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UNREAVELING THE KEY PATHOGENIC MECHANISMS IN A MARMOSET MODEL OF MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is a progressive neurological disease caused by a focussed autoimmune attack on the human central nervous system. The target of the attack is the protective myelin sheaths of neuro/axonal complexes in grey and white matter. A major question in MS research is the nature and specificity of the autoimmune attack and the mechanism(s) by which these are induced. The common marmoset provides a unique experimental autoimmune encephalomyelitis (EAE) model for this research, which combines remarkable clinical and pathological similarity to MS, with close genetic and immunological proximity to humans. By successive refinement of the disease induction protocol we were able to identify the core autoimmune principle, being the activation of natural-killer type cytotoxic T-lymphocytes responding to a 23-mer peptide of myelin/oligodendrocyte glycoprotein (MOG34-56). The *in vivo* activation requirements of MOG34-56 specific T-cells in the naïve repertoire, the fine specificity for a mimicry peptide shared with the UL86 antigen of human cytomegalovirus (CMV) and the phenotype of ex vivo activated cell lines suggest that these may originate from the memory pool of CMV induced memory T-cells. Once activated in vivo they can find their way into the CNS and cause massive demyelination independent of autoantibodies. The underlying mechanism is possibly by cytolysis of myelin/oligodendrocyte complexes exposing peptide in the context of the MHC class Ib specificity Caja-E.

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