (35 BCG vaccinated and 39 unvaccinated) aged less than 3 weeks at the start of experiment and 68 naturally infected 'TB reactor' cows were used for this study. Six weeks after vaccination, the calves and the TB reactor cows were tested with the DSTc and the single intradermal comparative tuberculin (SICCT) test. In conclusion, the DSTc could differentiate *M. bovis*-infected from BCG-vaccinated cattle in Ethiopia. DST had higher sensitivity than the SICCT test, thus it could be used as a diagnostic tool for bTB if BCG vaccination is implemented for the control of bTB.

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9 Queval, C. J., Fearns, A., Botella, L., Smyth, A., Schnettger, L., Mitermite, M., Wooff, E., Villarreal-Ramos, B., Garcia-Jimenez, W., Heunis, T., Trost, M., Werling, D., Salguero, F. J., Gordon, S. V., Gutierrez, M. G. (2021). Macrophage-specific responses to human- and animal-adapted tubercle bacilli reveal pathogen and host factors driving multinucleated cell formation. PLoS Pathogens, 17(3), e1009410. https://doi.org/10.1371/journal.ppat.1009410

10 Bayissa, B., Sirak, A., Zewude, A., Worku, A., Gumi, B., Berg, S., Hewinson, R. G., Wood, J., Jones, G. J., ETHICOBOTS consortium, Vordermeier, H. M., Ameni, G. (2021). Field evaluation of specific mycobacterial protein-based skin test for the differentiation of Mycobacterium bovis-infected and Bacillus Calmette Guerin-vaccinated crossbred cattle in Ethiopia. Transboundary and Emerging Diseases, 10.1111/tbed.14252. Advance online publication. https://doi.org/10.1111/tbed.14252

Use of blood matrices and alternative biological fluids for antibody detection in animal tuberculosis.[11]

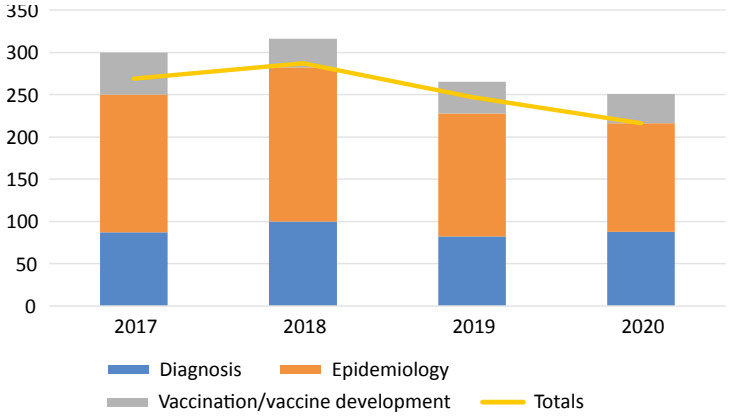
Dual Path Platform (DPP) and Multiantigen Print Immunoassay (MAPIA) were used to compare antibody levels in ten sample types including whole blood (fresh and hemolyzed), plasma (fresh and leftover from Bovigam testing), serum, saliva, broncho-alveolar lavage, urine, diaphragm extract, and bile collected from cattle aerosol-infected with *Mycobacterium bovis*. High correlation in measurements was found between all blood-derived specimens, broncho-alveolar lavage and diaphragm extract, supporting their potential use in antibody assays as alternative test specimens in serologic assays for bTB.

HMEJ-based safe-harbor genome editing enables efficient generation of cattle with increased resistance to tuberculosis.[12]

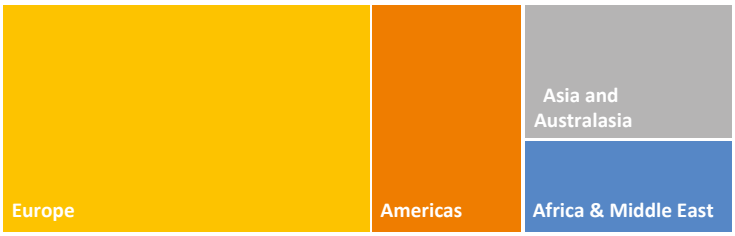
The authors demonstrated that a homology-mediated end-joining (HMEJ)-based method can be used to create gene-edited cattle that displays precise integration of a functional gene at the *ROSA26* locus, increasing the knock-in efficiency of reporter genes compared to the traditional HDR-based method in bovine fetal fibroblasts. Moreover, gene-edited cattle exhibited predictable expression of the functional gene natural resistance-associated macrophage protein-1 (*NRAMP1*), a metal ion transporter which appears to increase resistance to bovine tuberculosis.

Trends in published research

Total records &
Main topics



Country/ Region of
first Author (2017/2020)



11 Lyashchenko, K. P., Sikar-Gang, A., Sridhara, A. A., Johnathan-Lee, A., Elahi, R., Greenwald, R., Lambotte, P., Esfandiari, J., Roos, E. O., Kerr, T. J., Miller, M. A., Thacker, T. C., Palmer, M. V., & Waters, W. R. (2021). Use of blood matrices and alternative biological fluids for antibody detection in animal tuberculosis. Veterinary Immunology and Immunopathology, 239, 110303. https://doi.org/10.1016/j.vetimm.2021.110303

12 Yuan, M., Zhang, J., Gao, Y., Yuan, Z., Zhu, Z., Wei, Y., Wu, T., Han, J., Zhang, Y. (2021). HMEJ-based safe-harbor genome editing enables efficient generation of cattle with increased resistance to tuberculosis. The Journal of Biological Chemistry, 296, 100497. https://doi.org/10.1016/j.jbc.2021.100497

Ongoing research

Non-exhaustive list of ongoing projects on bTB funded by STAR-IDAZ IRC and STAR-IDAZ Network Members reported in 2021:

Research Area	Country/ Organisation	Research projects
Challenge model	Nigeria (NVRI)	• Direct molecular detection of Bovine TB in small and large ruminants in Plateau State
To identify protective mechanisms in *M. bovis* infected animals	Argentina (IRTA)	• Genetic factors involved in susceptibility/resistance to Bovine TB and in the immune response associated with the diagnosis of infection • Study of the potential trained innate immune response induced by *M. bovis* strains in immune cells from cattle and analysing the connection of trained immune phenotypes with mutations in NOD2 gene
	Italy	• Study on bovine immunopathogenetic pathways during the *Mycobacterium avium* subsp *paratuberculosis* infection to understand the resistance mechanisms to bovine paratuberculosis - IZS UM 6/19 • Implementation of advanced molecular and flow cytometry methods for buffalo tuberculosis diagnosis - IZS ME 6/19 • Standardization of a new diagnostic protocol of IFN-γ for bovine and swine tuberculosis *M. bovis* diagnosis - IZS
	Mexico	• Molecular and cellular mechanisms associated with *Mycobacterium bovis* control in granulomas in naturally infected cattle. • Identification of biomarkers of natural resistance to bovine tuberculosis
Development of a novel attenuated vaccine allowing DIVA	Argentina (IRTA)	• Development of an attenuated mutant strain in phoP that has shown better protection than BCG in mice.
Subunit vaccines	Argentina (IRTA)	• Development of subunit vaccines based on *M. bovis* antigens formulated in nanocarriers
Other	Spain	• The badger (*Meles meles*) and animal tuberculosis in Spain: badger -bovine interaction in hotspot areas and measures to control the disease in the interface - Servicio Regional de Investigación y Desarrollo Agroalimentario de Asturias (SERIDA) - RTI 2018-096010-B-C21
	Spain	• Quantitative epidemiology for the characterization of barriers and tools for the control and eradication of bovine tuberculosis in high and low prevalence areas - Universidad Complutense de Madrid (UCM-VISAVET) - RTI 2018-096010-B-C21

3. Brucellosis

Global network

Under the STAR-IDAZ project, an expert group on brucellosis was formed in 2014 to conduct a first research gap analysis. Lead summaries for a vaccine roadmap were developed based on these inputs and circulated to that same group of experts for comments in 2018. In order to improve the commitment of the experts in collaborating with the STAR-IDAZ IRC, and to formally establish a STAR-IDAZ IRC Working Group (WG) for brucellosis, SIRCAH presented at the 2019 International Brucellosis Society (IBS) Meeting, that was held as a satellite of the Conference of Research Workers in Animal Diseases (CRWAD) meeting in November 2019, in Chicago. The aim of the presentation was to introduce the activities and *modus operandi* of the STAR-IDAZ IRC, and to call for volunteers to revise the draft research roadmap for brucellosis vaccines and to update the research gap analyses for brucellosis diagnostics and disease control. After the meeting, IBS proposed a list of experts to join the STAR-IDAZ WG on brucellosis, and it was agreed that a first meeting of the WG should be held alongside the next Global Brucellosis meeting, that was supposed to be held in September 2020 in Italy. As the Global meeting was postponed to 2021, due to the COVID-19 pandemic, the meeting of the STAR-IDAZ IRC WG was also postponed, so as to hold the two events back-to-back.

A draft version of the STAR-IDAZ IRC **roadmap** for the development of brucellosis vaccines is available on the STAR-IDAZ IRC website.

DISCONTOOLS research needs

R&D needs for brucellosis:

- A better understanding of the epidemiology, diagnosis and immunoprophylaxis of brucellosis in less common livestock species (camelids, yaks, water buffaloes).
- **Improved vaccines** (more protective, stable, affordable, and less pathogenic), including immunologically tagged vaccines and complementary DIVA tests.
- A better understanding of latent infection in animals.
- **Socio-economic studies** under different situations to prioritize interventions in developing countries.
- **Molecular methods for typing** of *Brucella* strains.

Recent developments

Development of *Brucella melitensis* Rev.1 ΔOmp19 mutants with DIVA feature and comparison of their efficacy against three commercial vaccines in a mouse model.[13]

In this study, the authors described the development of a Rev.1 Outer membrane protein 19 (Omp 19) deletion mutants that contained sufficient residual virulence. Furthermore its protective immunity was similar to the commercial vaccines. Thus, the study showed that a vaccine prepared using a *B. melitensis* Rev.1 ΔOmp19 can differentiate infected from vaccinated animals (DIVA) through the ELISA test that detects the Omp19 protein.

13 Uslu, A., Erganis, O. (2021). Development of *Brucella melitensis* Rev.1 ΔOmp19 mutants with DIVA feature and comparison of their efficacy against three commercial vaccines in a mouse model. Molecular Immunology, 133, 44–52. **https://doi.org/10.1016/j.molimm.2021.02.006**

Comparative analysis of the main outer membrane proteins of *Brucella* in the diagnosis of brucellosis[14]

In this study, six recombinant *Brucella* outer membrane proteins, omp10, omp16, omp19, omp25, omp31 and BP26, were expressed in prokaryotic cells and utilized as diagnostic antigens analysed by indirect ELISA in clinical sera of humans, bovines and goats with brucellosis. BP26 showed the highest diagnostic accuracy in human (96.45%) and goat serum (95.00%), while omp31 showed the strongest ability to detect *Brucella* in bovine serum (accuracy of 84.03%). The results of this study indicate that omp31 and BP26 are candidate antigens with high potential application value in the clinical diagnosis of brucellosis, showing also higher diagnostic specificities than LPS and Rose Bengale Ag antigens.

Development and evaluation of a gold nanoparticle based Lateral Flow assay (LFA) strip test for detection of *Brucella* spp.[15]

The fabrication and validation of a Lateral Flow immunoassay (LFA) strip test, developed for detection of *Brucella* spp. from clinical samples (bovine aborted fetal stomach contents) is described. Over 115 clinical samples tested, the relative sensitivity (DSn) and relative specificity (DSp) of the LFA strip test was reported to be 78.57% (95%CI: 49.2-95.3); 93.07% (95%CI: 86.2-97.2) and 80.0% (95%CI:51.9-95.7); 94.0% (95%CI:0.795-0.925) using respectively culture and PCR as reference diagnostic tests. Thus, the LFA strip test described could be used as a rapid penside diagnostic test for screening of brucellosis.

Control of *Brucella melitensis* in endemic settings: A simulation study in the Nile Delta, Egypt.[16]

The authors simulated and described different control scenarios on the seroprevalence of brucellosis among the small ruminant population in a hypothetical endemic setting, using compartmental models. The study shows that vaccination of young replacement animals only can effectively reduce the prevalence of small ruminant brucellosis in endemic areas if a high vaccination coverage is achieved. Moreover, the results show the potential success of strategies requiring a vaccination coverage of 50% of young replacements and 25% of adult animals each year.

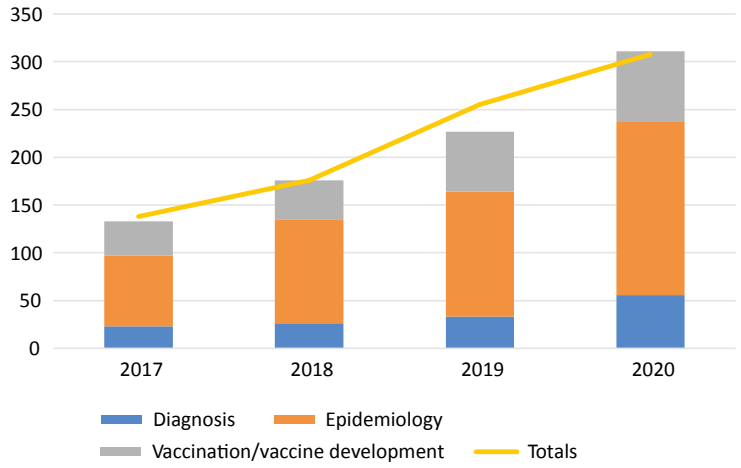
14 Bai, Q., Li, H., Wu, X., Shao, J., Sun, M., Yin, D. (2021). Comparative analysis of the main outer membrane proteins of Brucella in the diagnosis of brucellosis. Biochemical and Biophysical Research Communications, 560, 126–131. **https://doi.org/10.1016/j.bbrc.2021.04.127**

15 Prakash, C., Kumar, B., Singh, R. P., Singh, P., Shrinet, G., Das, A., Ashmi, M., Abhishek, Singh, K. P., Singh, M. K., Gupta, V. K. (2021). Development and evaluation of a gold nanoparticle based Lateral Flow assay (LFA) strip test for detection of Brucella spp. Journal of Microbiological Methods, 184, 106185. https://doi.org/10.1016/j.mimet.2021.106185

16 Hegazy, Y. M., Schley, D., Ridler, A., Beauvais, W., Musallam, I., Guitian, J. (2021). Control of Brucella melitensis in endemic settings: A simulation study in the Nile Delta, Egypt. Transboundary and Emerging Diseases, 68(4), 2364–2375. https://doi.org/10.1111/tbed.13897

Trends in published research

Total records &
Main topics



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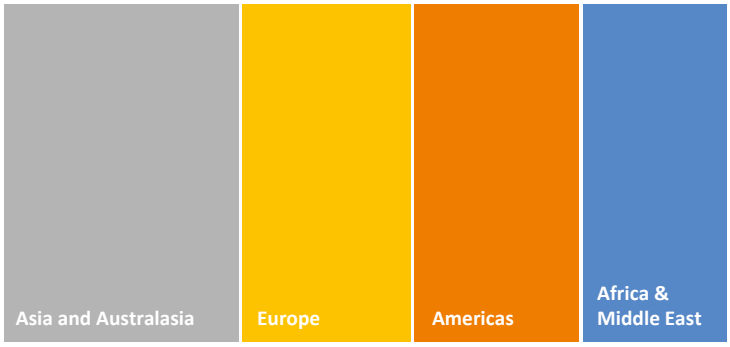


Ongoing research

Non-exhaustive list of ongoing projects on brucellosis funded by STAR-IDAZ IRC and STAR-IDAZ Network Members reported in 2021:

Research Area	Country/ Organisation	Research Projects
Vaccine development	Argentina (IRTA)	• Using a nanovaccine platform to develop a safe and effective immunogen against small ruminant brucellosis • Identification of novel virulence determinants in *Brucella* spp. and their application in the obtention of live attenuated vaccine candidates
	Nigeria (NVRI)	• Brucella antigen S19 development
	Spain	• Ovine brucellosis: *B. ovis* and *B. melitensis* safe vaccines and DIVA strategies - Centro de Investigación y Tecnología Agroalimentaria de Aragón (CITA,) University of Navarra, University of Salamanca - PID2019-107601RA-C31; PID2019-107601RA-C32; PID2019-107601RA-C33
	UK	• Develop a glycoconjugate vaccine – APHA (AgResults, BactiVac, Commecial partner)
Diagnostics	Argentina (IRTA)	• Validation of a competitive ELISA (cELISA) for epidemiology surveillance and diagnosis of caprine brucellosis • Identification of *Brucella* spp using LAMP (loop mediated isothermal amplification) • Indirect ELISA for detection of antibodies against *Brucella abortus* in bulk and individual milk samples in dairy cattle • Competitive ELISA for detection of antibodies against *Brucella abortus* in bovine serum samples • Competitive ELISA for detection of antibodies against *Brucella melitensis* in goat serum samples
	Mexico	• Serological techniques based on Phage Display technology: *Brucella* peptides selection by means of Phage Display technology • Serological techniques based on Phage Display technology: *Brucella* peptides selection to diminish Yersinia and Salmonella cross reactions • Serological techniques based on Phage Display technology: ELISA standardization with Brucella peptides selected from phage display technology
	Israel (KVI)	• Development of molecular typing of *Brucella melitensis* by whole genome sequencing with cgMSLT method
	UK (DEFRA)	• Developing Improved Detection and Control Tools for Brucellosis - APHA
Control strategies	Argentina (IRTA)	• Unraveling the molecular basis for natural resistance to Brucella infection • Epidemiological surveillance of brucellosis in dairy farms of Argentina
	UK (DEFRA)	• Developing Improved Detection and Control Tools for Brucellosis - APHA
Others	Argentina (IRTA)	• Epidemiology of *Brucella abortus* and *Brucella melitensis* infection in cattle and small ruminants of Argentina • Is there a link between Brucella virulence and streptomycin resistance (SmR)?
	European Commission (EC)	• Bruce-GenoProt - A comprehensive proteogenomic analysis of Brucella to understand the epidemiology, biology, virulence mechanisms, and host-pathogen interaction
	Mexico	• Improved knowledge of the sRNA regulation on Brucella virulence factors: Bioinformatics strategies to match sRNAs and regulated virulence factors • Improved knowledge of the sRNA regulation on Brucella virulence factors: Experimental strategies to corroborate interaction/regulation between sRNAs and virulence factors-genes

4. Foot-and-mouth disease (FMD)

Global network: Global Foot-and-Mouth Research Alliance (GFRA)

Website: https://www.gfra2021.com/home-site/

Partners ca.
27

Budget
NA

Start date:
2003

Overview

The Global Foot-and-Mouth Research Alliance (GFRA) was launched in 2003 with the aim of establishing and sustaining global research partnerships to generate scientific knowledge and discover the tools to successfully prevent, control, and eradicate FMD. The GFRA has, to date, 27 partners coming from all regions of the world and many stakeholders, including STAR-IDAZ.

The GFRA Members conducted research gap analyses on FMD diagnostics, vaccinology, epidemiology biotherapeutics and disinfectants, immunology, pathogenesis and molecular biology. These are now periodically updated during the groups' biannual meetings. These meetings also provide an opportunity for researchers to network and exchange new knowledge about the disease and the development of control tools.

Aim and priorities

Aim: to establish and sustain global research partnerships to generate scientific knowledge and discover the tools to successfully prevent, control and eradicate FMD.

Objectives

- Facilitate research collaborations and serve as a communication gateway for the global FMD research community;
- Conduct strategic research to better understand FMD;
- Development of the next generation of control measures and strategies for their application;
- Determine social and economic impacts of the new generation of improved FMD control; and
- Provide evidence to inform development of policies for safe trade of animals and animal products in FMD-endemic areas.

News

The **VI Global Foot-and-Mouth Disease Research Alliance (GFRA) Scientific Meeting** will be held **virtually,** due to the COVID-19 pandemic, from 1 – 3 November 2021.

A meeting to update the GFRA research gap analyses was held in Buenos Aires, Argentina, in June 2018. The purpose of the meeting was to bring together FMD experts worldwide to analyse and discuss vacant areas and pending challenges in relation to the control of the disease on a global scale. The meeting also served as a basis for developing STAR-IDAZ IRC FMD research roadmaps.

Three draft roadmaps (one on diagnostics, one on vaccines and one on disease control strategies) were drafted by SIRCAH and, after being revised by the STAR-IDAZ IRC Scientific Committee, were sent to GFRA experts' groups. For the final expert validation of the roadmaps, SIRCAH organised a satellite workshop alongside the GFRA Scientific Meeting that was held in Bangkok, Thailand, in October 2019. About 30 experts participated in the workshop, bringing a well-balanced range of specialisms (across diagnostic, vaccine and epidemiology) and wide geographical representation. The experts identified the main priority leads for each of the roadmaps and looked into the details of the identified challenges for each of these leads. The roadmaps were updated based on the received inputs and the final version was circulated after the meeting for validation by the group.

The validated versions of the STAR-IDAZ IRC **roadmaps** are available on the STAR-IDAZ IRC website.

DISCONTOOLS research needs

R&D needs for FMD:

- Faster diagnostics and sensitive pen side tests along with the development of more effective and specific tests for differentiating between antibodies due to infection and vaccination.
- Sufficient panels for test validation across all serotypes and species.
- Knowledge about virus transmission and persistence in vaccinated populations and reliability of tests to differentiate vaccinated from infected animals.
- Support for fundamental immunology and for animal studies.
- Knowledge on circulating isolates in endemic regions for selecting the vaccine antigens in endemic settings.
- Better serological predictors of protection afforded by vaccination.

Recent developments

The detection of long-lasting memory foot-and-mouth disease (FMD) virus serotype O-specific CD4+ T cells from FMD-vaccinated cattle by bovine major histocompatibility complex class II tetramer.[17]

The authors identified CD4+ T-cell epitopes in the FMD virus (FMDV) capsid and phenotyped the CD4+ T cells that recognize them using bovine major histocompatibility complex (BoLA) class II tetramer. Two epitopes were identified in the structural protein VP1, one in VP3 and one in VP4. Among the four epitopes in the FMDV capsid identified, three of them have not been previously reported. All the four epitope-expanded T-cell populations produced IFN-γ in vitro, indicating a long-lasting Th1 cell phenotype after FMD vaccination. They also demonstrated, utilizing FMDV epitope-loaded tetramers, that FMDV-specific CD4+ T cells were still present in cattle blood samples four years after the animals had been vaccinated against FMDV.

Foot-and-mouth disease virus infection in the domestic dog (*Canis lupus familiaris*), Iran.[18]

Five puppies died after being fed lamb carcases from animals that had died during an outbreak of FMD in Iran. At post-mortem examination, virological and microscopic examination of the cardiac tissue of one of the puppies provided evidence of FMD virus replication in the canine heart. These findings demonstrate for the first time that FMD virus can internalise and replicate in dogs and highlight the danger of feeding diseased animal carcases to other species.

Development of two rapid lateral flow test strips for detection of foot-and-mouth disease virus SAT 1 and SAT 3.[19]

In this study, the authors have developed two lateral flow immunochromatographic (LFI) strip tests for the detection of FMDV SAT 1, and SAT 3 using monoclonal antibodies (mAb). The results showed that SAT 1 strip test detected 14 out of 15 SAT 1 field isolates. While SAT 3 strip test detected all four SAT 3 isolates tested, even if showing a weak signal for UGA 10/97, and furthermore showed no cross-reactivity with other FMDV serotypes. The authors report diagnostic specificities of the SAT 1 and the SAT 3 tests as 100%, which are higher than double antibody sandwich (DAS) ELISA. On the other side, the sensitivity of the SAT 1 test strip is lower than that of DAS ELISA, while the diagnostic sensitivity of the SAT 3 test strip is similar to that of DAS ELISA.

17 Mitoma, S., Carr, B. V., Harvey, Y., Moffat, K., Sekiguchi, S., Charleston, B., Norimine, J., Seago, J. (2021). The detection of long-lasting memory foot-and-mouth disease (FMD) virus serotype O-specific CD4+ T cells from FMD-vaccinated cattle by bovine major histocompatibility complex class II tetramer. Immunology, 10.1111/imm.13367. Advance online publication. **https://doi.org/10.1111/imm.13367**

18 Waters, R. A., Wadsworth, J., Mioulet, V., Shaw, A. E., Knowles, N. J., Abdollahi, D., Hassanzadeh, R., Sumption, K., King, D. P. (2021). Foot-and-mouth disease virus infection in the domestic dog (Canis lupus familiaris), Iran. BMC Veterinary Research, 17(1), 63. **https://doi.org/10.1186/s12917-021-02769-1**

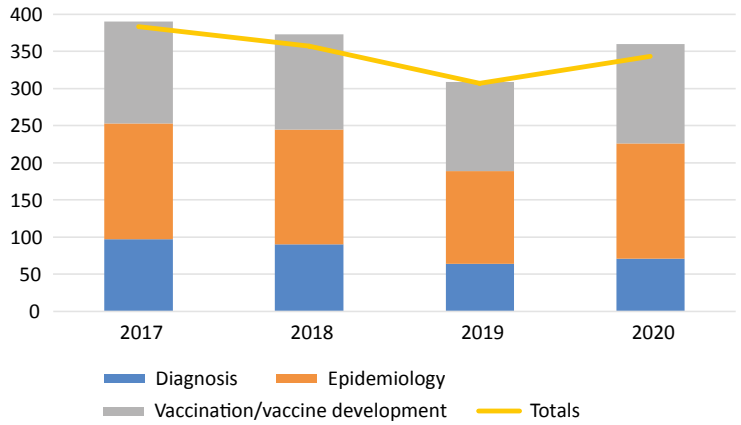
19 Yang, M., Mudabuka, B., Dueck, C., Xu, W., Masisi, K., Fana, E. M., Mpofu, C., Nfon, C. (2021). Development of two rapid lateral flow test strips for detection of foot-and-mouth disease virus SAT 1 and SAT 3. Journal of Virological Methods, 291, 113967. **https://doi.org/10.1016/j.jviromet.2020.113967**

The selection of naturally stable candidate foot-and-mouth disease virus vaccine strains for East Africa.[20]

Naturally stable East African FMDV strains for each of the A, O, SAT1 and SAT2 serotypes were identified to produce an improved multivalent FMD vaccine. Furthermore, they investigated their potential for protecting ruminants against strains that have recently circulated in East Africa. They found a high diversity in stability between and within serotypes. In this study, in comparison to non-African A serotype viruses reported to date, the East African strains resulted less stable. In a second step, candidate vaccine strains were adapted to propagation in BHK-21 cells with minimal capsid changes and used to generate vaccinate sera that effectively neutralised a panel of FMDV strains selected. Thus, for the development of FMD vaccines, tools to predict and assess FMDV vaccine stability were combined with cell culture adaptation and serological tests.

Trends in published research

Total records & Main topics



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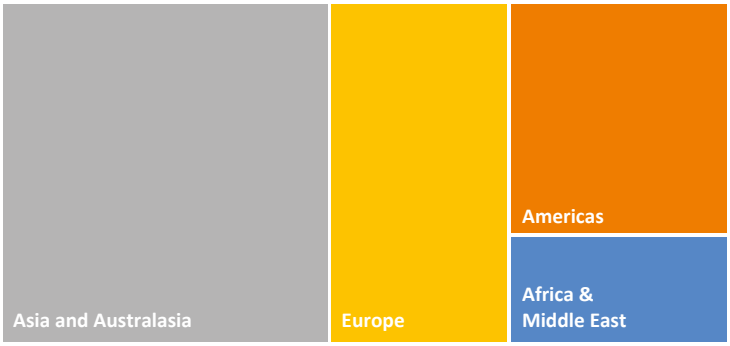


20 Jackson, B., Harvey, Y., Perez-Martin, E., Wilsden, G., Juleff, N., Charleston, B., Seago, J. (2021). The selection of naturally stable candidate foot-and-mouth disease virus vaccine strains for East Africa. Vaccine, 39(35), 5015–5024. **https://doi.org/10.1016/j.vaccine.2021.07.001**

Ongoing research

Non-exhaustive list of ongoing projects on FMD funded by STAR-IDAZ IRC and STAR-IDAZ Network Members reported in 2021:

Research Area	Country/ Organisation	Research Projects
Vaccine development	Argentina (IRTA)	• Development of rationally designed vaccine based on non-replicative FMDV - PICT 2016-1327 • Evolutionary studies of FMDV strains showing diverse pathogenicity in the mouse model - PICT 2017-2581 • Designing RNA vaccine • Characterization of the profile of the immune response in cattle, pigs and buffaloes, in response to vaccination and infection (only cattle) • Development of an in vitro method to assess vaccine purity (in terms of absence of non-structural proteins) in formulated vaccines, a new ELISA to evaluate antibody levels related to protection and to quality of the immune response, a method to quantify antigen payload in formulated vaccines
	Belgium	• RI 20/81 FMDV_PerIstOmics - From proteogenomic host response signatures of persistent foot-and-mouth disease virus (FMDV) infection to diagnostic markers and therapeutic control - ICRAD
	France	• FMDV_PersIstOmics - From proteogenomic host response signatures of persistent foot-and-mouth disease virus (FMDV) infection to diagnostic markers and therapeutic control - ICRAD
	Italy	• Identification of useful criteria for the arrangement of possibilities in case of emergency vaccination against foot-and-mouth disease and evaluation of costs of the different control strategies - IZS LER 4/19
	Nigeria (NVRI)	• Development of mouth improved foot-and-mouth disease (FMD) virus vaccine in Nigeria using indigenous isolates • Use of Different adjuvants to improve the potency of in-activated FMD vaccine in Nigeria e.g montanide ISA-206,201,50 and gel
	Spain	• Development and optimization of new vaccines and antiviral strategies. The foot-and-mouth disease virus as a model - Universitat Pompeu y Fabra- AGL2017-84097-C2-1-R • Mono and multivalent peptidic vaccine constructions against FMD virus: optimized production and studies of structure, stability and biodistribution - Spanish National Research Council (CSIC) - AGL2017-84097-C2-2-R
	UK (DEFRA)	• SE1130: To identify and isolate FMDV epitopes sequence • TPI is involved in defining correlates of vaccine protection through some externally funded research activities

Research Area	Country/ Organisation	Research Projects
Diagnostics	Argentina (IRTA)	• Development of a novel ELISA test that were transferred to CSRIO, The Pirbright Institute, FLI, South Africa
	European Commission (EC)	• FMDV_PersIstOmics - From proteogenomic host response signatures of persistent foot-and-mouth disease virus (FMDV) infection to diagnostic markers and therapeutic control - ERANET ICRAD co-funded call
	France	• PREPMedVet: Preparedness and Response in an Emergency context to Pathogens of MEDical and VETerinary importance - ANR
	Italy	• New diagnostic methods for genomic detection (CRISPR-Cas) and antigenic detection (LFD multiplex) - IZS LER 2/20 • Spreading analysis and characterization of apoptosis virus in central eastern Africa in global control strategies of the disease - IZS LER 13/19 • New, universal ELISA test for demonstration of antibodies for surveillance of foot-and-mouth disease - IZS LER 11/19
	Nigeria (NVRI)	• Continuous isolation and molecular characterization of current circulating serotypes • Development of NSP and SP diagnostic kit (in-house ELISA)
	UK (DEFRA)	• SE1130. Develop new lineage-specific rRT-PCRs and Implement simple tool to monitor sequence mismatches in lineage-specific rRT-PCRs - Comparative performance of Ag-LFDs for FMDV detection and typing and performance of RT-LAMP for FMDV detection - Compare antibody binding to intact and degraded viral capsids and prepare recombinant viral capsid for use as antigens on the Luminex system • SE2722: environmental sampling for detection of FMDV - assessing use of pen side PCR and LAMP for detection of FMDV in environmental samples; SE2722: generation of sequence data from environmental samples collected on farms and at livestock markets • SE2944 - Testing of Oxford NanoPore sequencer for FMDV and report of capabilities
Control strategies	France	• PREPMedVet: Preparedness and Response in an Emergency context to Pathogens of MEDical and VETerinary importance -ANR
	UK (DEFRA)	• SE2944: Characterise molecular clock rates for FMDV; results which underpins the further development of analytic tools to assess viral prevalence from sequence data • SE2722: assessing use of environmental surveillance to detect circulation and transmission of FMDV on affected farms and at livestock markets - collection of data on on-farm aerosols; development of methods to measure virus survival in aerosols; incorporation of these data in a predictive model of airborne transmission between farms

5. Helminths

Global network: Livestock Helminth Research Alliance (LiHRA)

Website: http://www.lihra.eu/

Partners ca.
24

Budget
NA

Start date:
2014

Overview

The Livestock Helminth Research Alliance (LiHRA) was founded in December 2014, comprising of international partners with a recognised expertise in different disciplines applied to livestock helminth research. LiHRA unites diverse areas of expertise in the field of helminth infections of livestock and aims to be a leading research alliance in the field of livestock helminth infections with a mission to develop sustainable control strategies and promote their implementation by the livestock industry.

LiHRA has 24 member organisations from 14 European countries and 6 associated organisations from New Zealand, Argentina, USA, Mexico and Canada.

Aim and priorities

Aim: to speed up the pace of development and innovation in livestock helminth research

Objectives

- Stimulate collaborative research by enabling exchange of ideas and mobility of young researchers;
- Initiate and coordinate research initiatives at the international and national level;
- Facilitate knowledge exchange with the livestock industry and other stakeholders to respond to their needs;
- Respond to global changes that impact on livestock, farming practices and helminth infections and identify areas for future research;
- Foster technology exchange and standardisation of diagnostic procedures, clinical trial and monitoring approaches throughout Europe.

News

The next meeting will take place online in November 2021. In these meetings, members present overviews of their current research areas and discuss pathways for collaboration or new ideas to be explored. Moreover, LiHRA coordinates responses to international grant calls.

Together with the COST Action **COMBAR**, LiHRA coordinated the development of the STAR-IDAZ helminth research roadmaps and produced a **summary document** highlighting the key research needs for control of helminth infectious diseases in ruminants.

DISCONTOOLS research needs

R&D needs for nematodes:

- Development and implementation of **holistic control strategies** using improved diagnostics, host genetics, nutrition and pasture management to reduce the reliance upon anthelmintics and the threat of anthelmintic resistance.
- Easy-to-use **diagnostics** to identify those animals requiring treatment and tests for early detection of anthelmintic resistance.
- **Anthelmintics with new mode of action** than currently available.
- Development of **complementary control measures**: vaccines, bio-active forages, nutraceuticals.

R&D needs for liver fluke:

- More information about how the predicted effects of **climate and environmental change** are influencing the survival and development of the environmental stages of the parasite.
- An understanding of the **immune responses** to fluke (innate and adaptive; protective and suppressive) in naturally exposed ruminants.
- **Genome mapping** to aid in identification of drug resistant isolates, improving our understanding of drug resistance to different flukicides; develop tools for diagnosis; and differentiating between species and identifying hybrid species.
- Pen-side tests, herd level tests to identify heavily infected beef herds, tests for diagnosis for acute infection or pre-patent infections.
- **Drugs** that are effective against the young immature stages of the parasite.
- **Vaccines** targeting all stages and suitable for any host species.
- Good control programmes no longer reliant on the exclusive use of anthelmintic prophylaxis to address the problems with drug resistance.

R&D needs for *Taenia solium* cysticercosis:

- Better knowledge of the **distribution of infection** and delineation of areas of high prevalence, particularly of neurocysticercosis.
- Further information on the effectiveness and cost-benefit of (alternative) control/elimination strategies of the infection in humans and pigs in different epidemiological settings.
- Studies on *T. solium* **egg survival**.
- Availability of **simple tests** to detect *T. solium* infections in humans, of pen-side diagnostic tests for individual pigs and for detection of infected carcasses in the abattoir.
- A serological test which is able to **detect living cysts** in the brain.
- A **serum bank** with well documented serum and cerebrospinal fluid samples to study sensitivity, specificity, reproducibility of serological tests.

R&D needs for *Echinococcus*:

- Harmonised **reporting systems** for alveolar echinococcosis (AE) and cystic echinococcosis (CE) in humans and animals.
- Standardization of validated **molecular tools** for the detection of *Echinococcus* spp. eggs for assessing the degree of contamination of matrices, water and food.
- Well-designed, integrated, long lasting **CE control programmes** based on deworming of dogs, vaccination of lambs and culling of old intermediate hosts.
- Improved specific and sensitive **fast tests** for the diagnosis and monitoring of control programmes of CE in livestock and intestinal infections in dogs.
- European manufacture and registration of the **EG95 vaccine** for livestock and political will and funding to undertake control programmes.

Recent developments

Phage display-based vaccine with cathepsin L and excretory-secretory products mimotopes of *Fasciola hepatica* induces protective cellular and humoral immune responses in sheep.[21]

In this study, the authors report the use of Excretory/secretory (E/S) products and cathepsin L mimotopes from *Fasciola hepatica* to immunise experimentally infected sheep against liver flukes. The resulted level of protection was measured by fluke burden, morphometric measurements, faecal egg counts, observing the humoral and cellular immune responses elicited. After challenge test, vaccinated sheep had a reduced mean fluke burdens compared to controls by 52.39% and 67.17%, respectively for vaccinated group with E/S products and cathepsin L1 (SGTFLFS); no effect was observed in animals inoculated with cathepsin L1 (WHVPRTWWVLPP). Sheep immunised with phage-displayed mimotopes induced mixed Th1/Th2 immune response and the epitope SGTFLFS from cathepsin L1 proved to be highly immunogenic.

In vitro anthelmintic evaluation of three alkaloids against gastrointestinal nematodes of goats.[22]

In this study, the authors assessed the *in vitro* anthelmintic activity of the alkaloids berberine, harmaline and piperine on gastrointestinal nematodes (GIN) of goat and their possible cytotoxic effects in Vero cells. The three alkaloids inhibited the egg hatch of GIN eggs. Piperine was the most active compound against goat GIN eggs with an EC50 (effective concentration 50%) of 0.0074 mM (0.0021 mg/mL), while the EC50 of berberine was 1.32 mM (0.49 mg/mL) showing a ovicidal action of 90%, while Harmaline (EC50 = 1.6 mM - 0.34 mg/mL) showed moderate ovicidal action (80.30%). In the larval motility assay, piperine and harmaline reduced larval motility in 2.75 and 25.29%, respectively, while larvicidal efficacy was evidenced only with the alkaloid berberine, which showed a percentage of inhibition of larval motility of 98.17% (2.69 mM =1.0 mg/mL). Furthermore, having all alkaloids showed low toxicity to Vero cells, the results suggest that berberine and piperine have anthelmintic potential on goat gastrointestinal nematodes with low toxicity to mammalian cells.

21 Villa-Mancera, A., Olivares-Pérez, J., Olmedo-Juárez, A., Reynoso-Palomar, A. (2021). Phage display-based vaccine with cathepsin L and excretory-secretory products mimotopes of Fasciola hepatica induces protective cellular and humoral immune responses in sheep. Veterinary Parasitology, 289, 109340. **https://doi.org/10.1016/j.vetpar.2020.109340**

22 da Silva, G. D., de Lima, H. G., de Sousa, N. B., de Jesus Genipapeiro, I. L., Uzêda, R. S., Branco, A., Costa, S. L., Batatinha, M., Botura, M. B. (2021). In vitro anthelmintic evaluation of three alkaloids against gastrointestinal nematodes of goats. Veterinary Parasitology, 296, 109505. **https://doi.org/10.1016/j.vetpar.2021.109505**.

Comparison of genetic parameters and estimated breeding values for worm resistance in meat sheep obtained using traditional and genomic models.[23]

Estimates of genetic parameters and breeding values for traits that indicate the resistance to gastrointestinal nematode infection in Santa Inês sheep, using the pedigree-based BLUP or including genomic information were compared. The host resistance was assessed using fecal nematode egg counts (FEC), FAMACHA score (FAMACHA) and resistance to gastrointestinal nematode infection (RGNI) by a combination of FEC, FAMACHA, body condition score, and hematocrit. Single- and multi-trait analyses were used to estimate genetic and breeding values. Multi-trait analyses provided higher estimates of predictive ability than those obtained using single-trait models. The heritability estimates showed that all traits evaluated are suitable for genomic selection. Even if low accuracies were obtained, the use of the genomic model provided more accurate estimates of breeding values in comparison to the pedigree-based model.

Haemonchus contortus hepatocellular carcinoma-associated antigen 59 with poly (lactic-co-glycolic acid): a promising nanovaccine candidate against *Haemonchus contortus* infection. [24]

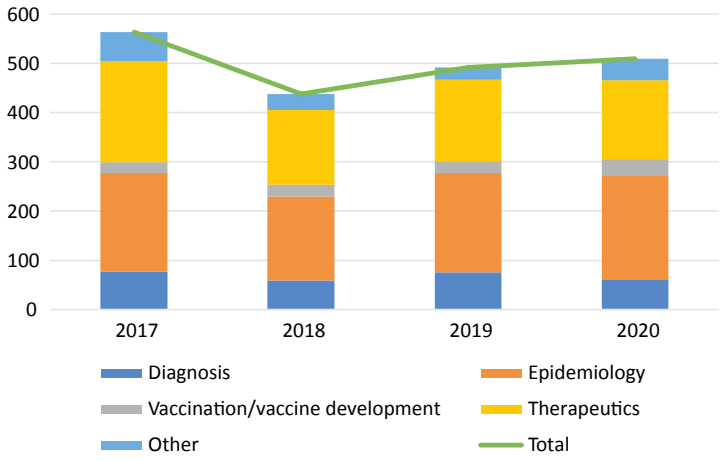
In this study, the challenge test over 15 goats for a nonovaccine candidate against *H. contortus* infection is described. The vaccine was developed merging the *H. contortus* recombinant Hepatocellular carcinoma-associated antigen 59 (HCA59) with the poly (lactic-co-glycolic acid) (PLGA) nanoparticle adjuvant. Following immunization, high level of sera IgG, IgA, and IgE, as well as significantly high production of IL-4 and IL-9 was produced in the vaccinated rHCA59 group. After challenge with *H. contortus* third stage larvae (L3), the level of IL-17 and TGF-β in rHCA59 group increased. Meanwhile, the fecal eggs and the abomasal worm burdens in rHCA59 group was reduced by 44.1% and 54.6%, respectively. The results showed that rHCA59-PLGA nanoparticles conferred partial protection and thus could be a good candidate for the development of nanovaccines against *H. contortus* infection in goats.

23 Dos Santos, G. V., Santos, N., Figueiredo Filho, L., Britto, F. B., Sena, L. S., Torres, T. S., Carneiro, P., Sarmento, J. (2021). Comparison of genetic parameters and estimated breeding values for worm resistance in meat sheep obtained using traditional and genomic models. Tropical Animal Health and Production, 53(2), 283. **https://doi.org/10.1007/s11250-021-02705-3**

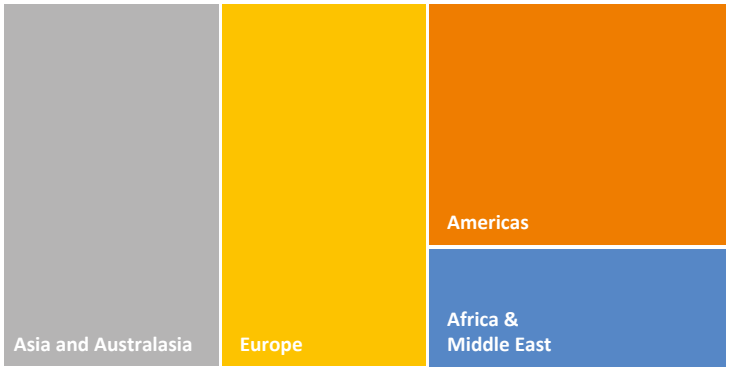
24 Wang, Q., Muhammad, T. A., Muhammad, W. H., Muhammad, A. M., Muhammad, H., Yan, R., Xu, L., Song, X., Li, X. (2021). Haemonchus contortus hepatocellular carcinoma-associated antigen 59 with poly (lactic-co-glycolic acid): A promising nanovaccine candidate against Haemonchus contortus infection. Veterinary Parasitology, 292, 109398. **https://doi.org/10.1016/j.vetpar.2021.109398**

Trends in published research

Total records &
Main topics



Country/ Region of
first Author (2017/2020)



Ongoing research

Country / Organisation	Project Title
Argentina (ANPCyT)	• ANPCYT-PICT-2017- 4148 - Transcriptomics and genomics applied to the study of drug-resistance in *Fasciola hepatica*
Austria (but colleagues from Italy and Germany are involved in the research)	• Anthelmintic resistance in small ruminants in Austria
Belgium (FWO)	• Role of glycosylation in the immunogenicity of the nematode specific activation-associated secreted proteins (ASPs) and its implication in vaccine efficacy
Czech Republic (Ministry of Education, Youth and Sports)	• LTC19018 - Pilot strategic plan of combating against the resistant strains of parasitic worms in the populations of Czech farm ruminants
Czech Republic and USA (Ministry of Education, Youth and Sports, Czech Republic)	• LTAUSA19 - Novel strategies for designing antiparasitic molecules as human and veterinary drugs
Denmark, Netherlands (Danish Council for Independent Research)	• Parasites and Plants - Parasites and Plants: Exploring the mechanistic activity of a bioactive livestock forage

Country / Organisation	Project Title
European Commission - UK, Ireland, Belgium, Spain, Norway, Germany (Horizon 2020)	• PARAGONE: vaccines for animal parasites
European Commission (COST Association - Horizon 2020)	• COMBAR - Combatting anthelmintic resistance in ruminants
	• Plants4Nemavax - Plant-based production of glyco-engineered nematode vaccines
Finland (Academy Of Finland, decision 310549)	• LipidET - Ellagitannin-lipid interactions – Molecular aspects, mechanisms and antimicrobial effects
Foundation for Science and Technology (FCT)	• MERINOparasite - Identification of genetic markers underlying genetic resistance to internal parasites in the Merina Branca sheep breed using the OvineHD Beadchip array
France - public-private partnership (CEVA)	• UREV - Rational use of eprinomectin in dairy cows : development of a targeted-selective treatment strategy (decision tree) against GIN in adult dairy cows
France (CASDAR)	• FASTOChe - Grazing of forage species rich in bioactive secondary metabolites in small ruminants: health, zootechnical, economic, environmental, and social interests
France and Switzerland (FRENCH ANNEX of the FIBL) (Région Auvergne Rhône-Alpes)	• ParCapAURA - Control of parasitism by Gastrointestinal Nematodes in goat farming to develop grazing systems in the Auvergne Rhône-Alpes region
Germany (Federal Office for Consumer Protection and Food Safety)	• TRFH - Triclabendazole resistance of *Fasciola hepatica* in German sheep flocks
Greece, Albania (EC - INTERREG IPA II)	• COMPLETE- Competitive livestock entrepreneurship and health protection for sustainable rural economic development
Ireland (University College Dublin)	• Flukeomics - Transcriptomic analysis of the ruminant immune response to liver fluke infection
Ireland, New Zealand (Teagasc Walsh Fellowship)	• Drug resistance and susceptibility in sheep nematodes; fitness and the role of anthelmintic combinations in resistance management
Italy (MINSAL)	• Control of the endoparasites and of the immune, inflammatory and microbiome intestinal status in equine - IZS LT 8/20 • Bovine gastrointestinal strongylosis: evaluation of anthelmintic resistance in livestock in Campania region. IZS ME 9/20 • Innovative diagnostic pathways and new monitoring /control protocols for endoparasitosis in livestock animals and for correlated drug resistances - IZS LT 10/19 • Surveillance on Lake fish species and related parasites in the lakes of Tuscany and Lazio regions - IZS LT 12/20
Italy, Argentina (CONICET-CUIA)	• COMB-ANT - New strategies for the diagnosis and sustainable control of parasites in cattle: evaluation of a combination of anthelmintics
Italy, Greece, Switzerland, France, Algeria, Tunisia, Australia (PRIMA)	• ECHINO SAFE-MED - New sustainable tools and innovative actions to control cystic ECHINOcoccosis in sheep farms in the MEDiterranean area: improvement of diagnosis and SAFEty in response to climatic changes
Norway, Denmark, Scotland (The Research Council of Norway, BIONÆR)	• BarkCure - Condensed tannins from Norwegian pine and spruce bark - antiparasitic effects and potential commercial exploitation
Poland (Polish National Research Center	• Multivariable biostatistical model based on in vitro methods for prediction of anthelmintic resistance in goats
Slovakia (VEGA national agency)	• COPRODIA - Diagnostic challenges and forgotten parasites of domestic animals

Country / Organisation	Project Title
Spain	• PID2019-108782RB-C22: *Fasciola hepatica*: only a coordinated in line attack could beat the master of evasion - Spanish National Research Council (CSIC) • PID2019-105713GB-I00: Extracellular vesicles in the control of fascioliasis in livestock - University of Valencia. • RTI 2018-093463-J-100: Your resources are my resources: parasite migration and the fibrinolytic system of the host in fasciolosis- Spanish National Research Council (CSIC) • PID2020-114466RR-I00: Water restriction, and gastrointestinal parasite infection in meat sheep: biomarkers associated to stress tolerance and modulation through sainfoin inclusion - Centro de Investigación y Tecnología Agroalimentaria de Aragón (CITA) • RTA2017-00010-C02-00: Immunological, genetic and molecular approaches for the control of fasciolosis in ruminants - Instituto Galego do Calidade Alimentaria (INGACAL)/ Universidad de Santiago de Compostela • PID2020-119035RB-I00: New tools for drug discovery and detection of anthelmintic resistance against gastrointestinal nematodosis in small ruminants - University of León
Spain (MINECO)	• TRICOSCREENING - Control of ovine gastrointestinal nematode infections: design, synthesis and clinical efficacy of new molecules with anthelmintic effect. subproject 1: evaluation of the anthelmintic activity of new molecules by in vitro and in vivo assays against nematodes
Spain- Greece (Junta de Andalucía-Fondos Feder)	• REGINPRUM - Resistance to anthelmintics of gastrointestinal nematodes in small ruminants: alternative control strategies
Sweden (Stiftelsen lantbruksforskning / Swedish Foundation for Agricultural Research)	• Improved diagnosis and targeted treatment of parasitic roundworms in laying hens
Sweden (Stiftelsen lantbruksforskning/ Swedish Farmers Foundation for Agricultural Research)	• Molecular tools for detection of gastrointestinal parasites and anthelmintic resistance in sheep
Switzerland	• Assessment of FAMACHA in sheep
UK (DEFRA)	• Project VM0544 To develop and refine molecular tools for detection of anthelmintic resistance (initially focusing on benzimidazole resistance in *Nematodirus battus* of sheep) and to identify routes of transmission of anthelmintic resistance - Moredun Research Institute • Project VM0543 To undertake research to inform, update and enhance uptake of the UK industry guidelines for prescribers and farmers regarding sustainable use of anthelmintics in sheep and cattle - Queen's University Belfast
USA (NIAID)	• Wormscreen - Screening *C. elegans* mutant strains for new clues about ivermectin and its mode of action

6. Porcine reproductive and respiratory syndrome (PRRS)

Global network

Under the STAR-IDAZ project, an expert group was formed on porcine reproductive and respiratory syndrome (PRRS) and, in 2013, this group conducted the first research gap analysis. No formal Working Group (WG) has since been established. SIRCAH drafted a research roadmap for PRRS vaccines and organised a meeting with the above-mentioned experts alongside of the 2018 Conference of Research Workers in Animal Disease (CRWAD) to validate it. The experts validated the **roadmap**, that was published on the STAR-IDAZ IRC website. SIRCAH will start working on the development of roadmaps for diagnostic development and control strategies for PRRS, that will need then to be submitted to the WG for validation.

DISCONTOOLS research needs

R&D needs for PRRS:

- **Whole genome analysis** to obtain correct genetic trees as a basis for epidemiological studies (evolution) and to identify the parts of the genome that are linked to the ability to spread, pathogenicity, virulence, immune evasion and immunogenicity.
- **Continuous validation of diagnostics** with the appearance of new PRRS virus isolates. It is important to monitor the genetic sequences of new viruses to ensure that they are detected in the existing PCR/ELISAs. To achieve this, a pan-European PRRS database should be created that would allow simultaneous comparison of PRRS isolates representing most countries in Europe.
- **New generation vaccines** that provide universal protection and that allow differentiating vaccinated animals from infected ones (DIVA). To achieve this, new approaches to vaccine production should be considered, such as multivalent vaccines or subunit vaccines.

Recent developments

Gut microbiome associations with outcome following co-infection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2) in pigs immunized with a PRRS modified live virus vaccine.[25]

In this study, the authors identified gut microbiomes associated with improved outcomes in vaccinated pigs with PRRS modified live virus (MLV) and co-challenged with PRRSV and porcine circovirus type 2 (PCV2b). It provides evidence towards the gut microbiome playing a role in PRRS vaccine efficacy. Results showed high growth outcomes associated with several gut microbiome characteristics, such as increased bacterial diversity, increased *Bacteroides pectinophilus*, decreased *Mycoplasmataceae* species diversity, higher Firmicutes: Bacteroidetes ratios, increased relative abundance of the phylum Spirochaetes, reduced relative abundance of the family *Lachnospiraceae*, and increased *Lachnospiraceae* species C6A11 and P6B14.

25 Constance, L. A., Thissen, J. B., Jaing, C. J., McLoughlin, K. S., Rowland, R., Serão, N., Cino-Ozuna, A. G., Niederwerder, M. C. (2021). Gut microbiome associations with outcome following co-infection with porcine reproductive and respiratory syndrome virus (PRRSV) and porcine circovirus type 2 (PCV2) in pigs immunized with a PRRS modified live virus vaccine. Veterinary Microbiology, 254, 109018. **https://doi.org/10.1016/j.vetmic.2021.109018**

Mitigation of Airborne PRRSV Transmission with UV Light Treatment: Proof-of-Concept.[26]

In this article, the authors report the test of effectiveness of ultraviolet (UV) in inactivating aerosolized PRRSV, specifically, four UV lamps, UV-A (365 nm, both fluorescent and LED-based), "excimer" UV-C (222 nm), and germicidal UV-C (254 nm) were studied. Results show that, while UV-A lamps could not reduce PRRSV titers for tested doses, the two UV-C lamps effectively irradiated fast-moving PRRSV aerosols with short treatment times (<2 s). Models were utilized to estimate the UV doses needed for target percentage (%) reductions on PRRSV titer. Further research is needed to scale up the concepts under conditions that mimic a swine facility more closely, where ultraviolet lamps could be installed near ventilation intakes to make sure air that enters the area doesn't carry aerosolized virus.

Comparison of ZMAC and MARC-145 cell lines for improving porcine reproductive and respiratory syndrome virus isolation from clinical samples.[27]

Virus isolation of PRRS from over 375 clinical samples was compared using the commonly utilised MARC-145 cell line with the ZMAC cell line derived from porcine alveolar macrophages. ZMAC cells were found to allow better isolation of a wide range of PRRSV field strains; moreover, not all of the ZMAC-obtained PRRSV isolates grew in MARC-145 cells.

A broadly neutralizing monoclonal antibody induces broad protection against heterogeneous PRRSV strains in piglets.[28]

In this study, the monoclonal antibody mAb- PN9cx3 exhibited broad-spectrum recognition and neutralizing activities against PRRSV-1 and PRRSV-2 strains in vitro. In vivo experiments revealed that the administration of two 10-mg doses of mAb-PN9cx3 before and after the inoculation of piglets with heterologous PRRSV isolates resulted in significant reduction of the PRRSV-induced pulmonary pathological changes and virus loads in porcine alveolar macrophages (PAMs) compared with the results obtained with mAb-treated isotype controls. In conclusion, this novel immunologic approach involving the use of mAbs, particularly mAb- PN9cx3, that seems to confer cross-protection against serious illness resulting from infection with heterogeneous PRRSV-2 isolates, could be a powerful addition to the current PRRSV prevention and eradication tools.

Genetic characterization of a new NSP2-deletion porcine reproductive and respiratory syndrome virus in China.[29]

In this article, the authors report the complete genomic sequence of a new NSP2-deletion isolated in Hebei Province, northern China. The PRRSV-HB-16-China-2019 strain's full-length genomic sequence shares 93.0% nucleotide similarity to NADC30 PRRSV. It was a recombination event between the NADC30-like strains (lineage 1) and a vaccine strains named RespPRRS MLV (lineage 5). Compared with other NADC30-Like strains, PRRSV-HB-16-China-2019 has a discontinuous 75-amino acid (75-aa from position 476 to 552) deletion.

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26 Li, P., Koziel, J. A., Zimmerman, J. J., Zhang, J., Cheng, T.-Y., Yim-Im, W., Jenks, W.S., Lee, M., Chen, B., Hoff, S. J. (2021). Mitigation of Airborne PRRSV Transmission with UV Light Treatment: Proof-of-Concept. Agriculture, 11(3), 259. doi:10.3390/agriculture11030259

27 Yim-Im, W., Huang, H., Park, J., Wang, C., Calzada, G., Gauger, P., Harmon, K., Main, R., Zhang, J. (2021). Comparison of ZMAC and MARC-145 Cell Lines for Improving Porcine Reproductive and Respiratory Syndrome Virus Isolation from Clinical Samples. Journal of Clinical Microbiology, 59(3), e01757-20. **https://doi.org/10.1128/JCM.01757-20**

28 Zhang, Z., Zhai, T., Li, M., Zhang, K., Li, J., Zheng, X., Tian, C., Chen, R., Dong, J., Zhou, E. M., Nan, Y., Wu, C. (2021). A broadly neutralizing monoclonal antibody induces broad protection against heterogeneous PRRSV strains in piglets. Veterinary Research, 52(1), 45. **https://doi.org/10.1186/s13567-021-00914-0**

29 Xie, C. Z., Wang, Z., Ha, Z., Zhang, Y., Xie, Y. B., Zhang, H., Nan, F. L., Zhang, J. Y., Zhao, G. Y., Li, Z. X., Li, C. H., Yu, C. D., Zhang, P., Hui-junLu, Jin, N. Y. (2021). Genetic characterization of a new NSP2-deletion porcine reproductive and Respiratory Syndrome Virus in China. Microbial Pathogenesis, 150, 104729. **https://doi.org/10.1016/j.micpath.2021.104729**

Trends in published research

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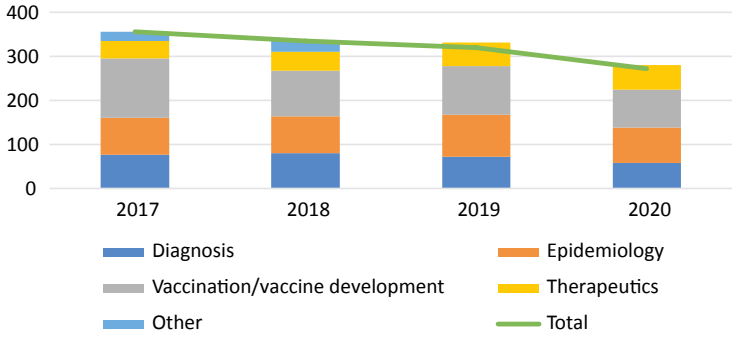

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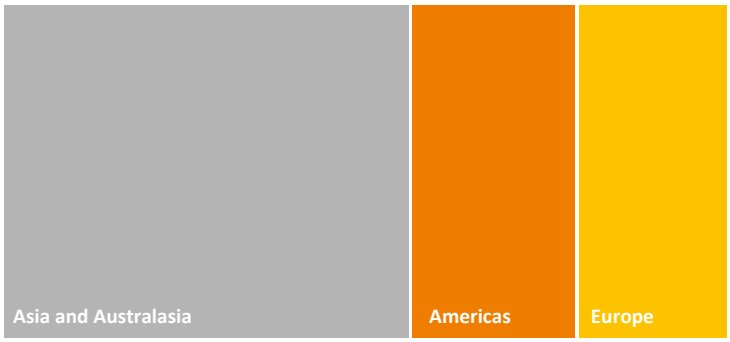

Ongoing research

Non-exhaustive list of ongoing projects on PRRS funded by STAR-IDAZ IRC and STAR-IDAZ Network Members reported in 2021:

Research Area	Country/ Organisation	Research Projects
Vaccines development	Belgium	• RF 19/6335 PigRResponSe - Unravelling the role of non-responding piglets and sows to vaccination against PRRSV
	France	• PRRS vaccine with macrophage tropism and interaction with maternally derived antibodies (VIP-unit) • Experimental evaluation of vaccination to control infection of pigs by Danish recombinant strain of PRRSV (VIP-unit)
	Italy	• Study on polymorphism of genes CD163 in order to control the PRRSV infection in pig farms (reproductive and respiratory syndrome of pigs) - IZS UM 2/20
	Spain	• PID2019-109718GB-I00: Evaluation of immune checkpoints during acute and chronic infection with porcine reproductive and respiratory syndrome virus - University of Córdoba
Diagnostics	Belgium	• TechPEPCon: New diagnostic platform (app on smartphone, new sampling swab, third generation sequencing) - ICRAD
	France	• Full genome sequencing and detection of genetic variation in PRRS genome (GVB-Unit)
	Italy	• Evaluation of the effect of genes polymorphism of the host on the resistance to PRRSV infection type I as alternative system in order to control the PRRS - IZS LER 14/18
Control strategies	France (ANSES)	• Experimental study of immunological and virological interactions between PRRSV and swine influenza viruses (VIP-unit)
	France	• Influenza/PRRSV coinfections in vitro/ex vivo - Establishment grant Région des pays de Loire, Immune Response in the context of Co-Infectious with Porcine Respiratory Pathogens • Using PRRSV RG systems, develop marker vaccines to differentiate infected and vaccinated animals (DIVA) • Study of aerial transmission of PRRS under experimental conditions (Episabe unit) • Epidemiological modeling of PRRS transmission (Episabe unit) • Link between pathogens, environment and level of organisation for epidemiological modelling • Optimising PRRS vaccination at farm level (VIP-Unit)
	Spain	• AGL2017-87073-R: Micro-epidemiology of precision of infection of the PRRS virus in epidemic farms- Universidad Autónoma de Barcelona

7. Coronaviruses

The coronaviruses (CoVs) of interest for the STAR-IDAZ IRC are infectious bronchitis virus (IBV), Middle East Respiratory Syndrome CoV (MERS-CoV), severe acute respiratory syndrome CoV 2 (SARS-CoV-2), and swine enteric CoVs, including porcine epidemic diarrhoea virus (PEDs), transmissible gastroenteritis virus (TGEv), and a new bat-HKU2-like porcine CoVs.

UK International Coronavirus Network

Website: https://www.liverpool.ac.uk/health-and-life-sciences/research/uk-international-coronavirus-network/

Partners ca.
24

Budget
£ 500,000

Start date:
2021

Overview

The network is an open and inclusive Global Coronavirus Research and Innovation Network. It will encourage new members throughout the life of this network. It is based on the same concept of existing global research alliances in the animal health area (such as the Global ASF Research Alliance – GARA, and the Global FMD Research Alliance – GFRA), with the main difference being they are self-funded while this network has funding provided by Defra and BBSRC.

Furthermore, it will align with existing networks, for example the Global Virus Network and the STAR-IDAZ IRC.

Aim and priorities

Aim: to establish and sustain global research and innovation partnerships to generate knowledge, tools and intervention strategies for control of animal and human coronaviruses.

Priorities: Animal and Human Coronavirus pathogen biology (including the seasonality, transmission, ecology and evolution of coronavirus), host response and effective intervention strategies.

Objectives

- Facilitate research collaborations and serve as a communication gateway for global human and animal coronaviruses research community;
- Conduct strategic research to better understand coronaviruses;
- Aim to develop the next generation of control measures and strategies for their application;
- Determine social and economic impacts of new generation improved intervention strategies;
- Provide evidence to inform development of socio-economic policies; and
- Integrate human, animal, and environmental health – in a One Health approach.

News

The network has been operational since September 2021 and will facilitate coordination of activities on Coronavirus with STAR-IDAZ, supporting in identifying research gaps and drafting research roadmaps on the topic.

DISCONTOOLS research needs

R&D needs for coronaviruses (CoVs) in pigs:

- Real time detection tool of various CoVs that is time sensitive and cost efficient.
- Readily available vaccine platforms based for example on virus/bacteria vector systems where genes of new strains can be inserted rapidly and which can be expanded rapidly if needed.
- Development of oral live vector vaccines that are not composed of whole live CoVs.

R&D needs for avian coronaviruses:

- Inactivated vaccines for IBV that are capable of inducing protective immune responses equal to that of current live attenuated IBV vaccines.
- What is the basis of cross-protection for IBV.
- Rationally designed live attenuated marker vaccines for IBV that induce broad range protection.
- Cost effective, reliable molecular tests for full S1 genotyping of IBV.
- IBV strain specific ELISAs.
- Knowledge on the host range of the different AvCoVs.
- Turkey CoV and guinea-fowl CoV specific ELISA tests are required to perform prevalence studies on these viruses.
- Koch's postulates need addressing for turkey CoV and guinea-fowl CoV.
- Relevance of IBV-like viruses in wild birds for poultry.

Recent developments

Killed whole-genome reduced-bacteria surface-expressed coronavirus fusion peptide vaccines protect against disease in a porcine model.[30]

In this article the authors report a synthetic biology-based vaccine platform that employs an expression vector with an inducible gram-negative autotransporter to express vaccine antigens on the surface of genome-reduced bacteria to enhance interaction of vaccine antigen with the immune system. A genome-reduced *Escherichia coli* was used to express SARS-CoV-2 and porcine epidemic diarrhea virus (PEDV) fusion peptide (FP) on the cell surface, a sequence highly conserved across coronaviruses. A PEDV challenge pig model was used to test the efficacy of PEDV FP and SARS-CoV-2 FP vaccines and both vaccines, even if not elicited sterilizing immunity, induced potent responses upon virus challenge: potentiated interferon-γ responses, reduced viral RNA loads in jejunum tissue, and provided significant protection against clinical disease. The coronavirus FP, as provided similar clinical protection to SARS-CoV-2 FP and PEDV FP, could be a target for a broadly protective vaccine using any platform. Furthermore, the genome-reduced bacterial surface-expressed vaccine platform, when using a vaccine-appropriate bacterial vector, can prove useful to produce readily scalable, inexpensive vaccines with easier storage and transport.

Multiple antigenic peptide-based flow through dot-blot assay for simultaneous antibody detection of infectious bronchitis virus and Newcastle disease virus. [31]

This study describes the development of a flow-through dot-blot assay (FT-DBA) using synthetic multiple antigenic peptides (MAP), namely, NP1 MAP (Nucleoprotein IBV) and HN MAP (Haemagglutinin-neuraminidase NDV), for simultaneous detection of antibodies to infectious bronchitis virus (IBV) and Newcastle disease virus (NDV). The kappa value indicates a substantial agreement between the FT-DBA test and the commercial ELISAs available. Thus, the FT-DBA test could be used for low cost, rapid and pen-side detection of IBV and NDV antibodies simultaneously.

Construction of porcine epidemic diarrhea virus-like particles and its immunogenicity in mice.[32]

In this study the authors report on the use of porcine epidemic diarrhea (PED) virus-like particles (VLPs), artificial nanoparticles similar to viruses that are devoid of genetic material and are unable to replicate, to induce immunity responses in mice. PED VLPs immunization induced Th2-dominant immune responses in mice and both IgG and IgA antibodies were produced. In addition, these antibodies protected against PED virus infection in Vero cells. The results indicate that PED VLPs induce strong immune responses in mice, suggesting that the VLP-based vaccine can be a promising vaccine candidate.

30 Maeda, D., Tian, D., Yu, H., Dar, N., Rajasekaran, V., Meng, S., Mahsoub, H. M., Sooryanarain, H., Wang, B., Heffron, C. L., Hassebroek, A., LeRoith, T., Meng, X. J., Zeichner, S. L. (2021). Killed whole-genome reduced-bacteria surface-expressed coronavirus fusion peptide vaccines protect against disease in a porcine model. Proceedings of the National Academy of Sciences of the United States of America, 118(18), e2025622118. **https://doi.org/10.1073/pnas.2025622118**

31 Tomar, P., Joshi, V. G., Mahajan, N. K., Jindal, N. (2021). Multiple antigenic peptide-based flow through dot-blot assay for simultaneous antibody detection of infectious bronchitis virus and Newcastle disease virus. Biologicals: Journal of the International Association of Biological Standardization, S1045-1056(21)00069-5. Advance online publication. **https://doi.org/10.1016/j.biologicals.2021.07.005**

32 Kim, J., Yoon, J., Park, J. E. (2021). Construction of Porcine Epidemic Diarrhea Virus-Like Particles and Its Immunogenicity in Mice. Vaccines, 9(4), 370. **https://doi.org/10.3390/vaccines9040370**

Application of chitosan as a natural disinfectant against porcine epidemic diarrhoea virus.[33]

The disinfectant effect and mammalian-cell toxicity of chitosan against PEDV was investigated using Vero cells. A 0.01% solution of chitosan was determined to be an effective disinfectant and no evidence of toxicity was observed during the cell toxicity test. Moreover, chitosan promoted cell proliferation. For these reasons, chitosan is a promising candidate for an effective and safe disinfectant against PEDV and other coronaviruses.

Update on the phylodynamics of SADS-CoV.[34]

In this study the authors performed an upgraded phylodynamic reconstruction of SADS-CoV (Swine Acute Diarrhea Syndrome Coronavirus), also known as PEAV (Porcine Enteric Alphacoronavirus) based on all whole genomes available on 21 June 2021. Results showed a very close relationship between SADS-CoV and HKU2-like CoV, although the direct progenitor of SADS-CoV is so far unknown. It is known that horseshoe bats are reservoirs for Rhinolophus bat coronavirus HKU2-like (HKU2-like CoVs) but the transmission path from bats to pigs is still unclear. A recombination hypothesis suggests that wild rats, which are frequent in farms, may have played a key role. The authors conclude that, due to the high recombination and cross-species capabilities of Coronavirus, SADS-CoV represents a possible high-risk pathogen for humans which needs a constant molecular monitoring.

Animal reservoirs and hosts for emerging alphacoronaviruses and betacoronaviruses.[35]

In this article the authors reviewed endemic and emerging infections of alphacoronaviruses and betacoronaviruses in wildlife, livestock and compani on animals. Furthermore, they provided information on the receptor use, known hosts, and clinical signs associated with each host for 15 coronaviruses detected in humans and animals. This information can be used to facilitate a One Health approach to improve strategies for preparedness, response and control to current and future coronavirus disease threats.

33 Kim, S. J., Nguyen, V. G., Kim, C. U., Park, B. K., Huynh, T. L., Shin, S., Jung, W. K., Park, Y. H., Chung, H. C. (2021). Application of chitosan as a natural disinfectant against porcine epidemic diarrhoea virus. Acta Veterinaria Hungarica, 10.1556/004.2021.00001. Advance online publication. **https://doi.org/10.1556/004.2021.00001**

34 Scarpa, F., Sanna, D., Azzena, I., Cossu, P., Giovanetti, M., Benvenuto, D., Coradduzza, E., Alexiev, I., Casu, M., Fiori, P. L., Ciccozzi, M. (2021). Update on the Phylodynamics of SADS-CoV. Life (Basel, Switzerland), 11(8), 820. **https://doi.org/10.3390/life11080820**

35 Ghai, R. R., Carpenter, A., Liew, A. Y., Martin, K. B., Herring, M. K., Gerber, S. I., Hall, A. J., Sleeman, J. M., VonDobschuetz, S., Behravesh, C. B. (2021). Animal Reservoirs and Hosts for Emerging Alphacoronaviruses and Betacoronaviruses. Emerging Infectious Diseases, 27(4), 1015–1022. **https://doi.org/10.3201/eid2704.203945**

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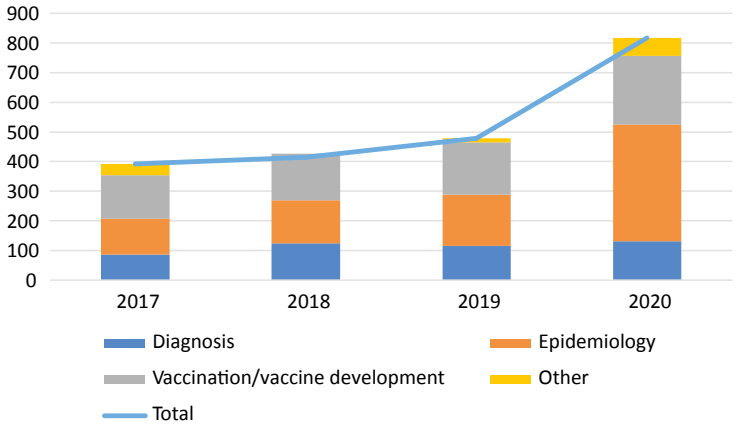

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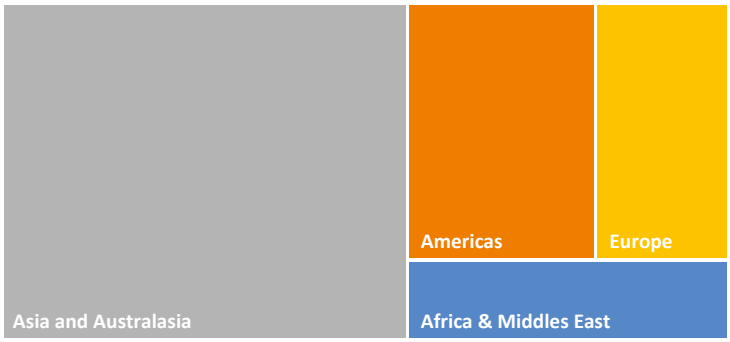


Ongoing research

Non-exhaustive list of ongoing projects on CoVs funded by STAR-IDAZ IRC and STAR-IDAZ Network Members:

Country/Organisation	Research projects
Argentina (INTA)	• Domestic and wildlife surveillance project for SARS-CoV-2 infection
France (ANSES)	• Bats as reservoir of orofecal pathogens with the main objective: epidemiological assessment of circulation of leptospirosis and virus (coronavirus and others) in bats • Development and validation of animal models (ferrets and hamsters) of SARS-CoV2 infection to test therapeutics and preventive molecules • In vivo assays in hACE2 transgenic mice of blocking peptides; Identification of antiviral molecules • Study of the role of cellular cyclophilins in coronavirus replication and in host restriction with two main objectives: understanding the mechanism in domestic animals and exploring it in wildlife

Country/Organisation	Research projects
Germany (FLI)	• Implementing SARS-CoV-2 animal infection studies
Hungary (NAK)	• Epidemiology and genetic changes of TGEV and PEDV coronavirus diseases. • Investigation of IBV genetics and development of pancoronavirus detection via NGS adaptation
Italy (MINSAL)	• Susceptibility of mammals to SARS-CoV-2: risks of reverse zoonosis and possibilities in translational medicine
Netherlands (Royal GD)	• IBV vaccine development projects (in collaboration with industry) • Pathogenesis testing of current and new IBV strains, *in-ovo*, in-vitro and *in-vivo* • Testing of live and inactivated IBV vaccines in vaccination/challenge experiments, against different serotypes, interference between vaccines
Spain (INIA)	• Characterise the new variants of PEDV in Spain and the immune response that they generate: investigate the hypothetical presence of other viruses associated to PEDV in outbreaks of diarrhoea and development of diagnostic and research techniques for the PEDV and other associated viruses
UK (BBSRC)	• Analysis of the function of infectious bronchitis virus accessory proteins • Determination of cross protection and genetic plasticity of IBV with the aim to control the virus • Development of rationally attenuated live vaccines for effective control of infectious bronchitis • Investigation on how passage in eggs results in attenuation, is this due to selection or random mutation with the aim to reduce the risk of vaccine reversion • MERS-CoV as a model system as a classical three species zoonotic event: examining how MERS-CoV affects gene and protein expression in human, camel and bat cells and to study the interaction of key MERS-CoV proteins in these species • Modification of the infectious bronchitis virus spike protein for growth in Vero cells; potential for vaccine growth and production in cell culture • Molecular characterisation of the avian coronavirus infectious bronchitis virus to identify regions of the genome involved in virulence • Strategically funded institute research into Porcine Deltacoronavirus (PDCoV): characterising virus induced replication organelles, understanding the process of viral envelopment and identifying cellular proteins that are important for virus replication
UK (Defra)	• Investigation of SARS-CoV-2 survival on surfaces and transmission risk (e.g., animal fur) • Molecular and sero-based test development for SARS-CoV-2

8. Vector-borne diseases (VBD)

Global network

No global network on vector-borne diseases has been formed yet. Due to the width of the topic, which involves several diseases affecting different animal species and humans (e.g. Rift Valley fever), it was decided to focus the activities of the STAR-IDAZ IRC Working Group (WG) on vectors (i.e. insects and ticks) including pathogen transmission by the vector, rather than on specific diseases. Working Group members have been identified through nominations by the STAR-IDAZ IRC Executive and Scientific Committees. SIRCAH collaborated with the STAR-IDAZ IRC Scientific Committee to draft a research roadmap for "Vector transmission and control" which is currently being reviewed by WG members.

In order to showcase recent developments on VBD research, foster closer collaboration, and to introduce the roadmap for vector transmission and control, STAR-IDAZ IRC participated in the UK Vector Borne Disease Conference, organised by the University of Liverpool, UK. The event was held as a series of webinars in November 2020, and STAR-IDAZ IRC co-organised the session on the 23rd of November. There, along with a few invited scientific presentations and a general introduction to the STAR-IDAZ IRC, a talk was dedicated to introducing and discussing the research roadmap for focusing the research effort on vector transmission and control. Once comments have been received from the WG on the roadmap and summaries a virtual workshop will be convened to discuss the roadmaps, and possibly form subgroups to focus on the main topics that are defined in this first meeting. The first meeting is expected to take place in 2022, tentatively March 2022.

DISCONTOOLS research needs

The database contains information about several VBD (i.e., **African horse sickness**, **African trypanosomiasis**, **bluetongue**, **Crimean-Congo haemorrhagic fever**, **Rift Valley fever**, **theileriosis**, **West Nile virus**). The research needs are summarized in the **DISCONTOOLS e-book**.

Recent developments

Quantifying and modeling the acquisition and retention of lumpy skin disease virus by hematophagus insects reveals clinically but not subclinically affected cattle are promoters of viral transmission and key targets for control of disease outbreaks.[36]

Four model vector species (Aedes aegypti, *Culex quinquefasciatus*, *Stomoxys calcitrans*, and *Culicoides nubeculosus*) were fed on lumpy skin disease virus (LSDV) inoculated cattle and their acquisition and retention of LSDV examined. Findings showed that insects feeding on subclinical animals were 97% less likely to acquire LSDV than those feeding on clinically infected animals. Insects were also unable to acquire the virus from cattle in the seven days prior to clinical signs developing. Furthermore, all vector species studied acquired LSDV at a similar rate, but *Aedes aegypti* and *Stomoxys calcitrans* retained the virus for a longer time, up to 8 days. The determined basic reproduction number of LSDV in cattle mediated by each of the model species was highest for *Stomoxys calcitrans* (19.1), followed by *C. nubeculosus* (7.1) and *Ae. aegypti* (2.4), suggesting that these three species can be considered potentially efficient transmitters of LSDV.

36 Sanz-Bernardo, B., Haga, I. R., Wijesiriwardana, N., Basu, S., Larner, W., Diaz, A. V., Langlands, Z., Denison, E., Stoner, J., White, M., Sanders, C., Hawes, P. C., Wilson, A. J., Atkinson, J., Batten, C., Alphey, L., Darpel, K. E., Gubbins, S., Beard, P. M. (2021). Quantifying and Modeling the Acquisition and Retention of Lumpy Skin Disease Virus by Hematophagus Insects Reveals Clinically but Not Subclinically Affected Cattle Are Promoters of Viral Transmission and Key Targets for Control of Disease Outbreaks. Journal of virology, 95(9), e02239-20. **https://doi.org/10.1128/JVI.02239-20**

Tick saliva-induced programmed death-1 and PD-ligand 1 and its related host immunosuppression.[37]

In a study of what happens to immune cells when they are exposed to tick saliva of *Rhipicephalus microplus* (Rm), it was found that Rm-saliva contained a high concentration of PGE2. This increases the upregulation mechanism of two cellular membrane protein: programmed cell death protein 1 (PD-1) in T cells and programmed death-ligand 1 (PD-L1) in CD14+ and CD11c+ cells in cattle. Furthermore PD-L1 blockade increased IFN-γ production. These findings suggest that PGE2 in Rm-saliva has the potential to induce the expression of immunoinhibitory molecules in host immune cells and this could play a role in the future development of tick alternative control strategies.

CRISPR/Cas-9 mediated knock-in by homology dependent repair in the West Nile virus vector *Culex quinquefasciatus*.[38]

In this article the authors describe the first successful germline gene knock-in by homology dependent repair in *Culex quinquefasciatus*, a mosquito distributed in both tropical and subtropical regions of the world, vector of many animal and human diseases including West Nile Virus and avian malaria. An sgRNA expression cassette and marker gene encoding a fluorescent protein fluorophore (Hr5/IE1-DsRed, Cq7SK-sgRNA) was integrated into the kynurenine 3-monooxygenase (kmo) gene by CRISPR/Cas9. This inserted gene produces red fluorescence proteins, thus that edited mosquitoes with one or more edited gene fluoresce red. Moreover, authors targeted an eye colour gene for the insertion site of the fluorescence gene so that mosquitoes that inherited two edited genes from their parents would have white eyes instead of black. Both these traits facilitate to recognize edited mosquitos. Furthermore, homozygotes mosquitoes that had white eyes (which had inherited two copies of the edited gene) did not survive after pupation. This study provides an efficient method for engineering *C. quinquefasciatus*, providing a new tool for developing genetic control tools for this insect.

37 Sajiki, Y., Konnai, S., Ikenaka, Y., Gulay, K., Kobayashi, A., Parizi, L. F., João, B. C., Watari, K., Fujisawa, S., Okagawa, T., Maekawa, N., Logullo, C., da Silva Vaz, I., Jr, Murata, S., Ohashi, K. (2021). Tick saliva-induced programmed death-1 and PD-ligand 1 and its related host immunosuppression. Scientific Reports, 11(1), 1063. **https://doi.org/10.1038/s41598-020-80251-y**

38 Purusothaman, D. K., Shackleford, L., Anderson, M., Harvey-Samuel, T., Alphey, L. (2021). CRISPR/Cas-9 mediated knock-in by homology dependent repair in the West Nile Virus vector *Culex quinquefasciatus* Say. Scientific Reports, 11(1), 14964. **https://doi.org/10.1038/s41598-021-94065-z**

The bluetongue disabled infectious single animal (DISA) vaccine platform based on deletion NS3/NS3a protein is safe and protective in cattle and enables DIVA.[39]

A bluetongue virus (BTV) Disabled Infectious Single Animal (DISA) vaccine platform, based on live-attenuated vaccines (LAVs) without nonessential NS3/NS3a expression which could be applicable for many serotypes by the exchange of outer shell proteins, was studied. The deletion of 72 amino acids (72aa) in NS3/NS3a was sufficient to block virus propagation in midges. Furthermore, the prototype DISA vaccine based on LAV with the 72aa deletion enables DIVA, is completely safe and induces a longlasting serotype-specific protection in cattle.

Trends in published research

Even if the scope of the STAR-IDAZ IRC WG on VBD has been defined, the topic is too broad to be covered by keywords that could provide feasible estimates of published research on the matter.

Ongoing research

Non-exhaustive list of ongoing projects on vector-borne diseases funded by STAR-IDAZ IRC and STAR-IDAZ Network Members:

Research Area	Country/ Organisation	Research projects
Vector-host interaction	Netherlands (WUR)	• One health Pact (**https://www.onehealthpact.org/**) Predicting arbovirus Climate Tipping points
	Sweden	• Preparedness against emerging mosquito-borne viral threats
	Israel (KVI)	• PALE-Blu: Understanding pathogen, livestock, environment interactions involving bluetongue virus (under Horizon2020)
	Argentina	• Studies for the control of subtropical and/or vector-borne diseases (anaplasmosis, babesiosis, soft ticks, myiasis, trypanosomiasis, bluetongue and rabies) i109
	European Commission	• TICKITS (**https://cordis.europa.eu/project/id/890970**) SFTS virus tick cell interactions in a vector system
	Defra, UK (DEFRA)	• Understanding parameters determining transmission of economically important arboviruses in the UK

39 van Rijn, P. A., Maris-Veldhuis, M. A., van Gennip, R. (2021). The Bluetongue Disabled Infectious Single Animal (DISA) Vaccine Platform Based on Deletion NS3/NS3a Protein Is Safe and Protective in Cattle and Enables DIVA. Viruses, 13(5), 857. **https://doi.org/10.3390/v13050857**

Research Area	Country/ Organisation	Research projects
Vector biology and transmission control	WUR, Netherlands (WUR)	• One health Pact (**https://www.onehealthpact.org/**) Predicting arbovirus Climate Tipping points: surveillance; host range and reservoirs
	ACDP, Australia (ACDP)	• Generating genetically modified mosquitoes with reduced vector competence against viruses or to reduce population • Using novel Wolbachia to reduce mosquito vector competence • Vector competence of Australian ticks for African swine fever virus • Developing novel strategies to reduce vector competence in mosquitoes and ticks
	Spain (CSIC)	• Sialoma and saliva microtranscriptoma of *Ornithodoros* sp., African swine fever vector tickets. Design and evaluation of anti-*Ornithodoros* multiantigenic vaccines.- RTI2018-098297-B-I00
	Israel (KVI)	• PALE-Blu: Understanding pathogen, livestock, environment interactions involving bluetongue virus (under Horizon2020)
	Italy (MINSAL)	• Study of the interaction of some flaviviruses in the mouse and avian model IZS AM 4/18 • Development of a sampling protocol for populations of *Anopheles* spp. and verification of their potential role as vectors of emerging pathogens IZS LER 12/18 • Study of the potential role of new species of Culicoides and other bloodsucking arthropods in the transmission of the bluetongue virus (BTV) IZS SA 4/18 • Study of the interspecific interactions of the larval stages of Culicidae to evaluate the role of microhabitat diversity and inter-species competence IZS SI 3/19 • Role of migratory birds in the introduction of new vectors and pathogens in Sardinia IZS SA 2/20
	Argentina	• Studies for the control of subtropical and/or vector-borne diseases (anaplasmosis, babesiosis, soft ticks, myiasis, trypanosomiasis, bluetongue and rabies). i109
	European Commission	• PALE-BLU (**https://cordis.europa.eu/project/id/727393**) : Understanding pathogen, livestock, environment interactions involving bluetongue virus • COMBAT (**https://cordis.europa.eu/project/id/101000467**): COntrolling and progressively Minimizing the Burden of Animal Trypanosomosis • INFRAVEC2 (**https://cordis.europa.eu/project/id/731060**): major European biosecure insectaries for experimental infection and containment of insect vectors under Containment Level 2 and 3 (CL2/ CL3) conditions
	UK (DEFRA)	• Building capacity for vector-borne diseases • Developing capability for tick-borne diseases and human health • Field sampling and testing for Usutu virus in 2021
	BMGF	• ClinGlobal: novel ectoparasiticides for Africa, novel methods to assess acaricide resistance, anti-tick vaccines and appropriate challenge models.

Research Area	Country/ Organisation	Research projects
Vector biotype and vector control in the environment	WUR, Netherlands (WUR)	• One health Pact (**https://www.onehealthpact.org/**) Predicting arbovirus Climate Tipping points: metagenomics arboviruses; arbovirus pathogenesis and vaccine development
	KVI, Israel (KVI)	• PALE-Blu: Understanding pathogen, livestock, environment interactions involving bluetongue virus (under Horizon2020)
	Italy (MINSAL)	• Artificial Intelligence and Remote Sensing: innovative methods for monitoring vectors and associated ecological / environmental variables. IZS AM 1/18
	Argentina	• Studies for the control of subtropical and/or vector-borne diseases (anaplasmosis, babesiosis, soft ticks, myiasis, trypanosomiasis, bluetongue and rabies) i109
	European Commission	• PREPARE4VBD (**https://cordis.europa.eu/project/id/101000365/fr**) A Cross-Disciplinary Alliance to Identify, PREdict and prePARe for Emerging Vector-Borne Diseases (Rift Valley fever, ehrlichiosis, theileriosis and fasciolosis)
	BMGF	• Oxitec: Feasibility of a Self-Limiting *R. microplus* for Sustainable Tick Control
Other	Netherlands (WUR)	• OneHealthPact: Modeling arbovirus emergence in relation to climate change
	Nigeria (NVRI)	• Molecular screening for Zika virus in mosquitoes in Jos, Nigeria • Molecular detection of trypanosomes in tsetse flies and cattle in Nigeria • Molecular screening of bluetongue virus in Nigeria • Screening *Leishmania* parasite in sandflies and in dogs • Screening for *Babesia* and theileriid parasite in ticks and in dogs using molecular techniques
	Australia (ACDP)	• Neurobiological and behavioral changes in mosquitoes after infection; Changes in fitness of vectors (mosquitoes and ticks) after infection; • Using AI/ML to identify mosquito phenotype.
	European Commission	• VECTRACK (**https://cordis.europa.eu/project/id/853758**): Earth observation service for preventive control of insect disease vectors • MOOD (**https://cordis.europa.eu/project/id/874850**): MOnitoring Outbreak events for Disease surveillance in a data science context • CANLEISH (**https://cordis.europa.eu/project/id/101007653**): Non-invasive volatiles test for canine leishmaniasis diagnosis
	UK (DEFRA)	• Advanced genetic analysis, molecular and serological diagnostics of bluetongue virus and related orbiviruses to protect UK livestock
	BMGF	• GALVmed: Novel therapeutic for animal African Trypanosomosis

9. Antimicrobial resistance – Alternatives to antibiotics

Global network

Antimicrobial resistance was identified as one of the priority issues by the STAR-IDAZ IRC, and it was decided a Working Group (WG) would be established to identify research gaps on this issue. Nevertheless, the topic is extremely broad and multifaceted, and many other initiatives are already existing in this area. In order to ensure progress and avoid duplications, it was decided that the STAR-IDAZ IRC WG should focus on the development of Alternatives to Antibiotics (ATA), where R&D was still a major need, and global coordination was lacking.

The STAR-IDAZ IRC WG was established in 2019 to identify research needs to support the development of alternatives to antibiotics and the reduction/rationalisation of the use of antimicrobials in livestock. This will ultimately help in the development of new non-antibiotic-based antimicrobial products and approaches for controlling infections and enhancing productivity, while maximising the life of existing and new therapeutics.

The first physical meeting of the WG was held in Bangkok, Thailand in December 2019, back-to-back with the 3rd International Symposium on ATA. Participants completed a questionnaire beforehand, which formed the basis of discussion at the workshop. The questionnaire covered the research needs on four main areas, i. alternatives to antibiotics acting directly on the pathogen, including establishing their mode of action (focusing on phages), ii. agents/compounds for their ability to enhance the hosts resistance to disease, including establishing their mode of action (focusing on immunomodulators), iii. mode of action of antibiotics as growth promoters and, iv. role of microbiome in the maintenance of health and how it might be manipulated. For each topic, experts were asked to identify the main research questions, research needs, possible solution routes, and dependencies.

Following the first workshop, the WG was divided into 4 subgroups focusing on: i) phages, ii) immunomodulators, iii) mode of action of antibiotics as growth promoters and iv) the microbiota. Some experts are involved in multiple subgroups. A gap analysis and research roadmap workshop was planned alongside the annual meeting of the European Federation of Animal Science (EAAP) in Porto, Portugal in September 2020. However, when this was postponed and rescheduled as a virtual meeting, the STAR-IDAZ IRC decided to advance the work of the WG independently. Thus, three webinars were held in early October 2020 to progress the gap analysis and develop the draft roadmaps on microbiota, immunomodulators, and phages. To validate the roadmaps and open the discussions on how antibiotic functions as growth promoters and how the marketability of ATA could be enhanced, STAR-IDAZ organized five webinars, that will take place during October/November 2021 in collaboration with the International Development Research Centre (**IDRC**):

- Alternatives to antibiotics acting directly on the pathogen, including establishing their mode of action (with a focus on **phage technologies**);
- Agents and compounds for their ability to enhance the hosts resistance to disease, including establishing their mode of action, with a focus on **immunomodulators**;
- The role of the **microbiome** in the maintenance of health, and how it can be manipulated;
- How **antibiotics work as growth promoters**;
- Taking new alternatives to antibiotics to market and the associated challenges.

DISCONTOOLS research needs

DISCONTOOLS does not cover antimicrobial resistance or alternatives to antibiotics as a separate topic, but disease specific information on effectiveness of control tools can be retrieved via targeted search in the database.

Recent developments

Oral delivery of *Bacillus subtilis* expressing chicken NK-2 peptide protects against *Eimeria acervulina* infection in broiler chickens.[40]

A stable strain of *Bacillus subtilis* carrying a chicken NK-lysin peptide 2 (cNK-2) to the gut was developed. A challenge test on eighty broiler chicks was performed to determine the effectivity of the oral delivery of this lytic peptide, with direct cytotoxicity against many apicomplexan parasites, in improving the control of coccidiosis when replacing the use of antibiotics in commercial broiler chicken production. The oral treatment with *B. subtilis*-cNK-2 improved growth performance, enhanced gut integrity, and reduced fecal oocyst shedding. Particularly it was able to reduce parasite survival and fecal oocyst shedding, to reduce coccidiosis-induced body weight loss, and to decrease gut damage based on the enhanced expression of proteins associated with gut integrity and intestinal health.

Overall assessment of antibiotic substitutes for pigs: a set of meta-analyses.[41]

A meta-analysis and network meta-analysis (NMA) was used to investigate the effects of feed additives as potential antibiotic substitutes (ASs) on bacteriostasis, growth performance, intestinal morphology and immunity. Among 16,309 identified studies, 37 were summarized to study the bacteriostasis effects of feed additives, and 89 were included in the meta-analysis and NMA (10,228 pigs). Comparing the results, authors suggest that antimicrobial peptides (AMPs) and plant extracts can be used as primary ASs for weaned piglets and growing pigs, respectively. While bacteriophages, zymin, plants, probiotics, oligosaccharides, lysozyme, and microelements can be considered as secondary ASs. Nucleotides and organic acids can be appraised as tertiary ASs. Further studies should assess the effects of combinational feed additives.

Antimicrobial peptides from black soldier fly (*Hermetia illucens*) as potential antimicrobial factors representing an alternative to antibiotics in livestock farming.[42]

In this review, the authors provide general information on currently verified functional antimicrobial peptides (AMPs) of *Hermetia illucens* known as black soldier fly insect (Diptera: Stratiomyidae). Furthermore, their potential medical value, the mechanism of their synthesis and interactions, and the development of bacterial resistance to AMPs in comparison with antibiotics are discussed.

40 Wickramasuriya, S. S., Park, I., Lee, Y., Kim, W. H., Przybyszewski, C., Gay, C. G., van Oosterwijk, J. G., & Lillehoj, H. S. (2021). Oral Delivery of Bacillus subtilis Expressing Chicken NK-2 Peptide Protects Against Eimeria acervulina Infection in Broiler Chickens. Frontiers in Veterinary Science, 8, 684818, **https://doi.org/10.3389/fvets.2021.684818**

41 Xu, B., Fu, J., Zhu, L., Li, Z., Jin, M., Wang, Y. (2021). Overall assessment of antibiotic substitutes for pigs: a set of meta-analyses. Journal of Animal Science and Biotechnology, 12(1), 3. **https://doi.org/10.1186/s40104-020-00534-2**

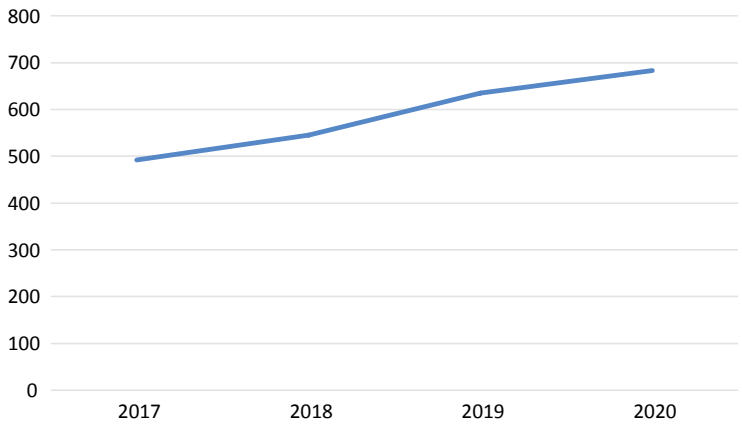
42 Xia, J., Ge, C., Yao, H. (2021). Antimicrobial Peptides from Black Soldier Fly (Hermetia illucens) as Potential Antimicrobial Factors Representing an Alternative to Antibiotics in Livestock Farming. Animals, 11(7), 1937. **https://doi.org/10.3390/ani11071937**.

Bacteriophage cocktail supplementation improves growth performance, gut microbiome and production traits in broiler chickens.[43]

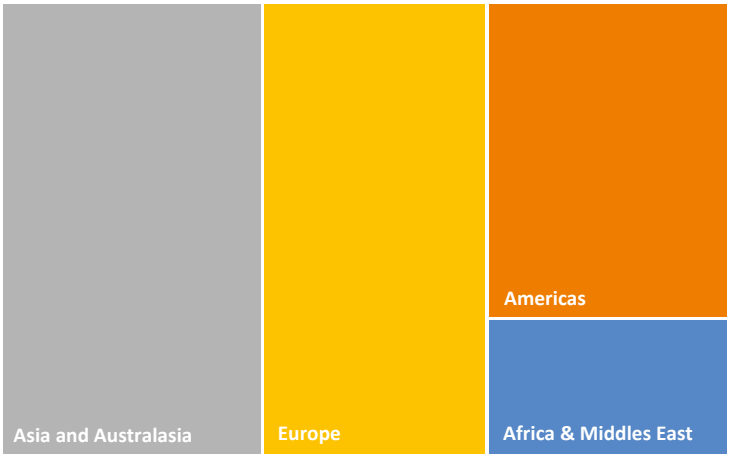
504 day-old broilers (Ross 308) were divided into 4 groups in a randomized study and treated respectively with CON (basal diet), PC (CON + 0.025% Avilamax®), BP 0.05 (CON + 0.05% bacteriophage), and BP 0.10 (CON + 0.10% bacteriophage). In the bacteriophage (BP) supplemented groups it was observed a significant linear effect on body weight gain (BWG) during days 1-7, days 22-35. The relative abundance of *Lactobacillus* was decreased in PC (65.28%), while it was similar in BP 0.05 and BP 0.10 (90.65%, 86.72%) compared to CON (90.19%). Particularly *Lactobacillus salivarus* presence was higher in BP 0.05 (40.15%) and BP 0.10 (38.58%) compared to the CON (20.04%) and PC (18.05%). Furthermore, authors conclude that a 0.05% BP addition was sufficient for supporting immune organs, bursa and spleen as well as enhancing gut microbiome, indicating the efficacy of 0.05% BP as a substitute antibiotic growth promoter in broiler diets.

Trends in published research

Total records & Main topics 44



Region of first Author (2017/2020)



43 Upadhaya, S. D., Ahn, J. M., Cho, J. H., Kim, J. Y., Kang, D. K., Kim, S. W., Kim, H. B., Kim, I. H. (2021). Bacteriophage cocktail supplementation improves growth performance, gut microbiome and production traits in broiler chickens. Journal of Animal Science and Biotechnology, 12(1), 49. https://doi.org/10.1186/s40104-021-00570-6

44 Cabi abstract search for the following keywords: prebiotics; probiotics; synbiotics; bacteriophages; antimicrobial peptides; medicinal plants; essential oils; plant extracts; phytochemicals

Ongoing research

Non-exhaustive list of ongoing projects on ATA funded by STAR-IDAZ IRC and STAR-IDAZ Network Members:

Area	Country/ organisation	Research projects
Phage technologies	Italy (MINSAL)	• Phage therapy as an Alternative to Antibiotics (ATA) in the control of infectious animal diseases: development of operational procedures for specific pathologies in farming models in Italy IZS LT 11/20 • Prevention and treatment of bacterial diseases of farmed marine fish species: approach to innovative strategies (bacteriophages) for national farming models IZS LT 3/18
	European Commission	• AVANT (**https://avant-project.eu/**): development of alternatives to antimicrobials for the management of bacterial infections in pigs, especially diarrhoea during the weaning period, as the major indication for antimicrobial use in livestock in Europe • PHAGOVET (**https://www.phagovet.eu/**): investigating phages as a cost-effective solution for controlling Salmonella and Escherichia coli in poultry production
The microbiome	Netherlands (WUR)	• Microbiome studies in various compartments and various species
	Belgium	• Probiotics for a health intestinal microbiome
	Spain	• Risk mitigating strategies and biomarkers in the new health and welfare paradigm of rearing calves (IRTA) • Nasal microbiota functionality and effect on the immune response of piglets (IRTA) • Analysis of the microbiota associated with porcine and ruminant neonatal diarrhea by high-throughput sequencing, and genomic characterization of the clostridia involved (TACYL) • Host response and microbiome interplay in swine dysentery and potential targets of disease control (Universidad de León) • Evaluation of the use of ruminal microbiota as a probiotic after birth to promote an optimal microbial colonization, ruminal function and efficiency after wearing (CSIC- EEZ) • Study of early interventions with probiotics in healthy ruminants: microorganism-host interaction (Asociacion Centro de Investigacion Coop en Biociencias CIC Biogune)
	Italy (MINSAL)	• Study of *Campylobacter* eco-epidemiology and antibiotic resistance in Italy (EcoCampy) IZS AM 3/20 • Study of the microbiome and related resistome in diagnostic and surveillance animal samples of antibiotic resistance, through a metagenomic approach IZS LT 01/20 • Endoparasite control and immune, inflammatory and intestinal microbiome status in equines IZS LT 8/20
	Argentina	• Analysis and modulation of the microbiome of livestock to increase production efficiency and reduce environmental impact I106
	European Commission	• HOLORUMINANT (**https://cordis.europa.eu/project/id/101000213**): holistic multi-omics approach to characterise the acquisition and evolution of microbiomes from different body sites, their inheritability and their influence on the host's resistance to disease and environmental efficiency of production • 3D-Omics (**https://cordis.europa.eu/project/id/101000309**): Three-dimensional holo'omic landscapes to unveil host-microbiota interactions shaping animal production

Area	Country/ organisation	Research projects
Immunomodulators	Nigeria (NVRI)	• Anti-coccidial effects of *Khaya senegalensis* and *Azadirachta indica* extracts on chickens experimentally infected with Eimeria species
	Belgium	• Immunomodulators for oral delivery affecting the GALT
	Sweden	• Coccidiosis control in broilers
	Spain	• Development of bionanoparticles for prevention and control of livestock viral diseases: engineered virus-like particles and extracellular vesicles pid2019-107145rb-i00 (INIA) • Nanoengineering host defense-based drugs into efficient drug delivery systems for intranasal administration-pid2019-107298rb-c22 (UAB) • Evaluation of immunomodulatory effects induced by probiotic strains (as alternative to antibiotics) on inflammation and tolerance regulatory mechanisms-RTI2018-098090-A-I00 (IRTA)
	Italy (MINSAL)	• Fight against the phenomenon of antibiotic resistance in the poultry sector thanks to the use of innovative products and procedures aimed at reducing the use of veterinary drugs IZS UM 01/20 • Study of the interaction between intestinal microbiota and *Giardia duodenalis* in dogs and the influence of pesticide treatment and the use of probiotics in the diet IZS VE 5/18
	European Commission	• AVANT (**https://avant-project.eu/**): development of alternatives to antimicrobials for the management of bacterial infections in pigs, especially diarrhoea during the weaning period, as the major indication for antimicrobial use in livestock in Europe
Others	Netherlands (WUR)	• Nanopore metagenome analyses
	Nigeria (NVRI)	• Effect of phyto-antioxidants on host pathogen interactions
	Belgium	• Biologicals for oral delivery that inhibit interactions of pathogens with the intestinal epithelium; targeted delivery of oral vaccines to the intestinal immune system
	Sweden	• Sino-Swedish Integrated Multisectorial Partnership for Containment of Antibiotic resistance (IMPACT)
	Spain	• New evidences on the clinical relevance of clostridia and their toxins in neonatal porcine and ruminant diarrhoea.-pid2019-108071rr-c22 (UCM) • Towards availability of antimicrobials "safe, effective and affordable"-rti2018-095586-b-c21 (INIA) • Optimization of diagnosis and treatment of postweaning diarrheas in pigs: towards a rational use of antibiotics. rti2018-095586-b-c22 (IRTA) • Integral control of salmonellosis in fattening pigs: development of new strategies in the farm-slaughterhouse interface-rti2018-093915-b-i00 (UNIZAR) • Understanding the host-pathogen interactions of *Campylobacter* infection in broilers, to design specific control strategies in poultry production- rti2018-095081-b-i00 (IRTA)
	Italy (MINSAL)	• Diffusion of antibiotic resistance factors in the environment: correlation with the territory and identification of wild / synanthropic animal species to be used as sentinels in surveillance IZS LER 2/19
	Argentina	• Studies on the generation of resistance to antimicrobials (antibiotics, antiparasitics, acaricides, antivirals) and development of prophylactic and therapeutic alternatives for their use in production animals I104 -
	European Commission	HealthyLivestock (**https://healthylivestock.net/**): a research programme to study the contributions of enhanced animal health and welfare on reducing the need to use antimicrobials in pigs and poultry APT (**https://armentavet.com/about-us/**): to address the issue of bovine mastitis, developed an innovative, non-invasive and antibiotics-free therapy that has proven to increase milk yield and quality, as well as reduce culling, using acoustic pulse technology (APT)

10. Influenza

Global network: OFFLU

Website: https://www.offlu.org/

Partners ca.
24

Budget
NA

Start date:
2014

Overview

OFFLU is the joint OIE-FAO global network of expertise on animal influenzas. It was established in 2006, initially to support the global effort to control H5N1 highly pathogenic avian influenza. Now OFFLU is a strong and functional network of world leading experts from OIE and FAO Reference Laboratories and Collaborating Centres, and from other institutes with leading expertise in diagnostics, epidemiology, bioinformatics, vaccinology, and animal production.

To date, Technical Activities of OFFLU have delivered guidance on diagnostic protocols, antigenic matching of vaccine strains with circulating field viruses, minimum biosafety guidelines for laboratory workers, and strategic guidance on animal influenza surveillance.

Aim and priorities

Aim: to reduce negative impacts of animal **influenza viruses** by promoting effective collaboration between **animal health** experts and with the human health sector.

Objectives

- To share and offer technical advice, training and veterinary expertise to international organisations and Member Countries to assist in the prevention, diagnosis, surveillance and control of animal influenza.
- To exchange scientific data and biological materials (including virus strains) within the network, to analyse such data, and to share such information with the wider scientific community.
- To collaborate with the WHO on issues relating to the animal-human interface, including pandemic preparedness for early preparation of human vaccine.
- To highlight influenza surveillance and research needs, promote their development and ensure co-ordination.

News

The OFFLU Steering and Executive Committee met virtually in July 2021 to review the progress in the work plan of OFFLU technical activities. Equine influenza experts participated in the OIE panel of equine influenza expert meeting virtually in July 2021 to update the vaccine recommendations for the equine industry in 2021. The OFFLU annual report 2020 can be found **here**.

The last update (September 2021) on global AIV with zoonotic potential can be found **here**.

To start developing a research roadmap on influenza virus, STAR-IDAZ published a **review on Animal influenza research**, in collaboration with USDA. The report identified what has been achieved by global research since the previous gap analysis and related activities carried out by USDA in 2013, OFFLU in 2014, by the EC in 2015 and by WHO in 2016 and 2017. The review includes information on avian, swine, equine and other influenza virus of veterinary interest, and will form the basis of a gap analysis workshop planned for next spring in Ames, Iowa, USA.

DISCONTOOLS research needs

R&D needs for avian influenza

Research to fill gaps in relation to pathogenesis, immunology, vaccinology, epidemiology and control.

- Cheap, stable and sensitive tests which allow high-throughput generic and subtype-specific multiplex serological screening.
- Rapid and sensitive methods of assessing infectious status of flocks.
- Easy to apply, single dose, cheap, marker vaccines that induce clinical broad protection and bring virus shedding to a minimum. Further development of recombinant vaccines is required.

Recent developments

Differences in highly pathogenic H5N6 avian influenza viral pathogenicity and inflammatory response in chickens and ducks.[45]

Two representative H5N6 viruses, A/Pavo cristatus/Jiangxi/JA1/2016 (JA1) and A/Anas crecca/shanghai/SH1/2016 (SH1) were characterized and compared for their pathogenicity and expression profiles of immune-related genes in chickens and ducks to identify the elements of the host immune-related response that were involved in different disease lethality. Results suggested that H5N6 HPAIVs had higher pathogenic and inflammatory effect in chickens than in ducks and that the TNF-α, IL-6, IFN-γ and iNOS levels were significantly higher in the lung of SH1 infected chickens compared to those of ducks. While JA1 was associated with greater pathogenicity in ducks and was accompanied by the excessive expression of iNOS in the brain.

45 Wang, B., Su, Q., Luo, J., Li, M., Wu, Q., Chang, H., Du, J., Huang, C., Ma, J., Han, S., Yuan, G., He, Y., Guo, M., Zhang, Q., He, H. (2021). Differences in Highly Pathogenic H5N6 Avian Influenza Viral Pathogenicity and Inflammatory Response in Chickens and Ducks. Frontiers in Microbiology, 12, 593202. **https://doi.org/10.3389/fmicb.2021.593202**

PB1 S524G mutation of wild bird-origin H3N8 influenza A virus enhances virulence and fitness for transmission in mammals.[46]

Eight H3N8 viruses, frequently recovered from wild bird species, were classified into seven different genotypes based on genomic diversity and their potential human health threat was investigated. Six of eight H3N8 viruses have acquired the ability to bind to the human-type receptor. Furthermore, experiments on guinea pigs demonstrated that three viruses transmitted efficiently to direct-contact guinea pigs without prior adaptation. In addition, they found that the PB1 S524G mutation conferred T222 virus airborne transmissibility between ferrets and that the 524G mutant increased viral pathogenicity slightly in mice compared with the WT (wild type). These results show the molecular basis of mammalian transmissibility of H3N8 influenza viruses. Authors, due to the potential human health threat, emphasized the need for continued surveillance of the H3N8 influenza viruses circulating in birds.

Efficacy of recombinant Marek's disease virus vectored vaccines with computationally optimized broadly reactive antigen (COBRA) hemagglutinin insert against genetically diverse H5 high pathogenicity avian influenza viruses.[47]

In this study the authors tested experimental vector herpesvirus of turkey (vHVT)-H5 vaccines containing either wild-type clade 2.3.4.4A-derived H5 inserts or computationally optimized broadly reactive antigen (COBRA) inserts with challenge by homologous and genetically divergent H5 HPAI Gs/GD lineage viruses in chickens. The HVT vector, a widely used replicating vaccine platform in poultry, with H5 insert provided clinical protection and significant reduction of viral shedding against homologous and heterologous challenge. In addition, the COBRA-derived inserts have the potential to be used against antigenically distinct co-circulating viruses and future drift variants.

Functional study of a role of N-terminal HA stem region of swine influenza A virus in virus replication.[48]

Results of this study demonstrated that Hemagglutinin (HA) protein of swine influenza A virus (SIV) could tolerate some mutations in functionally conserved B-loop and CD helix while attenuating influenza virus replication in both cell lines and porcine primary tracheal epithelial cells. Some B-loop or CD helix mutations generated virus mutants, replicated in MDCK and ST cell lines but failed to replicate in primary tracheal epithelial cells, in indicating that swine HA protein may function as a viral virulence and pathogenesis factor. Further studies are needed to explore those mutants as attenuated vaccine candidates that can effectively prevent or eliminate the spread of influenza virus within and between swine herds.

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46 Zhang, X., Li, Y., Jin, S., Zhang, Y., Sun, L., Hu, X., Zhao, M., Li, F., Wang, T., Sun, W., Feng, N., Wang, H., He, H., Zhao, Y., Yang, S., Xia, X., Gao, Y. (2021). PB1 S524G mutation of wild bird-origin H3N8 influenza A virus enhances virulence and fitness for transmission in mammals. Emerging Microbes and Infections, 10(1), 1038–1051. **https://doi.org/10.1080/22221751.2021.1912644**

47 Bertran, K., Kassa, A., Criado, M. F., Nuñez, I. A., Lee, D. H., Killmaster, L., Sá E Silva, M., Ross, T. M., Mebatsion, T., Pritchard, N., Swayne, D. E. (2021). Efficacy of recombinant Marek's disease virus vectored vaccines with computationally optimized broadly reactive antigen (COBRA) hemagglutinin insert against genetically diverse H5 high pathogenicity avian influenza viruses. Vaccine, 39(14), 1933–1942. **https://doi.org/10.1016/j.vaccine.2021.02.075**

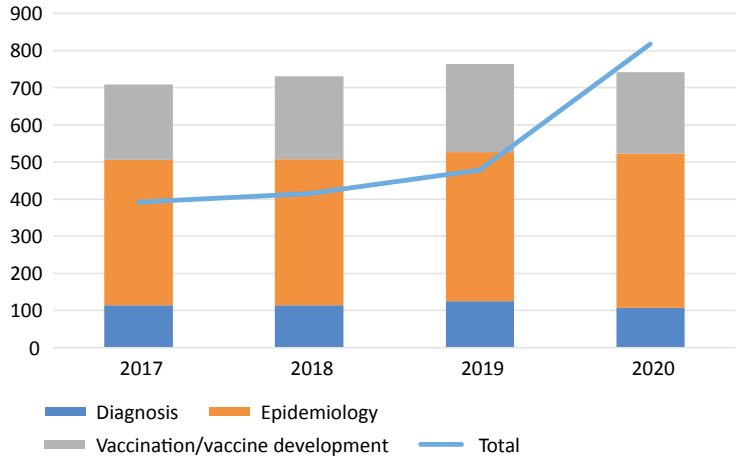
48 Wang, Z., Yu, J., Sheng, Z., Hause, B. M., Li, F., Kaushik, R. S., Wang, D. (2021). Functional study of a role of N-terminal HA stem region of swine influenza A virus in virus replication. Veterinary Microbiology, 258, 109132. **https://doi.org/10.1016/j.vetmic.2021.109132**

Global epidemiology of equine influenza viruses; "A possible emerging zoonotic threat in future" an extensive systematic review with evidence.[49]

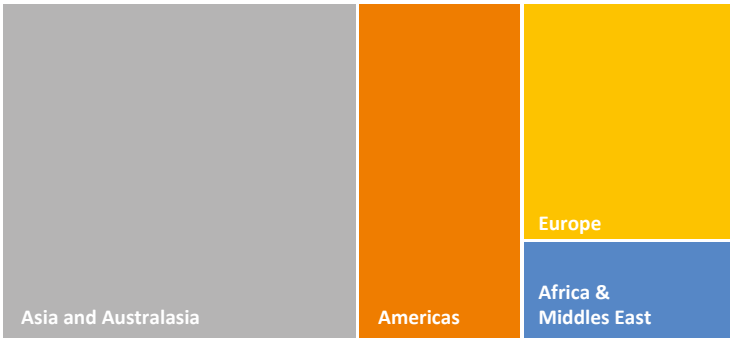
The findings of different research and review articles from Chinese, English, and Mongolian scientific literature, describing the evidence of equine influenza virus infections in humans were reviewed. Analyzing the epidemiological and Phylogenetic data from 962 articles, authors found a considerable experimental and observational evidence of H3N8 equine influenza viruses infecting humans in different parts of the World in the past. Several reports have highlighted the unpredictable nature of H3N8 EIVs emphasizing the need of continuous surveillance for H3N8 in equines and humans in contact with them for novel and threatening mutations.

Trends in published research

Total records &
Main topics



Country/ Region of
first Author (2017/2020)



49 Khan, A., Mushtaq, M. H., Muhammad, J., Ahmed, B., Khan, E. A., Khan, A., Zakki, S. A., Altaf, E., Haq, I., Saleem, A., Warraich, M. A., Ahmed, N., Rabaan, A. A. (2021). Global epidemiology of Equine Influenza viruses; "A possible emerging zoonotic threat in future" an extensive systematic review with evidence. Brazilian Journal of Biology, 83, e246591. **https://doi.org/10.1590/1519-6984.246591**

Ongoing research

Non-exhaustive list of ongoing projects on influenza funded by STAR-IDAZ IRC and STAR-IDAZ Network Members:

Area	Country	Research projects
Vaccine development	Belgium	• Vaccines against SIV
	Spain (IRTA)	• Swine influenza virus evolution associated to vaccination-AGL2016-75280-R
	Argentina	• Development of vaccines and technologies to improve prophylactic and therapeutic strategies for diseases that affect animal production and public health I102
	UK (DEFRA)	• Avian influenza (AI) threats to the UK
	BMGF	• Centivax inc, Universal influenza vaccine
Diagnostics	Netherlands (WUR)	• Detection and Identification of avian influenza in the Netherlands
	Nigeria (NVRI)	• Isolation and molecular characterization of Highly Pathogenic Avian Influenza
	Australia (ACDP)	• Australian Government Department of Foreign Affairs and Trade (DFAT) laboratory twinning project to enhance capacity to detect and manage zoonotic diseases, important transboundary animal diseases and emerging infectious diseases • FAO-ECTAD Indonesia project for provision of laboratory capacity building support for Ministry of Agriculture Directorate General of Animal Health Services (DGLAHS) laboratories in Indonesia [ACDP; FAO Indonesia; DGLAHS Indonesia • Project to support Singapore laboratory Animal Influenza test validation (2021) [ACDP; National Parks Singapore] • SO 17043 provider of OFFLU global proficiency test (PT) program for molecular detection of avian influenza viruses involving the OIE/FAO Reference Centres for Avian Influenza [ACDP; OFFLU] • ISO 17043 provider for the FAO-ECTAD Regional Office for Asia and the Pacific (FAO-RAP) regional proficiency test (PT) program for molecular detection of avian and swine viral diseases involving national animal health and veterinary diagnostic laboratories and provision of laboratory backstopping support [ACDP; OFFLU] • OIE Laboratory Twinning project with the Regional Animal Health Office No.6 (RAHO6) of Department of Animal Health, the Ministry of Agriculture and Rural Development, Vietnam, for enhanced diagnosis and characterization of emerging infectious diseases of pigs in the Southeast Asian Region [ACDP; RAHO6; OIE] • Development of ferret and chicken post-infection antisera and antigens for antigenic characterisation of regionally and inter-continentally circulating H5, H7 and H9 avian influenza viruses (ongoing) [ACDP; OFFLU] • Development of ferret and swine post-infection antisera and antigens for antigenic characterisation of swine influenza viruses circulating in Australia and the Indo-Pacific region (ongoing) [ACDP; WHOCCRRI; OFFLU]
	Argentina	• Development of diagnostic technologies and epidemiological studies for the control of diseases that affect animal production and public health I103
	European Commission	• SWINOSTICS - Swine disease field diagnostic toolbox (**https://cordis.europa.eu/project/id/771649**) • VIVALDI / Veterinary Validation of Point of/care detection Instruments (**https://cordis.europa.eu/project/id/773422**)
	UK (DEFRA)	• Mammalian influenza viruses (MIVs) threats to the UK

Area	Country	Research projects
Epidemiology, including molecular epidemiology	Netherlands (WUR)	• Monitoring and surveillance of avian influenza in the Netherlands
	Nigeria (NVRI)	• Molecular epidemiology of avian influenza in West Africa sub region • Phylogenetic and evolutionary analysis of avian influenza in the sub region • The role of Nigeria in the epidemiology of avian influenza in the sub-region
	Australia (ACDP)	• Genetic and antigenic surveillance of avian influenza A viruses in Australia and Oceania [ACDP; Wildlife Health Australia; WHOCCRRI] • Genetic and antigenic surveillance of H9N2 avian influenza A viruses in the Indo-Pacific region [ACDP; OFFLU] • Genetic and antigenic surveillance of swine influenza A viruses in Australia and the Indo-Pacific region [ACDP; WHOCCRRI; OFFLU]
	Spain (NEIKER)	• Development and validation of new isolation and typing strategies for avian influenza viruses-RTA2015-00088-C03-01
	Spain (UCLM)	• Avian influenza: Detection, pathogenesis and epidemiology at the wildlife domestic bird interface- RTA2015-00088-C03-02
	Spain (UAB)	• Avian influenza: study of the infection dynamics in autochthonous birds and the persistence of the virus in environmental conditions -RTA2015-00088-C03-03
	Italy (MINSAL)	• Qualitative and quantitative study on the evolution of the antigenic variability of swine and human influenza viruses circulating in Italy IZS LER 9/18 • Swine flu viruses in Northern Italy. Study of epizootic forms in farms and risk factors IZS LER • Study of the potential spread of influenza viruses through population movements of residential wild Anatidae IZS VE 7/18 • Swine flu: antigenic determinants of the viruses circulating in the Triveneto area for the correct control of animal infections IZS VE 15/18 • Study of the role of non-aquatic wild birds in the transmission of viral diseases to domestic populations IZS VE 11/19
	Argentina	• Development of diagnostic technologies and epidemiological studies for the control of diseases that affect animal production and public health I103
	European Commission	• DELTA-FLU (**https://cordis.europa.eu/project/id/727922**) Dynamics of avian influenza in a changing world • PREVENTER (H2020 **ICRAD**): Deciphering the role of influenza D virus in bovine and human respiratory diseases in Europe • PIGIE (H2020 **ICRAD**): Understanding the dynamics and evolution of swine influenza viruses in Europe: relevance for improved intervention and sustainable pig production
	UK (DEFRA)	• Environmental survival of influenza viruses

Area	Country	Research projects
Host-pathogen interaction	Netherlands, (WUR)	• Development of ex-vivo models for identification pathogenic avian influenza viruses
	Nigeria (NVRI)	• Interspecies transmission, pathology and control of influenza: 1. Studies on zoonotic and pandemic influenza virus in swine 2. Equine and canine influenza ecology 3. Human-animal interface study
	Australia (ACDP)	• Understanding the role of the cellular immune response in HPAI. This project involves building tools for influenza infection analysis in ferrets and chickens • Evaluating the effects of cell, age on the progression of influenza A virus infection in vitro. A range of susceptible cell lines will be evaluated for senescence assays
	Belgium	• Spreading between different host-species
	Italy (MINSAL)	• Evaluation of the replicative capacity and pathogenesis of swine influenza viruses through reverse genetics techniques and the use of respiratory organoids and 3D cell cultures of porcine origin IZS LER 13/18
	Argentina	• I105 - Study of animal pathogens and their interaction with the host and the environment: impact on productivity, animal and public health, and ecosystems in the "One Health" concept
	European Commission	• DELTA-FLU (H2020; until November 2022 **https://cordis.europa.eu/project/id/727922**) • FluNuance (H2020 ICRAD): to unravel the determinants of increased virulence in LPAI viruses in chicken, mallard, geese and pigeon in order to better predict the severity of emerging AIV strains
	UK (DEFRA)	• Enhancement of influenza diagnostic portfolio
Others	Netherlands (WUR)	• Serology of avian influenza, Protein array analyses Avian Influenza, Sequencing and bioinformatics
	Australia (ACDP)	• Investigation of the role and function of specific host genes in influenza infection • Assessing new therapeutics for prophylaxis and treatment of human infections with highly pathogenic avian influenza virus
	Italy (MINSAL)	• Innovative therapy of influenza and respiratory infections caused by viruses through the use of siRNAs (short interfering RNAs) IZS LER 3/18
	UK (DEFRA)	• Project 5: Pig Influenza Genetics, Intervention and Epidemiology (PIGIE): (Funded by EU and ICRAD/ERAnet, through Defra)

11.Mycoplasma

Global network: The International Organization for Mycoplasmology

Website: http://iom-online.org/

Partners ca.
500

Budget
NA

Start date:
1976

Overview

The International Organization for Mycoplasmology (IOM) was founded in 1976 as a nonprofit organization to promote the cooperative international study of mycoplasmas (Mollicutes) and mycoplasmal diseases and to disseminate knowledge about their characteristics, effects, transmission, and control.

IOM counts the participation of around 500 professionals that encompasses human, animal, plant, and insect microbiologists involved or devoted to the study of the Mollicutes.

The International Research Program of Comparative Mycoplasmology (IRPCM) (previously a consultative group sponsored by WHO and FAO) is currently a permanent standing committee of the IOM. It is composed of specific interest working-teams that regularly analyze and summarize recent developments in their respective interest areas, such as Avian Mycoplasmas, Porcine Mycoplasma, New and Emerging Mycoplasmas, Ruminant Mycoplasmas, Chemotherapy of Mycoplasma infections and others.

Members of the IOM also constitute the International Committee on Systematic Bacteriology Subcommittee on the Taxonomy of Mollicutes, the body that makes recommendations on minimum standards for the description of the class Mollicutes via the International Code of Nomenclature of Bacteria.

Aim and priorities

Aim: to promote the cooperative international study of mycoplasmas (Mollicutes) and mycoplasmal diseases and to disseminate knowledge about their characteristics, effects, transmission, and control.

Objectives

- Promote a cooperative study of mycoplasmas (Mollicutes) and mycoplasmal diseases;
- Advance and disseminate knowledge on all aspects of mycoplasmas (IRPCM):
  - a more complete understanding of the cellular and molecular biology of mycoplasmas, including those features that may be unique in the prokaryotic world to mycoplasmas;
  - Elucidation of the diversity of mycoplasmas;
  - Defining virulence factors of mycoplasmas pathogenic to humans, domestic and wild animals, and plants; and
  - Identifying more effective means of diagnosis, prevention, and control of mycoplasma infections and disease.
- Disseminate knowledge.

News

The 23rd Congress of the International Organization for Mycoplasmology originally scheduled for 5-9 July, 2020 in Tel Aviv, Israel will be held online on 1-4 November, 2021, due to current travel constraints.

More information regarding activities of Working teams can be found **here**.

DISCONTOOLS research needs

R&D needs for contagious agalactia (CA)

- Knowledge on the factors associated with reactivation of *Mycoplasma*, pathogenicity mechanisms and the contribution of the host immune response to lesion development in mammary gland and lung and disease.
- Further work on the transmission mechanisms: the role of pneumonia as part of the transmission process, role of insects, significance of aerosol transmission.
- A marker vaccine together with a suitable diagnostic means of distinguishing between vaccinated and infected animals. P48 is a prospective marker vaccine, but to-date has only been tested experimentally.
- Antibiotics with increased efficacy/distribution that could prevent the continued excretion of mycoplasma. Screening of novel chemicals and plant extracts against CA mycoplasmas is also possible. Future therapy is likely to remain with the use of antibiotics but new antibiotics may be restricted for human use.

R&D needs for contagious bovine pleuropneumonia (CBPP)

- Research on the establishment of infection (pathogenicity factors, immunopathology, virulence factors, genomics) and the persistence of infection in chronically affected animals (e.g. reservoirs).
- A pen side test capable of detecting both acute and chronic infections.
- A safer, more effective and better characterised vaccine to allow more effective disease control strategies to be implemented. DIVA technology is a critical gap in CBPP prevention and control tools. There is a debate regarding either the development of a new generation of potent CBPP vaccines/subunits or to rely on improvements in the current vaccines with regards to the biology of the vaccine strains and /or adjuvants and pH adjustments.
- An experimental animal model for CBPP disease.

R&D needs for *Mycoplasma bovis*

- Increased knowledge on host-pathogen interactions to develop safe and effective vaccines: mechanisms of host invasion, transmission within the host, predilection for specific sites, intermittent shedding, differences in resulting clinical signs, the role of variable surface proteins.
- The identification of protective antigens through genomic, bioinformatics, proteomic, immunological and biological approaches.
- The design of molecular typing schemes for *M. bovis* disease surveillance to support the development of more specific and sensitive tests.
- Effective antibiotic treatment regimens to address antibiotic resistance.

R&D needs for swine mycoplasmas

- More knowledge on i) the virulence factors and mechanisms in all three mycoplasmas and ii) the protective immune responses against *M. hyopneumoniae*.
- Further determination of mycoplasma genome to understand the way in which the pathogen regulates the immune response.
- Elucidation of the relationships between the bacterial, viral and mycoplasma infections.
- Knowledge on the economic impact of *M. hyorhinis* and *M. hyosynoviae* infection.
- Improved vaccines for *M. hyopneumoniae* and effective vaccines for *M. hyorhinis* and *M. hyosynoviae*.
- Improved use of antibiotics and treatment strategies to minimize potential for the development of resistance and for minimizing clinical disease due to *M. hyorhinis* and *M. hyosynoviae*.

Recent developments

Perspectives for improvement of *Mycoplasma hyopneumoniae* vaccines in pigs.[50]

This article provides a short overview of the pathogenesis and immune responses following *M. hyopneumoniae* infection, outline the major limitations of the commercial vaccines and reviews the different experimental *M. hyopneumoniae* vaccines that have been developed. The authors argue few efforts have been directed towards the development of attenuated vaccines, although such vaccines may have great potential. New vaccines should aim to target cell-mediated and humoral mucosal responses, as they are important for disease protection. Further research to develop better vaccines and to achieve a more sustainable control of *M. hyopneumoniae* infections are discussed taking in consideration the selection of proper antigens, administration route and type of adjuvant and carrier molecule. Furthermore, practical aspects, such as cost of the vaccine, easiness of production, transport, administration and possible combination with vaccines against other porcine pathogens are essential for success.

Protection against *Mycoplasma bovis* infection in calves following intranasal vaccination with modified-live *Mannheimia haemolytica* expressing *Mycoplasma* antigens.[51]

Novel live vaccine strains of *Mannheimia haemolytica* serotypes (St)1 and St6, expressing and secreting inactive yet immunogenic leukotoxin (leukotoxoid) merged to antigenic domains of *Mycoplasma bovis* Elongation Factor Tu (EFTu) and Heat shock protein (Hsp) 70 were constructed and tested for efficacy in cattle. After challenge, vaccinated cattle produced systemic antibody responses against leukotoxin and Hsp70, and concurrent reductions in temperature, middle ear infections, joint infection and lung lesions versus the control group. Moreover, a decrease in lung loads of *M. bovis* were detected in the vaccinated cattle. These results indicate that the attenuated *M. haemolytica* vaccine strains expressing Mycoplasma antigens can control *M. bovis* infection and disease symptoms in a controlled setting.

50 Maes, D., Boyen, F., Devriendt, B., Kuhnert, P., Summerfield, A., Haesebrouck, F. (2021). Perspectives for improvement of *Mycoplasma hyopneumoniae* vaccines in pigs. Veterinary Research, 52(1), 67. **https://doi.org/10.1186/s13567-021-00941-x**

51 Briggs, R. E., Billing, S. R., Boatwright, W. D., Jr, Chriswell, B. O., Casas, E., Dassanayake, R. P., Palmer, M. V., Register, K. B., Tatum, F. M. (2021). Protection against *Mycoplasma bovis* infection in calves following intranasal vaccination with modified-live *Mannheimia haemolytica* expressing *Mycoplasma* antigens. Microbial Pathogenesis, 105159. Advance online publication. **https://doi.org/10.1016/j.micpath.2021.105159**

Comparative secretome analyses of *Mycoplasma bovis* virulent and attenuated strains revealed MbovP0145 as a promising diagnostic biomarker.[52]

The secretomes of *M. bovis* HB0801 virulent (P1) and attenuated (P150) strains were compared and potential pathogenesis-related secreted proteins and biomarkers identified. Using also bioinformatics prediction, authors found that 178 proteins were commonly secreted by the P1 and P150 strains, and 49 of them were encoded by mycoplasmal core genes. Among these proteins, 34 were produced in higher quantity and uniquely expressed in P1, indicating a possible association with the virulence of *M. bovis*. Among them, MbovP0145 was confirmed to be more secreted by P1 than P150 strain, highly reactive with the antisera from naturally infected and P1 experimentally infected cattle but not with the P150 vaccinated calves, showing a potential as diagnostic biomarker.

Transfer of *Mycoplasma hyopneumoniae*-specific cell mediated immunity to neonatal piglets.[53]

The role of maternal cell mediated immunity (CMI) in protecting offspring against *M. Hyopneumoniae* was investigated. CMI was studied in piglets from vaccinated and non-vaccinated sows. Furthermore, the potential influence of cross-fostering before colostrum ingestion on the transfer of CMI from dam to piglets was also investigated. No difference was found in *M. hyopneumoniae*-specific CMI between cross-fostered and non-cross-fostered piglets. The results showed that different *M. hyopneumoniae*-specific T-cell subsets are transferred from the sow to the offspring. Further studies are required to investigate the role of these transferred cells on immune responses in piglets and their potential protective effect against *M. hyopneumoniae* infections.

Baicalin ameliorates *Mycoplasma gallisepticum*-induced inflammatory injury in the chicken lung through regulating the intestinal microbiota and phenylalanine metabolism.[54]

In this study the authors investigated whether baicalin alleviates *Mycoplasma gallisepticum* (MG) lung inflammatory injury through regulating gut microbiota. Baicalin significantly enriched the commensal bacterium *Bacteroides fragilis*, and gavaged with *Bacteroides fragilis*, alleviated MG infection-induced inflammatory injury in the lung. Furthermore, results showed that baicalin significantly reduced MG colonization and the pathological changes in the lung. It reduced the level of proinflammatory cytokines and suppressed proinflammatory protein expression and reversed peripheral accumulation of phenylalanine induced by MG infection. Those findings draw attention to the role of baicalin in inhibiting MG-induced inflammatory injury in the lung by remodelling the gut microbiota and phenylalanine metabolism.

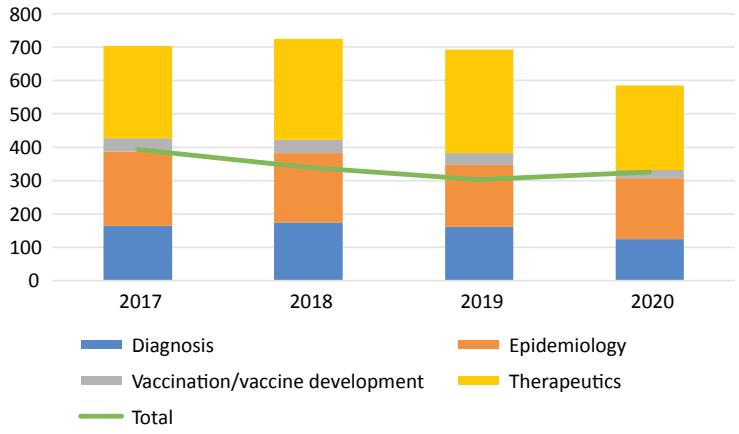
52 Zhang, H., Hu, G., Lu, D., Zhao, G., Zhang, Y., Zubair, M., Chen, Y., Hu, C., Chen, X., Chen, J., Chen, H., Yang, L., Guo, A. (2021). Comparative Secretome Analyses of Mycoplasma bovis Virulent and Attenuated Strains Revealed MbovP0145 as a Promising Diagnostic Biomarker. Frontiers in Veterinary Science, 8, 666769. **https://doi.org/10.3389/fvets.2021.666769**

53 Biebaut, E., Beuckelaere, L., Boyen, F., Haesebrouck, F., Gomez-Duran, C. O., Devriendt, B., Maes, D. (2021). Transfer of Mycoplasma hyopneumoniae-specific cell mediated immunity to neonatal piglets. Veterinary Research, 52(1), 96. **https://doi.org/10.1186/s13567-021-00968-0**

54 Wang, J., Ishfaq, M., Li, J. (2021). Baicalin ameliorates Mycoplasma gallisepticum-induced inflammatory injury in the chicken lung through regulating the intestinal microbiota and phenylalanine metabolism. Food and Function, 12(9), 4092–4104. **https://doi.org/10.1039/d1fo00055a**

Trends in published research

Total records &
Main topics



Country/ Region of
first Author (2017/2020)

Ongoing research

Non-exhaustive list of ongoing projects on *Mycoplasma* funded by STAR-IDAZ IRC and STAR-IDAZ Network Members:

Research Area	Country/ Organisation	Research projects
Detection/diagnosis	Nigeria (NVRI)	• Molecular characterization of mycoplasma mycoides subspecies mycoides isolated from cattle at slaughter in Nigeria
	Australia (ACDP)	• *Mycoplasma bovis* Science Programme – CSIRO Diagnostics Project
	Italy (MINSAL)	• Use of markers for the early identification of subclinical mastitis, study of genes related to genetic resistance to mastitis and control of somatic cells in milk in sheep and buffalo farms IZSLT
	UK (DEFRA)	• Research to underpin detection and diagnosis of Mycoplasma disease caused by *Mycoplasma* species exotic to Great Britain
Treatment/ Therapeutics and AMR	Nigeria (NVRI)	• Antibiotic therapy for the control of contagious bovine pleuropneumonia (CBPP) in Nigeria
Vaccine development	Belgium	• Mhyo vaccines: attenuated, inactivated and vaccine platform technology
Host-pathogen interaction	Belgium	• identification of protective epitopes on the surface of Mhyo
	Israel (KVI)	• Identification of virulence mechanisms in mammary pathogenic *Mycoplasma bovis* using unbiased whole genome random mutagenesis
	Italy (MINSAL)	• *Brucella* and *Mycoplasma* Lifestyle: pathogenesis and virulence (BruMLife) IZS AM 2/20
Epidemiology and control	Italy (MINSAL)	• Evaluation of *Mycoplasma synoviae* strains using the MLVA method, and creation of a database useful for understanding the epidemiology of this microbial species. Validation of the method and evaluation of any useful open access software systems IZS VE 4/19
	UK (UK)	• Research to underpin detection and diagnosis of Mycoplasma disease caused by *Mycoplasma* species exotic to Great Britain, particularly Epidemiology and Control objectives of this project

12. Mastitis

Global network

No global network on mastitis has been identified yet.

DISCONTOOLS research needs

R&D needs for environmental mastitis

- A standardised typing system to establish a likely environmental origin, mode of transmission or prognosis for mastitis cases.
- Tools for monitoring pathogen load in the environment.
- Improved knowledge of the innate immune system in the host response to, including but not limited to the role of macrophages, lymphocytes and cytokines. This is needed to develop improved vaccines.
- Continued efforts to bridge the gap in uptake of recent insights into environmental mastitis in veterinary practice and herd health management programmes. The impact of climate change, labour shortages and reduced use of antimicrobials on mastitis incidence and animal welfare is unknown.

R&D needs for *Staphylococcus aureus* mastitis

- A rapid, cow side or in-line pathogen specific diagnostic kit to timely implement pathogen-oriented treatment.
- A vaccine that prevents intramammary infection or accelerates cure after infection, or which contributes to increasing treatment efficiency. None of the vaccines studied to date have achieved these goals. Identification of protective immune mechanisms and correlates of protection is necessary. Apart from effective vaccines, we also need a good definition of effectiveness for mastitis vaccines.
- Improved therapies that utilize flexible treatments that are pathogen dependent. The use of peptide antimicrobials may offer the option of no withdrawal times, blanket fresh cow therapy and heifer treatments. Novel antimicrobial compounds that act intracellularly are under development. Narrow spectrum antibacterial agents that are not considered critical for human use are needed.

Recent developments

A 12 kb multi-allelic copy number variation encompassing a GC gene enhancer is associated with mastitis resistance in dairy cattle.[55]

The authors studied the biological mechanism underpinning the Clinical Mastitis (CM) genetic resistance on QTL located on chromosome 6. After mapping, they identified a ~12 kb multi-allelic copy number variant (CNV) as possible causal variant underlying this CM resistance QTL in the Dutch dairy cattle population. The multiplicated alleles are associated with increased group-specific component gene (GC) expression, a gene encoding a vitamin D binding protein, and low CM resistance. Furthermore, this allele showed multiple phenotypic expression for economically important traits such as increased milk yield and reduced fertility, apparently all related around the vitamin D pathway.

Nanomaterials and essential oils as candidates for developing novel treatment options for bovine mastitis.[56]

In this review authors summarize the current challenges in the treatment of bovine mastitis, highlighting the need for the development of innovative products, based both on new-generation nanomaterials (e.g., biological synthesized nanoparticles and graphene) and essential oils to address antimicrobial resistance.

Casein hydrolyzate for drying-off lactating mammary quarters in cows with chronic mastitis.[57]

In this research communication authors studied 60 cows with chronic mastitis dividing them in two treatment group: (a) three intramammary CH infusions (100 mg, 50 ml per infusion, with 24-h intervals) or (b) single intramammary CH infusion (300 mg, 50 ml). The quarters treated with three intramammary CH infusions had higher udder pressure index than those treated with single CH infusion, while the average milk yield and composite SCC of three functional quarters were not different among treatments. Thus, authors concluded that a single infusion of CH can be used as an alternative method for drying-off mammary quarters with CM during lactation.

55 Lee, Y. L., Takeda, H., Costa Monteiro Moreira, G., Karim, L., Mullaart, E., Coppieters, W., GplusE consortium, Appeltant, R., Veerkamp, R. F., Groenen, M., Georges, M., Bosse, M., Druet, T., Bouwman, A. C., Charlier, C. (2021). A 12 kb multi-allelic copy number variation encompassing a GC gene enhancer is associated with mastitis resistance in dairy cattle. PLoS Genetics, 17(7), e1009331. **https://doi.org/10.1371/journal.pgen.1009331**

56 Neculai-Valeanu, A. S., Ariton, A. M., Mădescu, B. M., Rîmbu, C. M., Creangă, Ş. (2021). Nanomaterials and Essential Oils as Candidates for Developing Novel Treatment Options for Bovine Mastitis. Animals, 11(6), 1625. **https://doi.org/10.3390/ani11061625**

57 Barcelos, M. M., Freu, G., Alves, B. G., Monteiro, C. P., Santos, M. V. (2021). Casein hydrolyzate for drying-off lactating mammary quarters in cows with chronic mastitis. The Journal of Dairy Research, 88(2), 185–188. **https://doi.org/10.1017/S0022029921000467**

Characterization of biofilms and antimicrobial resistance of coagulase-negative *Staphylococcus* species involved with subclinical mastitis.[58]

Biofilm formation and antimicrobial susceptibility in staphylococcal strains belonging to several species, isolated from the milk of cows with subclinical mastitis were investigated. Results revealed high genetic diversity among the strains and antimicrobial resistance patterns. More than 50% of the strains were resistant to ampicillin and penicillin G, with multi-resistance profiles (13.6%) also being observed. Furthermore, 65.9% of the strains formed biofilms, 72.7% carried the intercellular adhesion gene (icaA), while 36.3% carried the biofilm-associated protein gene (bap). Thus, this study revealed that a genetically diverse group of biofilm-forming Staphylococcus species can be involved in subclinical mastitis and since high antimicrobial concentrations cannot eradicate biofilm cells in vitro, their use may be ineffective. These findings support the need for alternative therapies aiming at disrupting biofilms for effective mastitis control.

Application of udder surface temperature by infrared thermography for diagnosis of subclinical mastitis in Holstein cows located in tropical highlands.[59]

The udder surface temperature (UST) was studied using infrared thermography (IRT) as a diagnostic tool for subclinical mastitis (SCM) and intramammary infection (IMI), and the influence of environmental conditions on the potential diagnosis of this disease in dairy cows located at high-altitude tropical regions was assessed. 105 cows from 3 dairy farms with mechanical and manual milking methods were enrolled in the study. SCM and IMI were diagnosed by somatic cell count (SCC) and microbial growth. Infrared images were taken with a thermal camera placed 1 m away from the udder during the morning milking, before any manipulation of the udder. The UST of healthy quarters ranged between (95% CI) 32.4 and 32.6°C, lower than SCM quarters (n = 88) at 32.9°C (95% CI: 32.7-33.1°C), MG quarters (n = 56) at 33.5°C (95% CI: 33.3-33.7°C), and IMI quarters (n = 50) at 33.5°C (95% CI: 33.2-33.7°C). Moreover, higher temperatures were observed for hand milking (n = 90) compared with machine milking (n = 185) while no relation between environmental conditions (wind speed, atmospheric temperature, relative humidity, and temperature-humidity index) and UST were observed. These findings suggest that UST can be considered a reliable, clinically useful method for MG and IMI diagnosis.

Changes in saliva proteins in cows with mastitis: A proteomic approach.[60]

The saliva proteome changes in cows with mastitis was studied using a Tandem Mass Tags (TMT) proteomics approach. A total of eight saliva and serum paired samples for healthy and mastitis cows were compared for the proteomic study, and eight additional samples for each group were analysed in the analytical and overlap performance studies. As a result, 2192 proteins were identified in saliva samples, being sixty-three differentially modulated in mastitis and 1299 proteins were identified in serum samples, being twenty-nine differentially modulated in mastitis. Particularly, Gamma glutamyl transferase (γGT) in saliva could be considered a biomarker of mastitis in cows.

58 Francisco, M. S., Rossi, C. C., Brito, M., Laport, M. S., Barros, E. M., Giambiagi-deMarval, M. (2021). Characterization of biofilms and antimicrobial resistance of coagulase-negative Staphylococcus species involved with subclinical mastitis. The Journal of Dairy Research, 88(2), 179–184. **https://doi.org/10.1017/S0022029921000285**

59 Velasco-Bolaños, J., Ceballes-Serrano, C. C., Velásquez-Mejía, D., Riaño-Rojas, J. C., Giraldo, C. E., Carmona, J. U., Ceballos-Márquez, A. (2021). Application of udder surface temperature by infrared thermography for diagnosis of subclinical mastitis in Holstein cows located in tropical highlands. Journal of Dairy Science, 104(9), 10310–10323. **https://doi.org/10.3168/jds.2020-19894**

60 Franco-Martínez, L., Muñoz-Prieto, A., Contreras-Aguilar, M. D., Želvytė, R., Monkevičienė, I., Horvatić, A., Kuleš, J., Mrljak, V., Cerón, J. J., Escribano, D. (2021). Changes in saliva proteins in cows with mastitis: A proteomic approach. Research in Veterinary Science, 140, 91–99. **https://doi.org/10.1016/j.rvsc.2021.08.008**

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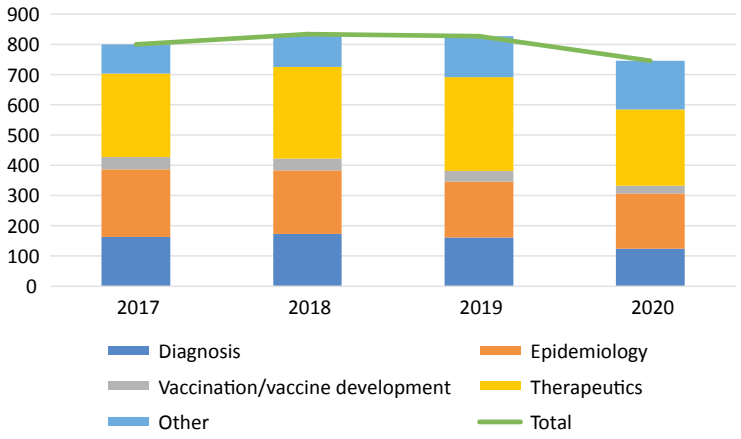

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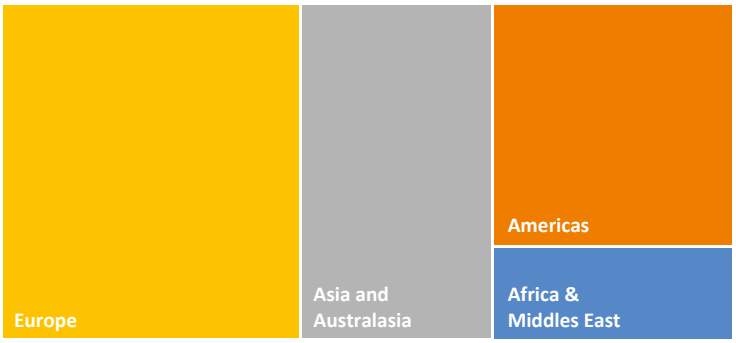

Ongoing research

Non-exhaustive list of ongoing projects on mastitis funded by STAR-IDAZ IRC and STAR-IDAZ Network Members:

Research Area	Country/ Organisation	Research projects
Early detection/ diagnosis	Netherlands (WUR)	Surveillance, monitoring and control of mastitis in cattle and other ruminants
	Nigeria (NVRI)	Control of mastitis amongst pastoralists in Plateau State (NVRI was a collaborating partner of SEBI, University of Edinburgh - project funded by Bill and Melinda Gates Foundation)
	Belgium	AI-based solutions for early detection of mastitis in milk
	Italy (MINSAL)	Use of markers for the early identification of subclinical mastitis, study of genes related to genetic resistance to mastitis and control of somatic cells in milk in sheep and buffalo farms IZS LT 5/20
	European Commission	**Biosens4PrecisionMastitis** (H22020; ICRAD)
Treatment/ therapeutics and AMR	Nigeria (NVRI)	Intramammary antibiotic injectables for treatment of mastitis udder of cows following CMT test confirmation
	Belgium	Alternatives to antibiotics
	European Commission	**APT** (H2020; SME project; until Mar2022): develop innovative non-invasive; antibiotics free therapies based on acoustic pulse technology **THERMUCNA** (H2020, MSCA IF; until Mar2023 **https://cordis.europa.eu/project/id/896775**): develop smart nanogels to deliver antimicrobial agents into the mammary glands of infected cows and cure ovine mastitis
Genetics of resistance	European Commission	**SMARTER** (H2020, until Oct2022): WP2 includes the identification of new disease phenotypes for endemic disease (proxies for foot rot, mastitis, parasites) linked to key production traits phenotypes
Vaccine development	Nigeria (NVRI)	OBVP Bludder Vaccine field trial study for small ruminant population of the pastoralists in Plateau State
	Italy (MINSAL)	Evaluation of the immunostimulating effect of a bivalent vaccine against the most common mammary diseases of sheep and goats IZS SI 4/18 Development of a recombinant vaccine for *Staphylococcus aureus* sheep mastitis starting from the genes coding for the main immunodominant antigens IZS SA 5/19
Epidemiology and control	Netherlands (WUR)	Surveillance, monitoring and control of mastitis in cattle and other ruminants
	Sweden	Control of *Streptococcus agalactiae* to reduce subclinical mastitis in pastoralist Camel herds in Kenya
	Spain	Deciphering the role of milk microbiota on the udder health status, colostrum quality and the development of the calf gut microbiota Pid2019-106038rr-i00 (neiker, instituto vasco de investigacion y desarrollo agrario sa)