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Functional genomics to identify cancer targets

William C. Hahn
Dana-Farber Cancer Institute, USA

Recent advances in genomics now make it possible to consider enumerating all of the genetic lesions in specific cancers. While these approaches will yield critical information regarding the identify, number, and types of alterations found in human tumors, a complementary approach to decipher the molecular basis of malignant transformation depends upon the application of genome scale tools to annotate the function of genes involved in cancer initiation and progression. Over the past several years, we have developed genome scale RNAi libraries and open reading frame expression libraries that permit a systematic evaluation of genes involved in cancer initiation and maintenance. Using these libraries, we have now performed screens in a panel of human cancer cell lines to systematically identify cancer vulnerabilities. By combining these functional approaches with information derived from mapping the structural abnormalities present in cancer genomes, we have identified several new oncogenes that contribute to cancer development. In addition, many commonly occurring and well-validated oncogenes and tumor suppressor genes remain refractory to molecularly targeted therapies. An alternative strategy for targeting such cancer drivers is to identify gene products that, when suppressed or inhibited, result in cell death only in the presence of an oncogenic allele. Through the use of systematic RNAi screens, we have identified several genes that act as synthetic lethal partners to known oncogenes. Taken together, these studies suggest that combining forward and reverse genetic approaches with information derived from the cancer genome characterization projects will yield a comprehensive list of cancer vulnerabilities and establish a general approach for the rational identification of oncogenic and co-dependent pathways in cancer.

Biography

Dr. Hahn is an Associate Professor at the Dana-Farber Cancer Institute and Harvard Medical School. He is the director of the Center for Cancer Genome Discovery and a Senior Associate Member of the Broad Institute. His laboratory focuses on using functional genomics to study cancer.