Dr. Karsten Rippe

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Genome Organization & Function

15 members of staff (biologist, physicist and chemists)

The Genome Organization & Function group at the BioQuant and the German Cancer Research Center is an interdisciplinary research team that combines molecular/cell biology and physics to develop quantitative descriptions that relate the dynamic organization of the (epi)genome with gene expression programs and functional cell states.

A special focus is put on the conformation and dynamic properties of the complex of DNA with histones and other chromosomal proteins referred to as chromatin. Both the DNA and the protein component of chromatin are subject to various post-translational modifications that include DNA/histone methylation, as well as acetylation and phosphorylation of histones. These so called epigenetic modifications define the cell's gene expression program and can be transmitted through cell division.

Understanding epigenetic regulation becomes increasingly important for medical diagnosis and therapy of cancer, developmental diseases and other pathologies. It is tightly related to chromatin (re)organization, which in turn is a key determinant of access to DNA sequence information for proteins involved in transcriptions as well as DNA replication and repair. The goal of the group is to provide an integrated view on how the dynamic balance between multiple activatory and inhibitory processes determines the stability and plasticity of epigenetic states.

To this end the group applies biophysical methods like fluorescence spectroscopy/microscopy-based techniques in living cells. This work is complemented with in vitro studies for example by analytical ultracentrifugation to elucidate how chromatin assembly, conformation, dynamics and accessibility are controlled. Furthermore, various modeling based projects with respect to the quantitative analysis of chromatin assembly, the chromatin fiber organization and the dynamic properties of nuclear subcompartments are conducted. The results from these studies are integrated into a systems biology approach to dissect epigenetic networks. The work has a number of implications for translational medical research with respect to understanding the complex effects of epigenetic drugs like histone deacetylase or DNA methylase inhibitors in treatments of cancer.

Special techniques

- Analysis of DNA/RNA and protein dynamics in living cells
- Fluorescence microscopy/spectroscopy
- Fluorescent labeling of proteins and nucleic acids in mammalian cell lines
- Genome-wide protein and nucleic acid interaction analysis
- Synthetic biology of chromatin
- Analytical ultracentrifugation
- Molecular dynamics simulation of protein-DNA complexes
- Monte-Carlo simulations of chromatin fibers
- Lattice models of DNA-protein interactions

Joint research projects

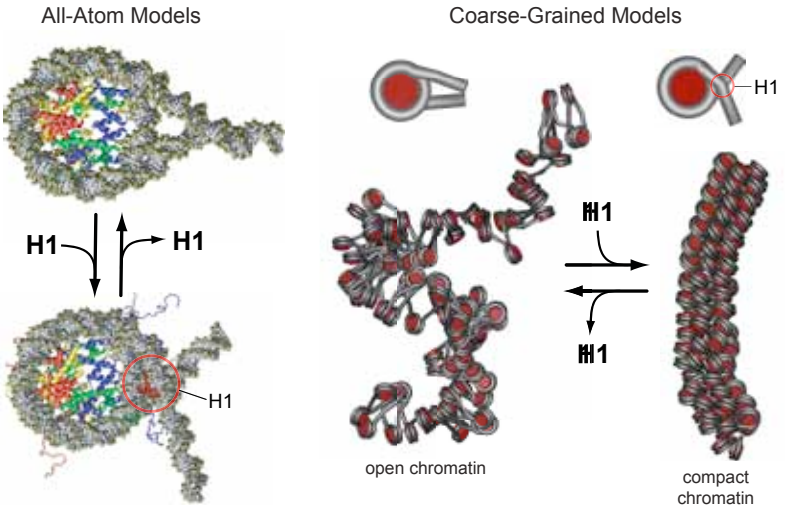
- EraSysBio Plus (EU)
- SysTec (BMBF)
- Systems Biology of Cancer (Helmholtz Association)

Selected cooperation partners

- Prof. Dr. Peter Lichter, German Cancer Research Center, Heidelberg, Germany
- Prof. Dr. Thomas Höfer, German Cancer Research Center & BioQuant, Universität Heidelberg, Germany
- Dr. Malte Wachsmuth, European Molecular Biology Laboratory, Heidelberg, Germany
- Prof. Dr. Gernot Längst, University of Regensburg, Germany
- Dr. Katalin Fejes Tóth, California Institute of Technology, Pasadena, USA

Selected publications

- Müller, K. P., Erdel, F., Caudron, M., Marth, C., Fodor, B. D., Richter, M., Scaranaro, M., Beoudoin, J., Wachsmuth, M. & Rippe, K. (2009). A multi-scale analysis of dynamics and interactions of heterochromatin protein 1 in the nucleus by fluorescence fluctuation microscopy, Biophys. J. 97, 2876-2885.
- Wachsmuth, M., Caudron-Herger, M. & Rippe, K. (2008). Genome organization: balancing stability and plasticity. Biochim. Biophys. Acta 1783, 2061-2079.
- Rippe, K., Schrader, A., Riede, P., Strohner, R., Lehmann, E. & Längst, G. (2007). DNA sequence- and conformation-directed positioning of nucleosomes by chromatin-remodeling complexes. Proc. Natl. Acad. Sci. USA 104, 15635-15640.



Model for chromatin fiber compaction induced by binding of linker histone H1. All-atom models of a nucleosome with and without linker histone H1 (left panel) were used to built coarse-grained models of this structure to evaluate the conformation of a DNA chain of 100 nucleosomes (right panel) in computer simulations. The change of the DNA geometry due to binding of linker histone H1 at the DNA entry-exit site of the nucleosome leads to a compaction of the chain into a condensed fiber structure with a diameter of about 30 nm. (Kepper, N., Foethke, D., Stehr, R., Wedemann, G. & Rippe, K. 2008, Nucleosome geometry and internucleosomal interactions control the chromatin fiber conformation, Biophys. J. 95, 3692–3705.)