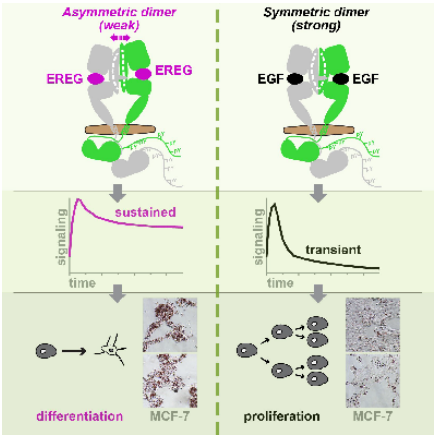
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

Biased agonism in receptor tyrosine kinase (RTK) signalling



The 58 growth factor receptor tyrosine kinases (RTKs) provide a useful palette of signaling mechanisms used in biology by receptors with a single transmembrane domain. Although initial studies of examples such as the epidermal growth factor receptor (EGFR) suggested a simple ligand-induced dimerization mechanism, it is now clear that these receptors are much more complex than this, with substantial diversity across the superfamily. Our studies of human EGFR activation by different activating ligands, combined with studies of invertebrate EGFRs, suggest a much more complicated picture for EGFR regulation. Early work with the *Drosophila* and *C. elegans* EGFRs suggested models for allosteric regulation of dimeric EGF receptors. More recently, we determined crystal structures of the human EGFR extracellular region bound to different activating ligands, revealing distinct structures with important implications for fine control of EGFR activation. Further investigation in cellular studies has revealed that certain EGFR ligands function as partial or biased agonists of the receptor, likely through a kinetic proofreading mechanism, to allow the same receptor to promote either cell differentiation or cell proliferation depending on the activating ligand.

Dr. Mark Lemmon

Profesor of Pharmacology
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Host: Dr. Sachdev Sidhu

Date: Thursday June 7, 2018
Time: 11 AM
Place: CCBR Red Room