Geneticists sequence *Escherichia coli* O157:H7 genome

In 1997 a team of geneticists led by Fred Blattner (University of Winsconsin, WI, USA) published the complete genome sequence of a non-pathogenic strain of *Escherichia coli* (K-12 MG1655). This week, the same research group describe the genetic sequence of *E coli* O157:H7, a pathogenic strain that was isolated from ground beef linked to an outbreak of haemorrhagic colitis in 1982 (*Nature* 2001; **409:** 529–33).

Blattner's research group has started to compare the two genomes in an attempt to understand which genes cause pathogenicity. Both genomes have about 4·1 million base pairs of DNA that were almost certainly derived from a common ancestor. Although the two strains share about 3500 common genes, within each genetic backbone is scattered hundreds of sections of DNA that are unique to one or other strain: the O157:H7 strain has 1387 genes unique to its genome and the non-pathogenic strain 528 genes. "The sheer magnitude of the differences [between the genomes] was totally shocking to us", says lead author Nicole Perna. "We couldn't just zoom in on areas of difference between the two species. The changes were scattered throughout."

Jeff Miller

Sequencing the *E coli* genome

Of particular interest to the investigators is how the two strains came to be so different. They suggest that at least some of the DNA unique to each strain could have been acquired by horizontal gene transfer—exchange of large banks of genes across entire families of bacteria. "If horizontal gene transfer has occurred", speculates Jonathan Eisen (The Institute for Genomic Research, Rockville, MS, USA), "then the fact that so many genes have been transferred to O157:H7 supports the suggestion that the continuing emergence of O157:H7 as a pathogen results from its ability to undergo rapid genetic change". Blattner agrees, saying "we are already seeing this with the ability of some bacteria to develop antibiotic resistance".

According to Eisen it remains to be seen which of these differences contributes to the virulence and pathogenicity of O157:H7. Once these features are identified, though, the way will be paved for the development of novel drugs and/or vaccines to target the pathogenic strain. In addition, he says that the genetic differences between the two strains will serve as diagnostic tools to determine whether someone is infected with *E coli* O157:H7. Perna agrees: "One of the first things we can do is improve our detection and surveillance before it [*E coli* O157:H7] becomes a public-health issue. We now have a far better distribution of genetic markers to help identify this in the field."

James Butcher

"Neural love triangle" leads to sexual receptivity

This week, US experts confirm that endogenous cannabinoids play a role in modulating reproductive behaviour. And in what has been dubbed a "neural love triangle", the researchers further reveal that certain sexual behaviours involve what commentator Nephi Stella (University of Washington, Seattle, WA, USA) calls "remarkable cross-talk" between three distinct signalling systems: cannabinoids, the neurotransmitter dopamine, and ovarian steroid hormones.

In rats, the main psychoactive ingredient in cannabis, Δ⁹-tetrahydrocannabinol (THC), is known to stimulate female sexual behaviour that is dependent on ovarian steroid hormones. THC is also known to modulate the dopamine neurotransmitter system. Moreover, previous research by Shaila Mani's team from Baylor College of Medicine (Houston, TX, USA), collaborating with Rockefeller University (New York, USA), demonstrated that dopamine and progesterone receptors interact to mediate sexual receptiveness in female rats. So Mani's group hypothesised that the neural basis of such behaviour might involve three signalling systems: endogenous cannabinoids, steroid hormones, and dopamine.

The researchers initially found that THC acts at the cannabinoid receptor-1 subtype (CB_1) to increase lordosis, a reliable indicator of sexual receptiveness in female rats. Further studies—involving intracerebral administration of receptor antagonists or antisense oligonucleotides—showed that lordosis could be facilitated by THC, progesterone, or dopaminergic agonists only if all three receptor systems were operative (*Proc Natl Acad Sci USA* 2001; 98: 1249–54). The authors suggest that, collectively, the data indicate an involvement of dopamine and progesterone-regulated pathways in THC signalling. So the endogenous cannabinoid system must cross-talk with steroid hormone systems to induce pleasure, concludes Mani.

Experts have hailed the findings as important. The three-way molecular cross-talk, perhaps the most complicated system found so far to underlie a sexual behaviour, is "remarkable", explains Stella, because the interaction "involves three very different types of signalling molecules: a lipid for the endocannabinoids, a catecholamine for dopamine, and a steroid for progesterone". Cindy Meston and Penny Frohlich (University of Texas, Austin, TX, USA) claim that the study resolves inconsistencies in the literature. And, "it suggests that the neurobiological processes underlying sexual behaviour may be best understood as complex interactions involving several hormone, neurotransmitter, and neuroanatomical factors".

The team are now investigating the mechanism of the interaction between the three systems. They propose that either separate activation of three receptor systems converges to mediate female sexual receptiveness or more likely that "THC initiates a signal cascade that promotes the release of dopamine, which then activates dopamine receptors. The signal cascade of dopamine . . . activates the progesterone-mediated behaviour", suggests Mani.

Kelly Morris