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Physiological and pathological roles of the neuronal beta-secretase BACE1 in Alzheimer’s disease

BACE1 is the neuronal beta-secretase responsible for the production of the neurotoxic amyloid-beta peptide that accumulates in the brain of Alzheimer’s disease patients. In the pathogenesis of the disease, the control of BACE1 expression is considered crucial to avoid amyloid-beta overload. Using mainly primary neuronal cultures, as well as animal models of Alzheimer’s disease, the candidate will investigate the molecular mechanisms of BACE1 expression. Previous studies performed on cell cultures, animal models and patients suggest a possible impairment in the translational component of BACE1 expression. Particular attention will be devoted to the characterization of the molecular machinery of BACE1 translation, with the aim to identify molecules interacting with the BACE1 transcript. Biochemical (protein purification, RNA band-shift assays, polyribosomal analysis) and molecular (gene transfection and silencing) procedures will be employed. Pharmacological and molecular tools will be also exploited to investigate how intercellular communication and signal transduction may affect translational control of BACE1 expression in the central nervous system. In parallel, the candidate will perform an evaluation of the physiological role of BACE1 in neuronal function by using neuronal cultures from wild type and BACE1 null mice and analyzing their behavior in terms of spontaneous and evoked activity.

Publications on this topic: