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Short Communication
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Autophagy: From Liver to Pancreas Tumor Pathogenesis

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Short Communication

Autophagy is a fine regulated mechanism of recycling. It has been firstly discovered in yeast. This *self-eating*, digestive mechanism is characterized by promoting the formation of double membrane vesicles by the interaction of several autophagic proteins at endoplasmic reticulum site [1]. Autophagy occurs during prolonged starvation and nutrient deprivation conditions. This protracted stress causes sub cellular organelles dysfunction, e.g. mitochondria; the autophagy machinery can internalize the non-functional organelles and drive them to the final digestion into the lysosome vesicles [2]. Mammalian cells can activate this process under stress also. Protracted autophagy, caused by low ATP level, can lead to a complete auto digestion and cell demise finally [3,4]. Altered autophagy process caused by the loss of function of autophagic key factors is implied in development of several diseases including neurodegenerative disorders and cancer [5]. Our studies focused on clarifying the autophagic processes in hepatocellular carcinoma. In particular, it was observed that autophagy can be activated in liver cancer cells by treatment with the deacetylase inhibitor panobinostat. The treatment caused an accumulation of autophagic genes transcripts and protein products Beclin1 and Map1LC3B. Furthermore, the formation and the maturation of autophagosomal vesicles were observed and followed in their maturation process (Figure1). The possibility to target autophagy as cell death molecular mechanism in liver cancer could offer new options for the palliative treatment of this, up to now, untreatable solid cancer [6]. The molecular mechanisms of autophagy represent a key role not only in liver cancer but also in other pathologies related to liver, pancreas and in general to all digestive tract. Notably, it would be interesting to clarify the role exerted by autophagy in NAFLD/NASH (non alcoholic fatty liver disease/non alcoholic steatohepatitis) [7,8] in order to amplify the knowledge of molecular mechanisms related to this disease and to improve the current therapy [9,10]. Protracted NASH develops frequently in hepatocellular carcinoma [11] and the role exerted by autophagy in this pathology of the liver could give new efforts in the prevention and treatment of liver cancer. Furthermore, it has been recently shown that autophagy plays a key role in pancreatic cancer and in particular autophagic mechanisms resulted activated in pancreatic stellate cells surrounding pancreatic adenocarcinoma [12]. Up to now, it is not known, the role exerted by autophagy in pancreatic neuroendocrine tumors and the role exerted by stellate cells surrounding such kind of tumor of the pancreas.

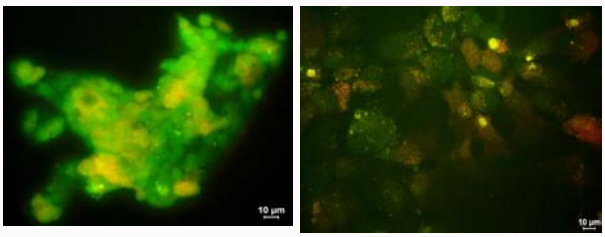

Figure 1: HepG2 (left panel) and Hep3B (right panel) hepatocellular cancer cell lines stably transfected with Map1LC3B-GFP-RFP tag. Treatment with panobinostat caused the green-red fluorescent *puncta* formation and the red visualization indicating the autophagosome maturation process. Magnification is 400X and scale bar indicates 10 µm.

The possibility to target autophagy, e.g. with mTOR (mammalian target of Rapamycin) inhibitors [13] and other analogues, could represent a new strategy for a future therapy and a better prognosis for patients affected by this highly recurrent and aggressive cancer of the pancreas.

References

1. Gray JV, Petsko GA, Johnston GC, Ringe D, Singer RA, Werner-Washburne M. "Sleeping beauty": quiescence in Saccharomyces cerevisiae. Microbiol Mol Biol Rev. 2004; 68: 187-206.

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2. Lippai M, Szatmari Z. Autophagy-from molecular mechanisms to clinical relevance. Cell biology and toxicology. 2016.

3. Denton D, Xu T, Kumar S. Autophagy as a pro-death pathway. Immunology and cell biology. 2015; 93: 35-42.

4. Kroemer G, Levine B. Autophagic cell death: the story of a misnomer. Nature reviews. Molecular cell biology. 2008; 9: 1004-1010.

5. Levine B, Kroemer G. Autophagy in the pathogenesis of disease. Cell. 2008; 132: 27-42.

6. Di Fazio P, Waldegger P, Jabari S, Lingelbach S, Montalbano R, Ocker M. ET AL. Autophagy-related cell death by pan-histone deacetylase inhibition in liver cancer. Oncotarget. 2016; 7: 28998-9010.

7. Puri P, Chandra A. Autophagy modulation as a potential therapeutic target for liver diseases. Journal of clinical and experimental Hepatology. 2014; 4: 51-59.

8. Di Fazio P. Comment on "A series of microRNA in the chromosome 14q32.2 maternally imprinted region related to progression of non-alcoholic fatty liver disease in a mouse model". Hepatoma Res . 2016; 2: 205-206.

9. Rotman Y, Sanyal AJ. Current and upcoming pharmacotherapy for non-alcoholic fatty liver disease. Gut. 2017; 66: 180-190.

10. Carr RM, Oranu A, Khungar V. Nonalcoholic Fatty Liver Disease: Pathophysiology and Management. Gastroenterol Clin North Am. 2016; 45: 639-652.

11. Okamoto K, Koda M, Okamoto T, Onoyama T, Miyoshi K, Kishina M, et al. A Series of microRNA in the Chromosome 14q32.2 Maternally Imprinted Region Related to Progression of Non-Alcoholic Fatty Liver Disease in a Mouse Model. PLoS One. 2016; 11: e0154676.

12. Sousa CM, Biancur DE, Wang X, Halbrook CJ, Sherman MH, Zhang L, et al. Pancreatic stellate cells support tumour metabolism through autophagic alanine secretion. Nature. 2016; 536: 479-483.

13. Capozzi M, Caterina I, De Divitiis C, von Arx C, Maiolino P, Tatangelo F. Everolimus and pancreatic neuroendocrine tumors (PNETs): Activity, resistance and how to overcome it. Int J Surg. 2015; 2: S89-S94.