

In touch with 19th century due to deciphering parasite

21-03-16 , 16:37



Dit is de omschrijving

New research published in the scientific journal eLife on Tuesday 22 March allows to trace back the successive epidemics of visceral leishmaniasis in the Indian subcontinent, the second deadliest parasitic disease after malaria. The reconstruction of the genealogical history of the Leishmania donovani parasite back to the 19th century was led by the Institute of Tropical Medicine in Antwerp (ITM) and the Sanger Institute (UK). The genome study lays the ground for molecular tools to produce an early warning system for surveillance and control of this neglected disease.

Visceral leishmaniasis (VL, also called black fever, kala azar in Hindi) mainly occurs in the Indian subcontinent, in East Africa and in South America, but has also been present for decades in Southern Europe. It is the second-deadliest parasitic disease after malaria. The World Health Organization estimates that between 200.000 and 400.000 new VL cases occur each year worldwide, with up to 50.000 deaths yearly. Reliable diagnostic tools and safe and effective drugs to treat this neglected disease are lacking. Until recently, antimonials, which cause toxic side effects, were the go-to drug against visceral leishmaniasis.

Scientists from the Institute of Tropical Medicine in Antwerp, Belgium, the Wellcome Trust Sanger Institute in the United Kingdom, the Banaras Hindu University in Varanasi, India and the BP Koirala Institute of Health Sciences in Dharan, Nepal, followed VL patients of the Indian subcontinent for years. They used the latest sequencing technologies to map the complete nuclear genome of 204 Leishmania donovani-strains and reconstruct the genealogical history of the parasite in the region. After five years of research, they hypothesise that a subtle genetic change contributed to resistance against antimonials.

"It was fascinating," said Prof. Jean-Claude Dujardin, one of the senior authors of the study. "While reading the book of life -the genome- of each strain, we could follow the successive epidemics of the disease back to the 19th century. Most interestingly, our results perfectly matched the historical records by British physicians in India, a touching dialogue between scientists with more than 150 years between them."

Deciphering a cryptic message

'TNBMM JT CFBVUJGVM'... Like a cryptic message in a Dan Brown novel, it doesn't make much sense at first glance. We made this code by replacing each letter by the next one in the alphabet. Reverse this operation and you get 'SMALL IS BEAUTIFUL' - just like parasites, according to some researchers.

Something similar happened within the genome of Leishmania donovani. The alphabet to describe DNA contains four letters, but a Leishmania genome is described using 35 million of these characters in different combinations. The researchers saw that a small letter shift scrambled most of a protein involved in the absorption of antimonials by the Leishmania parasite: resistance to antimonial drugs would thus originate from a tiny insertion of two bases of DNA. No wonder it took the scientists five years to go through the characters and discover the shifted sequence, a small needle in a giant haystack.

Dujardin: "This subtle but dramatic change in the sequence of one gene -which we call 'frame shift' in our scientific jargon- was only one of the adaptive skills presented by drug-resistant parasites. We discovered others, like multiplication of cassettes of genes, kind of survival kits to better control the action of the drug and subvert the host cell, or -the cherry on the pie- an incredible capacity of Leishmania to juggle with the number of chromosomes."

Contribution to science and society

The researchers are confident that the study results can provide new tools to fine-track *L. donovani* and provide early warning systems to monitor the success of the current programme for the elimination of VL in the Indian subcontinent. The results will also facilitate the detection of changes associated with the parasite's resistance to the few new drugs that are used in the region. Last but not least, it could guide research and development for new and more efficient anti-parasitic drugs.

Prof. Bruno Gryseels, Director of the Institute of Tropical Medicine, praised the researchers: "This is a scientifically fascinating study providing unprecedented insight in the adaptive evolution of parasites, and of micro-organisms in general. At the same time, the results are highly and directly relevant for the global fight against drug resistance in infectious diseases. Thus, it is a splendid illustration of the two sides of tropical disease research: scientific innovation and societal relevance."

Link

- The article '[Evolutionary genomics of epidemic visceral leishmaniasis in the Indian subcontinent](#)'