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Book of abstracts

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Novel NMDA receptor peptide antagonist

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NMDA receptor is one of the attractive targets for treatment of major depressive disorder (MDD). FDA approved the S-ketamine which is a non-selective NMDA receptor blocker for treatment of MDD in March, 2019. Unfortunately, ketamine shows undesirable side-effects. Thus, safer alternative are of a great demand.
Based on the known structure-activity relationships for ifenprodil binding site a set of peptides were designed by the virtual screening of the custom peptide library which contains all short peptides with up to 4 aminoacids. Molecular dynamics simulations with subsequent MM-PBSA binding free energy assessment were performed for 10 selected peptides and compared to known NMDA receptor ifenprodil-like antagonists. The selected peptides were synthesized and evaluated in radioligand binding assay ([H^3]-ifeprodil). The most promising peptide was tested and showed a weak inhibitory activity to NMDA/Gly-induced currents. We hope that this findings will aid the development of a safer antidepressants.