Water homeostasis is essential to animal survival. It is a complicated biological system which constitute of many hormones and receptors located in brain responsible for continuously monitoring osmolality within suitable physiological range and keep in balance. G-protein coupled receptors (GPCRs) are well-known as ligand-specific cell surface receptors responsible for transducing different sensory, chemotactic, hormonal and neuronal signals. It involves in many physiological processes including osmoregulation. Angiotensin II 1a receptors (AT1aR) from GPCR family A and secretin receptor (SCTR) from GPCR family B shared overlapping biological functions in osmoregulation. Both of these two receptors are highly expressed and co-localized in paraventricular nucleus (PVN). In addition, our research group has previously shown that SCTR and AT1aR were able to form heteromer in CHO cell by receptor BRET assays. Given that GPCR receptors may also self-associate or form dimers and higher-order oligomers to elicit specific cellular responses. Therefore, we hypothesized that AT1aR and SCTR may form heteromer in osmoregulatory centres and perform specific biological functions in hypothalamus.

Although the important role of SCTR/AT1aR heteromer in osmoregulation was confirmed, the in vivo role in central osmoregulatory centre is still unknown. In addition to drinking behaviour, ANGII and SCT are potent in stimulating VP release and expression in PVN. While Vp is one of the key components to access osmoregulation because of the physiological link between Vp release and drinking behaviour, therefore it is a spate of interest to understand whether SCTR/AT1aR heteromer regulate osmoregulation via the pathway of Vp release. In this study, we demonstrated that SCTR/AT1aR heteromer was involved in the regulation of Vp release and expression, as well as the central neural involvement in PVN.