

THE CUTTING EDGE

Giving vaccines *a shot* in the arm

Getting the best out of a potential lifesaver.

THE World Health Organisation ranks vaccines alongside clean water as the greatest weapons against global disease.

In Australia, countless lives have been saved by the routine vaccination of the population. Diseases like diphtheria and polio have virtually been eradicated, while other common childhood diseases of the past, including Hib, mumps and rubella, have been dramatically reduced.

An explosion in knowledge about diseases and how the body responds to them over the last two decades has led scientists into a new era of vaccine development.

They are working on a new generation of more potent, longer lasting vaccines designed to wipe out killers like malaria, HIV and cancer, halt flu pandemics and provide even better protection against diseases for which vaccines already exist.

GlaxoSmithKline's pursuit of new and better vaccines focuses on the use of new adjuvant systems, substances added to a vaccine to boost the body's immune response.

GSK Vaccine Medical Director Dr Su-Peung Ng says GSK has been developing a range of adjuvant systems which aim to tailor the type of immune response needed to achieve optimum protection against a particular infection.

Dr Ng says adjuvants are key components in the development of GSK's pipeline vaccines such as malaria and pre-pandemic influenza vaccines.

She says one of the biggest challenges with a pre-pandemic flu vaccine is being able to provide protection against an unknown strain of the virus.

"In a pandemic situation it would be a new strain, which the whole world would

not have previously encountered and would have no immunity against," she says.

"Therefore its effects would be very devastating."

The H5N1 bird flu virus almost always infects people in contact with birds, however, if the virus mutated so that it could easily be passed among humans we could face a pandemic. This is the strain that the World Health Organization considers the most likely threat.

"GSK and other vaccine companies are aiming to develop pre-pandemic vaccines that would be based on the prevailing avian flu strain H5N1," she says.

"And with the use of adjuvants in this setting, the objective is first of all to be able to use less antigen than conventional flu vaccines and secondly to develop vaccines that would provide cross protection against a different but related strain of virus to the antigen in the vaccine itself."

Associate Professor Tilman Ruff, from the University of Melbourne's Nossal Institute for Global Health, says stretching limited vaccine supplies will be vital in a pandemic.

"There is a huge problem with the global production and supply capacity for flu vaccine," he says.

"We can make a couple of hundred million doses a year but there are 6.5 billion of us on the planet and if there's a big pandemic ideally there would be enough doses for everybody.

"But that's not going to happen unless we can be smarter about stretching the current production capacity much further.

What is an adjuvant?

Adjuvants, from the Latin word *adjuvare* meaning 'to help', are compounds used to enhance a vaccine's ability to elicit a strong, durable, protective immune response making them more effective.

Conventional vaccine adjuvants were mainly based on aluminium salts. However, aluminium adjuvants do not always generate the optimal immune response, and they are often limited in their immunogenic strength.

Recent innovations in molecular

science have led to the discovery of a new generation of more powerful adjuvants, opening the door to the development of vaccines for very difficult disease targets.

The most frequently reported side effects of vaccines with adjuvant systems are local symptoms such as redness, swelling and arm pain.

People have also reported headache, fatigue and gastro with some vaccines with adjuvant systems. These are generally mild to moderate and temporary.



GSK Vaccine Medical Director Dr Su-Peung Ng.

“What adjuvants enable us to do for a number of vaccines is to actually get away with using a lot less of the antigen because it becomes that much more effective at stimulating the immune response.”

GSK has ongoing clinical trials of its pre-pandemic flu vaccine and is awaiting regulatory approval for its use in Australia and Europe. CO₂

Dr Ng says development of the malaria vaccine is also progressing well.

Studies to date have demonstrated promising results, but further clinical investigation is still required. These studies have been conducted through an international public-private collaboration, including African research institutions in five countries, GSK and the PATH Malaria Vaccine Initiative.

Associate Prof Tilman Ruff, who is also medical advisor to the International Department of Australian Red Cross and technical advisor on Pacific Island immunisation programs to the Australian Government aid program AusAID and UNICEF, says the GSK vaccine could be the first in the world for malaria, a disease which kills more than a million people every year, mostly children in Africa.

While cutting-edge novel adjuvant systems are used in the malaria and pre-pandemic flu vaccines, aluminium salts remain the most common form of adjuvant.

Dr Ng says aluminium salts have been used for about 80 years, including in a number of GSK vaccines.

She says that while not fully understood,

aluminium salts are thought to work by creating a “depot effect”, signaling to the body’s white blood cells to rally around the injection site. The influx of cells then more effectively carries the antigen to the rest of the immune system.

Dr Ng says newer adjuvant systems, range from purely synthetic to biological substances such as oil and water emulsions, vitamin E, detoxified proteins from bacteria, and natural plant derivatives.

Associate Prof Ruff says scientists are investigating other ways to enhance vaccine effectiveness, including the use of bacterial DNA or adding messenger molecules which help switch on the immune system.

Dr Ng says GSK believes adjuvant systems are key to future development of vaccines against challenging diseases with the objective of offering optimal protection while minimising side effects.

The technology has also paved the way for a new style of therapeutic vaccines which could be used in the treatment, rather than prevention, of diseases like cancer.

Studies are already investigating possible vaccines for prostate cancer, breast cancer, malignant melanoma and lung cancer which could one day be used to complement traditional treatments like chemotherapy and surgery.

“The concept is that if you can teach the body’s immune system to recognise cancer as a foreign agent, then you hopefully teach the immune response to fight more effectively the cancer cells themselves,” Dr Ng says. •

GlaxoSmithKline’s history of vaccine development dates back to the 1940s.

More than 30 different vaccines are now part of the GSK stable, protecting millions of children, adolescents and adults worldwide.

Supplying a quarter of the world’s vaccines, GSK distributes 35 doses of vaccine every second.

Many are combination vaccines, providing protection against up to six diseases at a time.

And with 25 vaccines in clinical development at the end of last year, GSK hopes to bring another five vaccines to the world in the next five years.

GSK credits much of its pipeline success to the decision 15 years ago to develop a new generation of more effective vaccines using adjuvants.



An Australian child born today can expect to be immunised against at least 13 different diseases in at least 30 vaccine doses in the first two years of life.

The National Immunisation Program Schedule includes vaccines for hepatitis B, diphtheria, tetanus, whooping cough, haemophilus influenzae or Hib, polio, pneumococcal disease, rotavirus, measles, mumps, German measles, meningococcal C, chickenpox and influenza from birth into old age.

In addition, females aged 12 to 26 will be vaccinated against human papillomavirus and high risk Aboriginal and Torres Strait Islander children will be protected against hepatitis A.

The latest Vaccine Preventable Diseases and Vaccination Coverage in Australia report shows 90 per cent of children born in December 2004 had received all vaccinations due by the age of one and 92.1 per cent were fully covered by the age of two, taking coverage targets close to their highest achievable levels in children.