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TCD team explains vital gene exchange

DICK AHLSTROM

A Trinity researcher has discovered how bacteria can 'share' genes, a process that speeds the evolution of drug-resistant bacteria

BACTERIA HAVE evolved a way to "share" genes, a process that is central to the development of drug-resistant strains including the hospital superbug MRSA.

Scientists at Trinity College Dublin have caught bacteria in the act of gene-transfer using "optical tweezers" and can finally explain how this gene-exchange occurs.

Trinity's Prof Martin Hegner led the work, which involved researchers at Trinity, including post-doctoral fellow Dr Wilfried Grange, and also colleagues in Switzerland and the US.

He and colleagues identified a protein, VirE2, that can exert a powerful physical force to pull a strand of genetic material, DNA, from one cell across into another.

Details of the work were published earlier this year in the important peer-reviewed journal *PLoS Biology*. It helps explain how a trait such as antibiotic resistance can jump between species of bacteria, Hegner explains.

Bacteria can transfer DNA via a process called conjugation. The donor injects DNA into a recipient and this DNA then becomes part of its own genome. "This is something which was already known, but it wasn't known how they do it," he says.

A principal investigator in Trinity's Crann research centre and a professor in the school of physics, Hegner decided to study this phenomenon in a plant/bacterial model, looking in particular at a bacterium called *Agrobacterium tumefaciens*.

The organism infects plants by transferring DNA into their cells, making it a good model for conjugation, Hegner says. The assumption had been that the host was effectively passive in receiving the DNA but this is only partly true, the researchers revealed.

"We found out that the bacteria is producing a protein which it introduces into the plant. This then waits on the plant side of the cell to receive the DNA from the bacteria," he explains. "This was the first time to describe what was going on on the host side of the [cell] membrane."

VirE2 is a protein that binds tightly to DNA and so is central to the conjugation process. It is capable of applying a force to the DNA which compacts it and then pulls it across from one cell into another.

The force is tiny, given the process is occurring at a molecular scale, but is huge given the minute size of the objects involved. A Newton is a measure of force required to give a mass of one kilo an acceleration of one metre per second, per second. The VirE2 protein is exerting a force equal to 60 million millionths of a Newton.

The VirE2 reaction also takes place at a startling speed, pulling across its 150,000 step DNA strand in just one thousandth of a second.

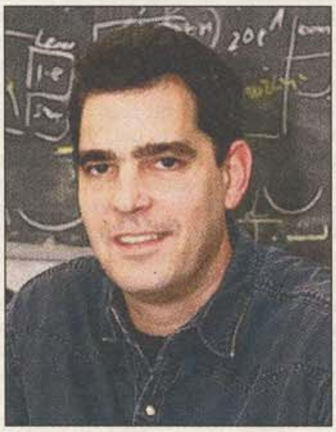
These astounding measurements were achieved using a new device based at the Crann centre, Hegner says. It employs a laser beam focused on a spot which acts like an "optical tweezer" that freezes the molecule in place.

This force can be varied, allowing the device to gauge the force exerted by the protein. The molecule is then free to move away once the beam is switched off. Only certain lasers can be used as optical tweezers, Prof Hegner says. Red and blue lasers are out as they tend to "roast the biological material".

This work is highly significant in that it helps explain how resistance can transfer so readily from organism to organism, he believes. Resistance, which is so disadvantageous to human health, is "definitely" driven by DNA transfer, he says.

Resistance could be inherent in the organism, but if this were so, then a strain with the resistance gene would start as a very small colony and more susceptible to attack by the host's immune system.

"If you spread resistance from one bacterium to another, [the colony] multiplies quickly and is able to break through the immune system," he argues. The organism must move quickly to overwhelm the host or its immune system will destroy the invader. Prof Hegner is the recipient of a Science Foundation Ireland Stokes Professorship that brought him to Ireland last October from the University of Basel. His team now includes five researchers.



Prof Hegner: his team caught bacteria in act of gene-transfer