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Expression of autophagy genes and markers of inflammation in the brain in a transgenic mouse model of Parkinson's disease

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Abstract — **The autophagy-lysosomal pathway is one of the main mechanisms for cleaning of brain tissue from "pathological" proteins that contribute to the neurodegenerative disorders including Parkinson's disease (PD) [1]. Levels of the regulatory factor Beclin1 (encoded by gene *Becn1*) and protein LC3-II are markers of autophagy activation. Cystatin C (encoded by gene *Cst3*) have a wide range of biological effects [2] including the autophagy induction through mTOR inhibition and regulation of inflammation, a marker of which are chitinases (chitoriosidase encoded by gene *Chit1*, and acidic-1 chitinase encoded by gene *Chia1*) upon activation of microglial cells. The aim of the work was to study gene (*Becn1, Cst3, Chia1, Chit1*) and protein (LC3-II) expression in the brain in a transgenic mouse PD model overexpressing the A53T-mutant alpha-synuclein at an early stage of the pathology progression (at the age of 5 months). The levels of gene expression were determined by qPCR. Protein expression was estimated with immunohistochemical analysis in frozen brain sections. Autophagy activity was suppressed in the striatum and amygdala (according to LC3-II marker) and in the frontal cortex (according to mRNA level of *Becn1*) in the transgenic mice compared to wild-type control. No changes were found in the expression levels of chitinases, while the expression of *Cst3* was reduced in the striatum and amygdala of transgenic mice that was associated with a reduced autophagy in these structures. This deficit in the cellular defense response may be a target for effective neuroprotection through therapeutic activation of autophagy at early stages of PD.**

Keywords *— **autophagy, Cystatin C, alpha-synuclein, mice, chitinase, microglia***

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