



**Supplementary Figure S4. CART fragments do not bind to any types of opioid or G protein-coupled receptors and the complete CART(55-76) is not acting as a DPP4 inhibitor.** MOR (A) and KOR (B) binding affinity of CART peptides to DAMGO and HS665 in  $[^3\text{H}]$ DAMGO and  $[^3\text{H}]$ HS665 competition binding assays in rat and guinea pig brain membrane homogenates, respectively. Values represent mean values $\pm$ SEM for at least three experiments performed in duplicate. Specific binding of  $[^{35}\text{S}]$ GTP $\gamma$ S in percentage (C) in the presence of increasing concentrations ( $10^{-10}$  -  $10^{-5}$  M) of the indicated ligands. In the enzyme inhibitory assay (D) the level of basal activity was defined as 100% and maximal inhibitory effect of sitagliptin was indicated with a dotted line. Points represent means $\pm$ SEM for at least three experiments performed in triplicates.