KINETIC CHARACTERIZATION OF NOVEL FLUORESCENT PIPTES BINDING TO MELANOCORTIN 4 RECEPTORS

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Melanocortin 4 (MC_4) receptors are central modulatory system for energy homeostasis, eating behavior and sexual functions. Ligand binding to these G protein-coupled receptors (GPCRs) is governed by a complex dynamic regulation [1]. The potential of targeting MC_4 receptors in drug discovery is set by the ability to quantify the formation and duration of the receptor-ligand complexes [2].

Fluorescence anisotropy method has been successfully applied in kinetic studies of ligand binding to these receptors among several other GPCRs [3, 4]. However the slow dissociation of the fluorescently labelled ligand NDP-α-MSH limits its use in kinetic studies of MC_4 receptors. To meet the need for fluorescently labelled ligands with improved kinetic properties two novel red-shifted fluorescent peptides UTBC101 and UTBC102 were designed.

Both of the novel ligands exhibited nanomolar level affinity to MC_4 receptors although they had quite different binding kinetics. UTBC101 had approximately 1.4 times and UTBC102 approximately 30 times faster dissociation compared to Cy3B-NDP-α-MSH ($\tau_{1/2}$ = 224 min) [3]. In screening assays UTBC102 covers a wider kinetic range due to its significantly shorter dissociation half-life, whereas UTBC101 covers a wider range of competitor potencies due its higher affinity. These ligands could become valuable tools for kinetic screening of novel MC_4 receptor specific ligands.

References

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