



Emerging Topics in Biological Networks and Systems Biology

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Transcriptional Networks in Cancer

Abstract:

Cancer is the most complex genetic disease known – mutations in more than 380 genes have been associated with formation of different types of malignant tumors in humans. Yet, the malignant phenotype is simple, characterized by unrestricted growth of cells that invade neighboring healthy tissue and in many cases metastasize to distant organs. One hypothesis explaining the complexity of cancer genotypes is that oncogenic mutations would commonly activate cell type specific upstream mechanisms, which would then drive the expression of a common set of downstream genes that would be responsible for the cancer phenotype. We are taking a systems-biology approach to identify such mechanisms, and to understand how lineage-specific factors collaborate with oncogenic signals to drive cell proliferation. For this purpose, we have developed computational and experimental methods to identify direct target genes of oncogenic transcription factors that are commonly activated in major forms of human cancer. Also, we have used high-throughput RNAi screening to identify genes required for cell cycle progression. Combining these data-sets allows identification of specific transcription factors and gene regulatory elements that drive growth in particular tissues and tumor types. This analysis has identified MYC and CDK4/6/7/CCRK families as common targets of lineage-specific oncogenic pathways. The same mechanisms were also identified by analysis of common genome-wide association signals from multiple cancer types. Our results indicate that lineage-specific oncogenic transcription factors commonly regulate the same set of target genes important for growth control, and pave the way for development of broadly active antineoplastic and chemopreventive agents against cancer.

About:

Professor Jussi Taipale obtained his Ph.D. at the University of Helsinki in 1996 and continued at the University of Helsinki for his post doctorate before moving to Johns Hopkins University (Baltimore, MD, USA). Since 2003, he has headed an independent research laboratory focusing on systems biology of growth control and cancer. He has published 64 articles of which thirteen are in the most prestigious scientific journals (Nature, Science and Cell), won numerous awards and grants (e.g., Anders Jahre Prize for Young Researchers, EMBO Young Investigator, ERC Advanced Grant and Vetenskapsrådet Distinguished Professor Program (Rådsprofessor)) and is internationally recognized as a leader in the field of genomics and systems biology. In 2012 Professor Taipale was elected as Member of the Nobel Assembly at the Karolinska Institutet, which awards the Nobel Prize in Physiology or Medicine.