

## INTERNSHIP PROPOSAL

**Institute and Group:** IBS, Group Membrane

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**Research project title:** Structural studies of a human GABA<sub>A</sub> receptor

**5 Keywords to describe the project:** Ion channel, membrane transport, biochemistry, structure,

**Description of the project (aims, experimental techniques, recommended background):**

Ligand-gated ion channels mediate fast synaptic transmission in the brain. The mechanisms by which neurotransmitter binding opens an ion-selective transmembrane channel in the receptor, thereby transmitting an electrical signal into the target cell, remains to be explained at the atomic level. The student will undertake the expression, purification and structural analysis of a pentameric GABA<sub>A</sub> channel-receptor. We already have a very good HEK cell line that produces large amounts of this receptor, but the student will also perform transient transfections of mutants. He/she will investigate a diverse set of tensio-active molecules (detergents, nanodiscs...) to find the best biochemical environment for the receptor. He/she will characterize the properties of the binding of selective toxins that bind to this receptor and try to image the complex by electron microscopy.

The host team has a long-standing expertise of membrane protein structural biology, and of ion channels. Protocols for the projects are partly established, and thus the student will have opportunities to discover all aspects of a structural project, from molecular biology to cristallography or EM.

**Relevant publications of the team:**

1. Hassaine G, Deluz C, Grasso L, Wyss R, Tol MB, Hovius R, Graff A, Stalberg H, Tomizaki T, Desmyter A, Moreau C, Li XD, Poitevin F, Vogel H, Nury H . X-ray structure of the mouse serotonin 5-HT<sub>3</sub> receptor. *Nature* **2014** 512:276-281
2. Hassaine G, Deluz C, Li XD, Graff A, Vogel H, Nury H . Large scale expression and purification of the mouse 5-HT<sub>3</sub> receptor  
*Biochim Biophys Acta*. **2013** 1828:2544-2552
3. Nury H, Van Renterghem C, Weng Y, Tran A, Dufresne V, Baaden M, Changeux JP, Sonner JM, Delarue M, Corringer PJ  
X-ray structures of general anaesthetics bound to a pentameric ligand-gated ion channel *Nature* **2011**, 469:428-31