

Characterization of the immune response generated in the placenta of cattle experimentally infected with *Neospora caninum* in early gestation

Stephen Maley¹, David Buxton, Colin Macaldowie, Ian Anderson, Stephen Wright, Paul Bartley, Irma Esteban-Redondo, Clare Hamilton², Anne Storset³ and Elisabeth Innes

¹Moredun Research Institute, Pentlands Science Park, Bush Loan, Edinburgh, EH26 0PZ, Scotland

²Department of Zoology, Trinity College, Dublin 2, Ireland

³Department of Food Safety and Infection Biology, The Norwegian School of Veterinary Science, Oslo 0033, Norway

Abstract

The placenta and foetuses of cattle injected either intravenously (iv) or subcutaneously (sc) at 90 days gestation (dg) with Nc1 tachyzoites were serially examined at 14, 28, 42 and 56 days post inoculation (dpi). Inoculation of parasite by either route led to foetal death and histopathological changes in the placenta and foetuses, with iv injection resulting in more severe clinical outcome and histopathology (compared with sc injection). To help determine why infection with *N. caninum* may result in foetal death the objective of this study was to identify, using immunohistochemistry, immune cells expressing CD3, CD4, CD8, gamma delta ($\gamma\delta$) TCR and NK cell antigens and, using in situ hybridisation, cells expressing mRNA for interferon- γ (IFN- γ) in the placenta of these cattle.

Pathological changes in the placenta consisted of necrosis of the foetal villi and necrosis and inflammation in the adjacent areas of the maternal septum and inflammation at the base of the maternal carun-

cle. The inflammatory infiltrate, in the placentae of animals that contained dead foetuses, consisted largely of CD3⁺ lymphocytes, CD4⁺ cells, NK⁺ cells and $\gamma\delta$ TCR⁺ cells, with CD8⁺ cells present to a lesser extent. mRNA for IFN- γ was identified in cells that infiltrated the maternal septa in one animal at 14 dpi and another at 28 dpi. Placentae from animals injected s/c, but containing live foetuses, were found to have distributions of immune cells similar to uninfected controls and no evidence of IFN- γ production. While direct tissue destruction by the parasite may play a role in causing foetal death, it may also be that in an attempt to control the parasite, neospora infection acquired in early gestation triggers the dam to generate a T helper 1 type immune response at the materno-foetal interface, resulting in recruitment of T helper cells and cytotoxic T cells, and production of IFN- γ . Whilst this immune response would be effective at eliminating the parasite it may, at the same time, be incompatible with foetal survival.