Oncogene-induced senescence (OIS) is triggered by B-RafV600E in human hepatocytes

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Abstract

Hepatocellular carcinoma (HCC) is one of the common malignant tumors in the world. Hepatocarcinogenesis is a stepwise process in which multiple genes are altered. This process occurs via activation of oncogenes, inactivation of tumor suppressor genes, reactivation of developmental pathways and activation of growth factors and their cognitive receptors. We focused one of the signaling pathways, specifically the MAPK signaling pathway which is associated with cell growth, proliferation and migration in HCC. B-Raf mutation has been reported in 61% of melanoma, 53% of papillary thyroid cancer and 11.5% of colorectal cancer patients. In the case of hepatoma, 23% of B-RafV600E mutation was reported. In this study, we want to evaluate the B-RafV600E function in hepatocarcinogenesis. The overexpression B-RafV600E caused cell growth arrest and showed senescence-associated beta-galactosidase (SA-β-gal) staining. Moreover, overexpression of B-RafV600E caused activation MAPK Kinases pathway and cell cycle arrest.

Introduction

Hepatocellular carcinoma (HCC) is one of the common malignant tumors in the world. Hepatocarcinogenesis is a stepwise process in which multiple genes are altered. This process occurs via activation of oncogenes, inactivation of tumor suppressor genes, reactivation of developmental pathways and activation of growth factors and their cognitive receptors. We focused one of the signaling pathways, specifically the MAPK signaling pathway which is associated with cell growth, proliferation and migration in HCC. B-Raf mutation has been reported in 61% of melanoma, 53% of papillary thyroid cancer and 11.5% of colorectal cancer patients. In the case of hepatoma, 23% of B-RafV600E mutation was reported. In this study, we want to evaluate the B-RafV600E function in hepatocarcinogenesis. The overexpression B-RafV600E caused cell growth arrest and showed senescence-associated beta-galactosidase (SA-β-gal) staining. Moreover, overexpression of B-RafV600E caused activation MAPK Kinases pathway and cell cycle arrest.

Discussion

Our results suggest that B-RafV600E overexpression induce human hepatocyte senescence, was detected by senescence-associated beta-galactosidase (SA-β-gal) staining and cell morphology change. Moreover, cell growth arrest as well as p16INK4a accumulation were observed in B-RafV600E human hepatocyte.

Further Study

- We focus to find the detail molecular mechanism or the factors can induce human hepatocyte senescence after B-RafV600E overexpression.
- In other hand, p53 depletion or Akt pathway could induce the senescence overcome. So we want to determine what the mechanism is if the human hepatocyte might overcome the senescence?

Reference