“When your heart skips more than a beat: Cx43 hemichannels in cardiac pathology”

Connexin 43 (Cx43) is the most abundant connexin forming junctional channels in cardiac ventricles. In multiple cardiac pathologies, Cx43 is found remodeled at the lateralized side of intercalated disks of unhealthy cardiomyocytes. We recently demonstrated that remodeled Cx43 protein functions as non-junctional channels, called hemichannels, in a Duchene muscular dystrophy mouse model (Dmdmdx). These mice were susceptible to arrhythmias upon β-adrenergic stress; however, arrhythmias were prevented using Cx43 hemichannel blockers, genetically reducing Cx43 levels or genetically preventing Cx43 remodeling. At the cellular level, pharmacological or genetic blockade of Cx43 hemichannels prevents an abnormal increase in membrane permeability, plasma membrane depolarization and isoproterenol-evoked triggered activity. Currently, we are investigating whether the opening of remodeled Cx43 hemichannels is a general mechanism to alter cardiomyocyte excitability or specific to cellular dysfunction associated with Duchene muscular dystrophy pathology. Exciting data suggest that, independent of the pathology, opening of remodeled Cx43 hemichannels is sufficient to promote cardiac stress-induced arrhythmias and ventricle infarction.