Major scientific achievements of Dr. Hugues ABRIEL (1999-2017)

1. Ubiquitylation-dependent regulation of ion channel density at the cell surface: roles in physiology and disease- Since 1999 and the seminal papers by Abriel et al., it is clear that ion channels can be ubiquitylated (classical post-translational modification) and upon its modification the channels are tagged for internalization and eventually degradation. This regulatory mechanisms was found to be altered in the case of a channelopathy leading to early onset hypertension (Liddle's syndrome)1. Abriel's group further demonstrated that other ion channels (in particular voltage-gated channels responsible for the generation of the cardiac action potential) were also the target of the same ubiquitin ligase enzymes of the Nedd4 family2. All these channels, Nav family3, hERG4, and KCNQ15, possess so-called PY motifs permitting the interaction with the Nedd4 enzymes. More recently, this Nedd4-dependent mechanism was shown to be important in regulating the number of Nav1.7 channels at the surface of sensory neurons in a mouse model of neuropathic pain6.

2. Biochemical and biophysical characterization of ion channel variants in cardiac and neurological disorders (channelopathies)- Dr. Abriel has been involved in the biochemical and biophysical characterization of many genetic variants found in ion channel genes causing severe human disorders. First, the amiloride sensitive sodium channel ENaC expressed in the kidney was found to be mutated in Liddle's syndrome patients. He showed that this was caused by altered internalization1 since these channels could not be tagged by ubiquitylation. Second, he was involved in demonstrating the mutation-induced alteration in biophysical properties of several variants of the cardiac sodium channel Nav1.5 described in 2004;10,11,2014. Albesa M, Grillo LS, Gavillet B, Abriel H. Nedd4-2-dependent ubiquitylation and regulation of the cardiac potassium channel hERG1. J Mol Cell Cardiol. 2011;51:90-98.

3. Molecular and cellular biology of the cardiac sodium channel Nav1.5: interacting proteins and distinct cellular pools- The cardiac sodium channel Nav1.5 is mutated in a large number of cardiac channelopathies. Dr. Abriel's group has been pioneering in demonstrating that this channel interacts with a number of regulatory proteins such as syntrophins15, dystrophin15, ubiquitin ligases3, calmodulin, MAGUK proteins such as SAP9716 and CASK17, and others (reviewed in18). Importantly, it was subsequently demonstrated that some of these interacting proteins (syntrophins, calmodulin, and SAP97) are mutated in patients with different forms of cardiac arrhythmias. In addition, Dr. Abriel's team showed for the first time that different populations of Nav1.5 channels interacting with different proteins are found in cardiac cells leading to the concept of "multiple pools of sodium channels"19,20.