Subtle differences can lead to major changes in parasites

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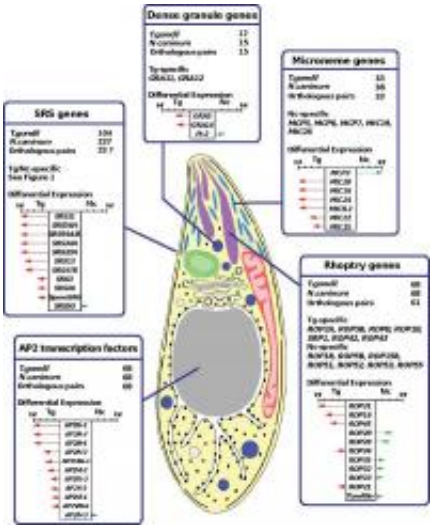

Groups of genes which are different between the parasites and how they relate to particular parts of the cell. [DOI:10.1371/journal.ppat.1002567]

Researchers have found the subtle genetic differences that make one parasite far more virulent than its close relative.

They looked at the evolution of these parasites and found that although their genome architecture still remains similar, the two split from their common ancestor 28 million years ago, approximately four times longer than the human-gorilla split.

Toxoplasma is arguably the most successful parasite. It can spread to any

cell type in any warm blooded vertebrate species. It can cause blindness and spontaneous abortion. Alternatively, the *Neospora* parasite can infect far fewer hosts. It is a veterinary pathogen and causes a high number of abortions in cattle, costing the UK farming industry millions of pounds a year. The parasites, though different, are closely related.

"The question we wanted to answer was; what causes this difference in virulence between *Toxoplasma* and *Neospora*?" explains Dr Adam Reid, first author from the Wellcome Trust Sanger Institute. "We used genome sequencing to probe the parasites for differences that might underlie the way they spread and how they have diverged."

The team found that a gene that helps the *Toxoplasma* pathogen to evade the host's immune system and enter the cell, is missing from neospora. The lack of this single gene means *Neospora* cannot evade the immune response in mice and may not be able to evade the immune response in other species. This could explain why *Neospora* has a more limited host range.

"Our results do not imply that *Toxoplasma* has in some way gained the gene, but that *Neospora* has actually lost the gene," says Professor Arnab Pain, senior author from the Wellcome Trust Sanger Institute. "We speculate that the loss of this gene in *Neospora* may be an adaptive change. Reducing *Neospora*'s virulence may increase its chance of survival in the host species."

The team also found that although the genetic differences between the two parasites are minor, there is a significant difference in the number of surface proteins found in both parasites. *Neospora* has more surface proteins, nearly twice as many as *Toxoplasma*, but fewer are active. Although this is difficult to interpret, the researchers hypothesise that a larger number of proteins are needed to restrict the parasite's host range.

"We were investigating these two parasites because they represent a big problem for the farming industry and in the case of *Toxoplasma* – for public health too," says Professor Jonathan Wastling, senior author from the University of Liverpool.

"Collectively, our results indicate that the ecological niches occupied by both parasites are influenced by subtle, adaptive, genetic changes. This project is an excellent example of how humans and animal medicine can learn from each other to provide better outcomes for both"

The next step for the team is to examine the genomes of other parasites within the same family as *Toxoplasma* and *Neospora* to better characterise the function of the genes and surface proteins. By deciphering which of these surface proteins are involved in the cell invasion process, it may be possible to develop vaccines for both of these parasites

More information: Reid et al 'Comparative genomics of the apicomplexan parasites Toxoplasma gondii and Neospora caninum: Coccidia differing in host range and transmission strategy' Published online in *PLoS Pathogens*, DOI:10.1371/journal.ppat.1002567

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