Prof. Julia Stingl

Role of genetic polymorphisms in drug metabolizing cytochrome P450 enzymes expressed in the brain for affective disorders, (BrainCYP)

Project Coordinator: Prof. Julia Stingl, Federal institute for drugs and medical devices, Bonn, Germany.

Project Partners: Dr. Roberto Viviani, University Ulm, Ulm, Germany,
Prof. Magnus Ingelman-Sundberg, Karolinska Institute, Stockholm, Sweden,
Prof. Rachel Tyndale, University of Toronto and Centre for Addiction and Mental Health, Toronto, Canada.

Cytochrome P450 (CYP) enzymes are proteins that help eliminate external substances such as drugs and toxins ingested or absorbed by an organism. Many drug-metabolising enzymes can also modify substances produced by the organism itself. The BrainCYP project focuses on two P450 enzymes, CYP2C19 and CYP2D6, which vary genetically in humans. These enzymes are expressed in the brain, and are able to metabolise CNS active substances such as antidepressants, antiepileptics, cannabinoids, and tryptamine derivatives. The genes coding these two enzymes occur in the population with variants that exhibit extreme effects on their activity. For example, some individuals have no functioning CYP2D6 protein in their organism, while others have so much CYP2D6 that its function is enhanced 10-15 times. Evidence pointing to the importance of these CYP variants to brain function is derived from studies showing differences in the susceptibility to affective disorders as well as differences in brain activity obtained with modern neuroimaging methods. Accordingly, this genetic variation may have practical implications for the treatment of mental disorders. BrainCPY brings together groups that work with laboratory animals carrying the two CYP genetic variants and groups that use neuroimaging to assess the impact of genetic variants on brain function..

Structure of the BrainCYP project: