Identification and Characterization of Cancer Stem Cells in Hepatocellular Carcinoma

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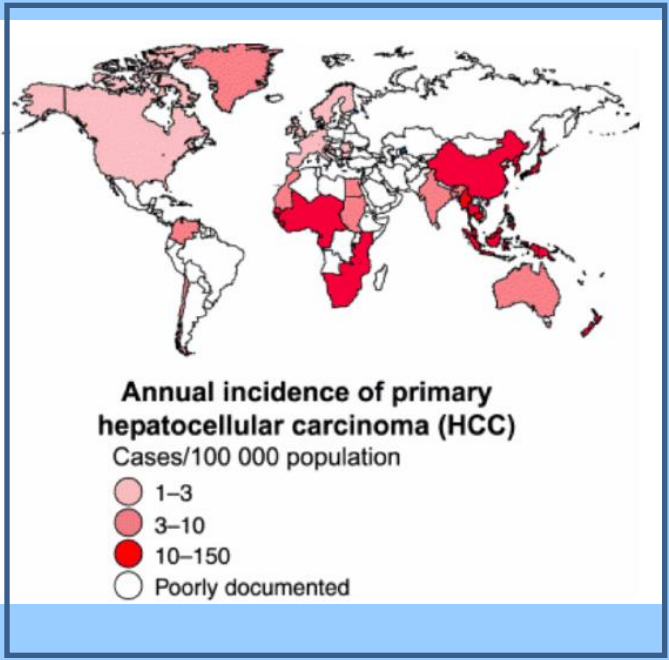
Hepatocellular Carcinoma (HCC)



HCC

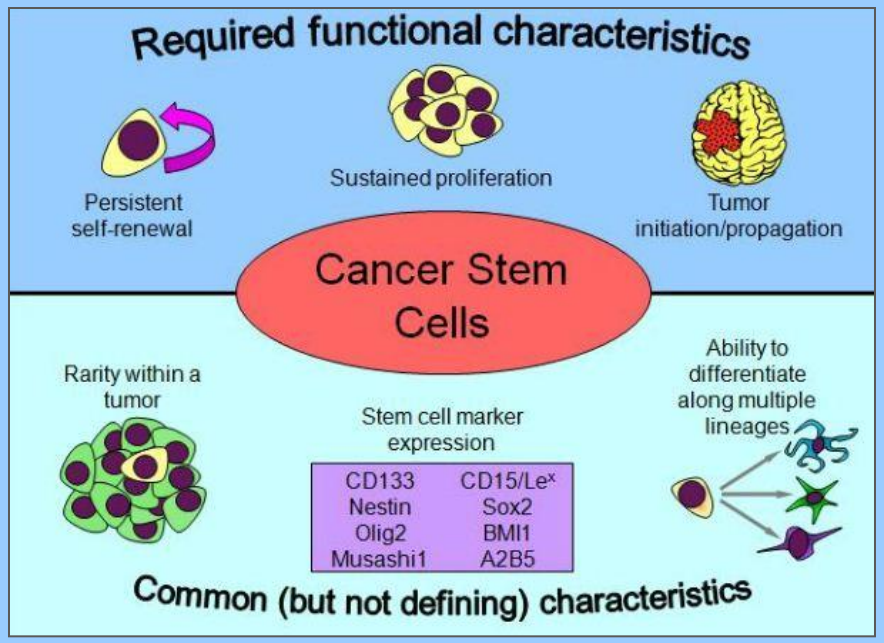
- 5th most common cancer
- 3rd leading cause of cancer death
- High incidence geographic regions: Southeast Asia, China, sub-Saharan Africa

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.
- Properties of CSCs – persistent **self-renewal**, sustained **proliferation**, **tumor initiation**.
- 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 – ?

Characteristics of $CD133^+$ subpopulation in HCC

- $CD133^+$ 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.

Tang KH, et al. ***Hepatology*** 2011

Knowckdown of CD133 can inhibit tumorigenicity of HCC cell lines.

Tang KH, et al. ***Hepatology*** 2011

Acknowledgments

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Thank You

Questions or Comments