showed more non-muscle myosin IIb. Mechanical induction was mediated via focal adhesions; vinculin assembled earlier in ASCs. Inhibiting fibronectin-integrin binding using alpha 5 or V integrin siRNA blocked mechanosensing process as ASCs fail to 'feel' myogenic 10kPa gel and to show myogenic mRNA expression. Together these data imply enhanced mechanosensitivity for ASCs, making them a better therapeutic cell source for fibrotic muscle.

3648-Pos Board B509

Noninvasive Detection of Spontaneous Muscle Activity in Amyotrophic Lateral Sclerosis in Frequency Domain

Faezeh Jahanmiri Nezhad[1], xiaoyan Li[2], William Zev Rymer[2], Ping Zhou[2].
[1]University of Illinois, Chicago, IL, USA, [2]Rehabilitation Institute of Chicago, Chicago, IL, USA.

Changes in Calcium ion balance in muscle fraction has been connected to occurrence of spontaneous bioelectrical activities. These changes would result in an unstable membrane potential and therefore, involuntary action potentials start to fire on individual single muscle fibers, called fibrillation potentials. Evidence of fibrillation potentials is a hallmark of muscular degenerative diseases, such as Amyotrophic Lateral Sclerosis (ALS). Detection of fibrillation potentials is typically done by inserting needle electrodes. However, there are some uncertainties, reported by some studies with regard to origins of detected fibrillation potentials, suggesting that these oscillatory potentials could be an artifact of needle insertion and a result of muscle fibers injured by the needle. In this work, baseline electromyographic (EMG) signals from control subjects and subjects with ALS are compared. The signals are recorded non-invasively using high-density surface EMG electrodes. The data are analyzed in frequency domain, since fibrillation potentials are not detectable on surface EMG in time domain. Significant differences at some frequency bands are observed, and different underlying reasons are discussed.

3649-Pos Board B510

Recombinant MG53 Protein can Increase Membrane Repair Capacity and Improve Pathology in Dystrophic Mouse Muscle

Noah Weisleder[1,2], Norio Takizawa[2], Tao Tan[2], Christopher Ferrante[2], Pin-Jung Chen[2], Rosalie Yan[2], Xiaoli Zhao[1], Chuanxi Cai[3], Hiroshi Takeshima[4], Jianjie Ma[1,2].
[1]Robert Wood Johnson Medical School, Piscataway, NJ, USA, [2]TRIM-edicine, North Brunswick, NJ, USA, [3]University of Louisville, Louisville, KY, USA, [4]Kyoto University Graduate School of Pharmaceutical Sciences, Kyoto, Israel.

Duchenne muscular dystrophy (DMD) and other dystrophies arising from mutations in the dystrophin/dystroglycan complex produce pathology, at least in part, due to sarcolemmal membrane fragility, and several other forms of muscular dystrophy have been linked to defective membrane repair. A therapeutic approach to increase the capacity of muscle cells to reseal their membranes following mechanical disruption could address both of these mechanisms and acts as a therapy for improving muscular dystrophy pathology. MG53, a muscle-specific TRIM-family protein, is an essential component of the acute membrane repair machinery. In an effort to translate these basic science findings into therapeutic interventions for muscular dystrophy, our studies found that membrane injury in many cell types leads to exposure of phosphatidylserine (PS) to the extracellular space that can be bound by purified recombinant human MG53 protein (rhMG53). PS is normally sequestered on the inner leaflet of health cells until a disruption in the membrane causes PS to flow onto the outer leaflet of the membrane. rhMG53 binding increases the capacity of targeted cells to repair membrane damage when provided in the extracellular space. This membrane repair action of extracellular rhMG53 could be inhibited by competition with additional PS. Intravenuous delivery of rhMG53 to wild type mice can ameliorate cardiotoxin-induced damage to skeletal muscle fibers. Subcutaneous injection of rhMG53 allowed for delivery of rhMG53 to the bloodstream and reduced the severity of pathology in the *mdx* rodent model of muscular dystrophy. These findings suggest that recombinant MG53 protein can enhance the membrane repair capacity in skeletal muscle, and potentially act as a therapeutic agent for the treatment of muscular dystrophy.

3650-Pos Board B511

High-Throughput Optical Assays for Assessing Drug-Induced Q-T Prolongation in Human iPS Cell-Derived Cardiomyocytes

Chien-Jung Huang[1], Nick Callamaras[1], Ursula Germann[2], Sandra Lechner[1], Jennings Worley[1].
[1]Vertex Pharmaceuticals Inc, San Diego, CA, USA, [2]Vertex Pharmaceuticals Inc, Boston, MA, USA.

Prolongation of the Q-T interval, an important electrocardiogram (ECG) parameter, has been a major cardiac safety concern because it can lead to potentially fatal arrhythmia. The identification of compounds with potential Q-T prolongation liability is becoming critical in the discovery and selection of candidates for drug development. To assess the effects of compounds on the duration of cardiac action potentials, which are related to the Q-T interval, we have developed plate-based membrane potential dye and Ca2+ indicator assays using human induced pluripotent stem (iPS) cell-derived cardiomyocytes. With the use of sub-second fluorescence resonance energy transfer (FRET) probes, the change of membrane potential in cardiomyocytes can be monitored. To determine whether these assays are predictive for human cardiotoxicity, we have examined the pharmacological effects of selected reference drugs known to target different classes of cardiac ion channels and receptors. We have demonstrated that these optical assays are highly sensitive to the inhibition of cardiac ion channels and able to accurately track drug-induced change of action potential duration in human iPS-derived cardiomycocytes.

3651-Pos Board B512

In Vivo Application of Dynamic Hyaluronic Acid Material for Myocardial Infarction Therapy

Jennifer L. Young, Jacquelyn Schaefer, Jeremy Tuler, Pamela Schup-Magoffin, Rebecca Braden, Karen L. Christman, Adam J. Engler.
University of California, San Diego, La Jolla, CA, USA.

Tissue-specific elasticity arises from developmental changes that occur in the environment over time, e.g. ~10-fold myocardial stiffening from E3 to E10 in the chick embryo. Recently, we have shown that pre-cardiac mesodermal cells plated on top of a thiolated hyaluronic acid (HA) matrix engineered to mimic this time-dependent stiffening improves cardiomyocyte maturation compared to cells on static compliant matrices. Here we determined cell-matrix interactions using in vitro encapsulation assays and in vivo injections. Improved pre-cardiac and embryonic stem cell (ESC) distribution and viability was observed when cells were encapsulated and bound to immobilized, thiolated fibronectin conjugated to the HA matrix. Though not toxic to cells, we also assessed HA's local and systemic biocompatibility. Prior to assembly, HA was injected subcutaneously into Sprague-Dawley (SD) rats and samples were removed over a post-injection time course and subject to histological, immunological, and mechanical analysis. Histological analysis showed minimal infiltration of host cells and capsule formation around the matrix. Hematological analysis showed no significant systemic immune response was elicited in pre- vs. post-injection animals for all time points. Most importantly, atomic force microscopy (AFM) analysis showed dynamically increasing hydrogel stiffness over time similar to that previously found in vitro. HA was also injected into the hearts of healthy SD rats and subject to histological analysis over a post-injection time course. Though injection volume prevented mechanical measurement in the myocardium, hydrogel porosity increased, which we previously correlated with increased stiffness over time for subcutaneous injections. These in vitro data indicate that the combination of cells and developmentally appropriate matrix stiffness may significantly improve cell differentiation while in vivo data indicate the injectable feasibility of the HA matrix into the myocardium in future regenerative studies for treating heart failure post-myocardial infarction.

3652-Pos Board B513

Adjuvant Mitigating Effect of Magnetic Field Exposures up to 72 Hours after UVC or X-Rays Damages Induction in Cell Cultures

Patrick M. Mehl.
The Catholic University of America, Washington DC, DC, USA.

Finding a good and long lasting mitigating approach against ionizing radiation is a continuous challenge. Pyruvate or tocopherol derivatives have been chosen for their low toxicity to confirm their intrinsic mitigating properties on L929 mouse fibroblasts against radiation damages up to 72 hours after exposures using colony forming unit assays.
60Hz magnetic fields (EMF) interact with cells through the induced electrical field Eind at the membrane surface. In our theoretical model, Eind produces a counter-ion migration from within the Debye layer resulting into a potential change of the membrane surface capable to activate cell signaling such as stress responses. EMF mitigation is presently observed but decreases with time after radiation exposures. To mimic EMF, changing transiently the intracellular redox potential with 100 microM ferricyanide increased strongly cell survival after lethal radiation. 0.1 to 4 Gauss EMF up to 4 hours with mitigating chemical agents are shown to promote cell survival, increasing the equivalent dose ratio from 1.25 (no EMF) to around 2 (with EMF) for pyruvate derivatives.
After UVC or X-rays, cells stop within their cell cycle for repair transiently cumulating in G2/M phase. Cells are subject to two different programmed death pathways: apoptosis (G2/M phase) and autophagy (G1, S phases). Flow cytometry shows EMF stimulation unlocking the G2/M blockage towards a transient