



# Interplay of autophagy and cancer stem cells in hepatocellular carcinoma

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## Abstract

Liver cancer is the sixth most common cancer and the fourth leading cause of cancer deaths in the world. The most common type of liver cancers is hepatocellular carcinoma (HCC). Autophagy is the cellular digestion of harmful components by sequestering the waste products into autophagosomes followed by lysosomal degradation for the maintenance of cellular homeostasis. The impairment of autophagy is highly associated with the development and progression of HCC although autophagy may be involved in tumour-suppressing cellular events. In regards to its protecting role, autophagy also shelters the cells from anoikis- a programmed cell death in anchorage-dependent cells detached from the surrounding extracellular matrix which facilitates metastasis in HCC. Liver cancer stem cells (LCSCs) have the ability for self-renewal and differentiation and are associated with the development and progression of HCC by regulating stemness, resistance and angiogenesis. Interestingly, autophagy is also known to regulate normal stem cells by promoting cellular survival and differentiation and maintaining cellular homeostasis. In this review, we discuss the basal autophagic mechanisms and double-faceted roles of autophagy as both tumour suppressor and tumour promoter in HCC, as well as its association with and contribution to self-renewal and differentiation of LCSCs.

**Keywords** Liver cancer · Autophagy · Cancer stem cells · Hepatocellular carcinoma · Tumour progression · Suppression · Sirtuin 1

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## Abbreviations

|            |  |
|------------|--|
| HCC        | Hepatocellular carcinoma                                 |
| HBV        | Hepatitis B virus  |
| HCV        | Hepatitis C virus  |
| CSC        | Cancer stem cell   |
| PI3K       | Phosphatidylinositol 3-kinase                            |
| VPS34      | Vacuolar protein sorting 34                              |
| mTORC1     | Mammalian target of rapamycin complex                    |
| ULK1       | Unc-51 like kinase 1                                     |
| ATG        | Autophagy related protein                                |
| FIP200     | Focal adhesion kinase family-interacting protein 200 kDa |
| AMPK       | 5' Adenosine monophosphate-activated protein kinase      |
| PI3P       | Phosphatidylinositol triphosphate                        |
| LC3        | Microtubule-associated protein 1A/1B-light chain 3       |
| PE         | Phosphatidylethanolamine                                 |
| SQSTM1/p62 | Sequestosome-1/ubiquitin-binding protein p62             |