Belgian scientists develop way to detect superparasites

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This is a typical village in Siraha district, Nepal, where leishmaniasis (also known as Kala-azar) is observed regularly. Scientists of the Antwerp Institute of Tropical Medicine developed a test for the "super" version of the *Leishmania* parasite, which is at the same time resistant to the classical drug against it, and more resilient to the human immune system (a biological first). Credit: © ITG

Belgian scientists of the Institute of Tropical Medicine (ITM) in Antwerp, Belgium made a breakthrough in bridging high tech molecular biology research on microbial pathogens and the needs of the poorest of the poor. After sequencing the complete genome of *Leishmania donovani* (a parasite causing one of the most important tropical diseases after malaria) in hundreds of clinical isolates, they identified a series of mutations specific of 'superparasites' and developed a simple assay that should allow tracking them anywhere. This EU-funded research was done in collaboration with the Wellcome Trust Sanger Institute in UK

and clinical partners of the Banaras Hindu University (India) and the BP Koirala Institute of Health Sciences (Nepal); it is published in the last issue of the *Journal of Infectious Diseases*.

Leishmania is a unicellular parasite that is transmitted through the bite of sandflies and occurs mainly in Latin-America, East-Africa, Asia and countries around the Mediterranean Sea. The parasite causes a disease called leishmaniasis which can range from self-healing cutaneous to deadly visceral disease, depending on the infecting species. Recently, the World Health Organisation estimated up to 1,6 million of new cases of leishmaniasis every year, affecting essentially the poorest of the poor. In comparison to these figures, the hundreds of imported cases reported among travelers appear a drop of water in the ocean. Some of these parasites are more dangerous than others, among them those causing visceral leishmaniasis, a clinical form which is lethal in the absence of treatment.

Recently, the same group of scientists reported among these (already) dangerous microbes, the existence of 'superparasites' in the Indian sub-continent, which are drug resistant and at the same time also better equipped to cope with our immune system. To our knowledge, it is the first time such a doubly armed organism is found in nature. (see "Do our medicines boost pathogens?", 21 dec 2011.) These superparasites could jeopardize current efforts to control this devastating disease.

The European Commission currently supports a series of research projects to develop new drugs against this type of parasites or to protect the few existing ones against the development of resistance (See http://www.leishrisk.net/leishrisk/). In the context of the Kaladrug project, the Belgian scientists of ITM, together with British colleagues of the Wellcome Trust Sanger Institute and Indian and Nepalese clinical colleagues, unraveled the DNA code of Leishmania using state-of-the-art genomic technologies while aiming to discover features allowing to track

superparasites. The scientists found a series of mutations that were specific for these drug resistant and more virulent microbes and developed an easy-to-apply assay that would allow to detect them rapidly. "Thanks to the discovery of these mutations, made possible through funding by the European Commission, the spread and emergence of these drug resistant parasites can be more efficiently monitored, contributing to a better and more adequate control of the parasite and the disease it causes." says Dr Manu Vanaerschot (ITM), first author of the paper. "We hope that this finding will ultimately pave the way to a field applicable drug resistance detection device not only for pentavalent antimonials but for all antileishmanial drugs. This is an important breakthrough which will help immensely in the control of the menace of leishmaniasis", says Shyam Sundar, from the Banaras Hindu University, a world authority in clinical research.

Technological revolutions during the last years have allowed a huge effort of sequencing the genome of hundreds of microbes. This type of research provides an unprecedented potential for new solutions to fight these pathogens by revealing their Achilles heal, so to say. These technologies can reveal the microbes true identity, offering new targets for drugs or vaccines and allowing scientists to track them. "Through the application of the latest technologies on precious clinical material to identify easy-to-use markers we strengthen our position among the world top in the field of translational research for infectious diseases and at the same time benefit those, often poor, patients that are usually most neglected in the society", says Prof Dujardin (ITM), coordinator of the Kaladrug project. "This project also clearly highlights the inestimable value of involving local clinical partners in the affected regions. Here, the European Commission plays an important role by funding fundamental research that at the same time provides solutions for clinical or epidemiological challenges."

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