Improving Elbow Function Post-Trauma: Rodents now, Humans next.

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Human Joints

• Typically, joints are made of hard (bone) and soft (cartilage, ligament and capsule) tissues.

• Joints are categorized based on their structure or function.

• Human joints are essential for holding bony structures like skull, and ribs and spine intact.

• They also assist in activities of daily living *i.e.*, grooming, locomotion and feeding oneself.
Articulating Joints

• In specific, articulating joints are designed to provide a certain range of motion depending on the location and function.

• Synovial joints a joint capsule holding synovial fluid for lubrication.

• Any injury to the soft tissue of the joint, leads to fibrosis.

• This can reduce the range of motion.
Elbow Post-Traumatic Joint Contracture

• 50% loss of elbow function leads to 80% loss of upper extremity function.
• Damage to joint soft tissues at elbow, mainly the capsule tissue, leads to fibrosis and reduces elbow function.
• Reducing post-traumatic scarring of the capsule tissue is the key in restoring the lost range of motion.
Treatment

• Splinting and physiotherapy with or without application of heat/ultrasound is a non-invasive approach.

• Invasive approaches including, arthroscopic or a full capsule release surgery fails to restore the range of motion at joints to pre-injury level.

• Contraction occurs due to increased myofibroblast activity.
Soft Tissue Fibrosis

• Myofibroblasts exhibit increased contractile force on ECM and produce excess collagen.

• Fibroblasts, the primary precursors of myofibroblasts use the increased ECM stress as a biomechanical cue to further promote myofibroblast differentiation apart from biochemical factors.

• Actin-myosin cytoskeleton is responsible for converting this mechanical signals into cellular.
Blebbistatin

• Our group has previously used RJCFs to demonstrate the Blebbistatin action to reversely inhibit this contractile force via collagen gel compaction assay *in vitro*.

• By this approach we can dampen the biomechanical feedback loop and reduce excessive ECM stress.

• This drug can be delivered in PLGA pellets for *in vivo* exploration.

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Rodent Model Study

• Long-Evans model has an elbow anatomy and functions comparable to humans.

• Anterior capsulotomy will be performed along with lateral collateral ligament transection and elbow subluxation to mimic severe elbow joint trauma.

• Blebbistatin loaded PLGA pellets will provide a local sustained delivery at the injured joint.

• Uninjured arm will serve as internal control for post-sacrifice histological and biomechanical analysis (using a custom-built biomechanical test apparatus).
Thanks You…

…Questions?