



Discovery, verification and validation of a biomarker profile for depression (MOODMARKER)

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This project aims at identifying a biomarker profile for major depressive disorders (MDD). We will use an iterative strategy of biomarker profile discovery, verification and validation. Discovery: To identify a biomarker profile, proteomics will be conducted for CSF and CSF extracellular vesicles (CSF-EVs; WP1) and post-mortem limbic brain tissue from MDD patients having died by suicide and matched controls (WP2; with in situ validations in WP3), as well as for limbic brain tissue from chronic social stress (CSS) and control mice (WP4). Verification: The CSF/CSF-EVs biomarker profile will be verified in a new, larger cohort of MDD patients (WP5). Proteomic findings will be verified in human brain samples at the mRNA (transcriptomics) and epigenetic (genome-wide methylation & miRNome) (WP6, WP8). In limbic brain from CSS/control mice, for a specific cell type implicated by the biomarker profile, RNA will be extracted for the study of the transcriptome (WP7) and the miRNome (WP8). Validation: Blood plasma-EVs will be obtained from MDD patients before and during antidepressant treatment and proteomics will be applied (WP9). CSS/control mice will receive an antidepressant drug or vehicle, and plasma-EVs and limbic brain tissue will be collected for proteomics (WP10). Data from most WPs will be investigated using deep bioinformatics pathway analyses (WP11). The establishment of this MDD biomarker profile is expected to be diagnostic, prognostic and treatment responsive.