I (and/or my co-authors) have something to disclose.

Detailed disclosure information is available via:

- The course syllabus,
or
- AAOS Disclosure Program on the AAOS website at http://www.aaos.org/disclosure
**PRP Regulatory Process**

FDA Position
- CBER (CFR 1271)
- Exempt from study
- 510(k) for centrifuge

"PRP to be used with bone graft to enhance bone graft handling properties"

**PRP and Cartilage**

- Matrix synthesis
- Chondrogenesis
- Decrease pain
- Anti-inflammatory
- HA synthesis
- Anti-infective

**PRP and MSCs**

- MSCs to serum
- MSCs to PRP

**Benefits of Collagen**

- Assessment of subchondral healing: comparison of microfracture to autologous matrix-induced chondrogenesis in a rabbit shoulder model
- Microfracture
- Surgical Control
- Collagen Scaffold
**BioCartilage**

- Micronized cartilage scaffold
- Aseptically processed w 5 year shelf-life
- Mix into paste with PRP or BMC
- Retention of:
  - ECM: Type II collagen, Aggrecan, Decorin
  - GF: TGF, FGF, PDGF, VEGF, BMP-7, EGF, IGF, etc.

**In vivo model**
- Five horses, two 10 mm defects/knee
- Microfracture + Biocartilage

**Outcomes**
- Arthroscopic 2, 6, and 13 months
- Gross, MRI, uCT, and Histology

**2nd Look Arthroscopy**

2 mo 6 mo 13 mo

Microfracture

Biocartilage

**Macro and MRI**

Overall Repair Score (13 mo)

<table>
<thead>
<tr>
<th></th>
<th>Microfracture</th>
<th>Biocartilage</th>
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</thead>
<tbody>
<tr>
<td>Frontal</td>
<td>2.4</td>
<td>2.6</td>
</tr>
<tr>
<td>Posterior</td>
<td>2.4</td>
<td>5.0</td>
</tr>
</tbody>
</table>

Type II Collagen Staining

**Case Example**

- 24 yo NFL lineman in contract year
- Years of medial pain

**Defect Evaluation**
Microfracture

Biocartilage/PRP/BMAC

1 year post op MRI

Growth Factor and Catabolic Cytokine Concentrations Are Influenced by the Cellular Composition of Platelet-Rich Plasma

PRP and OA

It doesn’t work!

It works!

It might work!
Safety and efficacy of LP-PRP vs Saline
- 15/group
- 3 weekly inj
- Improvement @ 12 mo
  - 78% vs 7%

PRBCT HA (50) vs ACP (50)
- All w blood draw
- US aspiration and injection
- Clinical/Biochemical Outcomes

Results
Responders
- Low BMI
  - < 25 vs > 34
  - K-L < Grade 2
PRP fold not a factor

LP vs LR PRP and OA
LP-PRP better than HA, LR-PRP and Placebo

Combination PRP + HA
Synergistic analgetic actions of hyaluronic acid and platelet-rich plasma on cartilage regeneration in osteoarthritis therapy

LP-PRP better than HA, LR-PRP and Placebo

Results
Less pain at 6 mo and 1 year w/ PRP
p=0.009 at 6 month (VAS 34 vs 48)
p=0.004 at 1 year (VAS 43 vs 57)
My Algorithm for OA

1st injection + HA Response?

= 1-2 weeks
2nd injection Response?

No

STOP?

Yes

?? 3rd injection

Stem Cells

...DREAM

I HAVE A DREAM

...OR REALITY?

“Their language is intentionally imprecise and exploits the vulnerability of patients with debilitating diseases”

The U.S. has the world’s highest density of online “stem-cell” tourism in the world

How do they work?

“Medicinal Signaling Cells”

1. Recruit other stem cells
2. Secrete bioactive factors
   - Angiogenesis
   - Mitosis
   - Anti-scarring
   - Anti-apoptotic
3. Local modulation
   - Anti-inflammatory
   - Immunomodulatory
     - Reduce T cell surveillance

MSC Strategies

WHERE?

BONE MARROW, ADIPOSE TISSUE, SYNOVİUM, PERIPHERAL BLOOD...

WHAT?

CONCENTRATED OR EXPANDED

HOW?

IA INJECTION OR SURGICAL DELIVERY

Cultured BM MSCs in OA and FCD

Cultured Marrow MSCs
- Improved MOCART
- Similar clinical and MRI
- 1 vs 2 surgery advantage

Autologous Bone Marrow-Derived Mesenchymal Stem Cells Versus Autologous Chondrocyte Implantation
An Observational Cohort Study
AJSM, 2010

Cultured Adipose MSCs
- Improved WOMAC
- Decreased defect size
- Increased cartilage volume
**BMAC**

- EPCs, HSCs and MSCs
  - 14 x concentration
  - ≈30K in 50 cc BMA
- Phenotypic stability
- “PRP made from BM with MSCs” w increased WBCs and less fibrinogen

**Why Concentrate BM?**

![Image of BMC and BMA at 96 hrs]

- BMC at 96 hrs
- BMA at 96 hrs

**Does BMC make sense in OA?**

![Image of a basketball player and a medical illustration]

**BMAC has IL1-RA**

<table>
<thead>
<tr>
<th></th>
<th>BMA</th>
<th>BMC</th>
<th>PRP</th>
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<tbody>
<tr>
<td>IL-1ra</td>
<td>++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>IL-1ra :IL-1β</td>
<td>-</td>
<td></td>
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<tr>
<td>MSC</td>
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<td></td>
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<tr>
<td>TGF-β1, PDGF</td>
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<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>IL-1β, IL-8</td>
<td>+</td>
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</tbody>
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Fortier, Kennedy, et al KSSTA, in press
7 Studies in 314 Patients w Knee OA
- Jadad Scale (quality): 3 High and 4 Low

Source
- 4 BMC, 2 Adipose, 1 Cord Blood

Results
- Pain: No or inconclusive impact
- Function: MSCs alone or combined improved function at 3, 12, and 24 mo (inconclusive vs hyaluronic acid)

Evidence weak w heterogeneous patients and low quality, incomplete outcomes and small sample sizes

Systematic review of BMAC for FCD or OA
- 11 Studies
  - 5 Prospective
  - 1 Retrospective
  - 5 Case Series/Reports
- 3 Studies for OA
- 8 Studies for FCD

Paucity of high quality studies, BMAC safe, recommend judicious use until better evidence exists

Conclusions
- BioCartilage for any defect that you might consider MST as a scaffold delivery for PRP/MSCs
- LP PRP for OA is becoming a dominant treatment strategy
- FDA regulatory process of MSCs is a moving target with increasing oversight and business risk aversion as therapeutic options expand
- BMC for OA basic science supports it but clinical evidence lacking at this time