A Kappa model for hepatic stellate cells activation by TGFB1
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**Introduction**

Chronic hepatitis is associated with the development of fibrosis, which results in the abnormal deposition of extracellular matrix (ECM) and a series of destruction of liver functions. The terminal stage of fibrosis is cirrhosis, which carries the major risk of occurrence of hepatocellular carcinoma (HCC). The matrix reorganization is therefore the major regulator of events related to the fibrosis-cirrhosis-cancer progression and hepatic stellate cells (HSC) are the main actors of the extracellular matrix remodeling.

- Upon liver injury, damaged hepatocytes produce signals including inflammation that in turn promote TGFB1-dependent activation of parenchymal HSC (HSC(TGFB1)). Activated HSC production tissue repair and other fibrosis-related through Senescence and Apoptosis (2) or deactivation towards normal HSC (HSC0), that can be reactivated more fibrotic.
- Upon analysis from data, activated HSC(TGFB1) progress toward a Malignant (MPF) state that escapes to controls, leading to fibrosis.

**Kappa**

- It offers a graphical interface for easy modeling.
- Rules locally modify the state of a system.

**Tools**

- Stochastic simulation allows:
  - 8 input every 90 hours
  - 8 inputs of each 24 hours
  - 16 inputs of each 90 hours

**Results**

- Model: A Schematic representation of the model, built using biological data.

**Conclusion / Perspectives**

**Conclusion**

- Stochastic HSC (HSC) are key regulators.
- Future research is necessary to further HSC activation and deactivation.
- The terminal stage of fibrosis is cirrhosis, which carries the major risk of occurrence of hepatocellular carcinoma (HCC). The matrix reorganization is therefore the major regulator of events related to the fibrosis-cirrhosis-cancer progression and hepatic stellate cells (HSC) are the main actors of the extracellular matrix remodeling.

**Perspectives**

- Dynamic ECM deposition induced by activated HSC and MPF lead to an increase of ECM, which may also contribute to activation of HSC (4).
- Future challenges will be the integration of new agent BOM to take into account these interactions.