## Project Nº 43

**Title:** Regulation of serotonin (5-HT) function by a VGLUT1 dependent glutamate pathway.

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<th>Department/Laboratory</th>
<th>Department of Pharmacology and Toxicology (Neurpharmacology research area)</th>
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### Summary:

It is widely accepted that in many patients altered serotonergic function may contribute to the aetiology and pathophysiology of affective disorders and frequently co-morbid with anxiety disorders. Moreover, drugs affecting the serotonergic function have had success in the treatment of major depression. Still, although the molecular mechanisms underlying the 5-HT dysfunction are unknown, experimental evidences suggest an important role for both local and long-loop feed back mechanisms of control over the 5-HT activity in the brain stem including the excitatory (glutamate) and inhibitory (GABA) neurotransmitter systems. Further, clinical and pre-clinical studies have linked major depression to an imbalance in the excitatory-inhibitory ratio in different brain areas. In keeping with this, unraveling the mechanisms of 5-HT neuron control might provide new insights into depression pathophysiology. In addition to the inhibitory 5-HT₁A autoreceptors, cortico-raphe glutamatergic descending pathways are suggested to modulate 5-HT activity in the DRN. Here we will study how decreased VGLUT1 levels in the brain stem affect glutamate regulation of 5-HT function.

VGLUT1+/− mice (C57BL/6) and wild type (WT) littermates will be used. In addition, adenovirus overexpressing VGLUT1 (pDEST-B1-pSyn-B5-VGLUT1Venus-B2 y pDEST-B1-pSyn-B5-VGLUT1mCherryminisog -B2) will be used to rescue the phenotype observed in VGLUT1+/− mice. Specifically, the functionality of the inhibitory 5-HT₁A autoreceptor will be assessed using biochemical (5-HT levels by HPLC, 5-HT1A mRNA expression) and pharmacological approaches (GTP-Gamma binding, in vivo recording of body temperature) in all the groups.
**References**


**POSSIBILITY OF PhD**

YES*

* (PhD grant required)