

10<sup>th</sup> International Conference on

# Neuroscience and Neurochemistry &

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## SMART steroids: Steroidal molecules as rapid-acting therapeutics

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Neurosteroids are compounds synthesized in the nervous tissue from cholesterol or steroidal precursors from peripheral sources. It is believed that neurosteroids execute their effects by modulating the activity of different membrane receptors, including the glutamatergic ionotropic receptors, e.g. N-methyl-D-aspartate receptors (NMDARs). The NMDARs play an important role in development, synaptic plasticity, learning and memory, however, abnormal activation of NMDA receptors have been shown to mediate neuronal degeneration/cell death. To find novel potentially beneficial drugs to treat neurological damage or neuro-degeneration is one of the most investigated areas in contemporary pharmacology and neuroscience. Therefore, we have designed and synthesized a library of SMART steroids- steroidal molecules as rapid-acting therapeutics. SMART steroids are neuroactive molecules, targeting primarily NMDARs, show neuroprotective properties and minimal side effects in animal models. Our screening pipeline currently covers physicochemical and biological properties like: Solubility (DLS); lipophilicity (logP, logD,  $\Delta G_{solv}$ ); patch-clamp recordings from HEK293 cells assessing NMDAR inhibition rates and IC<sub>50</sub> values; caco-2 assay, treatment of glutamate and NMDA-induced neurotoxicity (survival rate, caspase-3, intracellular calcium levels, ROS); in vitro growth of postnatal neurons after neurosteroid administration; models of animal behavior (open field, elevated plus maze, forced swim test, etc.); PTZ-induced seizures; paclitaxel-induced peripheral neuropathy and; pharmacokinetic properties. Our results indicate that these compounds do afford neuroprotective effect and as such, SMART steroids may be beneficial in treatment of several neurological diseases like epilepsy, neuropathic pain, AD, PD and others. Broad patent portfolio has been developed protecting compounds, production and its use for treatment in neurology etc.

### Biography

Eva Kudova has been working at Institute of Organic Chemistry and Biochemistry in Prague, Czech Academy of Sciences (IOCB) since 2002. She completed her PhD in 2009 at Charles University in Prague. Then, she worked for two years in the lab of Douglas F Covey at Washington University School of Medicine in St. Louis, Missouri, USA. Since 2011, she works at IOCB as the Project Investigator (PI) at Targeted Research Group of Steroidal Inhibitors. Her main research interest is Steroidal Chemistry. She has been working in this field for more than 10 years. Her major avenue of investigation is design and synthesis of new neuroactive steroidal compounds and structure-activity relationship studies affording NMDARs ligands.

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