BİLKENT UNIVERSITY

MOLECULAR BIOLOGY AND GENETICS

DEPARTMENTAL SEMINAR

"Robust Network Modeling Identifies Personalized Therapeutic Strategies in Glioblastoma"

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Glioblastoma multiforme (GBM) is the most common and aggressive type of malignant human brain tumor. Molecular profiling experiments using gene expression and proteomics have revealed that these tumors are extremely heterogeneous, and this heterogeneity is one of the principal challenges for developing targeted therapies. We hypothesize that despite the diverse molecular profiles, it might still be possible to identify common signaling changes that could be targeted in some or all tumors. Using a network modeling approach, we reconstruct the altered signaling pathways from tumor-specific phosphoproteomic data and known protein-protein interactions. We then develop a network-based strategy for selecting therapeutic targets that were predicted by the models but not directly observed in the experiments. Among these hidden targets, we show that the mitogen activated protein kinase kinase 1 (MEK1) displays increased phosphorylation in all tumor lines compared to normal cells. By contrast, we show that protein numb homolog (NUMB) is present only in a subset of the tumors. We evaluate clinical data and find that presence of NUMB is directly correlated with the invasiveness of the tumors. Overall, our results demonstrate that despite the heterogeneity of the proteomic data, network models can identify common or tumor specific pathway-level changes. These results represent an important proof of principle that can improve the target selection process for personalized medicine.

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