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A Kappa model for hepatic stellate cells activation by TGFB1

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Introduction

Chronic liver disease is associated with the development of fibrosis, which results in the abnormal deposition of extracellular matrix (ECM) and a severe dysfunction of liver function. The terminal stage of fibrosis is cirrhosis, which constitutes the main risk factor of non-alcoholic liver cirrhosis (NASH). The matrix remodelling is therefore the major regulator of events related to the fibrofatty transformation (FAT) and Hepatocellular carcinoma (HCC) are the main actors of the extracellular matrix remodeling.

The understanding of the dynamics of HSC activation and regulation by TGF-β is necessary to induce HSC activation but chronic stimulation by TGF-β doesn’t allow to reach a final state characteristic of propagated high level of ECM.

Kappa

Kappa is a rule-based language for modeling systems of interacting agents. HSC (hepatic stellate cell) is an example.

Kappa

- Rule-based language for modeling systems of interacting agents
- Entities are graphical structures, rules are graphical rewrite rules
- Rules locally modified the state of a system
- Tools
  - Stochastic simulation abilities
  - Inputs are parameters on each individual at a site graph

Results

6 inputs of TGFB1 each 90 hours

Conclusions

- Revised HSC (HRS) are key regulators
- TGFB1 is necessary to induce HSC activation but chronic stimulation by TGFB1 doesn’t allow to reach a final state characteristic of propagated high level of ECM.

Perspectives

Because ECM deposition induced by activated HSC and MFB lead to an increase of stiffness, which may also contribute to activation of HSC (H). The future challenges will be the integration of a new agent MFB to take into account this information.