Institut Pasteur

Progress report

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Infravec2 first 18-month progress report

Summary of progress of Infravec2, the EU-funded global source for no-cost vector research products and services, after 18 months of operation from February 2017 to July 2018.

Problems addressed, importance for society and overall objectives

The challenge of vector-borne disease.

Insect vectors are responsible for major global human suffering due to the diseases they transmit. These include viral infections transmitted by insects, such as chikungunya, dengue, Zika, Japanese encephalitis and yellow fever, and parasitic diseases such as malaria and leishmaniasis. Zika Fever is only decades old as a known human disease, while malaria is as old as humanity itself. Insect vector-borne veterinary diseases such as bluetongue and Schmallenberg, caused by viruses, are responsible for large economic losses in European and global animal industries. Bloodfeeding insects can act as a bridge allowing unknown animal pathogens to jump into human hosts, and local diseases can explode into global epidemics after just a few mutations, as apparently happened with chikungunya and Zika viruses. The diseases transmitted by insect vectors can be controlled by attacking the vector, either eliminating it or reducing its ability to transmit the pathogen. Indeed, for many vector-borne diseases, vector control is the only effective means of control. The goal of the Infravec2 project is to support research on insect disease vectors, to understand the biology of disease transmission in order to develop new tools and strategies to control current and future public health threats.

Social importance of insect vector research.

Vector-borne diseases have historically been considered a problem of tropical countries. Within the space of a few decades, vector-transmitted diseases and epidemics have now also become a threat to temperate regions of the world including much of Europe. A contributing factor has been the spread of different invasive mosquito species, particularly the Asian tiger mosquito Aedes albopictus, worldwide including into Europe. The increased risk of vector-borne diseases for the European population is a trend that will continue as a consequence of the global movement and expansion of the range of mosquito vectors, and probably other social as well as climatic changes. Thus, vector-borne disease is now a durable and permanent new public health concern in Europe. Just as the vectors and diseases changed to move to new environments, we also must adapt our public health measures implemented to meet the new challenges with vector surveillance, research, and new forms of vector control.

Objectives of Infravec2 for insect vector research and control.
The overall objective of Infravec2 is to integrate key specialized research facilities necessary for European excellence in insect vector biology, open them for access for vector researchers, and develop new vector control measures targeting the greatest threats to human health and animal industries. Working safely with infected insect vectors requires sophisticated and expensive infrastructures, which are not commonly available to many researchers. The lack of access to these unique facilities is currently a significant bottleneck for vector biology research and vector control development. The important vectors range from mosquitoes, considered the world's most lethal animal, the less well known but common sandflies, the barely visible Culicoides midges and nymphal ticks, and numerous other groups. The 24 Infravec2 partners, including four commercial companies, run the major European facilities for the study of insect vectors. With EU funding, Infravec2 is able to offer access to these facilities at no cost to qualified researchers in Europe and worldwide. Access to these infrastructures and resources is boosting progress in innovative vector research, building a robust vector research community, and will facilitate the development of new vector control tools.

Work performed and main results achieved

Infravec2 is developing new resources and tools for research on insect vectors. Many current mosquito colonies used for research are old and poorly characterized, and have likely changed in different laboratories. Infravec2 is creating eight new insect vector colonies for research, initiated in Europe, Africa and South America. Two of these colonies are established, one of them is publicly available and is already being used by researchers, five are in the process of adaptation to rearing under controlled environmental conditions in insectaries, and the last one will be initiated in September 2018. A genetic fingerprint method is in development as an authentication tool to verify colony quality. The bacterial community, or microbiome, of all animals is recognized as an important factor in health and immunity. This is also true for insect vectors, and their microbiome is now known to influence how well they transmit disease pathogens. Thus, the microbiome of the new colonies is being catalogued to help understand the biological influence for disease.

New cultured clones of the human malaria parasite are being established from different geographic parasite strains, and consistently performing clones have now been generated. This is important for laboratory research on malaria, because the main strain in research use now is over 50 years old, and its geographic source is unclear.

Work is in progress to improve the genome sequences for two important but neglected vectors, a European mosquito and a European sandfly. With high-quality genome sequences, the catalog of their genes will be available for study, whereas currently the research on these vectors has been greatly limited by the absence of this essential modern research resource.

Progress was also made in developing new tools for genetic study of Aedes and Anopheles mosquitoes.

Infravec2 made progress in a key goal, developing common protocols and operating standards for insect vector facilities. This is important because the current lack of unified experimental and date reporting standards can lead to errors in understanding the degree of risk posed by vector-pathogen combinations, and consequent inadequate preventative response. The goal is to develop and disseminate the world's first common inter-laboratory standards of performance for vector competence assays under secure insectary conditions. In these experiments, vectors are exposed to a pathogen under controlled conditions to measure the level of infection, and therefore predict their ability to transmit the pathogen. In this project period, a baseline standardization trial was carried out for virus vectors at one partner site, and the same test in parallel at two other partner sites is in progress. For malaria vector infection, baseline growth conditions of Anopheles mosquito diet and density were tested, prior to the next step of testing infection in parallel at two different sites. For sandflies, conditions were standardized for infection of the vector with the human parasite, Leishmania. A specialist group studying sandflies and another group of virologists pooled their expertise and succeeded in infecting sandflies in the laboratory with a class of viruses transmitted to humans by this and other sandflies throughout the Mediterranean region. To date, research on this public health problem has been impeded by the lack of ability to study the vector-pathogen combination in the laboratory. This work is an important step towards being able to study a neglected human viral disease, as a step to developing new tools to survey and control it.

Progress beyond the state of the art and potential impacts

The Infravec2 project plan includes a set of methodological and technological innovations reaching beyond the current state of the art. Progress was made during the current period in several target areas. Development of new tools for genetic manipulation of Aedes aegypti made important strides. In the African malaria mosquito, a successful laboratory test showed that populations could be driven to levels too low to maintain malaria transmission. An experimental infection system for sandflies with phlebovirus does not yet exist, and functional research is currently not possible on this European vector-borne disease system. In this period, infections were obtained in the laboratory using this sandfly vector and virus, which is an important step towards a new experimental model. This will be novel, will lead to new biological insight, and potential management tools. Progress was also made in development of a new device, the ArboVec-Disk, a handheld field platform for vector identification and infection testing.

The absence of common standards and reproducibility is a major gap holding back the vector research field, and reducing the impact of infrastructures in vector control. Progress was made in developing comparable standards for experimental reproducibility, a step towards creating a large networked and interoperable secure insect facility. This will be a world first, and will unleash additional innovation, including development of the quantitative study of vector competence and environmental variation, and greater power to interpret results and develop control tools based on genome editing, small molecule screening, symbionts, and the microbiome.

The social impact and implications of insect vectors and vector control was strengthened by progress on an operational citizen science tool, which is a social science strategy to integrate public input into vector surveillance and control by web-based and crowd-sourcing approaches. Also, the broad historical meaning of insect vector control is being investigated in an historic, cultural and anthropological context. Archival research and other historical methods are being used to reconstruct knowledge of historical vector control practices, successes and failures, which may hold clues for current research. Tools are being developed to promote the active involvement of societies for the most effective vector control interventions to protect human and animal health. Unlike most human histories that utilize the world wars as a timeline of key events, periods of mosquito control can be categorized according to establishment of international health organizations, preferred pesticides, discovery of bio-controls, and advances in molecular technology.

Image: The major African vector of human malaria, Anopheles gambiae. Credit: Institut Pasteur.

Infravec2 project partners

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3 POLO D' INNOVAZIONE DI GENOMICA, GENETICA E BIOLOGIA SCARL Italy
http://www.pologgb.com

4 INSTITUT DE RECHERCHE POUR LE DEVELOPPEMENT France
http://www.ird.fr

5 Institut Pasteur de Nouvelle-Calédonie New Caledonia
http://www.institutpasteur.nc

6 UNIVERZITA KARLOVA V PRAZE Czech Republic
http://www.cuni.cz

7 CENTRE DE COOPERATION INTERNATIONAL EN RECHERCHE AGRONOMIQUE POUR LE DEVELOPPEMENT France
http://www.cirad.fr

8 IMPERIAL COLLEGE OF SCIENCE TECHNOLOGY AND MEDICINE United Kingdom
http://www.imperial.ac.uk

9 INSTITUT DE RECERCA I TECNOLOGIA AGROALIMENTARIES Spain

http://www.irta.es

10 EUROPEAN MOLECULAR BIOLOGY LABORATORY Germany
http://www.embl.org

11 THE PIRBRIGHT INSTITUTE LBG United Kingdom
http://www.pirbright.ac.uk/arthropod-supplies

12 CENTRO AGRICOLTURA E AMBIENTE GIORGIO NICOLI SRL Italy
http://www.caa.it

13 TropIQ Health Sciences B.V. Netherlands
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14 MAX PLANCK GESELLSCHAFT ZUR FOERDERUNG DER WISSENSCHAFTEN E.V. Germany
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15 FOUNDATION FOR RESEARCH AND TECHNOLOGY HELLAS Greece
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16 STICHTING KATHOLIEKE UNIVERSITEIT Netherlands
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