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The Triumph of Genomics Puts Neglected Infectious Diseases in the Spotlight

It took nearly 6 years and 250 scientists from 47 institutions to crack the genomes of three trypanosome parasites responsible for sleeping sickness, Chagas disease and visceral leishmaniasis. In July 2005, *Science* published the genome sequences of *Trypanosoma brucei*, *Trypanosoma cruzi* and *Leishmania major*, including a comparison of gene content and genome architecture. These three pathogens cause millions of cases of disease and death in humans and other mammals mainly living in tropical and subtropical regions of Africa, Asia and South America. To have their genome sequences available is more than welcome, as they provide the building blocks for further functional and structural analysis.

The three genome sequences offer a unique insight into the biology of each of the three species. They contain many species-specific regions, reflecting the different insects they are transmitted by, the different pathologies they cause and the distinct ways they hide from the human immune system. For example, 20% of the genome of *T. brucei* reveals genes related to the parasite's capacity to switch its major surface proteins periodically in the bloodstream of its mammalian host, enabling the evasion of the immune system. *T. cruzi* uses a similar mechanism but hides intracellularly, often inside muscle cells. *L. major* evades the immune system by infiltrating macrophages and suppressing their function.

Although detailed analysis of the variations among the parasites could lead to targeted therapy against each of them in particular, their genetic similarities have priority as they provide the foundation for developing possible drugs that target all three. Comparative genomics of the pathogens showed a common core of 6,200 genes. Among these are genes encoding a diverse set of enzymes that are crucial for the parasites' metabolism which could be vulnerable to disruption by drugs. Moreover, half of the genes of all three parasites have unknown functions, leaving the possibility of discovering many more potential drug targets.

Comments

According to the World Health Organization, Chagas disease alone affects between 16 and 18 million people and threatens about a quarter of the population of Latin America. Nevertheless, the illnesses caused by the trypanosome parasites are neglected even more than malaria and tuberculosis. Development of new medicines is unprofitable because of the predominant occurrence in resource-poor countries. As a result, vaccines are lacking, and the few existing drugs are inadequate because of toxicity and resistance. However, the triumph of the trypanosomatid sequencing project shows that science does exist for these diseases and might revitalize efforts to fight them. With the immediate availability of the genetic information worldwide, scientists have already begun to identify critical enzymes in key metabolic pathways and possible vaccine candidates. This work depends heavily on public investment and is done by various international nonprofit research groups. The triumph of genomics will not provide immediate relief to those suffering; however, now that the trypanosome parasites have been put in the scientific spotlight, a wealth of data is available to find new cures against them.

R.P. Verhoeff, Delft