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# $GABA_A$ receptor binding partners in the ER: A role in trafficking to the cell surface

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Fast synaptic inhibition in the adult brain is largely mediated by $GABA_A$ receptors ($GABA_A$Rs), members of a family of GABA-gated Cl-/HCO3- permeable ion channels. $GABA_A$Rs are heteropentameric assemblies of subunits classified as α(1-6), β(1- 3), γ(1- 3), δ, ε, θ and π. The most abundant subtypes of these receptors incorporate two α, two β and 1 γ subunit. The cell surface expression of $GABA_A$Rs, a prerequisite for normal function, is dependent on the appropriate assembly of receptor subunits and quality control within the endoplasmic reticulum (ER) resulting in forward trafficking. We have described a highly conserved and previously uncharacterized region within the extracellular N-terminal domain of receptor subunits adjoining the first transmembrane domain as a region important for processing of $GABA_A$Rs within the ER. Modifications of this region by insertion and site-directed mutagenesis in the α1, β3 and γ2 subunits were shown to impair $GABA_A$R trafficking to the cell surface even though the expression and co-assembly of mutated receptor subunits into heteropentamers were intact. To define the underlying molecular mechanisms, we have carried out proteomics and mass spectrometry to isolate proteins which can bind to the N-terminal extracellular domains of α1, α2, β2 and γ2 subunits, expressed and purified using the baculovirus/Sf9 cell system. This approach has revealed a number of proteins which are likely to associate with the extracellular N-terminal domains of $GABA_A$R subunits in the ER, including calnexin, BiP and calreticulin. The role of these proteins in $GABA_A$R trafficking was further characterized.

## Biography

Jasmina N Jovanovic received her PhD in Neuroscience from the Rockefeller University, USA, in 1998. She completed her postdoctoral studies at the University College London, UK, in 2003. As a recipient of The Grass Fellowship in Neuroscience in 2001, and The Grass Foundation Faculty Award in 2004, Dr. Jovanovic worked as a summer investigator at the Marine Biological Laboratory, in Woods Hole, USA. Dr. Jovanovic was appointed as a Lecturer/Group Leader at the UCL School of Pharmacy in 2003, and was promoted to Senior Lecturer in 2007. She serves as an editorial board member of the Journal of Biological Chemistry.

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