A new approach to identify genetic networks using microarrays data - (session: Other)

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BACKGROUND and AIM: DNA repair mechanisms play a vital role in maintaining genetic integrity and it is becoming clear that defects in repair pathways are connected to the pathogenesis of secondary AML (s-AML). In particular defects in mismatch repair (MMR) and in the S-phase checkpoint gene hMRE11 are frequently observed in sAML (Casorelli et al, DNA Repair 2003, 142:1-13). We are currently studying differential expression levels of a large panel of genes (DNA repair, cell cycle control, cell growth and apoptosis) in de novo APL versus sAPL. The microarray data set will be analysed by both „descriptive‰ and „simulation‰ approaches. We present some preliminary data on the simulation approach based on a neural network model. This analysis might help to distinguish constitutive genetic networks from circuits linked to contingent situations. MATERIAL AND METHODS: Data were retrieved from published data banks of large scale microarray studies on different cellular systems (38 human AML and ALL, 76 human primary and metastatic adenocarcinomas, time course of cell cycle analysis in synchronized human cells). The correlation coefficients among a set of 50 genes involved in DNA repair (Rad50, Mre11, Brca1, base excision and mismatch repair genes), signaling of DNA damage or cell cycle (ATM, p53, p21, cyclin 1, PML) were fed into a neural network architecture, where the genes represent the nodes and the correlation coefficients the synaptic weights. Through the analysis of the asymptotic behavior of the network we studied the behaviour of the genes. RESULTS AND DISCUSSION: In the analysis of the microarray data the DNA repair/signaling genes showed relatively low linear correlations among themselves. However, a very robust behavior of the networks was observed in different data bases. This highlights the role of the nonlinear filter constituted by the neural network in identifying genetic circuits. Through this analysis it is therefore possible to identify scenarios where the same genes act in a constitutive or in an inducible way. Examples of this behaviour will be presented. The possibility to extract a sub-network of interacting genes from the unknown universe of the whole genome, offers a new tool to quantitatively describe genetic regulatory networks.