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Infravec2: Expanding researcher access to insect vector tools and resources

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Most of the world first heard of the Zika virus during its explosive global emergence in 2015, after a history of mostly local transmission since its relatively recent description in East Africa in 1947. On the other hand, malaria is one of the most ancient, widespread, and lethal scourges of humanity, as old as the divergence of the human and ape lineages. Veterinary disease pathogens, some well-established such as bluetongue virus, and some newly emergent such as Schmallenberg virus, are responsible for large economic losses in animal industries. These pathogens could not be more distantly related to each other. However, the common thread is that these (and many other) disease pathogens are transmitted by insect vectors, and the diseases can be controlled by eliminating the vector or reducing its efficiency.

The tools and methods used to study insect vector-borne diseases caused by these and other disparate pathogens are quite similar. However, working safely with infected 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. The important vectors range from mosquitoes, considered the world's most lethal animal (1), the less well known but common sandflies, the barely visible *Culicoides* midges and nymphal ticks, and numerous other groups.

To help resolve the infrastructure gap, researchers and companies running the top European vector biology facilities formed a consortium called Infravec2 (website: <https://infravec2.eu/>). The objective of Infravec2 is to provide access to rare and unique vector facilities and resources to European and other eligible scientists. Access to these

infrastructures and resources will boost progress in innovative vector research and facilitate the development of new vector control tools.

Infravec2 is funded by the European Union (EU) Horizon 2020 program on European Research Infrastructures (INFRAIA grant agreement 731060), and will run from 2017-2021. Infravec2 is an Advanced Community, which follows the Infravec1 Starting Community project (2009-2014). Infravec1 was a response to the need of European vector laboratories to carry out research that required complex laboratory facilities and infrastructures not readily available to most researchers. Infravec1 integrated a community of European and African vector scientists and helped advance European leadership in the field of vector biology (2). Much of the scientific focus of Infravec1 concerned malaria transmission in Africa.

During the Infravec1 project period, however, new disease vectors such as *Aedes albopictus*, responsible for human viral diseases, such as chikungunya and dengue, arrived in Europe and became a stable part of the northern hemisphere disease landscape (3, 4). Consequently, the Infravec2 project was aligned to respond to these new public health threats. The nascent Infravec2 consortium carried out a survey of the vector research community to determine research interests and infrastructure gaps. The results of the survey were published (5), and were incorporated into the design of the Infravec2 project.

The Infravec2 consortium and infrastructure is oriented towards providing tools needed for the study of vectors of human and animal arboviruses (dengue, chikungunya, West Nile,

Zika, and bluetongue), parasites (malaria and *Leishmania*), and emerging threats such as sandfly-transmitted phleboviruses, and tick-borne diseases. Access to the infrastructures and resources will be available by an online shopping format beginning August 2017 on the Infravec2 website. Users will request the materials and submit a brief justification, which will be evaluated by an independent committee. Materials will be provided at no cost to the end user, and the provider is reimbursed by the EU for the actual cost. Thus, Infravec2 represents research funding for vector biologists from the EU. Eligible researchers are those in the EU, 16 associated European countries, and 130 other countries (eligible country list: <https://infravec2.eu/the-project/>).

Infravec2 will also strengthen the vector infrastructure by stocking it with new defined biological resources. New mosquito colonies and *Plasmodium falciparum* strains will be created for distribution. Many current mosquito colonies are old and poorly characterized, and have likely diverged genetically and phenotypically in different laboratories. The new Infravec2 colonies, initiated in Europe, Africa and South America, will be characterized for genetic diversity and microbiome. A genetic fingerprint will be developed as an authentication tool for colony standardization.

In addition, Infravec2 will strengthen the infrastructure by developing comparable operating standards for vector experimental infection. Currently, insectaries at different institutes operate as independent silos, and comparability or reproducibility across facilities has not been systematically evaluated. Poor or unknown levels of data reproducibility is recognized as a major current scientific problem in different fields (6, 7).

Transposed to vector biology, the lack of unified experimental standards may lead to errors in understanding the degree of risk posed by vector-pathogen combinations, and consequent inadequate preventative response. Multi-site trials will be carried out by Infravec2 to identify the levels of cross-facility variation for experimental infection of vectors with arboviruses and malaria, sources of variation will be identified, and ameliorative protocols will be developed. The common operating standards will be disseminated to the community. Vector competence measured under secure insectary conditions will be compared to natural vector competence, to develop methodologies that provide more accurate exploitation of insectary-based results in public health risk assessments.

The integration and reinforcement of existing European vector facilities by Infravec2, and provision of access to the community supported by EU funding, will significantly strengthen research capacities in vector biology. An important challenge will be ensuring long term sustainability of the integrated facility. Once established, Europe will be home to the world's largest secure insectary infrastructure. The consortium is developing multiple avenues to secure the future of the infrastructure for vector research.

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FIGURE LEGENDS

Figure 1. Geographic sites of the 24 Infravec2 partner institutes located in Europe, South America, Africa, and the South Pacific are indicated by blue pins. The complete Infravec2 partner list and contact information is available online (<https://infravec2.eu/partners/>; Map data, Google).