"Discovering Small Molecule Inhibitors of MYC and RAS"

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Abstract: The oncogenes c-MYC and K-RAS are among the most well-validated therapeutic targets in cancer, and yet little progress has been made in developing drugs that target these pathways. Indeed MYC and RAS, despite compelling genetic evidence, have been all but dropped in drug discovery programs. We propose to revisit these targets by bringing innovation in synthetic organic chemistry, genomics and computational science to bear on the problem. Specifically, we will screen synthetic, natural product-like small molecules for their ability to abrogate a gene expression signature of MYC or RAS activity in cancer cells, and we will subsequently use advanced approaches to quantitative proteomics, RNAi screening and chemical genomics to determine the protein targets of these candidate compounds.
At the end of this project, we expect to have discovered and validated inhibitors of MYC and RAS activity that are suitable for progressing further preclinical development. Given the large number of human cancers that are dependent upon MYC or RAS activity, we believe that this project has tremendous potential for future clinical impact.