

ANNOTATION

OF RESEARCH TOPIC FOR POSTDOC POSITION

Regenerace jaterního parenchymu a její souvislost s karcinogenezí primárních nádorů jater

Regeneration of liver parenchyma and its relation to carcinogenesis of primary liver tumors

Position available from: January 2019

Department: Biomedical Center, Faculty of Medicine in Pilsen, Charles University

Laboratory: Laboratory of Cancer Treatment and Tissue regeneration

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Input premise

Hepatocellular carcinoma (HCC) is the furthestmost common example of primary liver cancer, making it third most common cause of cancer mortality. Generally impaired wound-healing response along with chronic liver injury results in liver fibrosis; a condition caused by extracellular matrix accumulation and scar formation. Advanced stages of liver fibrosis progress to liver cirrhosis, categorized by disruption of liver parenchyma cells, nodule formation, blood flow distortion, and liver failure risk. Continuation of disease gradually results in HCC. A variety of etiologies, such as hepatitis B and C viral persistence, chronic alcohol abuse, non-alcoholic steatohepatitis (NASH), cholestasis, and autoimmune hepatitis can progress to HCC. Despite significant advances in understanding of fibrosis leading to HCC, the exact molecular mechanisms of the disease are yet needed to be described. Various studies suggest central role of IL-22 in regulating pathways underlying HCC. High levels of IL-22 have been implied to promote carcinogenesis within the liver as well as in other organs. Its role in activating varied anti-apoptotic and cell proliferative pathways may play role in development and progress of liver cancer. Hence, it is hypothesized that overexpression of IL-22 can lead to various downstream signaling pathways and can eventually activate genes that result in development of tumor by continuous proliferation of liver cells. For that reason, the possible role of IL-22 and its downstream signaling pathways in HCC needs to be deciphered. IL-22 may possibly increase the metastatic potential of tumor cells through certain pathways including JAK/STAT and PI3K/AKT pathways. In this study the potential role of IL-22 in enhancing Mcl-1 via different

pathways (JAK/STAT, PI3K/AKT) will be studied. The effects of inhibitors of these pathways (SOCS3, PTEN) will also be observed. As the role of IL-22 in metastasis of HCC is still unclear, that's why further studies would help to explain the cascade reactions through which it might cause carcinogenesis in liver cells. The proposed study aims to explore the potential role of IL-22 in inducing downstream signaling molecules (PI3K, PDK , AKT) triggered cell proliferation, cell metastasis and ultimately development into HCC.

Qualifications

- Ph.D. (or equivalent) degree in biology or medicine recently graduated
- Technical skills in quantitative histology, liver pathology, immunohistochemistry, experimental work– advanced experience
- High motivation, ability to conduct collaborative research
- Excellent English communication skills both in written and oral form
- Track record of publications in peer-reviewed journals: at least 5 publications in IF journals, two as a first author

The applicants should submit

- [Letter of Reference](#)
- [Application for post-doc grant at Charles University](#)
- Curriculum vitae
- List of publications
- Copy of university diploma
- Brief description of prior research, skills and experiences