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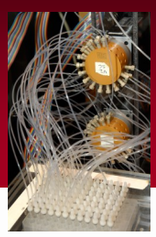
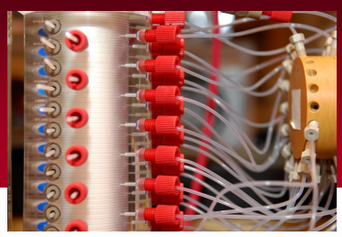


The Gene and Linda Voiland School of

Chemical Engineering and Bioengineering

2015 Seminar Series

Monday, March 23, 2015

12:10 p.m. Wegner G1

Aldrin Gomes
Department of Neurobiology, Physiology and Behavior
UC Davis, University of California

Dr. Gomes earned his Bachelor's of Science in 1991 from the University of the West Indies, St. Augustine, Trinidad and Tobago and his PhD in 1998 University of the West Indies, St. Augustine, Trinidad and Tobago. From 1999-2002 he was at University of Miami School of Medicine, Miami, FL as a Postdoctoral Fellow, and in 2002 became a Postdoctoral Associate there. In 2007 he joined UCLA, Los Angeles, CA, as an Assistant Research Physiologist and in 2008 he joined UC Davis as an Assistant Professor, becoming an Associate Professor in 2014.

His areas of interest include: Muscle Physiology and Proteomics, Proteasome, Protein Degradation, Troponin, Striated Muscle Diseases, and Proteomics.

Delineation of Molecular Pathways Involved in Cardiomyopathies Caused by Troponin T Mutations

Familial hypertrophic cardiomyopathy (FHC) is associated with mild to severe cardiac problems and is the leading cause of sudden death in young people and athletes. Although the genetic basis for FHC is well-established, the molecular mechanisms that ultimately lead to cardiac dysfunction are not well understood. To obtain important insights into the molecular mechanism(s) involved in FHC, hearts from two FHC troponin T (TnT) models (I79N and R278C) were investigated using label-free proteomics and metabolomics. Mutations in TnT are the third most common cause of FHC, and the I79N mutation is associated with a high risk of sudden cardiac death. Most FHC-causing mutations, including I79N, increase the Ca2+ sensitivity of the myofilament, however the R278C mutation does not alter Ca2+ sensitivity and is associated with a better prognosis than most FHC mutations. Out of more than 1200 identified proteins, 53 and 76 proteins were differentially expressed in I79N and R278C hearts, respectively, when compared to wild-type hearts. Interestingly, nearly 400 proteins were differentially expressed when the I79N and R278C hearts were directly compared. The three major pathways affected in I79N hearts relative to R278C and WT hearts were the proteasome, antioxidant systems, and energy production pathways. Further investigation of the proteasome system using western blotting and activity assays showed that proteasome dysfunction occurs in I79N hearts. Metabolomic results corroborate the proteomic data and suggest the glycolytic and galactose pathways are important pathways that are altered in I79N hearts relative to R278C or WT hearts. Our findings suggest that impaired energy production and protein degradation dysfunction are important mechanisms in FHCs associated with poor prognosis and that cardiac growth is not likely needed for a switch from fatty acid to glucose metabolism.