Gabrielle Rudenko Ph.D.

Assistant Professor
Department of Pharmacology
Life Sciences Institute 210 Washtenaw Ave #3163A 2216
Ann Arbor, MI 48109
(734) 615-9323
rudenko@umich.edu
My website

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Research Interests

Our lab seeks to determine the three dimensional structure of proteins that have important functions in the brain, by using x-ray crystallography. Our studies are augmented with biochemical and biophysical studies, as well as site-directed mutagenesis.

We are currently studying neuron:neuron adhesion molecules called neurexins and a transcription factor called DeltaFosB:

Neurexins are cell-surface proteins found exclusively in the brain and are play a role in synapse organization and adhesion. LNS/LG domains in neurexins undergo extensive alternative splicing at the mRNA level, to produce protein isoforms that bind different protein partners. The splice sites map close to each other in the protein, in loops located at one end of the module, likely forming part of a binding surface. We plan to solve structures of neurexin LNS/LG domains with their naturally occurring splice inserts. We will discover through these structures if the splice inserts are accommodated in loops, replace existing b-strands or insert new secondary structure elements. These structures should reveal not only how alternative splicing affects the LNS/LG protein fold, but also tell us how the recognition of binding partners and neuron adhesive properties are modulated.

DeltaFosB is a transcription factor whose levels are dramatically increased in the brain of laboratory animals, following chronic administration of electroconvulsive seizures, certain anti-depressants, anti-psychotics and drugs of abuse. On a molecular level, the induced DeltaFosB appears to have undergone modification(s) making it more stable, so that it persists in the brain for a relatively long period of time (weeks

to months!). The fact that DeltaFosB is stable for so long makes it unique and potentially important. Modification of DeltaFosB may affect its ability to turn genes on or off, in turn producing long-term changes to the brain, for example through regulation of synaptic plasticity. We are currently characterizing DeltaFosB biochemically, biophysically and structurally.

Selected References

Sheckler LR, Henry L, Sugita S, Sudhof TC, Rudenko G., Crystal structure of the second LNS/LG domain from neurexin 1alpha: Ca2+-binding and the effects of alternative splicing. J Biol Chem. 281(32) p. 22896-905 (2006).

Ulery PG, Rudenko G, Nestler EJ., Regulation of DeltaFosB stability by phosphorylation. J. Neurosci. 26(19) p. 5131-42 (2006).

Rudenko, G., Henry, L., Vonrhein, C., Bricogne, G., Deisenhofer, J. MAD-ly phasing the extracellular domain of the LDL receptor: a medium sized protein, large tungsten clusters and multiple non-isomorphous crystals. Acta Cryst. D59, 1978-1986 (2003)

Rudenko, G. & Deisenhofer, J. The low-density lipoprotein receptor: ligands, debates and lore. Curr. Opin. Struct. Biol. Dec;13(6):683-9 (2003)

Rudenko, G., Henry, L., Henderson, K., Ichtchenko, K., Brown, M., Goldstein, J., Deisenhofer, J. Structure of the extracellular domain of the LDL receptor at endosomal pH. Science, Vol 298 p. 2353-2358 (2002)

Rudenko, G., Hohenester, E., Muller, Y. LG/LNS domains: multiple functions - one business end? Trends Biochem. Sci. 26(6) p. 363-368 (2001)

Rudenko, G., Nguyen, T., Chelliah, Y., Sudhof, T.C., Deisenhofer, J. The structure of the ligand-binding domain of neurexin 1beta: Regulation of LNS domain function by alternative splicing. Cell, Vol. 99 p. 93-101 (1999)

Rudenko, G., Bonten, E., Hol, W.G.J., d'Azzo, A. The atomic model of the human protective protein/cathepsin A suggests a structural basis for galactosialidosis. Proc. Natl. Acad. Sci. USA Vol. 95 p. 621-625 (1998)

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