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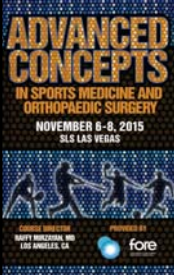
Disclosures

I have the following potential conflicts of interest:
Consulting payments/royalties and research support directly related to products discussed:

- Vericel, Regentis, Geistlich, Novartis, Cartiheal, SBM, **NuTech**
- SLACK publishing (Book)

FDA-status of devices discussed:
Many of the applications presented are considered off-label



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Harvard Medical School 



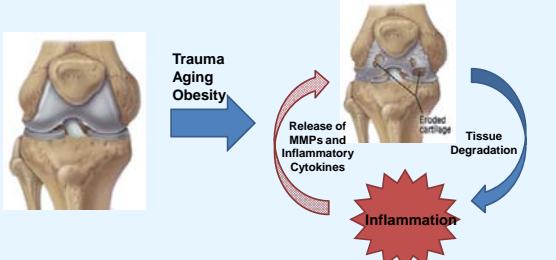
Amniotic Suspension Allograft Injection for Treatment of Osteoarthritis

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Progression of OA



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Stem cell functions

The diagram illustrates the functions of Stem Cells (MSCs). A central image of Stem Cells (MSCs) is surrounded by four arrows pointing to different functions:

- Regulate Immune System to Reduce Inflammation:** A diagram shows a Stem Cell interacting with T cells and B cells. It lists cytokines: TNF- α , INF- γ , IL-1 β , IL-4, and INF- γ .
- Prevent Scar Formation:** An image shows a surgical site with sutures.
- Home To Injury Site:** An image shows a cross-section of tissue with a dark spot indicating an injury site.
- Guided tissue regeneration:** An image shows a cross-section of tissue with a blue-stained area indicating regeneration.

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Injection

Allograft	MSCs derived from amniotic fluid and morselized amnion from the same donor are combined
Processing	Cryopreserved to maintain bioactivity
Stored	-80 Degrees Celsius
Packaging	Individual frozen vials in peel packaging
Safety	Aseptic tissue processing and extensive donor testing
Zero Age	Unlike PRP these tissues are obtained from younger donors, so donor age and tissue viability are not a factor.
Regenerative	Allograft amniotic tissues and stem cells have been shown to stimulate tissue repair and healing as well as possessing anti-scarring and anti-inflammatory properties.
Native Properties	Allograft amniotic tissues are known to contain: Collagen types III, IV, V and proteoglycans, hyaluronic acid, trophic proteins, growth factors and multipotent stem cells.
Regulatory	Products are regulated by the FDA as a 361 allograft tissue (HCT/P) Human Cellular and Tissue Based Products.

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Study Description

Safety study design:

- 6 patients
- Ave. age 55 (44-65) years
- All XR K-L 3
- Failed conventional non-op Tx
- Single intra-articular knee injection
- F/U 2w, 3mo, 6mo, 12mo
- PROM: KOOS, IKDC, SANE
- Labs: Inflammatory, Immune response

The images show microscopic views of cells. The top image is labeled 'ReNu 20X' and shows a cluster of cells. The bottom image shows cells with pink and yellow arrows pointing to specific features.

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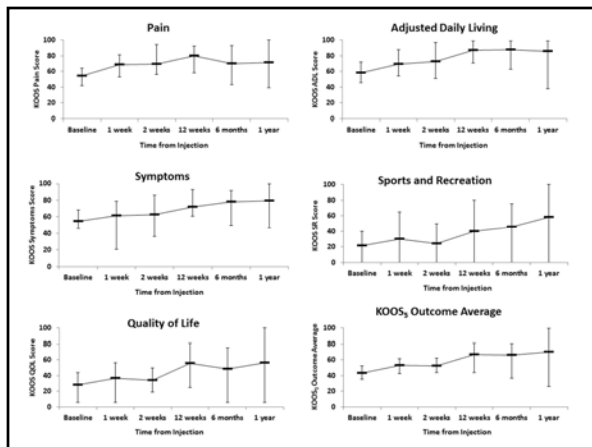
Results

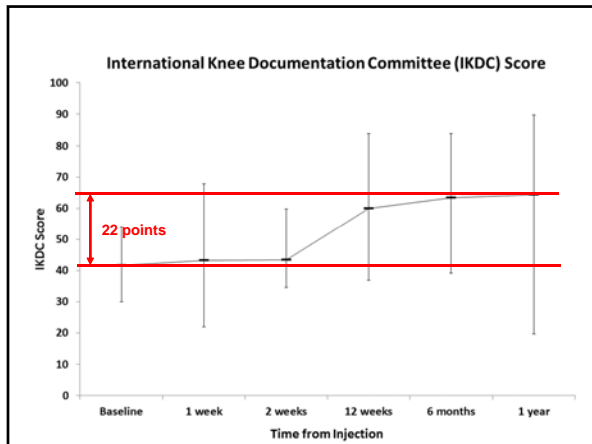
	General Laboratory Parameters				
	Baseline	2 weeks	3 months	6 months	1 year
	Mean Difference from Baseline (± 95% CI)				
Cr (mg/dL)	1.03 (0.7-1.5)	0.07 (± 0.1)	0 (± 0.05)	0.12 (± 0.08)	-0.03 (± 0.07)
HCT (%)	45.12% (40.6%-54.3%)	-1.3% (± 2.92%)	-2.55% (± 1.27%)	-2.13% (± 1.97%)	0.88% (± 2.61%)
WBC (cells/mm ³ x 10 ⁹)	8.22 (6.5-11.8)	-1.58 (± 1.64)	-0.87 (± 1.33)	-0.98 (± 1.29)	-0.98 (± 1.65)
PLT (cells/mm ³ x 10 ⁹)	241.17 (179-275)	-5 (± 29.27)	1.5 (± 18.89)	3 (± 15.42)	-20.17 (± 27.41)
ESR (mm/hr)	13.17 (1-29)	4.17 (± 7.29)	N.D.	0.83 (± 5.05)	N.D.
CRP (mg/L)	7 (0.71-18.2)	-3.07 (± 4.45)	N.D.	-1.13 (± 1.26)	N.D.

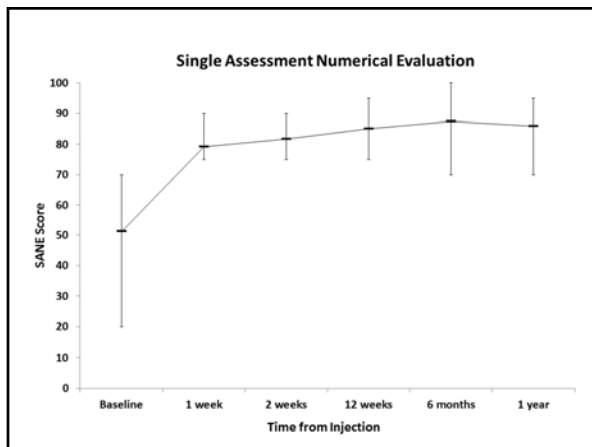
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Results

	Immunologic Parameters			
	Baseline	2 weeks	3 months	1 year
	Mean Difference from Baseline (± 95% CI)			
CD3+ T Cells (% of Lymphocytes)	71.5% (57%-89%)	-0.17% (± 2.79%)	0% (± 2.26%)	2.83% (± 3.37%)
CD3+CD4+ T Cells (% of Lymphocytes)	53.67% (49%-60%)	2% (± 3.08%)	-0.17% (± 1.63%)	2.17% (± 1.18%)
CD3+CD8+ T Cells (% of Lymphocytes)	17.5% (8%-38%)	-2.33% (± 2.61%)	-0.17% (± 1.55%)	0.5% (± 2.25%)
CD19+ B Cells (% of Lymphocytes)	11.5% (7%-17%)	1.17% (± 1.47%)	1.5% (± 1.58%)	1.5% (± 2.25%)
CD56+ NK cells (% of Lymphocytes)	12% (3%-18%)	-0.83% (± 1.55%)	0.17% (± 1.47%)	-0.83% (± 2.84%)
IgA (mg/dL)	164.17 (107-246)	N.D.	24.5 (± 12.97)	23.83 (± 23.71)
IgG (mg/dL)	749.83 (668-840)	N.D.	120.83 (± 67.06)*	119.33 (± 78.44)*
IgM (mg/dL)	120.67 (38-282)	N.D.	-7 (± 5.99)	6.33 (± 17.2)
IgE (mg/dL)	33 (14-57)	N.D.	0 (± 2.86)	5.5 (± 4.13)*







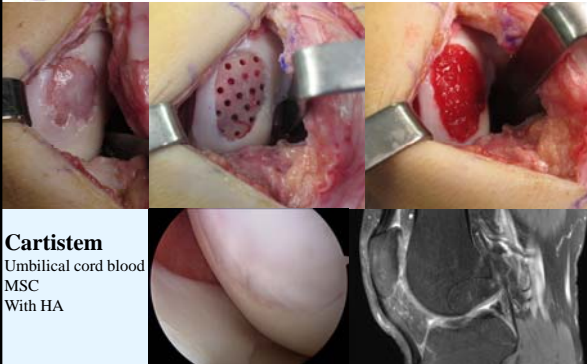
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Summary

- Amniotic suspension allograft injection demonstrated no adverse events in 6 pts.
- Small increase in IgG, decrease in CRP
- In small cohort, improvement in KOOS, IKDC and SANE (exceeds MCID)
- Larger RCT against NS and HA in progress (10 sites, 200 patients)

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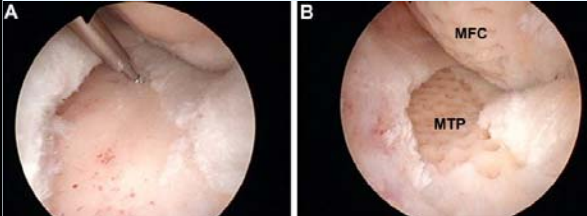
What else is out there?



Cartistem
Umbilical cord blood
MSC
With HA

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What else is out there?




A **B**
MFC
MTP

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Human clinical trials – March 2007


- Arthroscopic subchondral drilling & abrasion chondroplasty
- Continuous passive motion (CPM) 2 hours / day for one month
- Partial to full weight bearing 6 – 8 weeks




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Peripheral Blood Stem Cells (PBSC)

- Post-op day 4, 5 and 6
- Human granulocyte colony-stimulating factor (G-CSF)
- Neupogen 300 mcg – subcutaneously






- Post-op day 7
 - Apheresis
 - Fresh cells for injection
 - PBSC divided into vials & cryo-preserved






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PBSC + HA injections (once per week for 5 weeks)

1st Injection (Fresh cells) Frozen cells (2nd to 5th) PBSC 8 mls

PBSC + 2 mls Hyalgan Aspiration of haemarthrosis PBSC + HA injection

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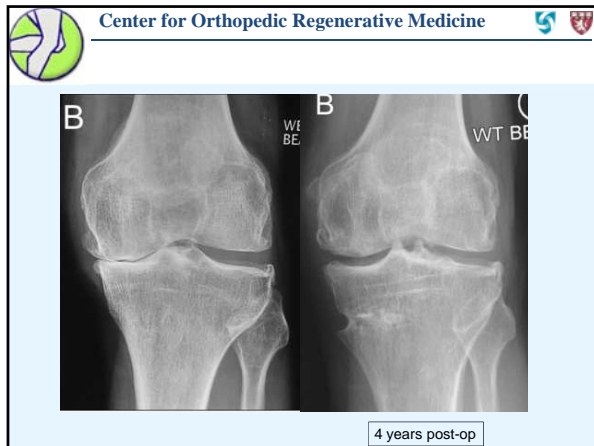
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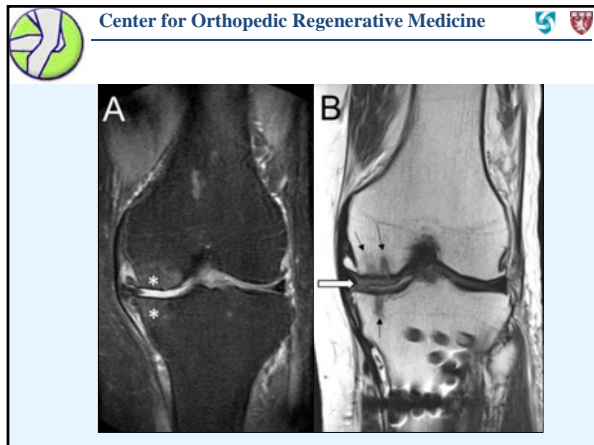
HIGH TIBIAL OSTEOTOMY AND CHONDROGENESIS


Image	Intra-operative	2 years	H&E
MFC			
MTP			



Fig 7. Findings of second-look arthroscopy and histologic assessment of medial femoral condyle (MFC) and medial tibial plateau (MTP) at 2 years in a 49-year-old male patient (same patient shown in Fig 6 primary).







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Summary

- Stem cells have great promise
- Big hype with little solid data
- Field is developing slowly
- First goal is symptomatic relief (injections)
- Second goal is structural repair through surgical implantation
- Far future goal is structural repair through injection
