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World Health Day 2014: EU-funded research to fight vector-borne diseases

The European Union is an important player in the fight against vector-borne diseases, the main theme of this year's 'World Health Day' which will be celebrated on 7 April.

Vectors are small organisms such as mosquitoes, bugs, ticks and freshwater snails that can transmit disease from one person to another. More than half of the world's population is at risk from these diseases! Yet, through simple preventive measures, such as vaccination, we can protect ourselves and our families.

EU support for vector-borne diseases research comes in number of ways. The funding of international collaborative research projects through the FP7 (2007-13) and Horizon 2020 (2014-20) framework programmes is a key element, as shown in the examples below. The European Research Council (ERC) is also financing a number of projects related to vector-borne diseases. In addition, the 'European and Developing Countries' Clinical Trials Partnership' (EDCTP) - a big player in malaria research – will be extended later this year.

EU health research on dengue – some examples

The world's fastest growing vector-borne disease is dengue, a mosquito-transmitted disease with a 30-fold increase in incidence over the last 50 years. 40 per cent of the world's population is now at risk from dengue and WHO currently estimates there may be 50–100 million infections worldwide every year. According to a report by the European Centre for Disease Prevention and Control, 610 cases of dengue fever were notified by 14 of 23 reporting EU/EEA countries in 2011 - much lower than 2010 but comparable to the number of 2009. A major dengue outbreak with more than 2000 reported cases started in October 2012 in Madeira, fortunately without severe cases or deaths.

By funding the following international research projects the EU helps to better understand the disease and the virus which causes it. This research is expected to result in new tools to keep dengue disease under control but also in global maps to show, and hence work against, the risk of dengue spreading to previously uninfected areas.

<u>DENFREE</u> aims to identify the key factors determining dengue transmission, infection outcome and epidemics, and to develop novel diagnostic tools to detect asymptomatic infections. The project shed new light on how subclinical infections - where the person does not feel the need to consult a clinician – contribute to the spread of the disease. It proposes a new slow-release system for insecticides which is simple to use and provides total protection against bites for 3 weeks.

<u>DengueTools</u> concentrates on better dengue diagnosis, surveillance, and the potential for dengue emergence in Europe in the context of climate change. The study improves our understanding of the epidemic potential of dengue, informs new models based on weather/climate data, and helps factor climate changes into surveillance and control. The DengueTools team is also developing novel tools for the surveillance of dengue and for the control of dengue in children.



<u>IDAMS</u> is currently working on the validation of important clinical signs and symptoms of dengue, and the evaluation of virological and immunological markers. The research team has updated global risk maps and burden estimates for dengue, and it has produced maps of the history of spread of each of the four dengue viruses. Finally, a new technical handbook with local dengue surveillance protocols for timely outbreak detection is currently in the works.

Examples of EU-supported malaria research

Malaria is the vector-borne disease responsible for most deaths worldwide. It killed some 627,000 people in 2012, roughly one person every minute. There are more than 200 million new cases every year, most of them in children and pregnant women in developing countries.

The EU, through its Research Framework Programme FP7 (2007-13), supported 67 international research projects worth €142 million. They covered all areas from basic research, vaccines, diagnostics and drugs to research on the mosquito vector as well as research capacity building and training researchers (see also MEMO/13/374).

For instance, <u>NANOMAL</u> is developing a pioneering smartphone-like device that uses cutting-edge nanotechnology to detect not only the malaria infection but also any drug resistance from a pinprick of blood (<u>IP/13/362</u>).

Special emphasis is also given to malaria transmission control. A complementary set of projects works on new ways of preventing mosquito reproduction and the development of the malaria parasite:

One example is <u>MALVECBLOK</u> which revealed the molecular events involved in reproduction and immunity of mosquitoes and identified environmental factors that may influence disease spread. Taken together, the project findings provide new concepts for innovative vector measures to control malaria transmission.

Another project, <u>ANOPOPAGE</u> investigated a malaria control strategy using Wolbachia bacteria, paving the way for future investigations into malaria epidemiology in Africa and into other Plasmodium-inhibiting bacteria that could be introduced into Anopheles mosquitoes.

Completing these efforts, <u>AVECNET</u> was a collaborative initiative between African and European researchers that is developing and testing new methods for malaria control, such as novel insecticide treated bed nets.

The <u>AnoRep</u> project seeks to better understand mosquito biology, and reduce the incidence of malaria. Specifically, it is looking at how mosquitoes reproduce. This is a question of fundamental biology, but it also has wide implications for disease control. If we can understand more about mosquitoes' fertility, we can intervene to reduce it. By developing ways to curb mosquitoes' success in reproducing, ERC Starting Grant holder Prof. Flaminia Catteruccia and her team hope to provide innovative contributions to the fight against malaria.

Finally, the European Union's <u>'European and Developing Countries' Clinical Trials Partnership' (EDCTP)</u> initiative has so far invested €50 million for malaria research, including 32 clinical trials on improved treatments and new vaccine candidates. Many of these trials help adapt existing malaria therapies and drugs to particularly vulnerable groups. For example, the Severe Malaria in Children network (SMAC) showed that three doses over two days of the drug artesunate are as effective as five doses over three days. This alternative regimen would lower the risk of incomplete treatment by the improved efficiency and reduce the cost of administering the treatment. The European Parliament is due to vote April 15 on a proposal to extend EDCTP funding under Horizon 2020.



Examples of EU research on other vector-borne diseases

<u>ANTIDotE</u> studies the mechanisms of tick feeding to develop a single, new vaccine which is capable of preventing tick-borne disease transmission to humans - by either interfering with transmission or with tick feeding. By targeting tick-bites, the project hopes to help decrease tick-borne diseases such as Lyme disease, tick-borne encephalitis and human babesiosis (<u>full story here</u>).

<u>ChagasEpinet</u>, a project run by European and Latin American scientists, concentrates on Chagas, a disease which is common in South and Central America. It is caused by the parasite Trypanosoma cruzi which is transmitted through the bites of cone-nose bugs, also known as 'kissing bugs'. The project could show for the first time that T. cruzi is not a homogeneous single species but it includes 6 'genetic lineages'. This knowledge allows identifying local 'mixtures' of lineages and unravelling local transmission cycles, ultimately paving the way for better vector control strategies.

BERENICE also focuses on Chagas. There are currently only 2 treatments for the disease, both fraught with frequent side effects which require stopping treatment in up to one in every ten patients. The BERENICE team plans to use nanotechnology to encapsulate one of the existing Chagas drugs, benznidazole, to improve drug delivery and reduce doses. Preclinical and early clinical trials are part of the study and will, hopefully, be able to show that the new benznidazole formulation will be more effective, have less unwanted side-effects, and cost less.

Kaladrug-R, a collaboration between European researchers and partners in India and Nepal, tackled drug resistance of leishmaniasis, another major vector-borne disease which is spread by sandflies The research team confirmed that drug underdosing is a major factor for emerging resistance and identified the genetic signature of resistant strains. This could help develop diagnostic tools to rapidly check if a patient is infected by a resistant strain or not, and modify treatment accordingly. The project also found out that resistance to antimonials can be reversed by giving them together with other commonly used drugs, which in itself do not work against the parasite. This finding paves the way to new combination treatments.

Africoleish aims to develop a package of safe and cost-effective treatments for East African patients of visceral leishmaniasis (VL), a form of the disease which is fatal if left untreated. Combination treatment is necessary in this population to avoid treatment failures and emergence of resistance, but existing combination treatments are difficult to administer, toxic, costly and long. The Africoleish team is currently running a series of studies on existing and novel oral drugs in the hope of developing a ground-breaking combination treatment against the disease which combines two oral drugs.

<u>WINGS</u> has worked on vaccines to protect humans against West Nile Virus, a vector-borne disease which is also affecting Europe. The project successfully developed a candidate vaccine consisting of a recombinant protein which showed complete protection in mice and non-human primates. The vaccine was well tolerated, protective against different circulating European strains and displayed higher immunogenicity and protective capacity than previous developments in this field. In addition, tools for the specific diagnosis of West Nile Virus infections have been developed, which eliminate the problem of cross-reactivity with related viruses, such as Dengue or tick-borne encephalitis.

<u>EUROWESTNILE</u> established a new biobank with the various West Nile Virus lineages and strains circulating in Europe and neighbouring countries; it also developed new animal models to understand West Nile virus pathogenicity and neuro-invasiveness and candidate vaccines against West Nile virus and Chikungunya virus. New tools and prototype kits for West Nile Virus diagnostics and surveillance able to detect any of the lineages and differentiate them from other co-circulating were developed.

<u>EDEN</u> and <u>EDENext</u> have investigated vector-borne diseases relevant for Europe and neighbouring countries such as Lyme disease, Crimean Congo Haemorrhagic Fever, rodent-borne Hanta virus diseases, mosquito-borne diseases, and leishmaniasis. The projects have analysed the introduction, emergence and spread of vectors and diseases to find out how these diseases transmit under changing environmental and socio-economic conditions. This has resulted in better models, maps and control tools for improved public health risk assessment and decision making.

QWECI, a European-African joint venture, has set out to understand why certain vector-borne diseases disproportionally affect certain parts of the world under specific climate conditions. Running in parallel in Ghana, Malawi and Senegal, the project studied the impact of climate variation especially on vector-borne diseases such as malaria, Rift Valley Fever and certain tick-borne diseases. Results include medical databases, an atmospheric database on the geographical distribution of pathogens and potential climate drivers, and a malaria prediction model to simulate seasonal disease patterns.

<u>HEALTHY FUTURES</u> develops disease risk mapping systems for malaria, Rift Valley fever and schistosomiasis in eastern Africa, taking into account changing environmental and socio-economic conditions. The new datasets created by the project will help model disease and understand disease-environment dependencies better.

With her <u>EPIFOR</u> project, ERC Starting Grant holder Dr Vittoria Colizza tackles the threat of the fast global transmission of diseases such as SARS, influenza, Lyme disease and West Nile virus. Bringing together mathematical, statistical and computational techniques her work enables better targeted interventions, and enhances our ability to control the spread of a disease, to understand more about its effect on the population and its impact on available resources.

The NANOSYM project examines trypanosomiasis (commonly known as "sleeping sickness"), a disease of sub-Saharan Africa transmitted by the tsetse fly. When the parasite is attached to the epithelium of the salivary glands the tsetse fly becomes capable of transmitting the disease to humans. ERC Starting Grant holder Dr Jan Van Den Abbeele's project aims to increase our knowledge of the flies' salivary glands, as well as the attachment process. The research team are using genetically modified bacteria that act as a 'Trojan horse' to prevent the parasite's development. The approach could, in turn, generate a parasite-resistant tsetse fly, which could be released into nature to halt the transmission of the disease. This innovative method could also be applied to other vector-borne diseases, such as malaria or dengue.

Links

The EU launches a new project to fight falsified medicines in developing countries IP/14/378

World Health Day 2014: Preventing vector-borne diseases http://www.who.int/campaigns/world-health-day/2014/en

European Centre for Disease Prevention and Control (ECDC): Vector-borne diseases http://www.ecdc.europa.eu/en/healthtopics/emerging and vector-borne diseases/vector-borne diseases/pages/index.aspx

European & Developing Countries Clinical Trials Partnership (EDCTP) www.edctp.org

Contribution of EU research to the fight against malaria http://ec.europa.eu/research/health/infectious-diseases/poverty-diseases/malaria_en.html