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NEWS AND COMMENTARY

Evolution of virulence

New gene, new disease

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History is filled with examples of novel infectious diseases suddenly appearing, and the origin of many of these is controversial, as in the case of the sudden emergence of syphilis in Europe in 1496 (Quétel, 1990). Biologists and historians studying these diseases usually pay little attention to the possibility that the infectious agent may have arisen *de novo*, preferring (often correctly, it should be said) to look for explanations in terms of transfer of pathogens between species or from other host populations. In a paper published in the latest *Nature Genetics*, however, Friesen *et al* (2006) give us evidence of a new disease emerging not because of interspecies or interpopulation transfer of pathogens but because of the interspecific transfer of a toxin gene that changed a previously benign microorganism into an important pathogen.

At first sight this story reads like something from a Greenpeace leaflet about the dangers of GM food, but in fact this event happened years before the development of DNA technology, probably around 1940 or 1941. The species that became pathogenic is a fungus called *Pyrenophora tritici-repentis*. It was originally described from a number of host species in the first third of the twentieth century as a saprophyte that could occasionally act as a pathogen, but in 1941 a new and damaging disease of wheat called yellow (or tan) spot was reported, and *P. tritici-repentis* was identified as the causative agent. Friesen *et al* (2006) argue that this change in virulence happened when a gene coding for a proteinaceous toxin called ToxA was somehow incorporated into the *P. tritici-repentis* genome following horizontal transfer from another fungal pathogen species, *Staganospora nodorum*, the causative agent of the snappily named *S. nodorum* blotch disease of wheat. Friesen *et al* were not there to observe this change first hand, but they produce a convincing collection of evidence to support their theory.

ToxA was initially identified in *P. tritici-repentis* but was not known for *S. nodorum* until the genome sequence of the fungus became available, enabling Friesen *et al* to identify a putative gene in the sequence with 99.7% similarity to the *P. tritici-repentis* ToxA gene. Further work revealed a similar structure of introns and exons, and similarities in the flanking regions of the two genes. The gene sequences and structures are thus very similar in both species, indicating a recent common ancestry, but what of the function of the proteins encoded by these genes? In *P. tritici-repentis*, ToxA is known to confer virulence when the fungus infects wheat plants carrying a particular gene called *Tsn1*, and Friesen *et al* were able to demonstrate that *S. nodorum* mutants with non-functional ToxA genes lost their ability to infect *Tsn1* carrying wheat plants. Furthermore, Friesen *et al* identified an *S. nodorum* isolate that was avirulent, producing no detectable lesions on any wheat plants. Insertion of the *P. tritici-repentis* ToxA gene into this avirulent line produced a line of *S. nodorum* that caused the characteristic yellow and brown blemishes on wheat that are typical of virulent strains of the fungus.

How to explain this very close similarity in the toxin genes present in two different species of fungus? There are a number of possible explanations: both fungi could have acquired the gene from a recent common ancestor, or the gene could have been transferred horizontally from one species to the other, or both species could have obtained the gene horizontally from a third species. These possibilities can be explored by looking at the patterns of diversity in the two fungi in question, and by searching for other species that carry the gene as well. It turns out that the *S. nodorum* ToxA gene is considerably more diverse than that of *P. triticarepentis:* Friesen *et al* were able to identify 11 haplotypes of the ToxA gene from 95 *S. nodorum* sequences, but only one haplotype from 54 *P. tritici-repentis* sequences. This difference in diversity suggests that the ToxA gene has been carried by *S. nodorum* for much longer than *P. tritici-repentis*. No other organism is known to carry this gene, despite five closely related wheat pathogens being screened in the study described here, making it unlikely (but obviously not impossible) that both fungi acquired the gene from a third party. The simplest explanation for these patterns is a single transfer from *S. nodorum* to *P. tritici-repentis*, presumably around 1940.

Bacteria are well known for their genetic promiscuity (Ochman *et al*, 2000), and the horizontal transfer of virulence genes is now recognized as being a significant phenomenon in many important diseases. The causative agent of cholera, the bacterium *Vibrio cholerae*, for example, only becomes virulent when a lysogenic bacteriophage virus carrying the cholera toxin gene inserts itself into the *V. cholerae* genome (Waldor and Mekalanos, 1996). Also, Rosas-Magallanes *et al* (2006) suggest that the ancestor of the bacteria that cause tuberculosis in humans and other animals only became able to cause significant pathology once it had acquired a gene that enhanced its ability to bind to host cells early on in infection. Evidence of gene transfer actually being associated with the recent emergence of new pathogens has not been forthcoming until now, however, and Friesen *et al* present not only the first good example of such an occurrence but also the first evidence of virulence gene transfer in a fungal, rather than a bacterial system.

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Further reading

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