Cologne Evolution Colloquium

SFB 680 Molecular Basis of Evolutionary Innovations

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Cancer genome analysis and evolution

The identification relevant cancer genome alterations from large-scale sequencing efforts and their evolution in time requires a systematic computational data analysis. Here, we present our approach to integrate various (epi-)genomic datasets to identify such alterations. This approach will be demonstrated on our recent cancer genome sequencing studies of small cell lung cancer and neuroblastoma.

Small cell lung cancer occurs in about 16% of all lung cancer patients and is particularly aggressive. To decipher the genomic landscape of these tumors we sequenced the genomes of 110 and the transcriptomes of 81 patient specimens. As key findings we reported the almost universal and bi-allelic mutational deactivation of the tumor suppressor genes TP53 and RB1, the emergence of oncogenic version of TP73 by genomic rearrangements, and the role of NOTCH family genes as tumor suppressors.

Neuroblastoma is the most frequent solid pediatric cancer with a diverse clinical outcome that ranges from spontaneous regression to an unfavorable course. To better characterize the etiology of neuroblastoma we performed whole-genome sequencing of 56 patient specimens together with their transcriptomes. We found that 12 of these samples harbored rearrangements affecting the TERT locus and that these alterations were limited only to patients having a high-risk to die from the disease. Together with transcriptional upregulation of TERT by MYCN amplifications and signatures of alternative telomere lengthening in the remaining high-risk cases our data suggests the critical involvement of telomere maintenance in this unfavorable group of neuroblastomas.

To reconstruct the subclonal architecture from genome sequencing data we present our recent computational approach that identifies subpopulations of point mutations. A first application of this methodology is given by a comparison of the subclonality between lung adenocarcinoma and small cell lung cancer.

Friday, December 18, 2015, 13:00
Institute for Theoretical Physics, New Building
Meeting Room First Floor

Hosted by Michael Lässig