Mitochondria are highly dynamic organelles with essential functions in the physiology of energy metabolism, controlled reactive oxygen species (ROS) formation and the regulation of intracellular Ca\(^{2+}\) homeostasis. In the nervous system, mitochondrial integrity is crucial for the maintenance and function of neurons. In fact, mitochondrial damage is a major feature of many neurological and neurodegenerative diseases, and cellular stress and death signaling pathways converge at the level of mitochondria. In particular, disturbed intracellular Ca\(^{2+}\) homeostasis, increased ROS formation, dysbalanced fusion and fission of the organelles, loss of the mitochondrial membrane potential, and the release of mitochondrial proteins such as apoptosis inducing factor (AIF) are prominent in many different paradigms of neuronal dysfunction and death.

The lecture will highlight novel insights into the molecular regulation of increased mitochondrial fission in models of neuronal cell death induced by oxidative stress, glutamate toxicity and oxygen glucose deprivation. In particular, the role of dynamin related protein-1 (Drp-1) and Bid will be discussed as potential targets for therapeutic approaches in models of neuronal death in vitro and in vivo. The data demonstrate that both factors interact in mediating mitochondrial damage and intrinsic pathways of cell death, while pharmacological inhibition of each factor preserves mitochondrial functions, thereby providing neuroprotective effects. In addition, further approaches of mitoprotection are discussed, including strategies of mitochondrial preconditioning, and pharmacological activation of small conductance Ca\(^{2+}\)-dependent potassium channels (SK), which prevent both, disruption of the Ca\(^{2+}\)-homeostasis and increased ROS formation. This approach is of particular interest for the further development of therapeutic strategies in neurological disorders, since SK channel activation mediates neuroprotection at the level of the plasma membrane and in mitochondria.

Overall, several lines of evidence expose mitochondria as key regulators in pathways of cellular stress with relevance to progressive neuronal dysfunction and death which is prominent in many neurodegenerative diseases and conditions of acute brain damage. Thus, novel concepts aiming at preserved mitochondrial integrity and function may provide effective neuroprotection.

**Publications**

