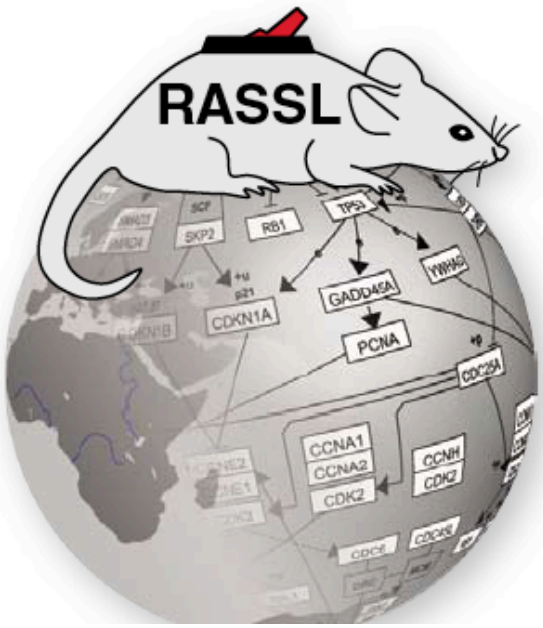
Hormone receptors direct the development and function of complex tissues, including those in the cardiovascular system. Our research focuses on the largest known family of receptors for hormones and drugs, the G protein–coupled receptors (GPCRs), which include over 700 human genes. We combine genetic knockouts, designer GPCRs, and bioinformatics techniques to gain a basic understanding of hormone signaling in mice and pluripotent stem cells.

We have engineered GPCRs called receptors activated by small synthetic ligands (RASSLs) that are unresponsive to endogenous natural hormones, but can still be activated by synthetic small-molecule drugs. We have expressed RASSLs in a wide variety of tissues to control responses such as heart rate, bone formation, and stem cell development. More recently, we have been using induced pluripotent stem (iPS) cells from patients with human genetic disorders in heart rhythm, such as long QT syndrome. These studies will allow us to directly examine the role of GPCR signaling in iPS–derived human tissues with specific human genetic diseases.

In parallel research efforts, our pathway-oriented bioinformatics team has produced a series of free, publicly distributed software packages called GenMAPP and WikiPathways, which are used by hundreds of researchers worldwide. We are expanding these open source programs to provide comprehensive genome-wide, pathway-oriented analysis for functional genomic experiments. These tools allow us to better analyze functional genomic data to advance our own studies of GPCR signaling in developing stem cells.



Recent Publications

Conklin BR, Hsiao EC, Claeysen S, Dumuis A, Srinivasan S, Forsayeth JR, Guettier JM, Chang WC, Pei Y, McCarthy KD, Nissenson RA, Wess J, Bockaert J, Roth BL (2008) Engineering GPCR signaling pathways with RASSLs. *Nat. Methods* 5:673–678.

Hsiao EC, Boudignon BM, Chang WC, Bencsik M, Peng J, Nguyen TD, Manalac C, Halloran BP, Conklin BR, Nissenson RA (2008) Osteoblast expression of an engineered G_s-coupled receptor dramatically increases bone mass. *Proc. Natl. Acad. Sci. USA* 105:1209–1214.

Hsiao EC, Yoshinaga Y, Nguyen TD, Musone SL, Kim JE, Swinton P, Espineda I, Manalac C, deJong PJ, Conklin BR (2008) Marking embryonic stem cells with a 2A self-cleaving peptide: A NKX2-5 emerald GFP BAC reporter. *PLoS ONE* 3:e2532.

Pico AR, Kelder T, van Iersel MP, Hanspers K, Conklin R, Evelo C (2008) WikiPathways: Pathway editing for the people. *PLoS Biol.* 6:e184.

Pico AR, Smirnov IV, Chang JS, Yeh RF, Wiemels JL, Wiencke JK, Tihan T, Conklin BR, Wrensch M (2009) SNPLogic: An interactive single nucleotide polymorphism selection, annotation, and prioritization system. *Nucleic Acids Res.* 37:D803–D809.

Members of the Conklin Laboratory

Katriina Aalto-Setälä
Wei Chun Chang
Bruce Conklin
Kristina Hanspers
Edward Hsiao
Allan Kuchinsky
Carlota Teresa Manalac
Kenta Nakamura
Jennifer Ng
Trieu Nguyen
Jason Park
Alexander Pico
Nathan Salomonis
Mark Scott
Matthew Spindler
Karen Vranizan