

Peripheral PrPSc accumulation pattern in sheep Scrapie

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Objective: To determine the temporal and cellular accumulation pattern of PrPSc in natural clinical and preclinical Scrapie.

Material and methods: Two flocks with a total of 80 sheep were analyzed for Prnp genotype and examined for PrPSc accumulation in the CNS and at various potential accumulation sites (CNS and non-CNS) by immunohistochemistry using monoclonal antibodies. Cellular specificity of PrPSc deposition was demonstrated by dual immunohistochemistry in lymphoid and intestinal tissues.

Results: None of 19 sheep younger than 12 months had PrPSc deposits in any tissue. Of 61 sheep older than one year, 13 had PrPSc deposits. Nine had deposits at sites within and outside of the CNS. Four had deposits restricted to non-CNS sites. All 13 animals with PrPSc deposits had involvement of the intestine with accumulation in gut associated lymphoid tissue (GALT) and the intestinal nervous supply. Other accumulation sites included lymphoid tissues unrelated to the gastrointestinal tract and placenta. PrPSc was not detected in bone marrow or mammary gland. PrPSc occurred only in sheep of Prnp genotype 136AA 171QQ.

PrPSc colocalized predominantly with follicular dendritic cells, peripheral neurons including their neurites and rare macrophages not confined to the germinal centers of lymphoid follicles

Conclusion: Results are consistent with experimental models of Scrapie and confirm early involvement of the intestinal tract with amplification of PrPSc in specific cells of the GALT, regional lymph nodes and the PNS during preclinical disease. The data provide a rationale to study specific immune cells (follicular dendritic cells) and their interactions with the peripheral nervous system in Scrapie pathogenesis.