My time at the ISHR World Congress was highly rewarding. I got to see some of the groundbreaking work of numerous heart researchers across the globe, make countless connections with individuals from all career levels, and meet some of the titans in the field. In relation to my work, the conference provided me with an opportunity to connect my research to areas of the heart that are not obviously related, allowing me to develop more well-rounded projects in the future. On a less scientific note, by going to the conference I was able to see some amazing sites in Osaka and Nara. I got to visit Osaka Castle, pet deer in Nara park, and eat a ton of good food. Overall, the conference was more than just an educational event, but an opportunity to experience how individuals can form strong collaborations while also embracing their culture.

May 9th – Day 1

Cardiolipin Regulates Metabolic Adaptations in Macrophages in Barth Syndrome - Katharina Ermer – From Katharina's figure, it looked like the cardiolipin was causing the bends that form the cristae. If a reduction in cardiolipin results in the dimer form of mitochondrial creatine kinase rather than the oligomer form, could it be that the double membrane space is required for the oligomer to form and the cardiolipin reduces this space by reducing the number of cristae?

May 11th – Day 3

Genetic Mitochondrial Cardiomyopathy: From Barth Syndrome to Beyond – Xi Fang – UCSD – Cardiolipin makes up 20% of the mitochondrial membrane. This lady does work on varying cardiolipin concentrations, which will be helpful when we begin putting this component in our model.

May 12th – Day 4

The R169Q-RyR2 CPVT Mutation Induces Ventricular Arrhythmias by Increasing its Openings at low Cytosolic Calcium Concentration –Celia Oughlis – INSERM UMR-S 1180 Universite Paris Saclay - R169Q mutation could be something to think about following the development of the model.

Lifestyle and Environmental Modulation of Cardiac Electrophysiology: The Impact of Feeding Behavior and Ambient Temperature on QT Prolongation in LQT3 Mice – Makoto Ono – Yamaguchi University - Found that QT interval was prolonged by increases in temperature. I am not sure if NaV1.5 is sensitive to temperature, but it could be interesting to look into as we try to understand NaV1.5 mechanisms.

Cardiac Sodium Channel NaV1.5 Drives Metabolic Reprogramming: Insights From Metabolomic Analysis – Iqra Mushtaq – Taipei Medical University – NaV downregulation causes loss of ATP. It said that the loss of cytosolic sodium increases glucose intake and glycolysis but does not explain how ATP is reduced due to this. I would have asked him how this occurred, but he was never at his poster. I will be on the look out for papers regarding this because it could help connect NaV to the mitochondria.

GRK2 Regulation of Beta-Adrenergic Signaling and Ca2+ Handling in the Heart – Shi Qiang Wang – Peking University – PKA phosphorylates CaV12 and RyR2 (S2808). This could be interesting to look into because phosphorylation of both of these proteins by the same kinase can give insight to a connection between them. She gave no insight into what structurally occurred, but when the RyR2 model is finished, I will try to look into it.

May 13th – Day 5

TMEM65 Controls Mitochondrial Ca2+ Extrusion – Diego De Stefani – University of Padova – TMEM65 and MCU are seen throughout evolution together. From what the lady we talked to at the banquet said, TMEM65 is a calcium efflux channel for the mitochondria. Structurally, they could have analogous regions, so when MCU is developed, it will be interesting to see if any comparison can be made (similar to how we can compare NaV and CaV).

Sarcoplasmic Reticulum-Mitochondria Communication in Diabetic HFpEF – Melanie Paillard – University Claude Bernard Lyon – Said that the MCU is a relatively low conductance calcium channel. I am not sure how accurate this is, but it is a nice fact to know.

CACNA1C L1520I Variant Associated with Long QT Syndrome 8 is a Gain of Function Mutation and Provides Insight into Channel Structure – Agnieszka Dyrda – Victor Chang Cardiac Research Institute – She was studying a L1520I mutation in CaV1.2. This mutation was inside the CTD, which has a similar structure to the NaV CTD. I am not sure if it has been proposed that the CTD and IQ motif interact in CaV, but I recommended she give our previous NaV paper a read. If she finds analogous structures between NaV and CaV it could help her explain how such a small mutation can have a large effect.

RyR2 as an Antiarrhythmic Drug Target – Bjorn Knollman – Vanderbilt University - We should try using QX-Flecainide and Methyl-Flecainide on our NaV and upcoming RyR2 model to see if we get specificity. Dantrolene seemed like a desirable one to model, but it requires CaM to have an effect.

Impact of Ca2+ Crosstalk Between Mitochondria and Sarcoplasmic Reticulum in Cardiomyocyte During Workload Transition – Ayako Takeuchi – Okayama University – Saw that the MCU was colocalized near RyR2, which allows for SR and mitochondria cross talk.

May 14th – Day 6

TRP Channel has an Outsized Impact on Ca2+ Overload in Dystrophic Cardiomyopathy by Adapting a Novel Structure – Annabelle Brusacoram – John Hopkins University – Mitochondrial creatine kinase phosphorylates at Y368, Y159, and Y155. The Y159A mutation causes the largest drop-in activity. We will not be able to see MitoCK function, but we could look at structural changes that relate to phosphorylation. She did not have any structural information, so I am not sure if this is related to oligomerization or dimerization.

Early Onset of Ca2+ Waves and Synchronization in Multicellular Clusters Facilitate Arrhythmogenesis in Human Heart Failure – Darya Kazakova – KU Leuven – R176Q reduced CaM affinity to RyR2 and increased calcium leak. R2474S reduced CaM affinity to RyR2 two-fold and increased calcium leak. R4496C did not reduce CaM affinity to RyR2 but increased calcium leak.

Mitochondrial Calcium Signaling and Redox Homeostasis in Cardiac Health and Disease – Eduardo Bertero – University of Genova – Aberrant cardiolipin remodeling destabilizes the MCU. Is this due to a macroscopic change in membrane composition or a specific interaction between cardiolipin and MCU? We could try modeling to test if it is a specific interaction.