

P025 Novel highly selective low-molecular radioligand for melanocortin-4 receptor: [¹²⁵I]THIQ.

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Melanocortin receptors (MCR) belong to the family A of G-protein coupled receptors. MC₄R is shown to have important roles for central regulation of food intake, energy balance and sexual functions.

I-THIQ, iodine derivative of low molecular weight compound N-[(3R)-1,2,3,4-tetrahydroisoquinolinium-3-ylcarbonyl]-(1R)-1-(4-chlorobenzyl)-2-[4-cyclohexyl-4-(1H-1,2,4-triazol-1-ylmethyl)piperidin-1-yl]-2-oxoethylamine (THIQ), has retained its high affinity and selectivity for melanocortin 4 receptors (MC₄R). Herewith we have used ¹²⁵I derivative of this compound ([¹²⁵I]THIQ) and checked its usability as radioligand of MC₄R. [¹²⁵I]THIQ binding to MC₄R expressed in COS-1 cells was fast, reversible and with high affinity. However, high non-specific binding and adsorption of the radioligand onto all materials complicated significantly the performance of experiments and interpretation of its results. Examination of a different buffer solution conditions reveal that higher BSA concentration and decreased buffer pH value during the solution preparation stage significantly minimized these undesired side effects. Fast binding kinetics of [¹²⁵I]THIQ makes it also valuable tool as a reporter ligand for characterization of binding of other reversible ligands to MC₄R, but its usability for characterization of slow, partially irreversible ligands is strongly limited.