Summary

The role of interferon-beta in Multiple Sclerosis

Laura van der Voort

Interferon-beta (IFN-β) is a widely used and was for a long time the only treatment for relapsing Multiple Sclerosis (MS). Clinical experience revealed a remarkable inter-individual variation in how well people did on IFN-β treatment. This was partly attributed to the natural variation in clinical disease course and partly attributed to the blocking of the biological activity of the drug by anti-IFN-β neutralizing antibodies (NAb). Our data demonstrates a role for MxA mRNA expression as a treatment response marker, as a low or absent MxA mRNA expression in IFN-β treated patients indicates the presence of NAb and is associated with the occurrence of clinical relapses. Recent studies suggest that the potential of IFN-β to modulate MS disease course is dependent on the pre-treatment activity of type I IFN pathways. These pathways are difficult to unravel as many genes, gene expression profiles and post-translational modifications of gene products are likely involved. In this thesis, we contribute to the suggestion that endogenous IFN-β activity effects disease severity, at least in some MS patients. We were unable to confirm the proposed role of interleukin-7 receptor (IL7R) on disease activity or on IFN-β treatment response, but our data did support a role for Interferon regulatory Factor 5 (IRF5) on treatment response modulation. Future work on type I IFN pathway differences in MS hold promise for an improved selection of patients eligible for IFN-β treatment and patients that will more likely benefit from alternative immunomodulatory agents.