University of Stuttgart

Stuttgart Research Center Systems Biology

SRC SB

Understanding mechanisms of cell signaling and gene regulation in single cells

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Host:
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Lecture Hall 0.106
Allmandring 31
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Systems Biology Seminar Talk

Abstract:

Long noncoding RNAs (lncRNAs) are increasingly recognized for their roles in human physiology and disease; however, mechanistic insights into most lncRNAs remain elusive. In this study, we explored the regulatory mechanisms of antisense lncRNAs at the X-chromosome inactivation (XCI) locus. We found that stochastic transcription plays a critical role in determining the mechanism of regulation for Xist and Tsix. At moderate transcription levels, RNA polymerases transcribe both Xist and Tsix from the same site, leading to significant deposition of the repressive histone mark H3K36me3, which inhibits Xist. At higher transcription levels, transcriptional interference occurs due to the simultaneous transcription of Xist or Tsix by many RNA polymerases. Our results highlight that transcriptional variability is not merely noise but a regulatory feature that enables a single locus to employ multiple regulatory mechanisms across a cell population. Additionally, we investigated how cells respond to dynamic stress environments, specifically in the context of changes in extracellular osmolarity, which are crucial in various physiological and pathological processes. We discovered that human cells can withstand gradual but not acute hyperosmotic stress. Gradual stress conditions do not activate typical stress pathways, including caspase and apoptosis signaling, unlike acute stress. Notably, we observed an unexpected accumulation of proline under gradual stress conditions, which protects cells from osmotic damage, similar to the Osmo protective mechanisms observed in plants and bacteria. This finding reveals a novel cell fate switch that enables survival in gradually changing stress environments by inhibiting caspase activation and utilizing proline for protection.

CV:

Dr. Gregor Neuert is an Associate Professor of Molecular Physiology & Biophysics at Vanderbilt University School of Medicine, with a distinguished interdisciplinary background that bridges technical physics and biophysics. He earned an M.Eng. in Technical Physics from Technical University Ilmenau, Montana State University, and the Pacific Northwest National Laboratory, where he specialized in surface science and solid-state physics. Dr. Neuert then shifted his focus to biophysics, completing a Ph.D. in Physics under Dr. Hermann Gaub at Ludwig Maximilians University in Munich, Germany. Following this, he conducted postdoctoral research as a DFG Fellow in the departments of physics and biology at MIT, studying the molecular mechanisms of signal transduction and gene regulation alongside Dr. Alexander van Oudenaarden. In 2012, Dr. Neuert established his independent research lab at Vanderbilt University, supported by an NIH Director's New Innovator Award. Dr. Neuert's research focuses on using quantitative methods to unravel molecular mechanisms involved in cellular signaling and gene regulation, contributing valuable insights to the fields of molecular physiology and biophysics.