Molecular Similarities Between Tumors

Using genomic analyses of molecular similarities between tumors to make "programmed" therapies

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Recent large scale genomic studies of cancer tissue, such as The Cancer Genome Atlas (TCGA, http://cancergenome.nih.gov/) provide unprecedented means to analyze many tumors together [1]. What one finds is both great heterogeneity and great similarity. Well curated databases such as the Catalogue of Somatic Mutations in Cancer (COSMIC, http://www.sanger.ac.uk/resources/databases/cosmic.html) detail the distribution of somatic mutations across many tissues and known oncogenes. Many of these genes are known targets for cancer drugs and gene pathways. Data on copy number alteration, allelic imbalance, and chromosomal break-points across these many tissue types inform the types of chromosomal and genetic alterations that take place in tumors and cancer cells [2]. Integrating both SNP, sequence, or mutation data with gene expression data gives insight into cancer drivers that are potential drug targets. What we propose is a methodology to design a regulatory sequence delivered to the cell by nanoparticle, viral particle or other drug delivery mechanism that can identify specific cancer cells by mutational status or multiple gene expression level signatures. Synthetic biology provides many of the tools to develop this: already a logical AND operation between multiple genes has been implemented on cancer cell lines [3]. Expanding the study beyond immortalized cell lines to patient tumors is the subject of the present proposal. Recent press on this topic includes: Biological 'Computer' Destroys Cancer Cells:

Diagnostic Network Incorporated Into Human Cells http://www.sciencedaily.com /releases/2011/09/110901142056.htm [1] Bell D, Berchuck A, Birrer M, Chien J, Cramer DW, et al. (2011) Integrated genomic analyses of ovarian carcinoma. Nature 474: 609-615. [2] Beroukhim R, Mermel CH, Porter D, Wei G, Raychaudhuri S, et al. (2010) The landscape of somatic copy-number alteration across human cancers. Nature 463: 899-905. [3] Xie Z, Wroblewska L, et al. (2011) Multi-Input RNAi-Based Logic Circuit for Identification of Specific Cancer Cells. Science 333: 1307-1311.

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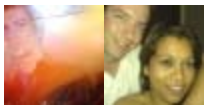

Russell Hanson

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