Submission to Molecular and Cellular Neuroscience

Dear Editors:

We wish to submit the enclosed manuscript entitled “PICK1 interacts with \(\alpha_7\) neuronal nicotinic acetylcholine receptors and controls their clustering” for publication as an Article in Molecular and Cellular Neuroscience.

\(\alpha_7\) neuronal nicotinic acetylcholine receptors (nAChRs) modulate network activity, neuronal survival and cognitive processes in the CNS. They are particularly abundant in the hippocampus, where they form clusters at the surface of GABAergic interneurons and modulate hippocampal inhibition and synaptic plasticity. The identity of proteins that interact with \(\alpha_7\) nAChRs to regulate their trafficking and localization remain unknown. We think our study would be of general interest to the readership of Molecular and Cellular Neuroscience, because we have identified the first scaffolding protein, PICK1, that binds to \(\alpha_7\) and show that it plays a role in \(\alpha_7\) clustering specifically in interneurons. PICK1 binds to the \(\alpha_7\) intracellular loop in yeast, mammalian and hippocampal cells, and colocalizes with the receptor at the surface of hippocampal interneurons. Although it does not affect receptor distribution in heterologous cells, PICK1 expression reduces \(\alpha_7\) clustering in interneurons.

These data show that PICK1 regulates surface clustering of \(\alpha_7\) nAChRs in GABAergic hippocampal interneurons, which may be important in inhibitory functions of \(\alpha_7\) in the hippocampus. These findings open new avenues to understand nicotinic receptor-dependent plasticity, addiction and pathology, and we therefore believe that the data should be of high interest to a broad range of neuroscientists.

We suggest [names of suggested reviewers] as possible reviewers (please see addresses of suggested reviewers below).

We respectfully request that this paper is not reviewed by [names of potential reviewers], all of whom are working on similar questions and would therefore have a significant conflict of interest in reviewing this manuscript.

In case of questions, please do not hesitate to call me at +41 44 635 33 10.

Thank you for considering this paper. We are looking forward to your reply.

Since

Christina Fuhrer, Ph.D.
Adjunct Professor for Neurobiology

Zurich, September 28, 2006