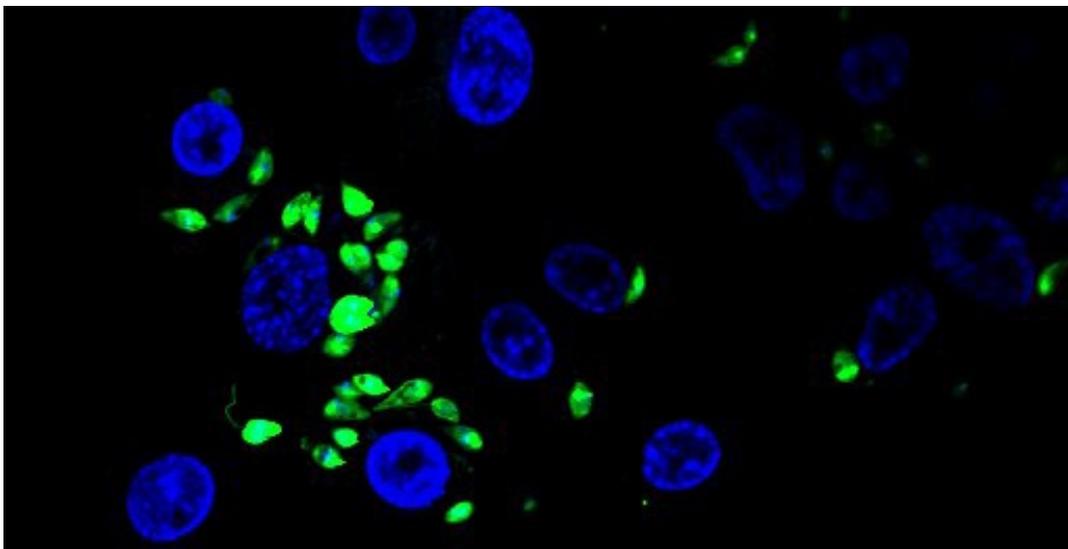




Scientists discover hidden parasites in patients with Leishmaniasis

Scientists develop a method allowing to sequence the genome of parasites that cause leishmaniasis directly in clinical samples

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Dit is de omschrijving

Scientists from the Institute of Tropical Medicine in Antwerp (ITM) led a study which developed a new method allowing to sequence the genome of parasites that cause leishmaniasis directly in clinical samples, without the need to isolate and cultivate the parasite. They found that the parasites in the patients were not the same as the cultivated ones, hence a lot of information may remain hidden inside the patient if working only with cultured parasites. The research was conducted with scientists from the Sanger Institute in the UK, Banaras Hindu University in India, BP Koirala Institute of Health Sciences in Nepal (BPKIHS). The findings were published in PLOS-NTD. Visceral leishmaniasis, also known as kala-azar, is a parasitic disease that affects 100,000 people each year and kills around 1 in 10 of its victims.

Over the last decade, scientists from Belgium, the UK, India and Nepal have united their efforts to sequence the genome of hundreds of Leishmania parasites. These studies are essential to support current programmes aimed at eliminating the disease. Prof Jean-Claude Dujardin, head of the Department of Biomedical Sciences at ITM, explains: “This scientific collaboration on Leishmania genomics has provided managers of elimination programmes with information about

previous epidemics, indications on the migration of parasites from one country to the other, the discovery of new parasite variants and the elucidation of some drug resistance's mechanisms."

Up until now, all genomic studies were done with parasites that were isolated from the patients and cultured in laboratories. In their paper, the scientists describe a DNA fishing method which allows to get rid of most human DNA present in clinical samples and enrich preparations in *Leishmania* DNA for later sequencing. ITM Dr Malgorzata Domagalska, responsible for the study and first author of the paper explains: "On the basis of previous experimental work, we suspected that culture of the parasites hid the truth, hence it was time to develop a method allowing to sequence the *Leishmania* genome directly in clinical samples without having to cultivate the parasites. However, this represents a major technical challenge, as DNA from human Kala-Azar samples may contain 99.99% of human DNA and only 0.01% of *Leishmania* DNA. Finding and sequencing the *Leishmania* DNA is like searching for a needle in a haystack." Dr Hideo Imamura, bio-informatician at ITM, illustrates: "This study generated Gigabytes of data that had to be filtered, controlled, corrected and analysed. As such, the project represented a major bioinformatic challenge. It was like separating all the ingredients of sushi, hand-picking tiny pieces of salmon and reconstructing an entire fish. In the end, our methods allowed to reassemble a high quality genome of *Leishmania* in most of the samples."

Besides this technological achievement, the authors of the paper made an important discovery. For several patients, they collected DNA both directly from patient samples and from cultured parasites isolated from the same patients. The scientists were astonished to see that in all comparisons, parasites were different in the patients and in the parasites isolated from these. Dr Domagalska clarifies: "This is likely due to both the presence of different types of parasites in a same patient, and Darwinian selection. Some parasites are 'happy' in the human environment, others in the culture medium." Domagalska concludes: "The next step in the genome conquest of parasites, not only *Leishmania*, should be done directly in clinical samples, as several features of the pathogens are hidden in the patients. This could guide research towards discovering new drugs and vaccines, which are desperately needed to deal with neglected diseases."

Visceral leishmaniasis is a tropical disease that occurs in the Indian sub-continent, East Africa, Latin America and Southern Europe. It is caused by *Leishmania*, a unicellular parasite that is transmitted to humans and animals by small insects. There is no vaccine against the disease and in the absence of treatment patients, essentially the poorest of the poor, die.

Link to paper: Domagalska MA, Imamura H, Sanders M, Van den Broeck F, Bhattarai NR, Vanaerschot M, Maes I, D'Haenens E, Rai K, Rijal S, Berriman M, Cotton JA and Dujardin JC. (2019) Genomes of *Leishmania* parasites directly sequenced from patients with visceral leishmaniasis in the Indian subcontinent. PLoS Negl Trop Dis 13(12): e0007900. <https://doi.org/10.1371/journal.pntd.0007900>

More information about kala-azar: https://www.who.int/leishmaniasis/visceral_leishmaniasis/en/