Identification and Characterization of Cancer Stem Cells in Hepatocellular Carcinoma

Xin-yuan Guan

Department of Clinical Oncology
The University of Hong Kong
Hepatocellular Carcinoma (HCC)

HCC
- 5th most common cancer
- 3rd leading cause of cancer death
- High incidence geographic regions: Southeast Asia, China, sub-Saharan Africa

Etiology of HCC
- HBV or HCV infection
- Aflatoxin B1 intake
- Alcohol abuse
- Obesity, diabetes and nonalcoholic fatty liver disease
Tumor-initiating cells (TICs) / Cancer stem cells (CSCs)

- CSC has been defined as a cell within a tumor that possesses the capacity to self-renew and to cause the heterogeneous lineages of cancer cells.
- Other common (but not defining) characteristics of CSCs – rarity within a tumor, stem cell marker expression, ability to differentiate along multiple lineages, chemoresistance, metastasis, etc.

- Origin of CSCs – largely unknown.
  e.g. for leukemia and colon cancer – normal stem cells
  e.g. for liver cancer – ?
CD133+ cells exhibit increased **tumorigenic** potential

CD133+ cells exhibit an increased potential for **self-renewal**

CD133+ cells exhibit a marked ability to **differentiate**

CD133+ cells preferentially express **“stemness” genes**

CD133+ cells are **more resistant to anticancer agents**, doxorubicin and 5-fluorouracil
Summary

Characteristics of CD133+ subpopulations, isolated from HCC clinical specimens and cell lines are consistent with the predicted behavior of cancer stem cells.

Ma et al., *Gastroenterology* 2007

CD133+ CSCs contribute to HCC chemoresistance through activation of the specific Akt/PKB and Bcl-2 survival pathway.

Ma et al., *Oncogene* 2008

Aldehyde dehydrogenase (ALDH) is preferentially expressed in CD133+ cells and can be used to better characterize the CD133+ HCC CSC population.

Ma et al., *Mole Cancer Res* 2008

miR-130b is overexpressed in CD133+ CSCs and regulates tumor growth and self-renewal via tumor protein TP53-INP1.

Ma et al., *Cell Stem Cell* 2010

CD133+ liver CSCs promote tumor angiogenesis through activation of the NTS / IL-8 / CXCL1 signaling cascade via MAPK signaling.


Knockdown of CD133 can inhibit tumorigenicity of HCC cell lines.

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Thank You

Questions or Comments

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