Donnelly Centre
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"Antiparasitic drug discovery: using recombinant yeast to find non-peptide ligands for nematode neuropeptide GPCRs"

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11:00 a.m. - 12:00 p.m.
James Friesen | Cecil Yip
Red Seminar Room
Donnelly Centre

Abstract:

Neuropeptides in the FMRFamide family (FLPs) are essential components of nematode neuromuscular systems and regulate essentially all physiological systems involved in motility, eating and reproduction. A large family of G protein-coupled receptors (GPCRs) that employ FLPs as endogenous ligands has been identified from the free-living nematode Caenorhabditis elegans as well as from many parasitic species. cDNAs encoding ~ 10 FLP-GPCRs have been functionally expressed in yeast (Saccharomyces cerevisiae) in a format that allows facile, multiplexed high-throughput screening assays to identify small molecule, non-peptide ligands that act as agonists or antagonists of these GPCRS. These assays are based on ligand-induced receptor activation, which leads to expression of an enzyme in the histidine biosynthesis pathway that is otherwise absent from this strain of yeast. The presence of an agonist in the culture medium permits growth of the recombinant yeast in the absence of histidine, providing a sensitive and highly specific endpoint for screening. Non-peptide agonists and antagonists of nematode FLP receptors are intriguing leads for possible development as novel anthelmintics.
We adapted these recombinant yeast strains for screening collections of synthetic and natural product chemicals obtained from multiple sources. This presentation describes the screening system and our results so far.

Host: Peter J. Roy