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MPI-NAT SEMINAR SERIES

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Circulomics: Using the physical biology of circular DNA to illuminate genome structure and function

The topological state of a genome, linear versus circular, is generally taken to be an important demarcation that separates domains of life. Although it is universally recognized that plasmids have essential biological roles in prokaryotes, the functions of endogenous extrachromosomal circular-DNA elements in higher organisms have remained obscure. Sporadic reports since the 1960s of narrowly defined subpopulations of circular DNAs in eukaryotes have hindered broader appreciation of the possible functions of this class of molecules. Nevertheless, circular-DNA species have been found in every eukaryotic system examined for their existence. With the availability of next-generation sequencing methods, we and others have begun to comprehensively identify, characterize, and investigate the functions of extrachromosomal-circular DNAs (eccDNAs) in human cells with a particular focus on their roles in health and disease. We have shown that eccDNAs exist as distinct and partially overlapping populations in both normal and aberrant cell types and have coined the term “circulome” to encompass the general repertoire of circular DNAs present as a component of any genome.

Our insights into the circulome have been aided by a multi-decade research program devoted to the physical biology of circular DNA. We have leveraged basic knowledge of the sequence- dependent and sequence-independent molecular behavior of looped and circular DNA to develop novel methods for eccDNA enrichment and characterization. In conjunction with novel bioinformatic approaches, this has generated a unique set of powerful tools to interrogate the circulome. Our methods meet the technical challenge of isolating and characterizing the Mbp-size eccDNAs (often called “double-minute” elements in their dimeric form) implicated in cancer progression and chemotherapy resistance. I will discuss how these capabilities offer new routes to understanding the mechanisms contributing to both normal and dysfunctional genome organization.

Monday, 23.01.2023, 11:00 am

Host: Donna Jovin

Ludwig-Prandtl Hall, hybrid

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