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Science Editor Dick Ahlstrom e-mail dahlstrom@irish-times.ie

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.

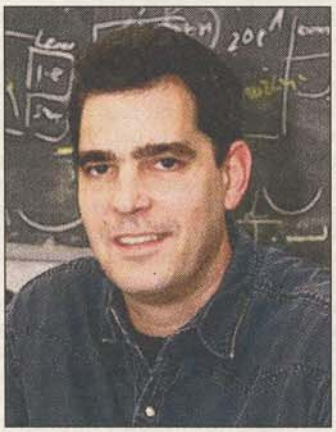
These astounding measurements were achieved using a new device based at the Crann centre, Hegner says. It employs a laser beam focused on a spot which acts like an "optical tweezer" that freezes the molecule in place.

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

Press Release

TCD Researchers Shed Light on Genetic Transfer Between Cells

Dublin, February 25, 2008 – Antibiotic resistance threatens to become a major problem in the next decades, with MRSA already a household name.

Important research led by Trinity College Dublin's Professor Martin Hegner published this week in the internationally peer-reviewed biological science journal *PLoS Biology,* sheds light on the mechanism by which bacteria transfer DNA to other cells, a process which can allow resistance to jump between species of bacteria.

Bacteria transfer DNA to other bacteria via a process called 'conjugation'. One bacterium injects DNA into another, and that DNA can then become part of the recipient's genome, which will be passed on to all clones that come from that cell. This means that a beneficial mutation – such as the ability to digest an antibiotic – that occurs in one cell can be passed on to other unmutated bacteria nearby.

It has always been thought that the donor cell was the important party in this process and that the recipient bacterium was passive; that the DNA was pumped across by the donor. However, the work led by TCD's Professor Martin Hegner, a Principal Investigator at TCD's nanoscience research centre, CRANN, and Professor in the School of Physics, with contributions from colleagues in Ireland, Switzerland and America, shows that the presence of specific proteins in the recipient play a key role in the import process.

The researchers studied a bacterium called *Agrobacterium tumefaciens*, which infects plant cells. As part of the infection process, the bacterium injects DNA into the plant, making it an excellent model of conjugation. Before DNA transfer, the bacterium transports proteins, including the DNA binding protein VirE2, into the plant.

VirE2 then plays a crucial role in DNA transfer. It binds to the beginning of the DNA strand and forces it to assume a tightly organised helical structure, causing the rest of the strand to be pulled into the host cell. The energy for this process all comes from the energy released by VirE2 binding to the DNA, rather then from any external source, or the donor cell.

For further details contact Keelin Murphy, CRANN Education & Outreach Manager,

PLoS Biology is ranked as the most highly cited general biology journal with an impact factor of 15.

CRANN, the Centre for Research on Adaptive Nanostructures and Nanodevices, is Ireland's first purpose built nanoscience research centre, housed in TCD's Naughton Institute. CRANN's mission is to deliver world class research and innovation in nanoscience and nanotechnology, of value both to its industry partners and to Ireland.

Professor Martin Hegner received MSc and PhD Life Science degrees from the Swiss Federal Institute of Technology Zurich in 1989 and 1994. He had post-doctoral appointments at the Institute of Physics University of Basel, Howard Hughes medical research laboratory in Eugene OR, and the University of California, Berkeley. He was appointed to the academic staff at the University of Basel in 1999, where he built up an interdisciplinary biophysics team in the department of Physics. In 2001 he received the *venia docendi* in experimental physics and became a fellow of the new National Center of Competence in Nanoscale Science Research in the University of Basel. In autumn 2007 he moved his research team to Trinity College Dublin to take up a position as Principal Investigator in CRANN, and Professor in the School of Physics.