Mathematical Measures of Network Complexity for Cancer Signaling Networks

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The 5-year survival for patients after diagnosis/treatment is strongly dependent on tumor type. Prostate cancer patients have a ¿99% chance of survival past 5-years since diagnosis, while pancreatic patients have ¡6% chance of survival past 5-years. Since each cancer type has its own molecular signaling network, we asked if there are "signatures" embedded in these networks that inform us as to the 5-year survival. In other words, are there statistical metrics of the network that correlate with survival? And further, if there are, can such signatures provide clues to selecting new therapeutic targets? From the KEGG Cancer Pathway database we computed several conventional and some less conventional network statistics. In particular we found a high correlation (R2 = 0.7) between degree-entropy and 5-year survival based on the SEER database. This correlation suggests that cancers that have a more complex molecular pathway are more refractory than those with less complex molecular pathway. We also found potential new targets by computing the betweenness - a statistical metric of the centrality of a node - for the molecular networks. We have also investigated algebraic and topological indices for network complexity for protein-protein interaction networks of 11 human cancers. We have found evidence that greater network complexity is associated with lower five year survival probabilities. Moreover, we identify several protein families (PIK, ITG, AKT) that are repeated motives in many of the cancer pathways. Our results can aide in identification of promising targets for anti-cancer drugs.