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REVERSAL OF CNS AUTOIMMUNITY BY INDUCTION OF ORAL TOLERANCE TO BRAIN ANTIGENS MEDIATED BY ANTIGEN PRESENTING CELLS OF THE LAMINA PROPRIA

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The phenomenon of oral tolerance is important for inducing non-reactivity to food borne antigens and commensal organisms by the immune system. In this study we have devised a method to induce tolerance to an auto-antigen, myelin oligodendrocyte glycoprotein (MOG), by oral administration of a chimeric immunoglobulin, Ig-MOG. Oral treatments with Ig-MOG ameliorated experimental autoimmune encephalomyelitis (EAE), an animal model of human multiple sclerosis (MS). Disease suppression was characterized by the reduction of pro-inflammatory cytokines and reduced T cell infiltration into the CNS. Intriguingly, Ig-MOG treatment led to a loss of T cell activation markers exclusively in the lamina propria, suggesting that lamina propria antigen presenting cells (LP APC) may be responsible for the induction of oral tolerance. Lamina propria APCs were unable to stimulate T cells with Ig-MOG, despite their ability to process and present whole proteins and to stimulate with MOG peptide. Upon oral Ig-MOG treatment, LP APCs acquired a “tolerogenic” phenotype, as Ig-MOG fed LP APCs lost their ability to stimulate T cells with MOG peptide and were able to transfer tolerance to naïve mice induced for MOG EAE. Transfer of tolerance by LP APCs was dependent upon antigen specific APC-T cell contact in the gut, and led to a “global tolerance” as Ig-MOG fed LP APCs were subsequently unable to stimulate T cells with diverse specificities. In conclusion, this study provides a novel mechanism of oral tolerance mediated by LP APCs which can be utilized to induce tolerance to auto-antigens and reverse autoimmunity.