

New vaccines needed

Monash University's Dr Gareth Forde is working to create the manufacturing technology for a new generation of DNA-based vaccines to treat illnesses including new strains of human flu. Vaccine development is crucial in a world where continuing outbreaks of bird flu have world health authorities worried and calling upon countries to stockpile their generic flu vaccines.

Bird flu is the perfect example of a health threat that can spread swiftly around the world. It is confined to birds and in particular poultry and although humans are infected only by rare intimate contact, it is deadly. About 75 per cent of people who contract bird flu die from it. As long as the strain exists in domestic poultry, there is a strong potential for the virus to turn into a human flu equivalent and spread around the world within a matter of months. In 1918, the Spanish flu had a devastating effect killing more people than World War 1.

The world does not have the capacity to produce enough vaccine if a sudden influenza pandemic were to occur. The other challenge is that influenza viruses changes from year to year so a vaccine which uses a disabled version of the current infectious strains takes too long to develop.

Dr Forde returned to Australia from Cambridge University in October 2005 with the help of a VESKI Fellowship. These were initiated to help talented and outstanding Australian ex-patriots in science ICT and design to return to Victoria. Since then he has worked quickly to commission an experimental scale plant for manufacturing DNA vaccines and Monash University has opened a BEL laboratory.

Dr Forde said that DNA vaccines are inherently safer, more stable, simpler, faster to develop and easier to manufacture. They are not in common use yet because the technology is so new. The first reported use of a DNA vaccine outside an experimental environment was to protect endangered California condors from West Nile virus in 2003. It worked well. DNA therapeutics have a huge potential, however, new industrial methods for mass production and delivery of this unique molecular technology are still being developed.

This is where Dr Forde's work can make an enormous contribution. The new vaccines are made using a particular form of DNA, which is found in self-contained circular units, know as plasmid, outside the normal chromosomal

structure. Plasmid DNA (pDNA) can be produced easily via fermentation and can contain regions for conferring important characteristics like resistance, for example.

Instead of employing disabled disease organisms to jolt the immune system into action, DNA vaccines are tailor made pDNA to induce cells to manufacture protein material to do the same job. Plasmids can be used not just for vaccines, but also for anti-cancer drugs (i.e. to deliver a protein or peptide) or for gene therapy.

Forde said they can be used to deliver a whole new generation of drugs. "They could allow us for instance to make therapeutic use of the information we now have about the human genome."



He explained that the plasmids can be designed from scratch to contain genes for one or many protein products. Control sequences and activity promoters can be added, and the resulting plasmid inserted into a rapidly multiplying bacterium for production. Because the end product is DNA, and does not contain a disabled disease organism, as in many standard vaccines, there is a reduced chance of side effects or triggering an adverse immune response.

Plasmid technology needs several steps to make it more efficient, cost effective and reliable before it can be fitted together in an industrial process and reach its potential.

It needs a cheap reliable method of extracting and purifying plasmid DNA for use on an industrial scale. It also requires a better delivery method to ensure engineered plasmids reach the appropriate cells and are taken up. Safety testing is also a priority to ensure they do not trigger autoimmune reactions.

Dr Forde and his team have been tackling these problems since his appointment to a lectureship in the Department of Chemical Engineering at Monash University in October 2004.

The benefit of this work to the Victorian community is more than medical, as commercial interest in plasmid technology is growing quickly. In gene therapy the number of clinical trials involving plasmid DNA worldwide has doubled since 2000 to 160, about 16 percent of the total number of clinical trials.

There has been an even faster increase in the development of bio-pharmaceuticals which in 2006 will account for 13 percent of the total pharma market (about US \$70 billion).

Dr Forde said that Melbourne is ideally poised to take advantage of this growth and to become a significant player in the industry.

“In this city the life sciences and biotechnology industries have grown organically out of the fantastic research institutions which are so very well established here.”

Dr Forde is interested in developing other types of affinity techniques for industrial processes. In Cambridge, he and his colleagues used special compounds known as zinc finger proteins, to

pluck plasmid DNA out of solution, free from potential contaminants.

He also wants to explore the use of specially engineered nano-particles, to have specific size and characteristics to help the uptake of biopharmaceuticals by cells. Better delivery methods to cells, such as this could decrease the required dosages, and reduce the cost per dose.

Dr Forde hopes that the technologies he and his colleagues are developing will lead to a new generation of cheaper, safer and more robust vaccines. He also hopes that the technology will make it easier to establish production facilities in countries where vaccines are needed most.

Expatriates a valuable resource

Gareth Forde's recruitment is part of a concerted effort to identify leading Australian expatriate scientists and bring them home.

In Victoria, that effort is being driven by VESKI (Victorian Endowment for Science, Knowledge and Innovation). This is an initiative to identify outstanding individuals and bring them to Victoria for the benefit of the Australian economy.

Fellowships are worth up to A\$100,000 a year for up to five years with matched funding from a host organisation.

VESKI's first catch was leading polymer chemist, Professor Andrew Holmes, who returned from Cambridge University in October 2004 to set up his research team at the Bio21 Institute at the University of Melbourne. His major research interests are in molecule design – from light emitting plastics, to solar panels, to drug design.

Professor Marcus Pandy, from the University of Texas, took up the Chair of Mechanical and Biomedical Engineering at the University of Melbourne. He is developing new tools to understand, prevent, and treat joint disease.

Dr Gareth Forde has relocated from Cambridge University to join the Monash University Department of Chemical Engineering. He is working on the manufacturing technology needed for a new generation of DNA-based vaccines and gene therapy products.

For further information visit www.veski.org.au.