

PROMEMO / DANDRITE Topical Seminar

Monday 15 January 2018
at 13:00 – 14:00

Aarhus University, building 1182, room 101

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Molecular Pathway Delineation of the Antidepressant Treatment Response

Over one third of major depressive disorder (MDD) patients do not show improvement during or after antidepressant treatment. The reasons for the heterogeneous antidepressant response need to be better understood in order to realize strategic and personalized treatment of MDD. With the aim of identifying molecular pathways associated with the antidepressant treatment response, we treated DBA/2J mice with the Selective Serotonin Reuptake Inhibitor paroxetine for 28 days. Following treatment, the mice were categorized into responders or non-responders based on the time they spent immobile during the forced swim test. Quantitative metabolomics and proteomics profiles were acquired for the hippocampus and plasma to identify molecular pathways that stratify antidepressant-treated sub-groups. Integration of mouse hippocampal metabolomics and proteomics data revealed significant purine/pyrimidine, glutamatergic and ubiquitin-proteasome system pathway differences between paroxetine responder and non-responder mice. In human MDD patient PBMCs, protein signatures from identified pathways including carbamoyl phosphate synthase 2, Aminoimidazole-4-carboxamide ribonucleotide transformylase/IMP cyclohydrolase, soluble guanylate cyclase- β 1, proteasome subunit α type-2 and ubiquitination levels significantly correlated with Hamilton Depression Rating Scale changes in response to antidepressant treatment. Our data indicate that purine/pyrimidine metabolism, glutamatergic and ubiquitin-proteasome system pathways can play a crucial role in the antidepressant treatment response, which may be used to predict and monitor the clinical antidepressant response. Our ongoing antidepressant engagement profiling with mass spectrometry coupled cellular thermal shift assay will add more valuable information to better understand the mechanisms of antidepressant action.

Host: Group Leader Anders Nykjær, PROMEMO, DANDRITE, Dept. of Biomedicine, Aarhus University