INTRAVENOUS IMMUNOGLOBULIN BINDS BETA AMYLOID AND MODIFIES ITS AGGREGATION, NEUROTOXICITY AND STIMULATORY PROPERTIES IN VITRO

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Intravenous Immunoglobulin (IVIG) is currently being tested for efficacy in patients with mild-to-moderate Alzheimer's disease (AD; Phase III clinical program). This clinical study is predicated on promising data from a number of smaller clinical programs, as well as observations of reduced levels of anti-amyloid beta (Aβ) antibodies in AD patients and the presence of these antibodies in IVIG.

IVIG is known to mediate beneficial effects in chronic inflammatory and autoimmune conditions by interfering with various pathological processes. To identify potential mechanisms responsible for the favorable effects observed in AD patients we have investigated the impact of IVIG on the in vitro aggregation, toxicity and stimulatory properties of Aβ.

The binding of Aβ-reactive antibodies in IVIG to plate bound Ab peptide was measured by ELISA and the capacity of IVIG to inhibit Aβ aggregation tested in a Thioflavin T fluorescence assay. In addition, we investigated the effect of IVIG on Aβ-induced cellular toxicity (SH-SY5Y neuroblastoma cell line and rat primary cortical neurons) and Aβ-mediated cellular activation (mouse microglial cell line).

We demonstrate that IVIG bound to Ab, inhibited its aggregation in a dose-dependent manner, and inhibited Aβ-induced toxicity in both SH-SY5Y cells and rat primary cortical neuron assays. Additionally, IVIG inhibited the Aβ-induced activation of mouse microglia as measured by surface marker expression and cytokine secretion.

Our in vitro results suggest that IVIG may impact on a number of the processes thought to be involved in AD pathogenesis and provide further support for the ongoing analysis of IVIG in this indication.