Mathematisch-Naturwissenschaftliche Fakultät
Institut für Pharmazeutische und Medizinische Chemie

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An alle Interessierten

Einladung zum Vortrag

Prof. Dr. Brian Freeman

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Molecular chaperones mediate a dynamic nuclear environment

The long-term objective of my laboratory is to understand the physiological relevance of a dynamic genomic environment. Within the nucleoplasm most proteins are highly mobile, yet the overall significance of the rapid action is not understood. As a molecular paradigm to investigate the process of protein-DNA dynamics we are currently focusing on the regulatory action of the p23 molecular chaperone with the Remodel the Structure of Chromatin (RSC) complex. Our recent work showed that the maintenance of accessible open chromatin is p23-dependent. In p23 null cells the number of Nucleosome Depleted Regions (NDRs) halved yet the average size of the prevailing NDRs doubled. We had suggested that the impact of p23 on NDRs resulted solely from reduced transcription factor (TF) dynamics since p23 broadly regulates TF DNA binding activities. Yet an increase in the occupancy of DNA sites linked to chromatin remodelers also is apparent in *p23*Δ cells. Previously we reasoned that the rise in DNA-bound remodelers was an indirect effect of recruitment by the more stably bound TFs. Alternatively, p23 might directly regulate the DNA interactions of chromatin remodelers. While the size discrepancy (>1 mDa remodelers vs. ~24 kDa p23) appears to create an unlikely scenario, p23 does share numerous genetic interactions with chromatin modifiers suggesting a physiological relationship. Significantly, our preliminary data demonstrate that p23 is sufficient to dissociate DNA-bound RSC in vitro. In vivo, p23 colocalized to RSC-associated sites and in p23 null cells the timing of RSC nucleation at activated gene promoters was considerably slower. While significant effort has been placed on defining how remodelers reposition nucleosomes, the mechanisms driving the transfer of remodelers between nucleosomes are not well understood. Our current studies support a model in which p23 triggers release of RSC after it has remodeled a nucleosome thereby facilitating its transition to the next RSC-target site. Hence, the actions of p23 in mediating dynamic protein action along the genome now extend from the chromosomal ends (telomeres) to transcription, DNA repair, and chromatin remodeling machinery.

Ort: Hörsaal 6D
Zeit: Mittwoch, 22 Oktober 2014, 17 Uhr c.t.
Gäste sind herzlich willkommen.

Professur für Pharmazeutische und Medizinische Chemie

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