hybridization and their spatial distribution relative to nuclei and each other evaluated using a bidirectional nearest neighbor (NN) colocalization analysis. Briefly, fluorescence signals were segmented (fig. 1B) and bidirectionally colocalized using a distance transformation-based approach (fig. 1C). Measured colocalization was compared against random signal distributions for each pair and compared with the observed patterns to assess the degree of spatial association between signal pairs (fig. 1D).

**Results:** Each CALM gene occupies a unique spatial strata around the nuclei, with CALM2 being the closest, CALM3 the furthest, and CALM1 exhibiting an intermediate distribution somewhere in between. CALM1, 2 and SCNSA all exhibit significant spatial attraction to the nuclei while CALM3 and RYR2 mRNAs are evenly distributed throughout the cytosol. CALM2 and SCNSA exhibit a similar spatial association to the nuclei, as well as RYR2 and CALM3, suggesting these pairs of mRNA may be co-translated.

**Conclusion:** Our preliminary results suggest that CaM and its effector targets may be co-translated within microtranslatomes that show distinct spatial distributions within the cardiomyocyte. In ongoing work, we are examining colocalization between signal pairs to directly evaluate the spatial association between mRNA for CaM and its effector targets.

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**PO-617-07**

**MODELS OF SEX-DEPENDENT EPIGENETIC TRANSCRIPTIONAL CONTROL OF CARDIAC ELECTROPHYSIOLOGY IN THE ADULT HUMAN HEART BASED ON THE GTEx DATABASE**

*Michael Pressler BS; Anelia Horvath and Emilia Entcheva PhD*

**Background:** The gene-tissue-expression database (GTEx) provides well-organized data sets for inferring links between gene expression patterns in adult humans (21 to 70 years old). These relationships can be parsed by organ, sex, age and other phenotypes of the donors. Computational machine learning models can help quantify such relationships.

**Objective:** The goal of this study was to create and test models that help reveal how chromatin modifiers, such as histone acetylation enzymes (HDACs and HATs), may exert transcriptional control of key cardiac ion channels (IC) via select transcription factors (TFs) in male and female adult human hearts.

**Methods:** We started with 689 GTEx donors and used gene expression (transcripts per million, TPM) data from the human left ventricle (LV). After filtering and normalization using geometric mean and log transform to allow correlative analysis and comparisons, we analyzed data from 84 female and 158 male LVs. Partial least-square (PLS) regression models that linked gene expression data for HDACs/HATs to TFs and to ICs gene expression were trained on male and female samples individually.

**Results:** The PLS models revealed notable co-regulation of cardiac ion channels by HDACs/HATs, with stronger clustering in male LV. The only exception was ATP1A1, encoding the Na/K pump, which showed orthogonal regulation by HDACs/HATs to most of the ion channels in male and female hearts. The HDAC/HAT effects appeared mediated by strong (+) TF regulators of ICs, e.g. MEF2A, and (-) TF regulators of ICs, e.g. RUNX1, in male and female hearts. Furthermore, PLS models revealed a stronger mediatory role for (+) TF regulation of ICs in males by SOD1 and NKX2-5 and (-) TF regulation of ICs in males by TGF1B. At the same time, HIF1A exhibited larger (+) TF effects on ICs in females. When male-trained PLS models of HDAC/HAT effects on ICs were created, they tended to underestimate effects on some ICs in females.

**Conclusion:** Analysis of GTEx cardiac data sets using machine learning techniques can provide valuable insights about co-expression and regulation of chromatin-modifying enzymes, transcription factors and key cardiac ion channels in a sex-specific manner. Such insights can drive the design of validation experiments to test the role of epigenetic modifiers on human cardiac electrophysiology.

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**PO-618:**

**Featured Posters: CIED at Pod 5**

**Friday, April 29, 2022**

**12:30 PM - 2:30 PM**

**PO-618-01**

**IMPACT OF PR INTERVAL PROLONGATION ON THE RISK OF HIGH GRADE CONDUCTIVE DISORDERS AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION**

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**Background:** The development of high-grade conductive disorder (HGCD) is one of the most frequent complications after Transcatheter Aortic Valve Implantation (TAVI). Variation in atrioventricular conduction time (PR interval) after TAVI and its specific impact on the risk of permanent pacing implantation (PPI) have been poorly described.

**Objective:** The aim of this study was to evaluate the impact of increase in PR interval after TAVI on the incidence of PPI for HGCD.

**Methods:** This is a single-center retrospective cohort analysis of 1466 patients undergoing TAVI from January 2010 to December 2018. We excluded patients with prior pacemaker, non-sinus rhythm, TAVI by transapical or transaortic approach and PPI after TAVI for sick sinus syndrome. We observed the variation of PR interval in the electrocardiogram before TAVI (baseline) and at day 1 (D1) of the procedure.