THE IMPLICATIONS OF AUTOPHAGY IN CROHN'S DISEASE

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Introduction: Inflammatory bowel disease comprises a variety of chronic inflammatory disorders, that affect the gastrointestinal tract, the most common ones being ulcerative colitis and Crohn's disease, that, if left undertreated, could pose a high risk for colorectal cancer. The aim of this study is to elucidate the role of autophagy in the physiology of the intestinal tract and in the pathogenesis of Crohn's disease (CrD) and the potential therapeutic application in its treatment.
Material and method. A comprehensive literature review was performed using major scientific databases, including the data from the years 2017-2024 of PubMed, Frontiers, Elsevier. Keywords: Inflammatory bowel disease, Crohn's disease, autophagy, colorectal cancer.
Results. Genetics, environment, abnormal gut microbiota and local immunity underlie the pathogenesis of CrD and the cross-link between them is autophagy - the programmed disposal of dysfunctional cellular components by vacuolization. This highly conserved process of cellular degradation regulates the intestinal immunity by promoting antigen presentation by dendritic cells, inflammatory factor synthesis, cellular proliferation and maturation and non-inflammatory cellular clearance. Up-to-date, the autophagosome formation is strictly coordinated by 36 autophagy related genes. Recent studies have linked the mutations in the ATG16L1 (autophagy-related 16-like 1 gene) and the NOD2 (nucleotide-binding and oligomerisation domain 2 gene) to around 50% of cases of CrD onset and progression risk. Among the many autophagy signaling pathways, AMPK/mTOR (Adenosine monophosphate kinase / Mammalian target of rapamycin) and NF-kB (Nuclear factor kB) are the most studied ones and the discovery of such autophagy promoters as metformin, dapagliflozin, palmatin and ginseng could prove beneficial in the course of treatment of CrD.
Conclusions. Moderating the inflammatory status in Crohn's disease by regulating the autophagic flux is feasible. However, more work needs to be done to develop a line of cell specific, harmless therapeutic agents, thus, preventing the colorectal cancer and surgery.
Keywords: Crohn's Disease, autophagy, autophagy-related genes, signaling pathways, therapeutic agents.