DOI 10.18699/BGRSSB-2018-189

# Features of the autophagy process during its induction by 48-h fasting and inhibition by chloroquine in the rat liver

O.S. Kozhevnikova*, D.V. Telegina, E.A. Zolotenkova, M.A. Tyumentsev, N.G. Kolosova
*Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia*
** e-mail: oidopova@bionet.nsc.ru*

**Key words:** liver, autophagy, chloroquine, senescent-accelerated OXYS rats

*Motivation and Aim*: Autophagy is a multi-stage process of delivery of cytoplasmic material to lysosomes for the subsequent degradation. It is the main mechanism of degradation of long-lived proteins and the only one – for organelle degradation. This process is involved in the maintenance of cellular homeostasis, the removal of damaged proteins and organelles, and is necessary to maintain cell metabolism in conditions of energy and nutrient deficiency. With age, the intensity of autophagy decreases. It is known that the pathogenesis of many age-related diseases, including neurodegenerative diseases, is associated with a disruption of autophagy, but the underlying mechanisms of these disorders have not been adequately studied. The liver plays a central role in controlling glucose and lipid homeostasis in response to fasting and feeding. The present work is aimed at studying the contribution of autophagy changes in the early development of age-dependent diseases in OXYS rats, a unique model of premature aging. Its purpose is to study the features of the process of autophagy when it is induced and inhibited in the liver of OXYS rats.
*Methods*: The work was performed on male OXYS and Wistar (control) rats at the age of 4 months ($n$ = 60). 48-h fasting was used for the induction of autophagy, and the chloroquine injections (50 mg/kg body mass) were used for its inhibition. The content of protein markers of autophagy (ATG7, p62 and LC3) was assessed by Western blot analysis and immunohistochemistry, autophagosome formation by means of electron microscopy (Microscopy Centre of ICG SB RAS).
*Results*: It was shown that the administration of chloroquine reduced the liver mass of rats of both strains, the body weight - only in OXYS rats. The chloroquine injections on a fasting background slowed down body weight reduction in Wistar rats, but not in OXYS rats. By the Sanger sequencing we confirmed the presence of non-synonymous single nucleotide substitution in the Pik3c2b gene in the genome of OXYS rats. The product of this gene is involved in the regulation of autophagy. According to our preliminary data, the activity of autophagy in the liver of OXYS rats has been reduced already at the young age.
*Acknowledgements*: Supported by the RSF 18-75-00031.