BMC Pharmacology

Meeting abstract

C-terminal mutation induces a folding defect in the serotonin transporter

Ali Elkasaby, Subhodeep Sarker* and Herwig Just

Address: Institute of Pharmacology, Center for Biomolecular Medicine and Pharmacology, Medical University of Vienna, 1090 Vienna, Austria

Email: Subhodeep Sarker* - subhodeep.sarker@meduniwien.ac.at

* Corresponding author

from 14th Scientific Symposium of the Austrian Pharmacological Society (APHAR)
Innsbruck, Austria. 21–22 November 2008

Published: 5 November 2008

BMC Pharmacology 2008, **8**(Suppl 1):A7 doi:10.1186/1471-2210-8-S1-A7

This abstract is available from: http://www.biomedcentral.com/1471-2210/8/S1/A7

Neurotransmitter transporters are responsible for terminating signal transmission. hSERT (the human serotonin transporter) is the plasma membrane Na^+/Cl^--dependent transporter which is responsible for uptake of serotonin from the synaptic cleft. A previous study has shown that deleting the C-terminus of SERT impaired transporter activity and compromised its delivery to the plasma membrane) [1]. However, this study did not provide a mechanistic explanation. Alanine-scanning mutagenesis strategy was used in order to delineate which part of the C-terminus of SERT was required for folding of the protein. Pairs of alanine substitutions by site-directed mutagenesis have been produced and we are currently in the process of testing the effect of these mutations on the functional properties and the cellular localization of SERT. The preliminary data show that the mutation in P601G602-AA and R607I608-AA (Sec24 binding site) causes intracellular retention and abolishes uptake and binding.

Acknowledgements

This work is supported by: SFB35-10 and stipend from Egyptian Ministry of Higher Education and State for Scientific Research.

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