Biochemical Studies of ATP-Binding Cassette Transporters

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Abstract

Membrane transport proteins constitute an important part of our genome and are target to many therapeutic drugs, but the complexities inherent to their hydrophobicity have significantly delayed their biochemical and structural studies. ATP binding cassette (ABC) transporters is a large family of proteins that use energy from ATP hydrolysis to move a diverse variety of molecules against their concentration gradient across the membrane. ABC transporters are involved in multiple processes: protection against xenobiotics, problems related to drug/drug interactions, development of multidrug resistance, etc, and their malfunctioning can cause terrible diseases such as Cystic Fibrosis or Stargardt. Despite the importance of these proteins, the molecular details of substrate/drugs recognition and the conformational changes that take place during their transport cycle are still unknown. I will present a general view of my biochemical, spectroscopic and structural studies of diverse ABC transporters, including my most recent research on a human transporter. Humans have near 50 ABC transporters, but the function of many of them remains unknown. Such is the case of the ABCB10 transporter, located in the mitochondrial inner membrane, where it is overexpressed in failing human heart. Diverse experimental evidence indicate that this transporter is necessary for the synthesis of heme and for protection of erythropoietic and cardiac cells against oxidative stress, but the identity of its physiological substrate and its molecular mechanism of transport are uncertain. It has been proposed that ABCB10 exports heme out the mitochondrial matrix (where heme’s final synthesis steps occur), although no substantial evidence is available. I will show that our preliminary studies have identified a putative substrate for ABCB10 and have recognized amino acids that are important for the binding of this substrate to the transporter. In addition, I will discuss our plans to extend our research approaches to better understand the function and molecular mechanisms of ABC transporter.

About the Speaker

Dr. Maria Zoghbi has been an Assistant Professor at the Molecular Cell Biology Department, University of California Merced (UCM) since 2016. She received her PhD in Physiology and Biophysics at the Venezuelan Institute for Scientific Research (IVIC) in 2003. She did her PhD research at the University of Massachusetts Medical School (UMass) as a visiting graduate student, and she stayed there to continue postdoctoral research until 2007. After that, she went to Texas Tech University Health Sciences Center (TTUHSC) to continue her postdoctoral training. Throughout the years, her research has been focused on understanding protein function and mechanisms using a combination of structural, biochemical and cellular approaches.