



Wednesday, September 15, 2021
4:00 P.M.

Ackert Hall, Room 120

Biochemistry
&
Molecular
Biophysics

Seminar

Pushing the nuclear envelope in muscle disease

Lori L. Wallrath

Biochemistry and Molecular Biology
Carver College of Medicine
University of Iowa



Mutations in genes encoding nuclear envelope proteins cause a collection of diseases called laminopathies. These include muscular dystrophies, cardiac diseases, fat disorders, and early onset aging syndromes. This seminar will focus on two such genes: *LMNA* and *TMEM43*. *LMNA* encodes A-type lamins, intermediate filaments that form a meshwork inside the nuclear envelope. *TMEM43* encodes a transmembrane protein that spans the inner nuclear membrane and interacts with lamins. To better understand disease mechanisms, mutations in *LMNA* and *TMEM43* were modeled in *Drosophila* where genetic and genomic tools are readily available. Larval body wall muscles and the heart were examined for defects caused by mutations in the *Drosophila* orthologues. The results showed that mutant lamins responsible for distinct clinical phenotypes have different patterns of mislocalization in muscle, suggesting mechanisms for the pathology. *LMNA* and *TMEM43* mutations that cause Emery-Dreifuss muscular dystrophy produced different myonuclear defects, suggesting distinct pathomechanisms. Taken together, these studies demonstrate the utility of *Drosophila* for determining the molecular defects associated with muscle disease-causing human mutations and set the stage for the identification of therapeutic targets.