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CONSTRUCTION OF DISCRETE MODEL OF HUMAN PLURIPOTENCY IN PREDICTING LINEAGE-SPECIFIC OUTCOMES AND TARGETED KNOCKDOWNS OF ESSENTIAL GENES

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A network consisting of 45 core genes was developed for the genes/proteins responsible for loss/gain of function in human pluripotent stem cells. The nodes were included on the basis of literature curation. The initial network topology was further refined by constructing an inferred Boolean model from timeseries RNA-seq expression data. The final Boolean network was obtained by integration of the initial topology and the inferred topology into a refined model termed as the integrated model. Expression levels were observed to be bi-modular for most of the genes involved in the mechanism of human pluripotency. Thus, single and combinatorial perturbations/knockdowns were executed using an insilico approach. The model perturbations were validated with literature studies. A number of outcomes are predicted using the knockdowns of the core pluripotency circuit and we are able to establish the minimum requirement for maintenance of pluripotency in human. The network model is able to predict lineage-specific outcomes and targeted knockdowns of essential genes involved in human pluripotency which are challenging to perform due to ethical constraints surrounding human embryonic stem cells.

Note: