Consiglio Nazionale delle Ricerche

ISTITUTO PER L'ENDOCRINOLOGIA
E L'ONCOLOGIA SPERIMENTALE
"G. SALVATORE"
2nd UNIT

Friday Seminar
21st April 2023, 14:30h CEST

Mathias Zeigler
University of Bergen, Norway

Dynamics of cellular NAD metabolism: How, where and when?

Host: Daniela Corda (daniela.corda@cnr.it)

Conference Room, CNR, P. Castellino Campus

Abstract:

NAD is a vital molecule in all organisms. It plays key roles as cofactor in metabolic redox reactions and as substrate for signal transduction processes. Given these critical functions, rapid degradation of host cell NAD has evolved as one of the favorite killing strategies used by microorganisms. NAD+-dependent signaling pathways include poly- and mono-ADP-ribosylation, protein deacetylation by sirtuins and generation of messengers involved in Ca2+ signaling. They mediate fundamental events such as transcription, DNA repair, cell cycle progression and vesicular transport. Moreover, they contribute to epigenetic regulation and the control of metabolism. All these signaling reactions include the degradation of NAD to nicotinamide. In fact, NAD turnover appears to be unexpectedly rapid in human cells suggesting that NAD-dependent signaling processes are highly active. The high rate of NAD consumption necessitates robust NAD biosynthesis, in particular, efficient recycling of the vitamin precursor nicotinamide. In addition, supplementation with related NAD precursors can restore reduced NAD levels observed in aging and neurodegenerative diseases. Indeed, a pilot study in Parkinson's disease conducted in Bergen yielded promising results. Our experimental research over the past years has identified some of the molecular mechanisms underlying cellular NAD homeostasis. We have developed and applied research tools to understand the dynamics of subcellular NAD pools, their generation and mutual communication. Our observations indicate an inter-organellar crosstalk of NAD pools and point to a role of mitochondria as NAD buffer. Moreover, we have identified a general NAD-dependent cell death pathway that was originally thought to be specific for axonal degeneration. Overall, NAD biology has emerged as a field of intense research efforts that have led to promising NAD supplementation approaches to improve human health.

Biosketch:

Mathias Ziegler received an M.D. from the Medical University in Moscow in 1986 where he was trained in Medicine and Biomedicine. In 1990, he obtained a Ph.D. in biochemistry at the Charité (Medical School) Berlin, where he studied mitochondrial biology. Following postdoctoral work in the USA, he started as independent group leader with a focus on NAD-mediated signaling mechanisms at the Free University Berlin. Since 2004 he has worked as full professor at the University of Bergen, Norway, now at the Department of Biomedicine. His current research interests are in principal mechanisms of the biology of NAD and other coenzymes, and their perturbations in neurodegenerative and other diseases.