

International Conference and Exhibition on
Pain Medicine

June 08-10, 2015 Chicago, USA

NPYFa, dualsteric chimeric peptide of met-enkephalin and NPPF, prevents opioid induced tolerance

Annu Mudgal and Santosh Pasha
CSIR-IGIB, India

Background: Methionine-enkephalin-Arg-Phe (MERF) is a known endogenous amphipathic analgesic peptide. Neuropeptide FF (NPPF) is reported for long lasting analgesia, role in opioid modulation and tolerance development. Based on these reports a dualsteric chimeric peptide NPYFa (YGGFMKKKPKQRFamide) was designed, having Met-enkephalin (opioid) and PKRF sequence of NPPF at C-terminal which can target both opioids and NPPF receptors. The aim of the present study was to determine opioid induced analgesia upon acute treatment and its tolerance development upon chronic exposure.

Results: NPYFa demonstrated early onset, dose dependent and prolonged anti-nociception. Antagonists (μ , κ and δ receptor) pretreatment studies alone or together and with NPPF receptors antagonist demonstrated κ -opioid receptors mediated anti-nociception. RF9, NPPF receptor antagonist exhibited additive effect to NPYFa acute analgesia, suggesting participation of NPPF receptors. In addition both Eu-GTP- γ S binding assay and FACS analysis further corroborated the observed acute analgesia showing significant binding with KOR and NPPF2 receptors suggesting its multiple binding nature. Further chronic (6 days) treatment effect of NPYFa showed up-regulation of protein expression of these receptors suggesting no tolerance development to the NPYFa acute analgesia.

Conclusions: Thus, NPYFa demonstrated potent, long lasting anti-nociception without tolerance development. Hence NPYFa may prove to be a potent analgesic probe with less tolerance development

annu.chemistry@gmail.com
spasha@igib.res.in

Notes: