

A mountain higher than Everest



Marshall Lightowlers

University of Melbourne
Veterinary Clinical Centre
250 Princes Highway
Werribee, VIC 3030
Tel (03) 9731 2284
Fax (03) 9731 2366
Email marshall@unimelb.edu.au

Challenging scientific hurdles are just the beginning for those who work on neglected tropical diseases. The really big problem is the reason the diseases are neglected in the first place: they are limited mostly to very poor people and hence there are no commercial markets for new treatments.

At our University of Melbourne laboratories we embarked in the 1980s on a quest to develop vaccines to help prevent parasitic diseases known as neurocysticercosis and hydatid disease. These infections are caused by the larval stages of cestode parasites. Both diseases are limited mostly to the poorest people in the world, so there is little or no commercial interest in them, notwithstanding their causing a great deal of morbidity and mortality. From the outset there seemed no prospect of securing the investment required to develop human vaccines for these diseases because they are not significant First World problems. However, livestock animals are critically involved in transmission of both hydatid disease (mostly sheep and goats) and neurocysticercosis (pigs) and this offers a relatively inexpensive alternative. That is, developing vaccines for livestock that would remove the source of parasite transmission and indirectly prevent new human infections.

When embarking on our vaccine development plans, there had never been any success in vaccinating against any parasitic disease of man or animals using any defined antigen, despite many man-years of effort towards this end in relation to numerous medically and economically important parasites. Hence the challenge was daunting. With luck and some good judgement, the program hit pay-dirt. We discovered recombinant proteins that could prevent infection with a parasite of sheep¹ that was closely related to the parasites which cause hydatid disease and neurocysticercosis. This sheep vaccine was the first recombinant vaccine against any parasite; it had been acclaimed a milestone in the history of parasitology². Using the knowledge gained in producing this first vaccine, we were subsequently able to develop an effective vaccine for livestock animals that transmit hydatid disease³ and develop a vaccine for pigs which can prevent infection with the parasite that causes neurocysticercosis⁴. Last year we published



the results of a field trial of the pig vaccine in which the vaccine achieved the complete elimination of parasite transmission by the animals involved in the trial⁵.

If we were to amortise the development costs in 2011 dollars, and include only the research done at or associated with the University of Melbourne leading to the cysticercosis and hydatid vaccines, a guesstimate would be in the order of \$15–20 million; a significant sum, but trivial is the context of investments in other yet-to-be-successful (if ever) projects. Implementation costs for an animal vaccine are relatively small, although they will still be challenging in those areas where livestock currently receive no vaccinations whatsoever. Nevertheless, our experience to date has been that the cost of goods for the vaccines is in the order of a few cents per dose and, hence, they should represent good value for money as disease control measures.

We are confident we have novel, inexpensive disease control tools that could reduce or eliminate new cases of hydatid disease and neurocysticercosis in many endemic countries^{6,7}. All we need to do is to have the vaccines manufactured on a commercial scale, have them registered for general use and have them used in the areas needed. Imagining our original scientific hurdle – developing a recombinant vaccine against a parasite – as Mount Everest, we seem to have ascended the mountain only to look beyond to an even higher peak, with its summit shrouded in cloud! The challenges involved in implementing much-needed disease control measures for infections that have no First World market, are enormous. However, with the support of philanthropic agencies, including the Wellcome Trust, the Gates Foundation and the Global Alliance for Livestock Veterinary Medicines, and the continued research funding support from the NHMRC, we are making progress towards implementation of the vaccines and, hopefully, achieving a demonstrable decline in the incidence of neurocysticercosis and hydatid disease. These are not to be the most important medical issues facing the countries in which the parasites are endemic, but at least we may be able to remove one or two of the debilitating and potentially lethal infections from the long list of neglected tropical diseases challenging poor people in developing countries.

References

1. Johnson, K.S. *et al.* (1989) Vaccination against ovine cysticercosis using a defined recombinant antigen. *Nature* 338, 585–587.
2. Cox, F.E.G. (1993) Milestones in parasitology. *Parasitol. Today* 9, 347–348
3. Lightowlers, M.W. *et al.* (1996) Vaccination against hydatidosis using a defined recombinant antigen. *Parasite Immunol.* 18, 457–462.
4. Flisser, A. *et al.* (2004) Induction of protection against porcine cysticercosis by vaccination with recombinant oncosphere antigens. *Infect. Immun.* 72, 5292–5297.
5. Assana, E. *et al.* (2010) Elimination of *Taenia solium* transmission to pigs in a field trial of the TSOL18 vaccine in Cameroon. *Int. J. Parasitol.* 40, 515–519.
6. Lightowlers, M.W. (2010) Eradication of *Taenia solium* cysticercosis: a role for vaccination of pigs. *Int. J. Parasitol.* 40, 1183–1192.
7. Lightowlers, M.W. (2006) Vaccines against cysticercosis and hydatidosis: foundations in taeniid cestode immunology. *Parasitol. Int.* 55 Suppl, S39–43.

Biography

Marshall Lightowlers completed a PhD with Neville Stanley and Harry Waring at UWA, followed by a postdoctoral stint at the IMVS in Adelaide. He joined Mike Rickard as a postdoc at the University of Melbourne in 1981 to work on immunity to taeniid cestode parasites. In 1991 he was appointed an NHMRC Fellow and has remained with the NHMRC fellowship scheme to this day. In July 2011, Professor Lightowlers was appointed Melbourne Laureate Professor at the University of Melbourne. He is based at the university's Faculty of Veterinary Science.