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

Stepanov A., Belyy A., Kasheverov I., Rybinets A., Dronina M., Dyachenko I., Murashev A., Knorre V., Sakharov D., Ponomarenko N., Tsetlin V., Tonevitsky A., Deyev S., Belogurov A., Gabibov A.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2016, Springer Science+Business Media Dordrecht.Objective: 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