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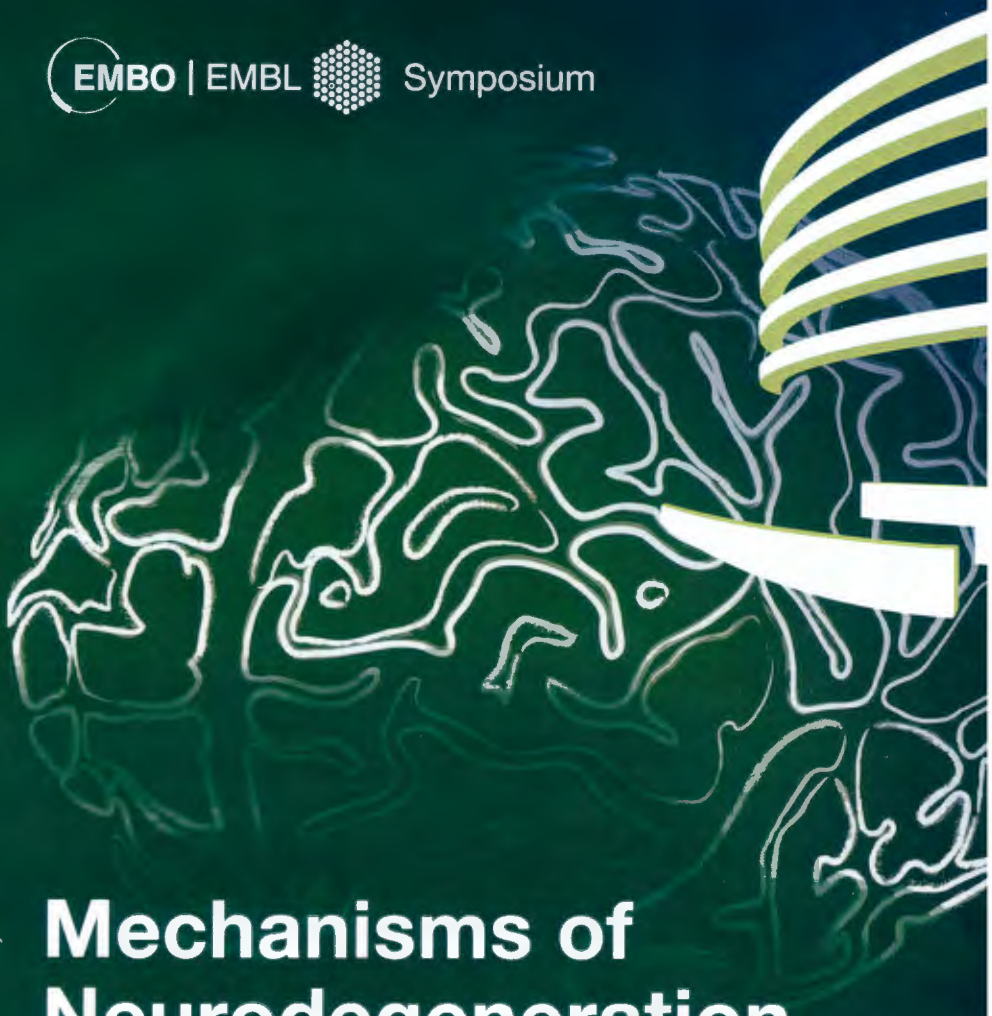

Mechanisms of Neurodegeneration

14–17 June 2017 | Heidelberg | Germany | EMBL Advanced Training Centre

Kuchkin Daniil

Abstracts of papers presented at the

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Scientific Organisers:
Bart De Strooper, KU Leuven, Belgium
Karin Dumstrei, The EMBO Journal, Germany
Todd Golde, University of Florida, USA
Christian Haass, German Center for Neurodegenerative Diseases, Germany

Conference Organiser:
Bronagh Carey, EMBL Heidelberg, Germany

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Analysis of mammalian amyloids interaction in yeast Saccharomyces cerevisiae

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Presenter: Daniil Kachkin

Protein misfolding and aggregation processes are central events in the pathogenesis of amyloid diseases such as Alzheimer disease (AD), Amyotrophic lateral sclerosis (ALS), Creutzfeldt-Jakob disease (CJD), type 2 diabetes (T2D) and etc. Existing data demonstrates that amyloids can interact with each other. Coexistence of various aggregates has been demonstrated for a series of proteins, such as PrP (mammalian prion), amyloid beta peptide (Ab) and tau peptide (associated with Alzheimer's disease). A number of authors have described presence and coexistence aggregates of Ab and PrP in CJD patients. Epidemiological research has demonstrated frequent combination of AD with T2D. Type 2 diabetes patients are twice as exposed to the risk of Alzheimer's disease development.We use an yeast model for amyloid interaction analysis. It has been a useful model organism in such fields of research as regulation of transcription, protein trafficking and cell biology, primarily because of its ease of genetic manipulation. This is no less so in the area of amyloid studies.For our research we chose the most socially important diseases (AD, T2D, CJD) and studied amyloids which are significant for their pathogenesis. We have obtained plasmids and strains with human amyloidogenic proteins are fused to CFP and YFP. Thus, by using FRET technique, we can analyze colocalization of different amyloids in yeast and their ability to interact in vivo. Also we showed that analyzed amyloidogenic proteins can form detergent-resistant aggregates in yeast which are similar to those formed in humans.We showed that some amyloids can physically interact with each other and those interactions can play an important role in disease pathogenesis. This work was supported by the grant from Russian Science Foundation (Project 14-50-00069); RFBR (Projects 15-04-06650 and 15-04-08159). Authors acknowledge the SPbSU Resource Centers «CHROMAS» and «Molecular and Cell Technologies» for technical support.

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Neurotoxic action of triclocarban involves apoptosis but not autophagy and estrogen receptor signaling

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Presenter: Malgorzata Kajta

Recently, an antimicrobial compound triclocarban (3,4,4'-Trichlorocarbanilide) has been positioned in the middle of the rank of potentially dangerous organic pollutants, but far before bisphenol A (BPA) that has been recognized as developmental risk factor. Although a growing body of evidence shows that triclocarban is present in human tissues, little is known about its impact on the nervous system. This study aimed at investigating the mechanisms of neurotoxic action of triclocarban with a particular concern on apoptosis and autophagy, and the interactions with the estrogen receptor-mediated signaling. We demonstrated that triclocarban (0.1-100 μM), that was used in environmentally relevant concentrations, induced apoptosis in mouse embryonic neurons in primary cultures as evidenced by loss of mitochondrial membrane potential, activated caspase-3, and apoptotic fragmentation of cell nuclei. In contrast to induction of apoptosis, triclocarban inhibited autophagic processes in mouse neurons as indicated by approximately 70% decrease in the level of autophagosomes. The use of selective antagonists (MPP, PHTPP, G15) and expression analyses point to impairment of the estrogen receptors ESR1 and GPR30, but not ESR2 in response to triclocarban. In this study, for the first time triclocarban has been identified as neurodevelopmental risk factor that induces apoptosis, impairs autophagy, and disrupts estrogen receptor signaling. Targeting the receptors could be asset in searching for effective neuroprotective strategies against Neural Disrupting Chemicals and their controlled use, especially during the early developmental stages. Acknowledgement: Supported by the Polish National Research Centre grant no. 2015/19/B/NZ7/02449 and the funds from KNOW sponsored by Ministry of Science and Higher Education, Poland.