CNS-targeted, microglial cell-mediated viral transfer of interleukin-10 during experimental Multiple Sclerosis

Derks S, Mercier D, Verhaagen J*, Drukarch B, Van Dam A-M
Research Institute Neurosciences VU, Dept Medical Pharmacology, VUmc, Amsterdam, *Netherlands Institute for Brain Research, Amsterdam

Multiple Sclerosis (MS) is a chronic, inflammatory disease of the central nervous system (CNS). In addition to the infiltration of immune cells, pro-inflammatory mediators (e.g. cytokines) are produced in or near lesions in the CNS. These inflammatory mediators contribute to the neuropathology of MS. Also anti-inflammatory cytokines, in particular interleukin-10 (IL-10), can be produced within the CNS and counteract the pro-inflammatory response. During chronic-relapsing experimental autoimmune encephalomyelitis (cr-EAE), an animal model for relapsing-remitting MS, only low levels of IL-10 are detected within the CNS which may explain the chronicity of the disease. Moreover, exogenous administration of IL-10 reduces the clinical symptoms of EAE (Cua et. al. 2001). However, there are two major problems facing the possible use of IL-10 as a therapeutic agent, 1) it does not easily pass the blood-brain barrier due to it's size; 2) peripheral treatment may induce unwanted side-effects in immune system function. Therefore, we hypothesize that the best way to manipulate chronic, inflammatory processes in the CNS during cr-EAE is local CNS treatment by non-invasive CNS-targeted, cell-mediated viral transfer of IL-10.
To this end, microglial cells (which are known to home to the brain; Imai et. al. 1997) infected with lentiviral vectors expressing rat IL-10 will be injected into the bloodstream of rats suffering from cr-EAE.
Currently, we aim to differentiate rat macrophages (NR8383) into microglial cells by culturing them with astrocyte-conditioned medium. In addition, we culture primary rat microglial cells. Both will be infected with lentivirus expressing rat IL-10.
Our poster presents the research plan of my PhD contract and the preliminary results achieved so far.

Cua D. Et al. (2001) J. Immunol. 166: 602-608
Imai F. et al. (1997) Neurosci. Lett. 237: 49-52

Sanne Derks, Dept. Medical Farmacology, VU medical center, Van der Boechorststraat 7, 1081 BT Amsterdam, t 020-4448096, e-mail s.derks@vumc.nl

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