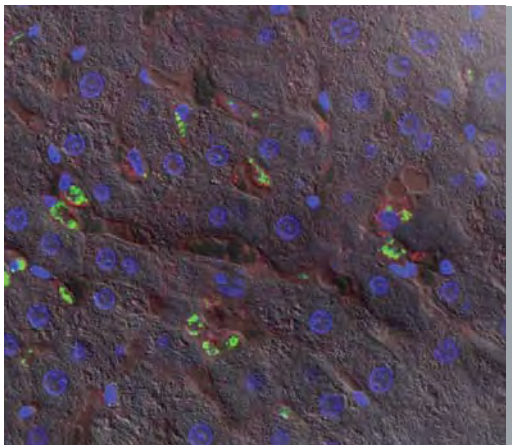
NEW STRATEGIES FOR RNAi DELIVERY

Viral diseases tend to be much more difficult to treat than those caused by bacteria, largely due to the fact that viruses use the person's own cellular machinery to propagate themselves. RNA interference (RNAi) technology has the potential to treat various intractable diseases, not only viral ones but also genetic disorders and cancers. It is able to do this by precisely suppressing the production of specific proteins from the host cell or a pathogen.

Led by Dr Thilak Gunatilake, a multidisciplinary group at CSIRO Clayton laboratories is collaborating with Dr Mark Tizard, Dr Tracey Hinton and Dr Paul Monaghan, at the Australian Animal Health Laboratory (AAHL), Geelong to overcome the major challenge of developing effective delivery vehicles for RNAi therapy. By using confocal and live-cell imaging at the AMMRF Linked Lab at the AAHL Biosecurity Microscopy Facility they are able to track fluorescently labelled delivery vehicles inside cells and whole animals. This enables them to establish the behaviour of capsules within the body and their effectiveness in delivering the RNAi 'payload'. This can be seen in the image where a thick section of liver from a rat that had been treated with green fluorescent capsules shows that they end up in a specific subset of cells.

The team also want to understand the role of various ligands (small bioactive molecules attached to the delivery vehicle) in directing RNAi to specific organs, cells or even sub-cellular targets with a view to developing these new reagents into practical therapeutics.



Confocal micrograph of a thick section of rat liver showing that the green capsules travel specifically to Kupffer cells (red). Nuclei are stained blue and tissue morphology is shown by differential interference contrast microscopy.

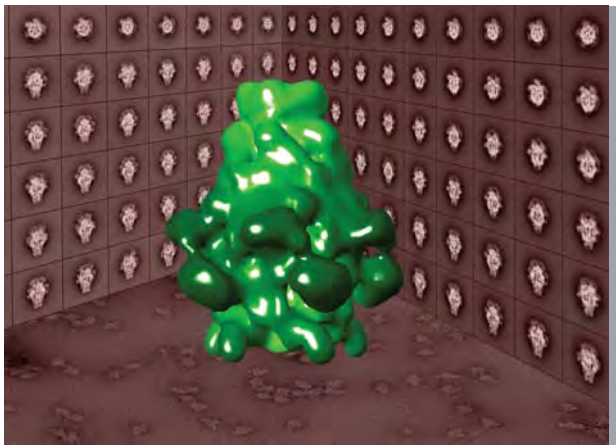
A POTENTIAL NEW BIOINSECTICIDE

The control of harmful insect populations is very important to both the agricultural and horticultural industries. For many years, synthetic insecticides were the most widely used control measures, but, owing to their various side effects, they have now been largely replaced by insecticides of biological origin. These are widely regarded as being more environmentally friendly and safer to humans, wildlife and beneficial insects.

Dr Michael Landsberg and A/Prof. Ben Hankamer are using single-particle analysis on the transmission electron microscope (TEM) in the AMMRF at the University of Queensland to determine the structure of a bacterial protein complex isolated from a native New Zealand grass grub. The protein is currently being investigated for its potential to be deployed as a new bioinsecticide. It is toxic to several insect pests, including a species of moth that has spread worldwide and infests plant crops such as cabbage, broccoli, Brussels sprouts, cauliflower, radish, turnip and mustard seed. It is also effective against the bronze beetle that affects apples and pears. The protein appears to be completely safe and shows no harmful effects towards helpful insects such as honey bees or other beneficial species such as worms.

The protein is an endochitinase and the researchers have identified the areas in the structure responsible for its toxicity. They have developed a hypothesis about how the toxin invades the host and has its effects. This in-depth knowledge could potentially enable the modulation and enhancement of the toxin's actions for maximum effectiveness.

Michael Landsberg et al. *PNAS*, in press



3-D model of the protein structure (green) as determined by single-particle analysis. The 'carpet' shows different views of the protein under the TEM and the 'wallpaper' shows steps in the 3-D reconstruction of the protein's structure from the TEM images.