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Genetically modified viruses – international issues

> Science cannot resolve moral conflicts, but it can help to more accurately frame the debates about those conflicts.
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> Heinz Pagels, *The Dreams of Reason*, 1988

'Viral-vectored immuno-contraception' is a cumbersome though useful technological term. It encapsulates the idea that a virus can be genetically modified to produce proteins from the host animal's eggs or sperm. This means that when infection occurs, antibodies are produced not only against the virus but also against the host's own reproductive gametes. These antibodies subsequently cause sterility in the target host by inhibiting sperm production or destroying ova.

Dr Hugh Tyndale-Biscoe first developed this idea in discussions with Dr Steve Robbins in CSIRO and it was proposed as a potentially new and humane way of controlling pest animals (Tyndale-Biscoe 1994). The idea attracted major supporters, the result being that CSIRO, state government organisations and other Australian partners invested heavily in research to see whether the idea could be applied to pests such as foxes, house mice and rabbits. Much of this exploratory work went on at the same time as research into RHD.

In the case of rabbits it was proposed to use an attenuated myxoma virus as the vector, essentially one that spread readily but didn't cause high rabbit mortality, while egg-membrane, or zona pellucida, proteins that form the outer coat on the rabbit's eggs were the reproductive proteins selected as the targets. Given the rabbit's legendary fecundity, a genetically modified virus that sterilised rabbits would be a major achievement. Furthermore, as myxoma virus only infects rabbits, it was a control method that would be rabbit-specific and would not affect any other species.

Significant progress was made in developing the concept by over a dozen different scientists in the research group (Kerr *et al.* 1999; Mackenzie *et al.* 2006), but it was Dr Peter Kerr and Barbara van Leeuwen and their team who summed up work on the final recombinant virus. A suitable myxoma virus, called Uriarra/2–53/1, had been selected as the vector because it caused low mortality among laboratory rabbits. Several recombinant viruses were subsequently made from it to see which of three zona pellucida proteins might be most useful for inducing antibodies that would reduce the fertility of rabbits. One of these proteins, called rabbit zona pellucida C (ZPC), stood out as being more effective than the others. This recombinant virus was additionally furnished with the capability of producing interleukin-4, a protein molecule normally secreted by cells of the immune system to enhance the immune response. Finally, a promoter was inserted at an appropriate point in the virus genome so that the virus expressed these products at the right time and in sufficient quantities to ensure the strongest possible immune response. The recombinant virus, incorporating ZPC with interleukin-4 controlled by a p28 late promoter, made all female test rabbits sterile. They failed to