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Chagas parasite invades genome

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How infection with *Typanosoma cruzi* - an intracellular parasite that can hide out in the cells of the body - results in the development of chronic Chagas disease has been a mystery. Now a study in the July 23 *Cell* reports the integration of *T. cruzi* DNA into the genomes of infected patients, as well as chicken and rabbit animal models, suggesting that horizontal gene transfer may play a role in *T. cruzi*host-parasite interactions.

T. Cruzi infects some 16 to 18 million people in Latin America, and one third of these infections are estimated to result in chronic Chagas disease, which may not manifest itself until decades after an initial infection. A "major controversy" in the area of chronic Chagas disease research has been whether the presence of the parasite or an autoimmune reaction is its potential cause, said David Campbell, from the University of California, Los Angeles, who was not involved in the *Cell* study.

"[The *Cell* study] provides a fascinating insight into possible mechanisms of Chagas disease... in that the parasites 'presence' may be as little as a piece of integrated DNA," Campbell told *The Scientist*.

Nadjar Nitz, Antonio Teixeira, and their colleagues, from the University of Brasilia, undertook the study after hypothesizing that genetic transfer might be occurring between *T. cruzi* and a host genome. Upon analyzing genomic DNA from 13 patients with Chagas heart disease by polymerase chain reaction and Southern blot analysis, they detected *T. cruzi* mitochondrial DNA, which is termed kinetoplast DNA (kDNA), in each patient.

To further investigate, Nitz, Teixeira, and their colleagues moved their research into rabbits, and once again detected kDNA in the genomic DNA of infected rabbits, although they could find no indication of nuclear *T. cruzi* DNA. Additionally, they infected chickens, which are resistant to persistent *T. cruzi* infection. Chickens' eggs injected with *T. cruzi* gave rise to hens and roosters with detectable kDNA, and when bred, gave rise to offspring with inherited kDNA.

"We give an account of horizontal gene transfer between eukaryotes far apart in the kingdom," said Teixeira, who speculates that such kDNA integrations could have all sorts of effects, from the disruption of genes to the production of chimeric proteins. Thus, Teixeira feels that Chagas disease might have a genetic disease component.

"I think that the results are provocative," said David Engman, from Northwestern University, who was not involved in the study. "It should not be surprising that kDNA is integrated, though, since the parasite seems to do naturally what many of us do every day using electroporation," he said.

Larry Simpson, from the University of California, Los Angeles, who was not involved in the study, agreed. "It makes sense that for an intracellular parasite, of which some die and their DNA gets degraded, that their repetitive DNA-containing sequences would get integrated," Simpson told *The Scientist*.

Both Engman and Simpson cautioned that it is not yet clear if the integration of kDNA is involved in the pathology of Chagas disease. "Much more needs to be done before this can be concluded," said

Engman. Nevertheless, the research brings exciting new questions, including whether "this also occurs during intracellular infection with other organisms [such as Leishmania]," he said.

Apart from its potential role in Chagas disease, the integration of *T. cruzi* kDNA into host genomes also raises questions of its effect on evolution. "If this process involves the germline, integrated kDNA could theoretically alter human genetics through disruption of protein-coding sequences and promotion of recombination events between kDNA integration sites," Engman told *The Scientist*.

While the results are unlikely to end the debate on what causes chronic Chagas disease, "these data open the door to completely new ways of thinking about the host-parasite relationship, the consequences of chronic infection, and an intracellular lifestyle," said Campbell.

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