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INSTITUTSKOLLOQUIUM

Gemeinsames Kolloquium der Physik und Chemie

Am Dienstag, dem **27. Oktober 2026**, spricht um **17:15 Uhr** im **Faraday-Hörsaal,**

Prof. Dr. Zhao-Qi Wang

State Key Laboratory for Microbial Technology,
Shandong University, Qingdao

zum Thema:

"Differential DNA Damage Vulnerability in Human Neuropathies"

Abstract:

Human genomic instability syndromes (GIS) are caused by mutations in the DNA damage response (DDR) modulators: ATM (Ataxia-Telangiectasia, A-T), ATR (Seckel Syndrome, SS), NBS1 (Nijmegen Breakage Syndrome, NBS) and MRE11 (A-T Like Disorder, A-TLD), affecting commonly the central central nervous system (CNS), among other organs. Intriguingly, A-T and A-TLD patients show cerebellar degeneration and ataxia, whereas NBS and SS patients display microcephaly with cerebral malformations and intellectual disabilities. The differences of these clinical features hint a heterogenic action mode of the DDR in different regions of the brain. Although the DDR is a universally conserved cellular mechanism, the spatiotemporal utilization of these pathways in distinct neural cell types renders a diverse vulnerability of specific brain regions to pathological processes. The cerebellar pathology represents a striking common hallmark across various human GIS. We investigated how these DDR modulators dictate the cell-type diversity and specificity in neuropathologies of human GIS. We found that knock-out of MRN in the mouse CNS results in cerebellar atrophy and ataxia due to a selective disruption of cerebellar granule cell progenitors (GCPs). GCPs, but not cerebral cortical progenitors, contain a high level of DSBs in the absence of Mre11, which consequently leads to the activation of P53 and apoptosis. Spatial transcriptomic analyses revealed that in the *Mre11*-mutant cerebellum, GCPs were widely depleted during cerebellogenesis. In contrast, the cerebral cortex was resistant to Mre11 deletion, as cell types and molecular pathways were unchanged. Transcriptomic module scoring indicated that spatiotemporal heterogeneity of repair pathway utilization determines regional pathological susceptibility to malfunctional DDR.

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Die Hochschullehrer der Institute für Physik und Chemie