Interferon-beta increases systemic BAFF levels in multiple sclerosis without increasing autoantibody production - DTU Orbit (27/07/2019)

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**Background:** Treatment with interferon-beta (IFN-beta) increases B-cell activating factor of the TNF family (BAFF) expression in multiple sclerosis (MS), raising the concern that treatment of MS patients with IFN-beta may activate autoimmune B cells and stimulate the production of MS-associated autoantibodies. **Objective:** To investigate whether BAFF levels are associated with disease severity/activity in untreated MS patients, and to assess the effect of IFN-beta therapy on circulating BAFF and anti-myelin basic protein (MBP) autoantibody levels. **Results:** Twenty-three patients with relapsing–remitting MS (RRMS) were followed longitudinally from initiation of IFN-beta therapy. Their blood levels of BAFF correlated positively at baseline with the expanded disability status scale (p <0.009) and MS severity score (p <0.05), but not with disease activity as determined by the number of gadolinium-enhanced lesions. The patients were followed for up to 26 months, during which the BAFF levels remained elevated without association to increased disease activity. IFN-beta therapy caused an increase in plasma BAFF levels after both 3 and 6 months of therapy (p <0.002). However, an 11% decrease in IgM and a 33% decrease in IgG anti-MBP autoantibodies (p <0.09 and p <0.009, respectively) was observed after 6 months. **Conclusion:** Pre-treatment BAFF levels correlate with high disability scores in MS, suggesting that high BAFF expression is a negative prognostic marker. Despite its known beneficial effects, IFN-beta therapy causes a sustained increase in plasma BAFF levels, which does not translate into increased levels of anti-MBP autoantibodies.