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largest (and smallest) APD-values were selected to create a maximum (and minimum) APD-map. This illustrated the variability-range per slice which, as an example for APD80 at 2Hz, was 196.37ms ± 6.59ms (maximum; mean ± SD), 187.00ms ± 6.57ms (minimum), and 191.69ms ± 5.44ms (average). Interestingly, even though the spread of activation differed significantly for the different stimulus sites, resulting APD-maps were comparable for all pacing rates in homogeneous slices (i.e. in the absence of pronounced source-sink mismatches).
Thus, APD heterogeneity in cardiac tissue slices shows a reproducible intrinsic pattern that prevails regardless of acute changes in stimulation site and frequency.
Claycomb. J Biol Chem. 1976/251:P6082-P6089.

2767-Pos Board B537
Pluripotent Cell-Derived Cardiomyocytes: One Cell Type as a Predictive Tool For the Assessment of Drug Efficacy and Safety on a Variety of Cardiac Targets
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The lack of a reliable and standardized in vitro cardiac myocyte cell culture model hampers the development of new cardiac drugs and leads to costly late stage failures of potential drug candidates.
Pluripotent stem cell-derived cardiomyocytes have the capacity to bridge this gap. The standarized production process, the availability of large frozen stocks, and the long-term stability in culture make them an attractive in vitro model.
Now cardiomyocytes originated from various species and different kinds of stem cells are available. These cells are only as good as the predictivity, as measured against human clinical data, of the assays that have been developed for them. Genetically selected mouse embryonic stem cell-derived cardiomyocytes were successfully used in a variety of electrophysiological assay systems including high throughput FLIPR fluo-4 and membrane potential assays (up to 1536 well format) as well as rubidium flux assays. The cells were also used in high content assay systems like automated voltage and current clamp and microelectrode array recordings and long-term recording in impedance-based assay systems. Each technique has their advantages and particular application. We can show high predictivity in their application in the assessment of drug efficacy and safety for many cardiac targets.
Furthermore, we have established and validated a cardiac cytotoxicity assay based on pluripotent stem cell-derived cardiomyocytes to predict drug-induced cardiac-specific cytotoxicity of different compound classes including anthracyclines as well as tyrosine kinase inhibitors.
Taken together, these assays can be implemented early in the drug optimization and development process and will reduce costly in vivo studies and will help to prevent late stage drug candidate failures.

2768-Pos Board B538
Exploring Stem Cell-Derived Cardiomyocytes with Automated Patch Clamp Techniques
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There is increasing interest for cardiomyocytes as models for studying cardiac cellular physiology and preclinical drug safety testing. Stem cell-derived cardiomyocytes have the potential for such a model and have the possibility for modeling human diseases. The present investigation is the first to describe current properties from stem cell-derived cardiomyocytes using multi-hole recordings with planar automated patch clamp technology.
In our study pluripotent stem cell-derived cardiomyocytes were biophysically and pharmacologically characterized. The cells are differentiated in large numbers and cryo-preserved, which make them suitable for automated patch clamping and facilitate their use in drug screening. We tested the cells in two different recording modes; single-hole and multi-hole, respectively. For multi-hole recordings up to ten cells are patched at the same time and the total current is measured per site. This recording mode can be useful for small currents (e.g. endogenous) and typically increases the success rate for useful data. For all experiments the whole-cell configuration was used and three different types of currents were studied; Na^+, Ca^{2+} and K^+. Using specific voltage protocols biophysical characteristics of each current was described and compared from single-hole and multi-hole experiments. We showed that currents recorded from these pluripotent stem cell-derived cardiomyocytes are similar to human cardiomyocytes and the response to known pharmacology is as expected. The $V_{0.5}$ values, I-V relationships, current kinetics and IC_{50} values determined for known blockers (TTX, nifedipine and cisapride) were comparable for the two recording modes. Clearly the success rate for usable data per measurement plate was significantly increased with the multi-hole technology. This is the first time current properties of stem cell-derived cardiomyocytes have been described from multi-hole recordings with planar automated patch clamp. Our study has shown that automated patch clamp is ready for stem cell-derived exploration.

2769-Pos Board B539
Individual Cell Electrophysiology (ICE) of Cardiac Myocytes _ Using Innovative 'Onion-Peeling' Technique to Study the ICE of Excitable Cells
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The action potential (AP) of a cardiac cell is a finely choreographed dance involving many ion channels and transporters interacting with one another via membrane potential and intracellular Ca^{2+}. The ionic mechanisms that cause arrhythmogenic APs (early or delayed afterdepolarizations, short or long AP duration) are still incompletely understood. Traditional voltage-clamp experiments measured one current from one cell and in most cases without Ca^{2+} transients. Data averaged from many cells were then used to build a canonical AP model. However, the canonical AP may be very different from the AP of any particular cell due to cell-to-cell variations. Recently, we developed an innovative *'Onion-Peeling' (O-P)* technique to achieve (***a***) a direct recording of ionic current under *in situ* condition (during AP, with Ca^{2+} cycling, in a physiological milieu, undergoing contraction) and (***b***) recording of *multiple* currents from a single cell to study how different currents interact and integrate to shape AP. Here we report the results of using *O-P* to investigate: (1) recording of key ionic currents (I_{Ks}, I_{Kr}, I_{K1}, $I_{Ca,L}$, I_{NCX} , $I_{Na\text{-}Late}$) during AP in the guinea pig ventricular myocyte; (2) effects of the Ca^{2+} transient on modulating these currents during AP; (3) changes of multiple currents under beta-adrenergic stimulation and how concerted changes in currents integrate to reshape AP. The ability to measure many currents in a single cell has also revealed two hitherto unknown characteristics of the currents in cardiac cells: coordination of currents within a cell and large variations of currents between cells. Hence, our *O-P* technique presents a significant step beyond the traditional way of measuring only one current in any one cell, and provides a powerful new tool for studying the individual cell electrophysiology.

2770-Pos Board B540
Electrophsiological Tools to Study Cardiomyocytes from Single Cell to Organ Level
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The electrophysiological properties of cardiomyocytes are fascinating yet complex. A finely tuned composition of different ion channel classes is necessary for the precise execution of an action potential. Modification of channel subsets by pharmacological substances or by genetic mutations can disturb the timing of electrical excitation cumulating in life threatening arrhythmias of the entire heart. Heart pathologies can be studied in different sets from cellular to organ level. Here we are going to discuss the advantages and limitations of different preparations and techniques applied in our lab, including 1) patch clamp analysis of adult cardiomyocytes cultivated for up to 7 days without showing major ion channel dedifferentiation, 2) microelectrode array (MEA) recordings of electrically coupled embryonic cardiomyocytes to study cardiac excitation, signal propagation and antiarrhythmic drug effects on a multicellular level, 3) Human stem cell derived cardiomyocyte technology and their potential for safety pharmacology screening, 4) acute and cultivated ventricular heart slices from different species including humans as test platform for drug screening in intact tissue and 5) Flex-MEA technology to perform extracellular recordings in intact beating hearts in a Langendorff preparation.
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2771-Pos Board B541
Quasi-*In Vivo* Electrocardiogram Measurement using Convolution of Field Potential Propagation in the *On-Chip* Cardiomyocytes Network Circuit
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Understanding the importance of spatial and temporal regulation of cellular community size and shape are keys to resolve mechanisms in highly complex heart system by new quasi-*in vivo* assay, which can predict the phenomenon *in vivo* using *in vitro* assay. For that, an *on-chip* cell network cultivation system has been