University of Stuttgart

Stuttgart Research Center Systems Biology

SRC SB

Systems Biology Seminar Talk

Forever young with Plan B – dissecting how cancer cells become immortal without telomerase

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10:00 CET

Lecture Hall 0.106
Allmandring 31
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Abstract:

Telomeres are repeat sequences that protect the ends of the linear human chromosome. They shorten at every cell division, which acts as a molecular clock that stops cells from dividing more than ~ 50 times. Most cancer cells circumvent this limit by activating TERT, the protein subunit of the enzyme telomerase that can extend the telomere repeats. However, some tumors do not activate telomerase but use aberrant DNA repair and recombination via the alternative lengthening of telomeres (ALT) mechanism. This pathway involves the histone H3.3 chromatin deposition machinery (ATRX and DAXX), the assembly of a PML compartment at the telomeres as well as the epigenetic network around the trimethylation of H3/H3.3 at lysine 9 (H3K9me3) via the histone SUV39H1/2 and SETDB1 methylases. We use a combination of fluorescence microscopy and molecular profiling methods to dissect ALT in single cells and apply our approach to neuroblastoma, a severe childhood tumor. Our multi-modal analysis relates ALT activity to cancer cell proliferation capacity and can be exploited for patient stratification and diagnosis as well as to identify specific vulnerabilities of ALT tumors.