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A Kappa model for hepatic stellate cells activation by TGFB1

Introduction

Chronic liver injuries, from the onset of non-alcoholic steatohepatitis (NASH) to chronic stimulation by TGFB1, progress toward a Myofibroblast (MFB) state that escape to control, leading to cirrhosis. The understanding of the dynamics of HSC activation and regulatory network is essential to identify markers and therapeutic targets likely to promote the reversion of fibrosis at the stage of progression. Here, we develop a combined model to characterize the dynamics of HSC activation and identify the key regulators.

Kappa

A rule-based language for modeling systems of interacting agents. It is based on the stochastic simulation algorithm (SSA) and is used to define events, their probability and delimit the state of a system.

Results

8 inputs of TGFB1 every 90 hours

Conclusion / Perspectives

Conclusions

- HSCs (Hepatic Stellate Cells) are key regulators having an essential role in fibrosis progression. However, drugs inhibiting HSC activation, such as TGFB inhibitor, don’t allow to reach fibrosis state characterized by preserved high level of ECM deposition.

Perspectives

- Due to the limited work on HSCs and MFB, further studies will be needed to improve the present model to account for new information.

Model

Schematic representation of the model, built using biological data.

Agent (HSC and MFB) are defined by different types of receptors. The state of each site may be active or activated.

8 inputs of TGFB1 every 90 hours

Conclusion / Perspectives

Conclusions

- Stochastic simulation algorithm is a key regulator having an essential role in fibrosis progression. However, drugs inhibiting HSC activation, such as TGFB inhibitor, don’t allow to reach fibrosis state characterized by preserved high level of ECM deposition.

Perspectives

- Due to the limited work on HSCs and MFB, further studies will be needed to improve the present model to account for new information.