Objective

GABA(A)Rs are the principal neurotransmitter receptors at the inhibitory synapses. The majority of these receptors are anchored at the inhibitory postsynaptic compartment by the central scaffolding function of gephyrin. A dysfunctional receptor clustering by gephyrin leads to abnormal neurotransmission and neurodevelopmental disorders, including anxiety disorders and epilepsy. Recent advances in the structural studies, most recently by cryo-electron microscopy (cryo-EM), have elucidated several heteropentameric GABA(A)R structures. All of these illustrate receptors in isolation. However, in a physiological synaptic context, GABAARs exist and function in close association the auxiliary protein LFPLH4 as well as with anchoring proteins including gephyrin, collybidin (CB) and the adhesion molecule...
neuroligin 2 (NL2).

To understand the architecture and function of this fundamental complex, I will work on the structural elucidation of the human GABA(A)R-gephyrin-CB-NL2 supramolecular complex by single-particle cryo-EM. Structural studies will be followed by validation using additional biochemical, biophysical and electrophysiological analysis of mutant constructs. These data will not only provide the first insights into the supra-molecular organization of a major human neurotransmitter receptor. As the dysfunctional GABAergic neurotransmission manifest itself in lethal neurodevelopmental disorders such as Alzheimer’s and also epilepsy, structural insight into the central complex will also help to understand the molecular basis of these disorders.

**Fields of science**

- natural sciences → biological sciences → neurobiology
- medical and health sciences → basic medicine → neurology → epilepsy
- medical and health sciences → basic medicine → neurology → dementia → alzheimer
- natural sciences → biological sciences → biochemistry → biomolecules → proteins
- medical and health sciences → clinical medicine → psychiatry → anxiety disorders

**Keywords**

- GABA(A) Receptor
- Gephyrin
- Cryo-EM
- Collybistin
- Neuroligin
- Inhibitory postsynapses

**Programme(s)**

- H2020-EU.1.3. - EXCELLENT SCIENCE - Marie Skłodowska-Curie Actions
- H2020-EU.1.3.2. - Nurturing excellence by means of cross-border and cross-sector mobility

**Topic(s)**

- MSCA-IF-2019 - Individual Fellowships
Call for proposal

H2020-MSCA-IF-2019

See other projects for this call

Funding Scheme

MSCA-IF - Marie Skłodowska-Curie Individual Fellowships (IF)

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Links

Contact the organisation
Website
Participation in EU R&I programmes
HORIZON collaboration network

Other funding

€ 0,00

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