BIOCHEMICAL CHARACTERIZATION OF THE TG2576 MOUSE MODEL: AGE-DEPENDENT LEVELS OF Aβ SPECIES AND OTHER APP PROCESSING FRAGMENTS IN PLASMA AND BRAIN

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Introduction: Tg2576, a mouse model overexpressing human APP with the Swedish mutation, is a widely used animal model to study amyloidosis.

Aims: To investigate the levels and variability of Aβ species and other APP fragments, in plasma and brain from Tg2576 mice of different ages up to two years, to improve the knowledge of this animal model and how it can be used in drug discovery.

Methods: Tg2576 female mice were purchased from Taconic (Georgetown, NY, USA), and aged at AstraZeneca’s animal facilities, kept under conventional housing and fed with standard rodent chew. Plasma and brains were collected from animals of different ages. Brains were sequentially extracted with diethylamine and formic acid to obtain the soluble and insoluble brain fractions, respectively. The levels of different Aβ species and other APP processing fragments were analyzed using commercially available ELISA (Invitrogen & Innogenetics) or MSD technologies. Extensive statistical analysis was performed on all data.

Results: We found that the levels of both endogenous mouse and transgenic human Aβ rapidly increased with age, in both the soluble and insoluble brain pools, preceding the plaque deposition detected by histological analysis. However, the levels of Aβ in plasma were stable over all ages studied. The obtained information on Aβ levels and variability is used to perform estimations of necessary sample size for upcoming efficacy studies.

Conclusions: This extensive biochemical characterization of the Tg2576 mouse model is used to design acute and long-term efficacy studies.