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Development of a recombinant immunotoxin for the immunotherapy of autoreactive lymphocytes expressing MOG-specific BCRs

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Abstract

© 2016 Springer Science+Business Media DordrechtObjective: Myelin oligodendrocyte glycoprotein (MOG) is one of the major autoantigens in multiple sclerosis (MS), therefore selective depletion of autoreactive lymphocytes exposing MOG-specific B cell receptors (BCRs) would be beneficial in terms of MS treatment. Results: Using *E. coli* we generated an efficient protocol for the purification of the recombinant immunotoxin DT-MOG composed of the extracellular Ig-like domain of MOG fused in frame with the catalytic and translocation subunits of diphtheria toxin (DT, *Corynebacterium diphtheriae*) under native conditions with a final yield of 1.5 mg per liter of culture medium. Recombinant DT-MOG was recognized *in vitro* by MOG-reactive antibodies and has catalytic activity comparable with wild-type DT. Conclusion: Enhanced pharmacokinetics (mean residence time in the bloodstream of 61 min) and minimized diminished nonspecific toxicity (LD50 = 1.76 mg/kg) of the DT-MOG makes it a potential candidate for the immunotherapy of MS.

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Keywords

Diphtheria toxin, Immunotoxin, Myelin oligodendrocyte glycoprotein, Prokaryotic expression