VolkswagenStiftung

Mapping the interactions of lamin-A/C in cell cycle and in mechanotransduction signaling

Initiative: zukunft.niedersachsen (nur ausgewählte Ausschreibungen)

Ausschreibung: Forschungskooperation Niedersachsen - Israel

Bewilligung: 17.02.2016

Laufzeit:

The nuclear lamina is a critical structural scaffold for the nuclear envelope in higher eukaryotes. It interacts simultaneously with a variety of inner nuclear membrane proteins and regulatory factors, thereby recruiting chromatin domains to the nuclear periphery, stabilizing heterochromatin structures and organizing components of signal transduction cascades. Lamins participate in a complex network of interactions involved in and modulated by cell and tissue specific functions. These interactions are difficult to study because of the insoluble nature of the lamin network and their highly dynamic response to the cell cycle, development, differentiation and mechanical stress. More than 300 mutations in lamins are associated with diverse pathologies, collectively termed laminopathies that include premature ageing, muscular dystrophies and cardiomyopathies.The project's goal is to elucidate the interaction map of A-type lamins and how these interactions change during cell cycle and as part of cellular mechano-sensing. With genetically encoded UV-activatable crosslinker amino acids direct interactions of lamins in living mammalian cells will be trapped with high specificity and sensitivity. The impact of lamin phosphorylation on these interactions will be studied and they will be mapped to specific lamin domains, where genetic mutations are associated with various laminopathies. This will provide unprecedented insights into the structure of the lamin network and the mechanism of nuclear lamina (dis)assembly during mitosis and remodeling in interphase cells.
In combination with genome-wide transcriptional profiling, the approach will be used to uncover signal transduction pathways that mediate mechanical inputs, such as matrix elasticity or externally induced deformations, and how these stimuli are translated into distinctive regulatory programs of gene expression.

Projektbeteiligte

Prof. Dr. Heinz Neumann
Universität Göttingen
Fachbereich Biologie
Angewandte Synthetische Biologie
Göttingen
Dr. Amnon Buxboim
The Hebrew University of Jerusalem
Faculty of Mathematics and Sciences
Institute for Life Sciences
Safra Campus
Jerusalem
Israel