Ackert Hall, Room 120
Wednesday, September 11, 2024
4:00 P.M.

Coffee and Cookies
Chalmers Hall, Room 168
3:45 P.M.

Biochemistry & Molecular Biophysics Seminar

Getting into shape: phosphoinositide roles in muscle cell remodeling

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Muscle contraction is essential for animal life. Muscle function depends on specialized cellular compartments, including plasma membrane domains that support ongoing myofiber signaling and integrity. Transverse (T)-tubules, invaginations of the muscle plasma membrane, form an extensive tubulated membrane network critical for excitation-to-contraction relays in both skeletal and heart muscles. Little is known about how the elaborate T-tubule network forms nor how it remodels with muscle growth, damage, aging and disease.

We developed the use of intact Drosophila body wall muscles as an ideal system to study the T-tubule membrane network. Using muscle-targeted genetic screens, we discovered functions that act within distinct programs for either T-tubule membrane formation versus regulated remodeling. Importantly, the identification of conserved genes involved in T-tubule regulation established fly models for several different human myopathy diseases. We found that factors involved in endocytic and autophagic membrane trafficking control T-tubule stability versus disassembly, and that targeting this regulation can revert myopathy-related defects. An emerging theme is that specific phosphoinositide lipids, as well as the lipid regulators and effectors, play key roles in T-tubule formation, remodeling and human disease.