The 59th iCeMS SEMINAR

Tue 14 September 2010
11:00-12:00

The Nose in a Dish: Functional Expression of Mammalian Chemosensory Receptors

Lecturer: **Hiroaki Matsunami, Ph.D.**
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Venue: 2nd floor Seminar Room (#A207)
Main Building, iCeMS Complex 1
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Hosted by: iCeMS (Institute for Integrated Cell-Material Sciences), Kyoto University

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Abstract of Dr. Matsunami's seminar on Sep 14.

In order to understand how odorants and pheromones are detected by the chemosensory receptors, it is essential to identify the receptors which are activated by a given chemical. Although these receptors, members of G-protein coupled receptors (GPCRs), were first identified in 1990's, functional data relating selectivity of how the receptors respond to their cognate ligands remains largely unclear.

Though in vitro systems has been widely used to interrogate receptor-ligand interaction, identifying cognate ligands for most of the chemosensory receptors including the ORs and the V2Rs has been difficult, because of poor surface expression in heterologous cells.

For functional cell surface targeting of ORs, we previously show that mammalian ORs require receptor-transporting proteins RTP1 and RTP2 for functional expression. Using this system, we have asked a series of fundamental questions regarding odorant receptor function, such as comprehensive identification of ligand-receptor pairs and how genetic variation of human odorant receptor genes affects their function and odor perception.

For the V2Rs, we find a very different mechanism regulating their surface expression. We show a mechanism by which a ubiquitously expressed endoplasmic reticulum chaperone, calreticulin, acts to block V2R trafficking that ultimately limits the functional cell surface-expression in heterologous cells. We identified calreticulin4, a homolog of calreticulin, shows highly enriched expression in the vomeronasal chemosensory organ in place of calreticulin. The mechanism of trafficking employed by V2Rs is likely unique, in that the transport of V2Rs was not facilitated by co-expression of the specific chaperone, calreticulin4. Rather, depletion of calreticulin was crucial for the V2Rs to be transported to the plasma membrane. Using this approach, we show activation of the V2Rs by their cognate peptide ligands.

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