IMOL SCIENCE CLUB

THE INTERNATIONAL INSTITUTE
OF MOLECULAR MECHANISMS AND MACHINES
POLISH ACADEMY OF SCIENCES

ONLINE SEMINAR

Prof. Aleksandra Trifunovic

TRANSCRIPTIONAL REGULATION OF MITOCHONDRIAL STRESS RESPONSE

October 6th, 2021, 2 P.M. CET
Online seminar via ZOOM

REGISTER AT WWW.IMOL.INSTITUTE

Transcriptional regulation of mitochondrial stress response

SPEAKER

PROF. ALEKSANDRA TRIFUNOVIC
Institute for Mitochondrial Diseases and Ageing,
Faculty of Medicine,
University of Cologne, Germany

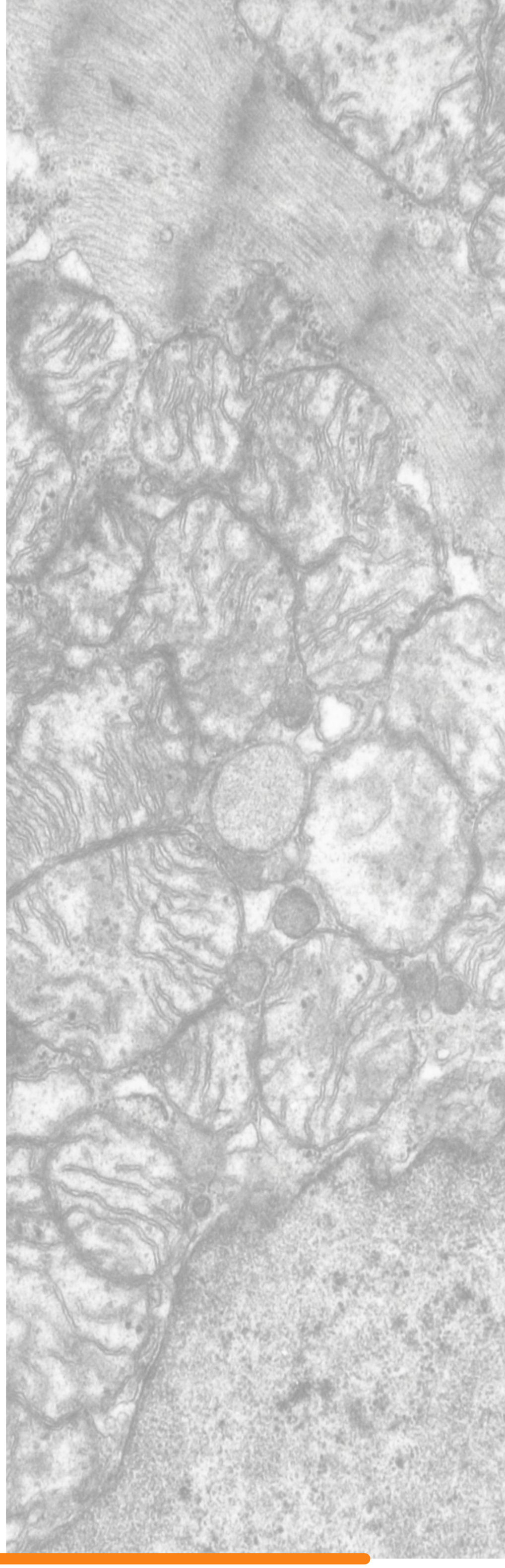
ABSTRACT:

Understanding of the mitochondrial stress response in mammals remains incomplete. Numerus studies over last years showed that unlike in C. elegans, mammalian UPRmt is not the primary response to mitochondrial dysfunction but rather part of more complex mitochondrial stress response sharing a signature of the integrated stress response (ISR), hence referred to as mitoISR.

We recently uncovered an intricate interplay between three transcription factors regulating the mitochondrial stress response: CHOP, C/EBPβ, and ATF4. Contrary to its previously proposed role as a transcriptional activator of UPRmt, we present strong evidence that CHOP, through its interaction with C/EBPβ, attenuates prolonged ISR and mitochondrial cardiomyopathy through regulation of ATF4 levels.

Our results argue that upon mitochondrial dysfunction, the interaction of CHOP with C/EBPβ is needed for the adjustment of an ATF4-regulated transcriptional program. Very early upon mitochondrial dysfunction, before OXPHOS deficiency occurs, Chop is increasingly expressed and forms a complex with C/EBPβ, which seems to facilitate the translocation of CHOP:C/EBPβ heterodimers to the nucleus, thus preventing overactivation of the ATF4-regulated transcriptional program.

Hence, contrary to its previously proposed role as a transcriptional activator of mitochondrial unfolded protein response, our results highlight a role of CHOP in the fine-tuning of mitochondrial ISR in mammals.



REGISTER AT WWW.IMOL.INSTITUTE

The International Institute
of Molecular Mechanisms and Machines
Polish Academy of Sciences

IMOL