

CHARACTERISATION OF THE INFERTILITY EFFECT INDUCED BY A RECOMBINANT MURINE CYTOMEGALOVIRUS EXPRESSING MURINE ZONA PELLUCIDA 3

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A recombinant mouse virus, murine cytomegalovirus, that has been engineered to encode the fertility antigen murine zona pellucida 3 (mZP3), is being developed for fertility control in mice. A single inoculation of the recombinant virus induces complete infertility in female BALB/c mice which persists for the breeding life of the animal. The extent of this autoimmune response was unexpected especially as the incorporation of mZP3 appears to have immunologically attenuated the growth of the recombinant virus. The histological features of the infection are an initial depletion in tertiary follicles by 21 days post inoculation followed by a progressive depletion of primordial follicles, leading to an almost complete absence of follicles by 150 days post-infection. High titre, long lasting, zona pellucida-specific antibody is present in infertile BALB/c mice although infertility has not been linked with either a critical titre or a dominant immunoglobulin isotype. However, our evidence suggests that anti-ZP3 antibody plays a primary role in infertility since antibodies are detected *in vivo* bound to the zona pellucida of ovaries from recombinant virus-infected mice, and passively transferred antibody from infected animals induces infertility in the absence of recombinant virus. In addition, an experiment in which immunoglobulin-deficient mice remained fertile after inoculation with the recombinant virus indicates that antibody is crucial for the immunocontraceptive effect to occur. Other immune mechanisms are also being explored.