modelers have already linked the mechanical and the electrical activity in their formulations and showed how those activities feedback on each other. Feed forward modeling is a step towards reproducing the neurological control of parameters on pacing frequency used here can be refined but is a valid starting point to implement the convergence of cardiac chronotropy and inotropy.

2810-Pos Board B580
TRPC1 and TRPC4 Channels Contribute to Basal Cardiac Calcium Signalling via a Constitutively Active Background Calcium Entry Peter Lipp1, Qinghui Tian1, Martin Oberhofer1, Karin Hammer2, Juan E. Camacho-Londono3, Petra Weissgerber1, Marc Frechtl1, Lars Kaestner1.
1Saarland University, Homburg/Saar, Germany, 2UC Davis, Davis, CA, USA.

Transient receptor potential (TRP) channels have been assigned to a wide array of important physiological functions but in cardiac myocytes TRPC channels are almost exclusively associated with diseases. Using TRPC1/C4 double KO or TRPC1 and TRPC4 single KO mice we investigated a putative physiological role of TRPC1/C4 channels in cardiac myocytes. We have used high-sensitivity imaging, video-imaging and electrophysiological analysis of single ventricular myocytes to investigate local as well as global calcium handling, contractility and electrical properties of the cells. For TRPC1/C4 dKO mice we found decreased global calcium transients, with both amplitude (20% reduction) and basal, diastolic calcium concentration (around 15%) affected. Cellular contractility was reduced by more than 35%. L-type calcium current density was constant but the calcium content of the sarcoplasmic reticulum (SR) displayed a 20% reduction. Calcium sparks showed an almost 20% reduction in amplitude while other spatiotemporal parameters were unchanged. Both Na/Ca exchanger and SR-calcium pump activity were unchanged. In Mn-quench experiments we found an almost 50% reduction of Mn entry in unstimulated conditions when comparing cells from TRPC1/C4 dKO and wt mice. Using myocytes from TRPC1 or TRPC4 single KO mice we observed a reduction of global calcium handling and SR-calcium content for both genotypes. From these data we concluded that both, TRPC1 and TRPC4 channels, play an important role for basal cardiac calcium handling.

This work was supported by the DFG, BMBF and the Medical Faculty.

2811-Pos Board B581
Relationship Between Ca^{2+} Alternans and T-Wave Alternans: Role of Calsequestrin and Sorcin Azade D. Petrosky1, Bernardo Zepeda1, Alexander B. Petrosky1, Dmytro Kornyeyev2, Paola Contreras2, Hector H. Valdivia2, Ariel L. Escobar1.
1UC Merced, Merced, CA, USA, 2Universidad de la Republica, Montevideo, Uruguay, 3University of Wisconsin, Madison, WI, USA.

Several pathologies are associated with defects in Ca^{2+} handling: One example is T-wave alternans (TW-Alt). TW-Alt is observed as alternating beat-to-beat changes in the T-wave of the electrocardiogram (ECG) and constitutes an important arrhythmic mechanism. The likelihood of TW-Alt increases when changes in the beat-to-beat response. To test if A2AR activation alters beat-to-beat stability of intracellular calcium transients and their propagation in atrial myocytes.

Barriga Montserrat1, Cristina E. Molina2, Anna Llach2, Nuria Cabello2, Alex Vallmitjana2, Raul Benitez3, Josep Padro2, Juan Cinca2, Leif Hove-Madsen1.
1UC Merced, Merced, CA, USA, 2Universidad de la Republica, Montevideo, Uruguay, 3Universitat Politecnica de Catalunya, Barcelona, Spain.

Adenosine A2A receptor activation decreases beat-to-beat stability of intracellular calcium transients and their propagation in atrial myocytes.

Acute Chemotherapeutic Treatment Induces Chronic Phosphorylation of the Cardiac Ryanodine Receptor

Doxorubicin affects the calcium handling and release and can also induce chronic changes in the calcium release and release properties of the cardiac ryanodine receptor (RyR2). To determine whether chronic changes in the calcium release properties are observed and how this relationship is related to the cell's capacity to activate the RyR2.

Sorcin was overexpressed in human atrial myocytes, 200 nM of the Adenosine A2A receptor (A2AR) agonist CGS21680, was added to human atrial myocytes for 24 hours. CGS21680 decreased the fraction of uniform responses at 1 Hz (from 23/36 to 15/36) and reduced the maximal frequency where a uniform response could be maintained (from 1.11 ± 0.10 to 0.80 ± 0.08 Hz, p<0.05). The frequency dependent reduction of uniform responses in the presence of CGS21680 was due to the concurrent increase in fraction of irregular responses (from 1.36 to 7.36/36 at 1 Hz and from 13.36 to 26.36/36 at 2 Hz). In cultured atrial HL-1 myocytes, CGS21680 also decreased the number of uniform responses of 50/80 to 35/80. Moreover, CGS21680 destabilized the propagation of the calcium transient. Overall, a uniform propagation of 38/80 calcium transients was observed in control conditions and only 22/80 transients showed uniform propagation after exposure to CGS21680. We conclude these simulation results indicate that simulations should incorporate both local control and regional expression variability.