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Cystatin C as regulator of autophagy in the brain of transgenic murine model of Parkinson's disease

T.A. Korolenko[1]*, A.B. Shintyapina[2], A.B. Pupyshev[1], V.M. Belichenko[1], E.L. Zavjalov[3], T.G. Amstislavskaya[1, 4], M.A. Tikhonova[1, 4]

[1] *Scientific Research Institute of Physiology and Basic Medicine, Novosibirsk, Russia*

[2] *Institute of Molecular Biology and Biophysics of Federal Research Center of Fundamental and Translational Medicine, Novosibirsk, Russia*

[3] *Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*

[4] *Novosibirsk State University, Novosibirsk, Russia*

** e-mail: t.a.korolenko@physiol.ru*

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Motivation and Aim: Cystatin C is one of the potent regulators of autophagy. Changes in the expression and secretion of cystatin C in the brain have been found in amyotrophic lateral sclerosis, Alzheimer's and Parkinson's diseases and in some animal models of neurodegeneration, demonstrating its protective role. Cystatin C is regarded to play an important role in amyloidogenesis and be promising approach for treatment of neurodegenerative diseases. In Parkinson's disease, serum cystatin C levels may predict disease severity and cognitive dysfunction, although the exact role of cystatin C remains unclear. The aim: to evaluate expression of cystatin C in transgenic mouse model of Parkinson' disease at early stage of disease development (5 m.o.) and estimate results as related to mechanism of autophagy activation.

Methods and Algorithms: 5-month-old male mice of B6.Cg-Tg(Prnp-SNCA*A53T) 23Mkle/J) (further – B6.Cg-Tg) and control C57Bl/6J strain were used. Total RNA was isolated from mouse brain areas (striatum, amygdala, hypothalamus, hippocampus). Gene expression levels were detected using qPCR-RT. LC3-II levels were evaluated in brain cryosections with immunohistochemical analysis. Cystatin C levels in plasma were determined by specific ELISA kits.

Results: Analysis of cystatin C (*Cst3*) gene expression in the striatum and, especially, in amygdala revealed a significant decrease in B6.Cg-Tg mice compared to controls. Low levels of *Cst3* expression were associated with suppression of autophagy: a marker of autophagy activation LC3-II was reduced in the striatum and s. nigra while expression of *Becn1* encoding another marker of autophagy activation was significantly decreased in the frontal cortex. Cystatin C concentration in plasma of transgenic mice was not changed vs. controls.

Conclusion: The results obtained provide further evidence of association between cystatin C and autophagy activity. Cystatin C may play a protective role in multiple neurodegenerative disorders including Parkinson's disease.

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