FGFR2 involvement in regulation of autophagy – implications in breast cancer progression

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Autophagy is a physiological process of recycling and removal of large molecules and damaged organelles. It is activated by many conditions including amino acids starvation, glucose deprivation, oxygen deficiency, growth factor withdrawal, exposure to drugs or cellular damage. Autophagy was shown to play dual role in oncogenesis i.e. it can promote or suppress growth of tumor cells. At the early stages of cancers, autophagy acts as a tumor suppressor by preventing the accumulation of damaged organelles and proteins. In more advanced disease autophagy protects cancer cells from metabolic and therapeutic stress and leads to cancer cell survival and development of resistance to therapeutics. Several studies suggested an involvement of tumour microenvironment in regulation of autophagy in cancer cell. Our team has proved that Fibroblast Growth Factor Receptor 2 (FGFR2) mediates communication between tumor stroma and neoplastic cell in luminal (ER-positive) breast cancer.

The aim of this project was to analyzed an impact of FGFR2-dependent signaling on the induction and/or inhibition of autophagy with plausible implications in luminal breast cancer cell response to anti-ER therapies. At first, we analyzed FGFR2-regulated expression/activation of autophagy regulators (i.e. LC3, p62, Beclin-1 and members of Atg family). To monitor progression from the autophagosome to autolysosome we used Premo™ Autophagy Tandem Sensor RFP-GFP-LC3B Kit, which relies on pH difference between the acidic autolysosome and the neutral autophagosome. We also evaluated an involvement of autophagy in FGFR2-promoted cell growth in the presence of tamoxifen (anti-ER drug) and chloroquine (autophagy inhibitor) in 3D growth assay. Combined therapy based on FGFR and autophagy inhibitors/modulators may have potential application for patients with developed resistance to anti-ER drugs.

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