

Migratory Cell Subsets in the Pathogenesis of Transmissible Spongiform Encephalopathies

Although transmissible spongiform encephalopathies (TSEs) have been recognized as species-specific diseases, the appearance of cross-species infection of cattle and humans in the early 1990's has illustrated the potential danger of these agents as zoonotic agents. The potential effect of BSE on the beef industry can be seen in the severe shift in European eating habits following the outbreak of "Mad Cow Disease" in Britain. The pathogenic agent of the TSEs has been established to be a pathogenic alteration of normal host proteins, the so-called prions. Nonetheless, relatively little is known regarding the pathogenesis or host response to prion infection. It now appears that the pathogenic prion protein is an uncommonly stable form of a normal host protein, capable of being absorbed through the intestinal lumen and somehow transported to secondary lymphoid tissue, and eventually the nervous system. Intriguingly, immune cells have been demonstrated to be involved in the spread of the prion protein in infected individuals, including B cells and the specialized follicular dendritic cells. Intriguingly, FDCs do not appear to host the prion protein in cattle, as opposed to other species. Using a panel of monoclonal antibodies we have raised against follicular dendritic cells, we will define both normal and prion-affected FDCs in sheep and cattle. Furthermore, we will analyze the migratory potential of prion-affected and prion-unaffected leukocytes through direct cell labeling and tracking techniques. In the simplest form, this data could be applied to assist in the development of a blood-based screening test for prion infection in food animals, and would lead to a greater understanding of the pathogenesis of TSEs. This project is being done in conjunction with Dr. Juergen Richt of the USDA-Animal Disease Research Service in Ames, IA.