Physikalisches Kolloquium — Physics Colloquium

Einladung — **Invitation**

Monday, 17 November 2025

Lecture Hall N24/H13, at 16:15
Coffee and cookies will be served in front of the lecture hall from 16:00

The guardian on the move: p53 dynamics and function in single cells

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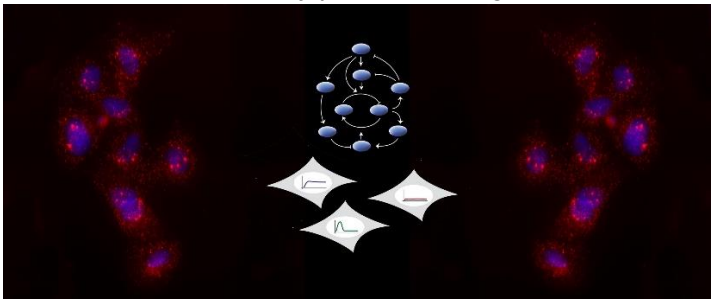
The tumor suppressor p53 is a central hub in the signaling network mediating the mammalian DNA damage response. It converts incoming signals into alternate cell fate decisions by changing the expression of hundreds of target genes. Combining quantitative fluorescent live-cell microscopy, computational data analysis and mathematical modeling revealed pulsatile accumulation of p53 protein upon induction of DNA double strand breaks. Initial studies indicated that these pulses are generated by an excitable network comprising positive and negative feedback resulting in uniform amplitude and duration. The strength of the insult is mainly encoded in the number of pulses, like a digital signaling system. We are now investigating how the molecular network regulating p53 dynamics shapes its response to acute and sustained stress. Our results suggest that the damage regulated kinase ATM is crucial for initiating the p53 response, while the check point kinase CHK2 sustains the response in the presence of persisting damage by moving the negative feedback between p53 and its ubiquitin ligase in a stable limit cycle. This leads to sustained p53 oscillations, whose duration depends on the initial amount of activated Chk2. Furthermore, we examined how varying levels of p53 affect stochastic gene expression at its numerous target gene promoters and revealed gene- and stimulus specific regulation patterns at the single cell level. Taken together, our systems biology approach provides evidence how specific dynamics of the tumor suppressor p53 enable individual cells to appropriately respond to varying type and doses of genotoxic stress and thereby prevent tumorigenesis.



Host: Prof. Dr. Christof Gebhardt, Institute of Experimental Physics

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