Institute of Applied Physiology
N27, Room 4.053
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Everybody welcome!

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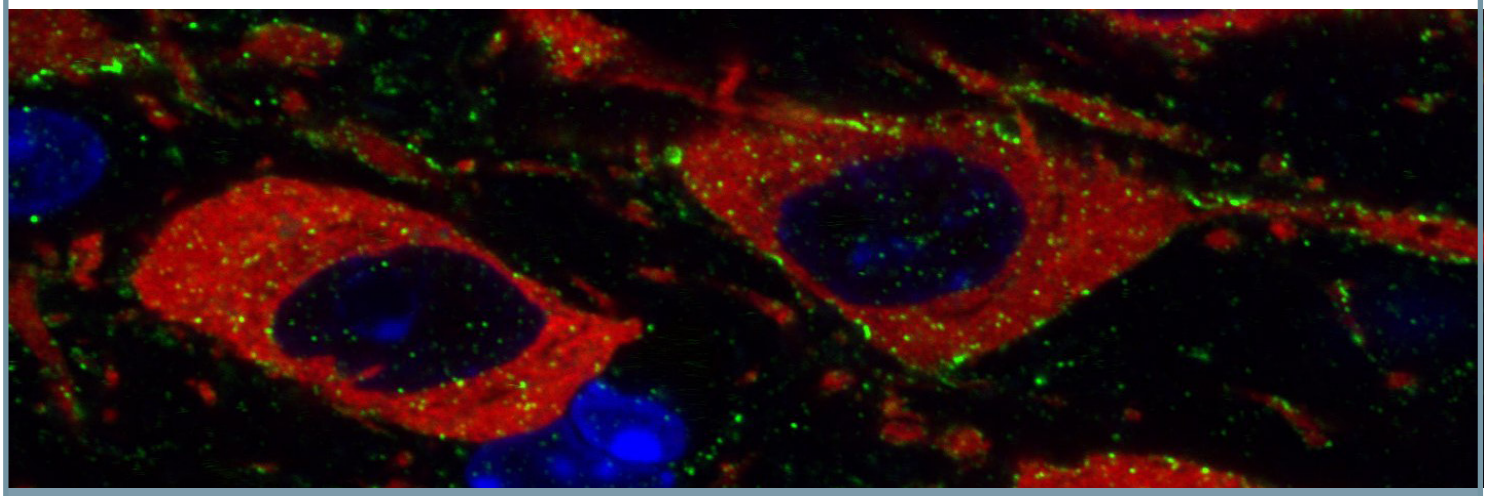

Physiology Seminar

Mitochondria – endoplasmic reticulum crosstalk as therapeutic target against aging, cancer and diabetes

Given by Univ.-Prof. Mag. pharm. Dr. rer. nat. Wolfgang F. Graier
Chair of Gottfried Schatz Research Center, Head of Division Molecular Biology and Biochemistry, Medical University of Graz

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Mitochondria are not only the master of cellular energy metabolism, but they are also involved in multiple vital processes, including signal transduction, biosynthesis, and gene expression. Mitochondria are crucially involved in most pathological processes leading to cell dysfunctions and, ultimately, cell death. The reason for such ubiquitous involvement of mitochondria in cellular physiology and pathology is mainly achieved by the intense interaction of the organelle with virtually all other cellular compartments. Accordingly, the endoplasmic reticulum (ER) – mitochondria axis received enormous attention. This interorganelle interface is organized in so-called, mitochondria-associated membranes (MAMs), the site where the exchange of substrates, products, and ions occurs. Particularly the latter one, namely Ca2+, appears to be a fundamental regulator of such inter-organellar communication. Recent studies revealed abnormal inter-organellar Ca2+ transfer as a hallmark in many diseases like Alzheimer, diabetes mellitus, cancer, and aging. Applying state-of-the-art techniques such as super-resolution fluorescence microscopy (pmid: 35778442, 31427612), single Ca2+ channels recordings in the inner mitochondrial membrane (pmid: 26275882 , 23397170), structure biology techniques like NMR or ITC (pmid: 27642082), and the design of genetically encoded biosensors (pmid: 26842907, 29127288, 31636543; www.ngfi.eu), we discovered posttranslational arginine methylation of the primary regulator of the mitochondrial Ca2+ uptake, MICU1 (pmid: 35778442, 27642082) that engages UCP2 as a crucial facilitator for mitochondrial Ca2+ uptake (pmid: 17351641) under distinct pathological conditions. Accordingly, we are now able to envisage the role of the ER-mitochondria axis for (re-)wiring (pmid: 35058562), e.g. as the instigator of ß-cell dysfunction has been identified. Hence, specific alterations in the ER-mitochondria axis have been identified in aging and cancer (pmid: 30458321, 33614647). Based on this work, we are currently successfully testing potential leading compounds uniquely designed to counteract cell aging- or cancer-specific settings at the ER-mitochondria interface. Our latest findings reveal an excellent specificity of these compounds that exclusively hits senescent or cancer cells and highlight the great potential of such strategies and compounds against aging-associated dysfunction and cancer growth.