VANDERBILT SCHOOL OF MEDICINE | Basic Sciences

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Biosketch

Dr. Olivares received his PhD in Molecular Biophysics and Biochemistry from Yale University where he studied how dimeric myosin motor proteins coordinate their biochemical cycles to move along actin filaments. He then completed his postdoctoral training at the Massachusetts Institute of Technology, where he used single molecule force spectroscopic techniques to probe how energy-dependent proteases mechanically unfold proteins during substrate degradation. Work in his lab focuses on creating new tools to visualize and manipulate force-sensing and force-producing machines within the cell and better understand the interplay between the physical and biochemical microscopic world.

Key Publications

"Effect of directional pulling on mechanical protein degradation by ATP-dependent proteolytic machines," ***Proceedings of the National Academy of Sciences U. S. A.*****, 114(31):E6306-13, 2017**

"Mechanochemical basis of protein degradation by a double-ring AAA+ machine," ***Nature Structural & Molecular Biology*****, 21(10):871-5, 2014**

"Single-molecule protein unfolding and translocation by an ATP-fueled proteolytic machine," ***Cell*****, 145(2):257-67, 2011**

"Probing how the cell nucleus senses and responds to mechanical forces, one molecule at a time"

Two fundamental questions my lab aims to address are: how does the **cell use mechanical forces to drive biochemical processes across lipid bilayers**, and how does the **nucleus sense and transform mechanical force into biochemically meaningful signals that influence cellular development and function**? Much evidence suggests that the nucleus can directly sense physical forces through protein complexes spanning the nuclear envelope (NE), though the molecular mechanisms of nuclear force sensing are not well understood.

Mutations or dysfunction within this network of membrane embedded and associated proteins lead to changes in NE architecture and to human disease including neurological disorders, cardiomyopathy, muscular dystrophy, and cancer. Though much work has been done to characterize how cell adhesion molecules and the underlying cytoskeleton sense and convert mechanical force into biochemically meaningful reactions, **a mechanistic understanding of nuclear mechanical signaling is lacking**.

Using a combination of single-molecule force spectroscopy, biochemical reconstitution of NE components responsible for mechanical signaling, and biophysical methods, **we hope to unravel the molecular details governing mechanical signaling at the nucleus.**