The central question behind our work is how the centrosome and primary cilium control cell function and influence development, and how defects in these structures cause a remarkable range of human disease, ranging from cancer, polycystic kidney disease, and obesity, to neurocognitive defects including mental retardation, schizophrenia, and dyslexia.

The centrosome consists of a pair of centrioles and pericentriolar material and organizes the cytoplasmic microtubules of most animal cells. Most importantly, the mother centriole (the older of the two in the pair) nucleates the formation of a primary cilium in most cells in the body. First seen by cell biologists in the 1950's, the primary cilium was ignored for many years until a combination of human and model organism genetics revealed that it is a critical sensory organelle with functions...
in many important processes. Defects in primary cilium structure and function cause a set of human conditions, called ciliopathies, that share a set of phenotypes that reflect the importance of the cilium in signaling pathways.

There are three main projects in the lab:

1) Ciliary biogenesis and function. In addition to the microtubules making up the interphase array and the mitotic spindle, many animal cells make a specialized microtubule structure, the primary cilium. This is a single, non-motile cilium that is able to act as a transducer of mechanical and chemical signals - sort of a cellular antenna. The microtubules of the ciliary axoneme grow directly from a centriole at their base, this centriole is often called a basal body. Some epithelial cells in the trachea, oviduct and brain produce hundreds of motile cilia on their surface, each with a centriole at their base. We are studying both the primary cilium and multiciliated cells for clues into ciliary structure and function, and centriole formation.

2) Cell cycle control of centrosome duplication. We have shown that duplication of the centrosome, the microtubule organizing center of animal cells, is dependent on the cell cycle kinase cdk2, and on cell cycle-specific proteolysis. We are working to determine the molecular mechanisms of centrosome duplication and to understand how centrosome duplication is controlled so that it happens once and only once per cell cycle. Cancer cells often have aberrant centrosome numbers, and we are investigating the relationship between aberrant centrosome number and the genome instability that is common in cancer cells.

3) Microtubule nucleation and organization. Microtubules are polymers of tubulin, which is a heterodimer of alpha-tubulin and beta-tubulin. We have identified a remarkable complex of proteins associated with a third type of tubulin, gamma-tubulin. Gamma-tubulin and its associated proteins are localized to the centrosome and are critical for initiation, or nucleation, of microtubule assembly. The gamma-tubulin complex (gammaTuRC) is a very large, ring-shaped complex and contains at least 6 proteins in addition to gamma-tubulin. We are determining the role of gamma-tubulin and its associated proteins in microtubule nucleation and organization.

Teaching

COURSES

2015-16
- Core Molecular Biology Laboratory: BIO 44X (Aut, Win)
- Foundations in Experimental Biology: BIOS 200 (Aut)

2014-15
- Biology PhD Lab Rotation: BIO 299 (Spr, Sum)
- Core Molecular Biology Laboratory: BIO 44X (Aut, Win)

2013-14
- Core Molecular Biology Laboratory: BIO 44X (Aut, Win)
- Foundations in Experimental Biology: BIOS 200 (Aut)

2012-13
- Core Molecular Biology Laboratory: BIO 44X (Aut, Win)
- The Nucleus: BIOS 200 (Aut)

STANFORD ADVISEES

Postdoctoral Faculty Sponsor
Jonathan Geisinger, Roberta Sala, Krishnakumar Vasudevan, Jennifer Wang

Doctoral (Program)
Publications

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