Chemical Genetics and Chemical Genomics: High Throughput Profiling of Drugs and Therapeutic Disease Genes

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With advances in determining the entire DNA sequence of the human genome, it is now critical to identify and catalog genes/proteins for specific cellular pathways (functional genomics/proteomics) and ultimately to formulate and modulate complex biological networks (bio-systemics). Our efforts have focused on the development of a "chemical genetic" approach that uses small molecules to probe the function of specific pathways and genes/proteins in human cells. Chemical genetics involves: (1) identifying small molecules that affect specific cellular pathways with unbiased phenotype-based screens; (2) characterizing their action mechanisms and identifying the proteins whose activity is affected by these chemical ligands; and (3) studying the biological consequences of inhibition or activation of the target protein using the small molecules as a tool. These procedures yield information that is similar to what could be learned from cloning a mutant gene from a genetic screen and using a conditional allele to study the function of the protein that it encodes. Chemical genetic approach has been complemented by various functional genomic/proteomic approaches, which will provide the relevant and creative directions for high throughput discovery of drugs and therapeutic disease genes in the "chemical genomic and medicinal genomic" approaches. These novel and innovative approaches have been applied to the elucidation of regulation mechanisms of cell aging and immortalization, and the identification of ways to directly control these events with small molecules in oncogenic and anti-oncogenic pathways.