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# Intracellular signaling: G proteins talking to G proteins

Dr. Philip J.S. Stork,
Professor, Vollum Institute, Oregon Health and Science University

Our laboratory studies the biochemical pathways governing cell proliferation and differentiation, with particular interest in the synergistic actions of hormones and growth factors in cell differentiation and proliferation. These pathways are mediated by multiple GTP binding proteins including both "heterotrimeric G proteins" as well as "small G proteins". Over the past number of years, we have examined how heterotrimeric G proteins, which are activated by hormones, interact with the small G protein pathways that are activated by growth factors. One of the best-studied small G proteins is the small G protein Ras. Ras is an important target of growth factor action and acts, in large part, by activating the MAP kinase cascade. Heterotrimeric G proteins that are coupled to cAMP (via the alpha subunit of Gs) can activate or inhibit MAP kinase signaling, depending on the cell type. I will discuss models that account for this specificity of action, focusing on the small G proteins Ras and Rap1, a Ras family member, as well as the MAP kinase kinase kinase B-Raf.

The major intracellular target of cAMP is the cAMP-dependent protein kinase (PKA). Additionally, two new targets of cAMP have been identified: Exchange Proteins Activated by cAMP (EPAC). Two EPACs have been identified, EPAC1 and EPAC2. Both are guanine nucleotide exchange factors for Rap. I will present a model that activation of Ras regulates EPAC2 function in part by recruiting EPAC2 to the plasma membrane via its Ras association (RA) domain. This property of EPAC2 to respond to Ras signaling suggests that EPAC2 can act as a coincidence detector for signals generated by growth factors (Ras) and G protein-coupled receptors linked to cAMP. For EPAC1, the RA domain does not bind to Ras and has no known binding partner. In the last part of the seminar, I will discuss new studies examining the role of the RA domain of EPAC1 in EPAC1 localization and function.

## September 16th, Wednesday 16:00~

## 医学研究科 F 棟 1 階セミナー室
## Building F, 1F, Seminar Room

連絡先　病態生物医学分野
(Department of Pathology and Biology of Diseases)
松田　道行 (Michiyuki Matsuda)　内線(ext. 4421)