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Novel everolimus-loaded nanocarriers for topical treatment of murine experimental autoimmune uveoretinitis (EAU).

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Abstract

In the present study, therapeutic effect of topically applied everolimus (EV)-loaded methoxy-poly(ethylene-glycol)-hexyl substituted poly (lactic acid) (mPEGhexPLA) nanocarriers on experimental autoimmune uveoretinitis (EAU) were investigated. EAU was induced in B10.RIII mice via immunization with human interphotoreceptor retinoid-binding protein peptide 161-180 (hIRBPp161-180) in complete Freund's adjuvant. Everolimus-loaded mPEGhexPLA (EV/mPEGhexPLA) nanocarriers were prepared by using a solvent evaporation method. On days 12-21 postimmunization (p.i.), the right eyes were treated five times daily either with 10 μl of 0.5% everolimus formulation or PBS (control). The EAU score of the eyes was determined histologically. On day 21 p.i., the peripheral immune responses were measured in serum, cervical lymph nodes (LN), and spleens via hIRBPp161-180-specific serum antibodies, cytokine secretion (ELISA), lymphocyte proliferation, and FoxP3+ regulatory T cells (Treg; flow cytometry). Compared to the PBS-treated mice, unilateral topical everolimus treatment significantly reduced EAU severity in both eyes ($p < .05$). The treatment reduced the antigen (Ag)-specific hIRBPp161-180-induced proliferation ($p < .05$), IL-2, IL-17, and IFN-γ secretion from cells isolated from the left and right cervical LN ($p < .05$). Under everolimus treatment, IL-10 secretion and $CD4^+CD25^+FoxP3^+$ Treg frequency from cervical LN were enhanced. The proliferative response and cytokine secretion as well as the frequency of splenic Treg were almost unchanged. Topical administration of an everolimus formulation improved EAU in both eyes. The effect might also be related to systemic immunosuppressive effects, as several systemic cellular immune responses were influenced.