Analysis of VPAC and secretin receptors in vertebrates: its implications on molecular and functional evolution of the secretin receptor family

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G-protein coupled receptors (GPCRs) are important in the pharmaceutical industry, as approximately one third of therapeutic drugs are targeted to modify functions of GPCRs. Information regarding essential structural motifs and domains for receptor-ligand interaction and intracellular signaling could be obtained by a comparative approach using selected animal models that have specific positions in vertebrate evolution. In the past 10 years, our lab has been working on the functional evolution of a family of peptides including pituitary adenylyl cyclase activating polypeptide (PACAP), vasoactive intestinal peptide (VIP), growth hormone releasing hormone (GHRH) and secretin (SCT). Receptors for these peptides carry out diverse physiological functions while their structures in early vertebrates remain unclear. In this study, several PACAP/VIP receptors (VPAC-R) and SCT receptors (SCT-R) from representative vertebrates were identified and characterized. Based on these recent data as well as our previous works, a revised evolutionary scheme for PACAP/VIP/SCT receptors is proposed. Our hypothesis provides explanations for the divergence of these receptors in relation to the widely accepted theory that indicates the presence of 3 rounds of genome duplication in early vertebrates. We believed that the works here should provide us with fundamental information for seeking the origin of this family of receptors in the vertebrates.