Background

- BMP and Wnt crucial for bone formation [1]
- Endochondral ossification: chondrocytes pass through a succession of states (proliferative and hypertrophic state)

Aim of this study

- model the switch between Sox9 (proliferative) program and Runx2 (hypertrophic) program
- experimental validation

Materials & Methods

Ordinary Differential Equations (ODEs) describe the temporal evolution of the various model constituents (numbers refer to interactions in Figure 1)

\[
\frac{d[\text{Runx2}]}{dt} = \frac{[\beta_{\text{cat}}]^{n_1}}{K_{n_1}^{n_1} + [\beta_{\text{cat}}]^{n_1}} + \alpha_{\text{Runx2}} \cdot \frac{[\text{Runx2}]^{n_2}}{K_{n_2}^{n_2} + [\text{Runx2}]^{n_2}}
\]

- The model predicts that:
  - activation of Wnt upregulates β-catenin and provokes the switch between the Sox9 state and the Runx2 state
  - activation of BMP inhibits the transition of β-catenin to the nucleus but cannot provoke a switch from the Runx2 state towards the Sox9 state
  - two stable states (bistability) are obtained for appropriate parameter sets

Discussion

- in absence of quantitative parameter information, the ODE model presented here provides qualitative predictions on changes in the concentrations of all modelled components
- the model is able to reproduce the switch between the Sox9 program and the Runx2 program for specific parameter sets
- the model behavior is in concordance with experimental results present in the literature [5]
- mathematical models can be used to enhance our understanding of signaling cascades and their interactions

References


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