Interactions of mitochondrial matrix proteins 17β-hydroxysteroid dehydrogenase type 10 and cyclophilin D in people with Alzheimer disease and multiple sclerosis

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The nucleus-encoded mitochondrial matrix protein 17β-hydroxysteroid dehydrogenase type 10 (17β-HSD10) operates via multiple enzymatic as well as non-enzymatic functions. Its overexpression or deficiency is associated with various pathologies. Increased levels of 17β-HSD10 in cerebrospinal fluid (reflecting probably its brain overexpression) were found in patients with Alzheimer disease (AD) or multiple sclerosis (MS). Both neurodegenerative diseases are accompanied by mitochondrial dysfunction. Cytosolic 17β-HSD10 is imported into the mitochondrial matrix via PINK1-Parkin-TOM/TIM pathway. Here, it binds to cyclophilin D (cypD) and, by preventing its translocation to the inner mitochondrial membrane, can regulate the opening of the mitochondrial permeability transition pore mediated by cypD. Under conditions of increased accumulation of mitochondrial amyloid β (Aβ), observed especially in AD, interactions of 17β-HSD10 and cypD could be eliminated which may lead to apoptosis and mitochondrial dysfunction. Using cerebrospinal fluid samples of people with AD or MS and mitochondria isolated from double transgenic McGill-R-Thy1-APP rats (one of the best animal models of AD with intracelular accumulation of Aβ), we estimated levels of 17β-HSD10, cypD, Aβ 1-42, total Aβ and of various complexes (17β-HSD10 – Parkin, 17β-HSD10 – total Aβ, 17β-HSD10 – cypD). In AD, our results indicate that up-regulation of 17β-HSD10 does not have to be followed by increased levels in mitochondrial matrix and that the ability of the protein to regulate cypD is weakened. In MS, on the contrary, it seems that up-regulation can lead to increased PINK1-Parkin-TOM/TIM transport and that 17β-HSD10 in mitochondrial matrix is fully functional. Supported by GA CR (P304-12-G069) and AZV CR (16-27611A) projects.

Speaker Biography

Zdenka Kristofikova studied at Czech Technical Univerzity in Prague (Ing., Department of Nuclear Chemistry) and at Univerzity of Defence, Faculty of Military Health Sciences in Hradec Kralove (PhD, Department of Toxicology), both in the Czech Republic. She works at National Institute of Mental Health as a senior researcher and a head of working group. She is interested in Alzheimer disease for a long time (Web of Sciences: 122 results, 594 sum of times cited, h-index 15).

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