

3-in-1: A novel approach to study membrane protein pharmacology

Membrane proteins make up about 25% of all proteins encoded by the human genome and are considered major drug targets. One type of membrane protein, the family of **ligand-gated ion channels** (LGICs), mediates crucial functions in the nervous system and has been implicated in numerous diseases. Most LGICs are molecular assemblies of more than one subunit, but conventional methods to study these proteins cannot easily address the contribution of individual subunits within such a protein complex. Recent advances in the field of **molecular biology** and **chemical biology** now allow to overcome this limitation by using of **inteins**, a family of self-splicing proteins, to link together individual subunits into one large protein containing all subunits required for full LGIC assembly and function. This will allow us to individually **manipulate a defined number of subunits** within LGIC complexes and therefore enable us to elucidate the function and pharmacology of these medically relevant proteins in unprecedented detail.

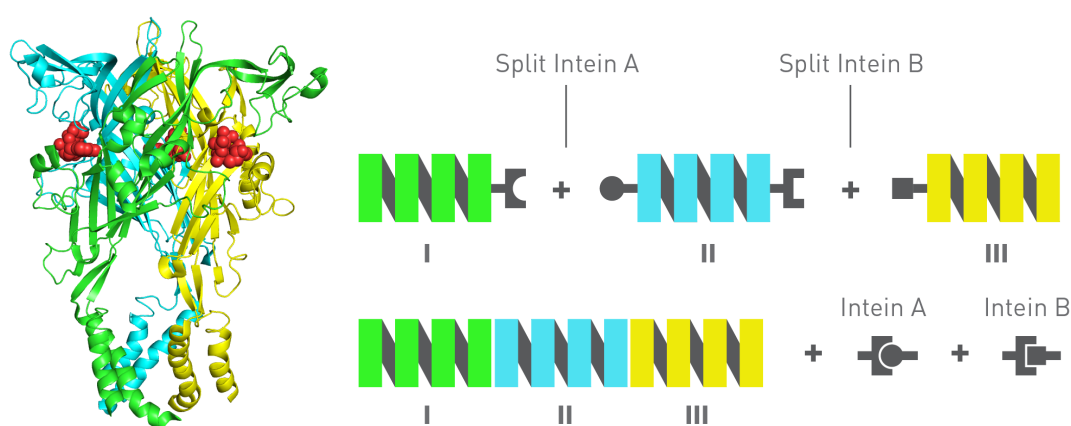


Fig 1: Left: Example of the structure of a trimeric LGIC with subunits indicated by different colors and the ligand shown in red ; Right: cartoon illustrating the use of (split)inteins in order to create a trimeric protein in which a defined number of subunits can be individually manipulated.

The development of such a cutting-edge approach will be broadly applicable to numerous types of proteins and will no doubt provide the foundation of many future studies in different fields.

The project will be carried out in the newly-established Center for Biopharmaceuticals, which provides state-of-the-art facilities and a very vibrant and international environment. The project will be supervised by Assoc. Prof. Stephan A. Pless (Stephan.pless@sund.ku.dk). For more information please contact us or visit our website: www.theplesslab.com