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News

Sequencing unlocks secrets of blood parasites

Possible drug targets revealed in flatworms that cause schistosomiasis.

Kerri Smith

Researchers have sequenced the genomes of two species of flatworm that cause the tropical disease schistosomiasis, revealing potential weaknesses that could be exploited by drug developers.

The *Schistosoma mansoni* genome was much larger than scientists expected.

Uniformed Services University of the Health Sciences

Schistosomiasis — also called bilharzia — is transmitted by water-borne snails, and affects more than 200 million people, many of whom live in Africa. Infections are usually chronic, rather than fatal. There is currently only one drug, praziquantel, in use against schistosomiasis and, although it is effective, scientists don't understand exactly how it works.

An international team led by Matthew Berriman at the Wellcome Trust Sanger Institute in Cambridge, UK, and Najib El-Sayed at the University of Maryland in College Park has sequenced the genome of the parasite found throughout Africa (*Schistosoma mansoni*). The Asian strain (*S. japonicum*) was tackled by the Schistosoma japonicum Genome Sequencing and Functional Analysis Consortium. Both genomes are published in *Nature*[1,2].

Small fluke, big genome

The two genomes confirm theories about the flatworm's biology — for example, it depends on its host for fatty acids that it can't make itself. But they also throw up some surprises. One is a new class of genes, thought to be involved in directing the movements of proteins around the organism's cells, each of which is seen in a number of different forms. The researchers think that this variation helps the parasite to hide from its host's immune system.

Another surprise is the size of the genomes. "This is a really big genome in terms of its overall length," says Berriman of the African schistosome genome.

"If you've got a full genome, you've got a benchmark."

Scott Lawton Natural History Museum

Karl Hoffman, a schistosomiasis researcher at Aberystwyth University, UK, and his team are already using the genome information to find targets for drugs and vaccines. Researchers are particularly interested, for example, in genes that are found in the worm's genome but not in the human genome, so that the proteins they make could be targeted by drugs or vaccines. That includes genes that, when knocked out, stop the female parasite producing eggs.

Berriman's group is also hunting for drug targets by looking for similarities. "We're now also looking for things that are very similar to the host and for which drugs already exist," he says. "If we can persuade [drug companies] they may already have things in their drug cabinet that could work, it could open up some new avenues." The drug cyclosporine, which is already used in humans as an immune suppressant, is one possible candidate.

Going straight

The genomes could shed light on the early evolution of animals — specifically, the point at which animals started to develop body plans that were straight rather than spherical like sea urchins. "Because schistosomes are flatworms, and flatworms occurred very early in this process, they allow us to get much closer in time to that split," says Berriman.

Scott Lawton, a researcher at the Natural History Museum in London, is excited by the possible insights the genomes could yield. In terms of discovering new genes, "it did fill in a lot of gaps", he says. It also shows which genes have moved around in the genome — for example, the *Hox* genes, which control body pattern in animals, are clustered together in many animals, but in schistosomes they are scattered around.

Although much of the *S. mansoni* data has been public for some time on the Wellcome Trust Sanger Institute website, assembling it all is still a milestone that the community has been "looking forward to", says Hoffman.

"It doesn't matter what organism you work on and at what level," Lawton says. "If you've got a full genome, you've got a benchmark."

References

1. Berriman, M. *et al. Nature* **460**, 352-358 (2009). | Article

2. Schistosoma japonicum Genome Sequencing and Functional Analysis Consortium *Nature* **460**, 345-351 (2009). | **Article**

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Knowledge about whole genome sequence will certainly help in developing drug/vaccine.Discovery of new genes involved in directing the movements of proteins around the organism's cells to hide it from host's immune system need to be investigated in detail in order to develop effective vaccine.Otherwise all solutions will be temperary in nature. Anurag chaurasia, ICAR, India

Report this comment Posted by: **Anurag Chaurasia** | 15 Jul, 2009

Since Luiza Freire (UFMG-Brazil) has been working in this very organism research, I wonder if is there any Brazilian involved in this publication? ADRIANO (Graphic Artist - scientific Illustrator)

Report this comment Posted by: **j.adriano desousa** | 16 Jul, 2009

I wonder what will happen to humans once we have eliminated all disease and parasites from our evolutionary process

Report this comment Posted by: **Jms rndll** | 17 Jul, 2009

RE: Human vs. disease/parasite evolution!? -- Nothing will happen to humans once we have eliminated all diseases and parasites from our evolutionary process. This is because we will never be able to eliminate all diseases and parasites from our body system, including the dreadful cancer and aging. They are just the integral (whether harmful or helpful) products and/or byproducts of our natural evolutionary process on Earth. Even if we could eliminate all diseases or parasites from our body system, there will be always an opportunity for new ones to replace them! That is the scientific and philosophical dynamism of our human vs. disease/parasite evolution! -- Best wishes, Mong 7/17/9usct2:03p; author "Decoding Scientism" and "Consciousness & the Subconscious" (works in progress since July 2007), "Gods, Genes, Conscience" (2006: http://www.iuniverse.com/bookstore/book_detail.asp?isbn=0595379907) and "Gods, Genes, Conscience: Global Dialogues Now" (blogging avidly since 2006: http://www2.blogger.com/profile/18303146609950569778).

Report this comment Posted by: **Mong H Tan, PhD** | 17 Jul, 2009

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Blood parasites belonging to the Apicomplexa, Trypanosomatidae and Filarioidea are widespread in birds and have been studied extensively. Microscopical examination (ME) of stained blood films remains the gold standard method for the detection of these infections in birds, particularly because co-infections predominate in wildlife. None of the available molecular tools can detect all co-infections at the same time, but ME provides opportunities for this to be achieved.Â However, it is not suitable for detection of species of Leucocytozoon and Plasmodium. BCM is a useful tool for diagnostics of blood parasite co-infections. Its application might be extended to studies of blood parasites in other vertebrates during field studies. Background. Commonly identified blood parasites include intracellular stages of Plasmodium, Haemoproteus, Leucocytozoon and â€œAtoxoplasma,â€ and extracellular stages of Try-panosoma and microfilariae from various filarial worms. Blood smears may be made on microscope slides or on coverslips. Coverslips have the advan-tage of being in view when mounted on slides and the sample is protected from being wiped off the slide.Â The parasite produces an anti-erythrocytic factor, which causes intravascular hemolysis and anemia, the principal clinical sign. Leucocytozoon is highly patho-genic in young Anseriformes and Galliformes.45 Fatal infections have been described in budgerigars. Diplostomid parasites are extremely difficult to distinguish morphologically, thus the use of molecular genetic methods allows us to understand the hitherto hidden diversity of parasites and their impact on the host, VasemÃ¤gi explained. "The developed methodology enables to analyze more material within one study than all previous molecular genetic research combined," said VasemÃ¤gi.Â Depending on the species eye parasites prefer specific niches within the eye. Some parasites infect the lens and fish develops cataract which renders it blind. List of Human Blood Parasites. There are many parasites that can invade the human body. Some of them are blood borne, meaning they are found in the blood rather than in tissues. These parasites can be transmitted from one person to another through exposure to infected blood (e.g. through blood transfusion or the sharing of a needle). Some are transferred by insect carriers, such as mosquitos. Blood donors are screened for possible parasite exposure, and donations are screened for some blood borne parasites, but some do still get through. Babesia microti. This parasite is responsible for Babesiosis, which is caused by infected red blood cells being spread by ticks.