

- 1) HEPATOCYTE (HC) primary target for several agents/conditions able to induce cell injury and death
 - most of agents/conditions leading to HC injury are able to generate ROS, HNE, and other free radicals
 - damaged HC can release ROS and other reactive intermermediates in the surrounding microenvironment
 - HC can also release IGF-1 and, under hypoxia, VEGF
 - during chronic liver diseases, surviving HC can proliferate in an attempt to repopulate injured liver

2) MONONUCLEAR CELLS (Mc) **KUPFFER CELLS (KC)**

- recruited Mc and resident KC become activated in conditions of chronic liver injury
- Mc and KC can act by phagocytosis of cell debris & apoptotic bodies as well as APC



- on activation, they can generate and release: ROS and other reactive intermediates; several GFs, CKs & mediators, including PDGF, bFGF, TGF β , TNF α , IL-1, PGs, etc; selected MMPs

3) **SINUSOIDAL ENDOTHELIAL CELLS** (SEC)

- partecipate to angiogenesis, being recruited and stimulated by GFs, mainly VEGF
- when injured/activated, SEC can potentially release: GFs & CKs like PDGF, bFGF, IL-1, TGFβ, IGF-1, PGs, ETs, VEGF; NO and ROS



4) **PLATELETS**



- when recruited/activated at the site of injury they can release: PDGF, EGF, TGFα, TGFβ, TXAs, IGF-1

5) T LYMPHOCYTES



- recruited to the liver under conditions of chronic liver injury induced by viruses (HBV, HCV), chronic alcohol consumption, auto-immune conditions, etc.
- may contribute to perpetuation of liver injury
- once activated, may release TNF α or IFN γ as well as other CKs

6) **HEPATIC PROGENITOR** CELLS (HPC)



- under certain conditions (i.e. chronic liver injury) may contribute to parenchymal repopulation
- HPC are bipotent cells, able to give rise to either HC or biliary epithelial cells (BEC)

7) BILIARY EPITHELIAL **CELLS (BEC)**



- BEC can actively proliferate in different conditions of acute & chronic liver injury
- BEC can establish cross-talks with surrounding cells and may release a number of mediators, including PDGF, TGFβ II, ETs and VEGF

8) **ENDOTHELIAL PROGENITOR** CELLS (EPC)

- circulating and/or bone marrow (BM) derived cells that may contribute to liver angiogenesis, possibly together with BM - derived monocyte lineage cells

