Poster J-3

Searching for Genes Involved in Novel Mechanisms of Tumor Cell Death Triggered by FGF2: Introducing New Methodological Approaches

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Short Abstract: Coefficient of Determination (CoD) is introduced to analyze gene expression data aiming to uncover genetic networks underlying the Y1 adrenocortical tumor cell death triggered by FGF2. CoD networks are searched for subnetworks modeled as logic circuits and the shortest path between FGF stimulus and phenotype (survival/death), modeled as Bayesian Networks. Initial probing revealed induction of the p190RhoA-GAP gene antagonising FGF2-cell death triggering, a likely relevant inference since RhoA activation is required for FGF2-cell death triggering.

Long Abstract:

This is a progress report on the analysis of cDNA-microarray data of gene expression aiming to uncover genetic networks underlying the Y1 adrenocortical tumor cell death triggered by FGF2. Tumor cell death triggered by FGF2 is a surprising phenomenon since FGF2 is a peptide growth factor that promotes proliferation and inhibits apoptosis of normal cells. Elucidation of FGF2 molecular mechanisms that leads to tumor cell death might reveal novel targets for drug development of interest in cancer therapy.

We have previously shown a clustering algorithm for searching statistical correlation in gene expression profiles [1]. In this communication the Coefficient of Determination (CoD) is introduced. CoD has been used for finding multivariate nonlinear relations between genes [2,3]. This method assesses the codetermination of gene transcriptional states based on statistical evaluation of reliably informative subsets of data derived from cDNA- microarray data. In our work, the resulting CoD network is searched for a) subnetworks which can be modeled and studied as logic circuits and b) for the shortest path with high CoDs connecting the FGF stimulus to the phenotype (life/death), which is modeled as a Bayesian Network in which evidences can be inserted an queries on the state of the genes are answered in silico. Initial probing into Bayesian Networks has shown induction of the p190RhoA-GAP gene antagonising FGF2-cell death triggering. This inference is likely to be biologically relevant considering that RhoA activation is required for FGF2-cell death triggering [4].

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