

# Regenerative Orthopedics

WHERE ARE WE NOW?

MD, CAQSM, RMSK

M

W. Scott Waugh, MD, RMSK

- ▶ Edmond, OK – Integrative Medical Solutions and Nonop Ortho
- ▶ Baylor University – Waco, TX
- ▶ University of Oklahoma College of Medicine - OKC
- ▶ VCU Family Practice Residency Program – Richmond, VA
- ▶ University of Oklahoma Sports Medicine Fellowship – OKC
- ▶ University of Oklahoma Sports Medicine Fellowship, Associate Clinical Faculty
- ▶ MSKUS.com Faculty

## History

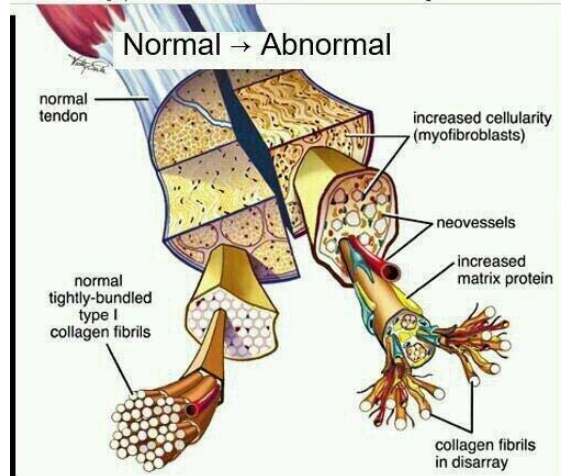
- ▶ 1950's: MSC's were initially discovered by Friedenstein and colleagues
- ▶ 1968: first successful bone marrow transplant (Allogeneic graft) took place to treat 2 siblings with Severe Combined Immunodeficiency
- ▶ 1978: stem cells were discovered in umbilical cord blood
- ▶ 1980's: stem cells were isolated in adipose tissue by scientists at UCLA working with Penn State University
- ▶ 1987: PRP was first used by Ferrari et al. following an open heart surgery, to avoid excessive transfusion of homologous blood products.

## Conditions

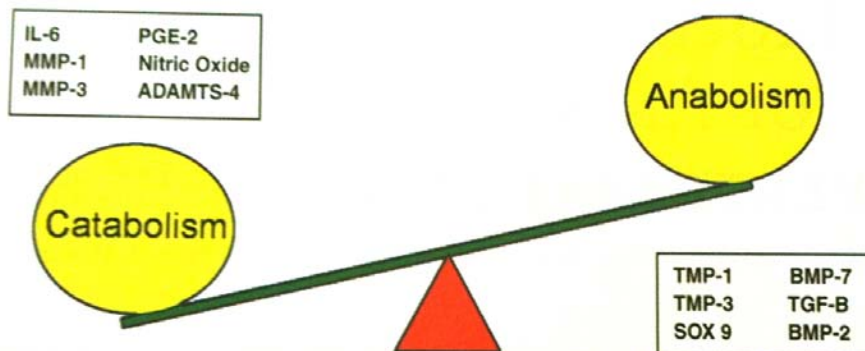
- ▶ Tendinitis
- ▶ Tendinopathy
- ▶ Partial tendon tear
- ▶ Ligament tear
- ▶ Muscle tear
- ▶ Joint inflammation
- ▶ Joint degeneration



# Pathophysiology of Tendinopathy

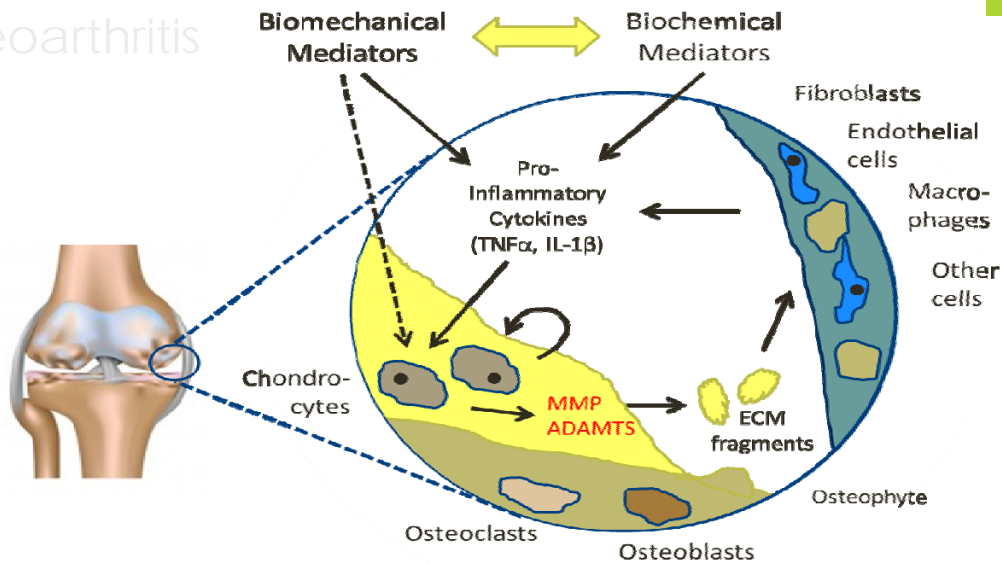


# Normal Cartilage Metabolism



# Pathophysiology of DJD

Osteoarthritis

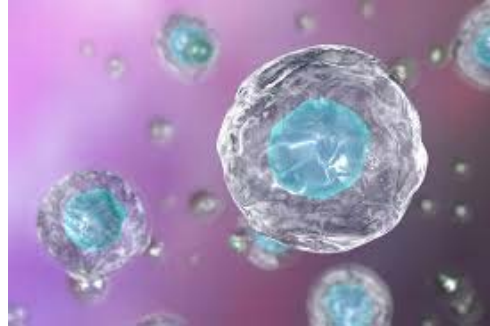


## Overlapping Theories of OA

- ▶ Biomechanical (overweight, injury, etc.)
  - ▶ Biomechanical insults activate the biochemical pathway (chondrocyte activation, protease release)
  - ▶ Treated with surgery, physical therapy
- ▶ Biochemical (cartilage degradation, lesions, chondrocyte activation and protease release, inflammation)
  - ▶ Biochemical insults reinforce the biomechanical pathway (instability, degradation, pain)
  - ▶ Treatment: Current drugs treat pain and/or inflammation indirectly. Attempts at biologic treatment with mixed results (e.g. anti-TNF-alpha approach)

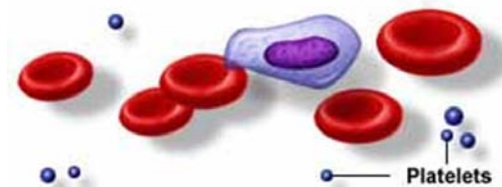
## Regenerative Therapies

- ▶ Platelet Rich Plasma
- ▶ Alpha-2-macroglobulin
- ▶ Placental tissue derivatives
  - ▶ Placental tissue matrix
  - ▶ Amniotic Fluid
- ▶ Exosomes
- ▶ Stem Cells



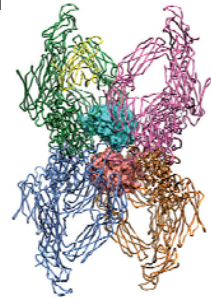
## Platelet Rich Plasma (PRP)

- ▶ Concentrated from the patient's blood
- ▶ Several different manufacturer's with different levels of platelets, red cells and white cells
- ▶ Platelet-derived growth factor (PDGF)
- ▶ Transforming growth factor (TGF)
- ▶ Vascular endothelial growth factor (VEGF)
- ▶ Epidermal growth factor (EGF)
- ▶ Fibroblast growth factor (FGF)
- ▶ Very good at treating tendinopathy and less good at treating joint disease



## Alpha-2-macroglobulin (A2M)

- ▶ A2M is a tetramer that is concentrated from the patient's blood
- ▶ It has a bait region, that upon cleavage, induces a conformation change trapping the protease
- ▶ It halts the biochemical mediation of joint osteoarthritis
- ▶ It is very useful in treating acute swelling post-injury and post-surgery



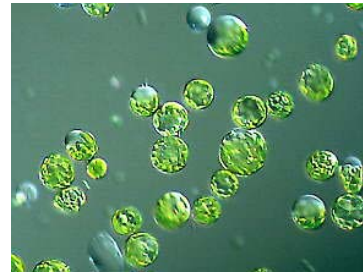
## Acellular Placental Products

- ▶ Placental Tissue Matrix (Skye Biologics)
  - ▶ Stable at room temperature
- ▶ Amniotic Fluid
  - ▶ Cryopreserved
- ▶ Safe, non-steroidal alternative to surgery
- ▶ Anti-inflammatory and anti-microbial
- ▶ Contains more than 200 growth factors



## Exosomes

- ▶ Culturally expanded placental stem cells secrete signaling proteins
- ▶ Small lipid vesicles
- ▶ Cell-cell communication
- ▶ mRNA and other proteins
- ▶ FAST - allows neighboring cells to produce required proteins without the need to initiate DNA transcription and translation
- ▶ Concentrated, potent anti-inflammatory and regenerative effects on soft tissue and joints



## Stem Cell Therapy

- ▶ All stem cells have 2 minimum qualities
  - ▶ Stems cells are renewable and have potency (not in-vivo)
- ▶ They do produce long-term effects by responding to signals from injured tissue in multiple ways
- ▶ MSC's secrete multiple anti-inflammatory factors and optimize the environment
- ▶ Now YOUR OWN body, along with the MSC's and production of cytokines, exosomes, growth factors and mRNA, has the opportunity to begin to regenerate the damaged tissue

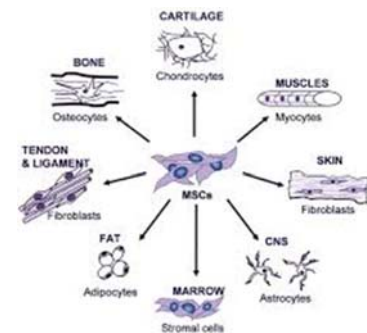
# Stem Cell Therapy

- ▶ Bone Marrow Aspirate
  - ▶ Excellent source of autologous MSC's
  - ▶ Good for large joint osteoarthritis
  - ▶ Limited by age and comorbidities
- ▶ Adipose
  - ▶ Also a good source of MSC's
  - ▶ More reliable with aging but still limited by comorbidities
  - ▶ Great for filling gaps in tendon tears



# Stem Cell Therapy

- ▶ Umbilical Cord Blood
  - ▶ Harvested from donated umbilical cord tissue after delivery
  - ▶ Contain live nucleated cells that contain 2-3% mesenchymal stem cells
  - ▶ No manipulation is performed
  - ▶ Cryopreserved, critical to know the cell count after re-warming
  - ▶ Effective for joint and tendon pathology





## UC VS. AMNIOTIC VS. BMAC/ADIPOSE

	UMBILICAL CORD	AMNIOTIC	AUTOLOGOUS ADIPOSE/ BMAC
COMPOSITION	LIVE NUCLEATED CELLS, GROWTH FACTORS, PROTEINS	FEW/NO LIVE CELLS GROWTH FACTORS, PROTEINS	LIVE NUCLEATED CELLS, GROWTH FACTORS, PROTEINS
STEM CELL TYPE	MSC & HSC	FEW/NO LIVE CELLS	MSC & HSC
CONCENTRATION	5M/CC, 10M/CC, 30M/CC	FEW/NO LIVE CELLS	DEPENDENT UPON PATIENTS AGE & HEALTH
QUALITY OF CELLS	9 MONTHS OLD/ROBUST	9 MONTHS OLD/FURTHER DIFFERENTIATED/ CELLULAR DEBRIS	DEPENDENT UPON PATIENTS AGE & HEALTH
ADVERSE REACTION	MINIMAL/SULFA SENSITIVITY	POTENTIAL RESPONSE TO CELLULAR DEBRIS	PAIN & POTENTIAL SURGICAL RISK
CONSISTENCY OF RESULTS	VERY CONSISTENT/BASED ON CONC. AND QUALITY OF CELLS	VARIABLE	VARIABLE/OPERATOR-DEPENDENT, PATIENT AGE & HEALTH DEPENDENT
EASE OF USE	DEFROST AND INJECT 30 MIN	DEFROST AND INJECT 30 MIN	SURGERY/PROCESSING 2-4 HOURS

## Summary

“We’re like children with nuclear weapons”

Sean Mulvaney, M.D.

## Ultrasound Imaging

- ▶ Point-of-care testing
- ▶ Patient education
- ▶ Dynamic imaging
- ▶ Inexpensive
- ▶ Quick
- ▶ Accurate needle placement



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MUSCULOSKELETAL  
ULTRASOUND  
DEMONSTRATION

