AN AUDIENCE WITH…

Rino Rappuoli

Global Head of Vaccines Research for Novartis Vaccines & Diagnostics. Rino Rappuoli is Global Head of Vaccines Research at Novartis Vaccines & Diagnostics based in Siena, Italy. He is co-founder of the field of cellular microbiology, a discipline that merged cell biology and microbiology, and is member of the US National Academy of Sciences (NAS) and of the European Molecular Biology Organization (EMBO). In 2005, he was awarded the Gold Medal by the President of the Italian Republic for his contributions to public healthcare.

The number of companies involved in vaccine development had been declining until recently. What were the underlying factors?
Until the 1970s, vaccine production was mainly supported by governments and was described in textbooks as having to be cheap, safe and efficacious. As soon as production became private, the word 'cheap' became the enemy of vaccination and the number of vaccine companies decreased markedly. When I was Chief Scientific Officer of Chiron, portfolio decisions were always on the side of biopharmaceuticals simply because there was more money. Because people will pay a lot when they are sick, modern society drives companies to invest only in illness (*Science* 297, 937–939; 2002). Instead, if they could think about the real value of vaccines in preventing diseases and the overall pharmacoeconomic cost-savings, we could have a healthy society.

What factors have influenced the recent resurgence of interest among biopharma companies in vaccine development?
Both scientific and societal factors have led to a resurgence in vaccines research and development since 2002. Following September 11, the US became aware of their exposure to bioterrorism because they no longer knew how to make vaccines. Another thing was avian flu — people realized that they were not prepared, and vaccines became part of the presidential campaign when Chiron failed to provide the US with the influenza vaccine in 2004. Scientific and technological advances are aiding the development of new generations of vaccines, such as a universal vaccine against meningitis B. Also, a pneumococcal vaccine (Prevnar; Wyeth) became a blockbuster, and with papilloma virus vaccines set to be potential blockbusters, pharma have now recognized that vaccines are worth investing in.

How has the vaccine industry responded to the challenges posed by avian influenza?
There are no more technical challenges. For example, we have developed a subunit H5N1 influenza vaccine licensed to be used in case of emergency, which is under late-stage evaluation by the EMEA as a pre-pandemic vaccine. One of the technical questions we had was: which strain do you need to use to make the vaccine? Today, my answer is that it doesn't matter because the vaccine made with the existing virus, when administered with the adjuvant MF59, will induce antibodies that will interact with a mutated virus. As vaccine developers, we have done our job by putting a tool into the hands of the policy makers. My recommendation would be to start vaccinating people and make sure that the pandemic never comes.

For diseases where there isn't sufficient market incentive to develop vaccines commercially, what approaches might translate the basic research into vaccine candidates?
A recent example of how you can tackle this problem was a meningococcus B epidemic in New Zealand in the 1990s. The Ministry of Health approached me at a meeting in 2000. Until then, nobody had told them that the technical solution was available — the problem was simply economic. The government gave NZ$200 million for the development of the vaccine and by 2004 we vaccinated every person aged 2 months to 18 years. By 2005 the epidemic was over — this is one of the things that I am most proud of.

For developing countries, through organizations such as the Bill and Melinda Gates Foundation and the Wellcome Trust, the money is becoming available for the first time. 'Advanced market commitments' have been created in which the G8 will give US$1–2 billion dollars to buy a vaccine for a neglected disease. However, the money cannot buy a vaccine unless it is developed and the technology required is present only in companies that already produce vaccines. The people upstream — academia, biotech — know the science, but translating it into a product stalls because the expertise is not there. To tackle this problem, we have created a new institute, to be known as the Novartis Vaccine Institute for Global Health, dedicated to the translation of research into vaccines that do not have a commercial interest.

Do you think it will ever be possible to create a vaccine for HIV?
I believe so because I am optimistic, but we cannot do it with the tools we have now. We are on the verge of new technologies that will help us to design novel adjuvants and to engineer antigens to stimulate a proper immune response. For example, recently, a paper described the structure of a conserved epitope of GP120 present on every single HIV virus (*Nature* 445, 732–737; 2007). We don't know how to tell the immune system to identify that epitope, but until recently, we had no idea of the epitope structure and now we do, so we are getting there.

What is your vision for the future of vaccine development?
My vision is that with all the technological breakthroughs — genomics, adjuvant technology, being able to engineer the immune system — we will be in a better position to achieve a key milestone for vaccines for infectious diseases: to begin eliminating meningitis by 2010. We have a vaccine against four of the subtypes A, C, Y and W in Phase III development. For the fifth strain, subtype B, we took a genomic approach to discover new antigens, and the vaccine is now in Phase II trials.

Apart from eliminating infectious diseases, the next big thing is cancer. I believe that by eliminating cancer-causing agents such as human papilloma virus and *Helicobacter pylori*, the cancer rate will decrease. Outside of this area, into metabolic diseases and therapeutic vaccines, I see an explosion of what vaccines will be doing in the future.