Lessons Learned from Advancements in Orthopedics

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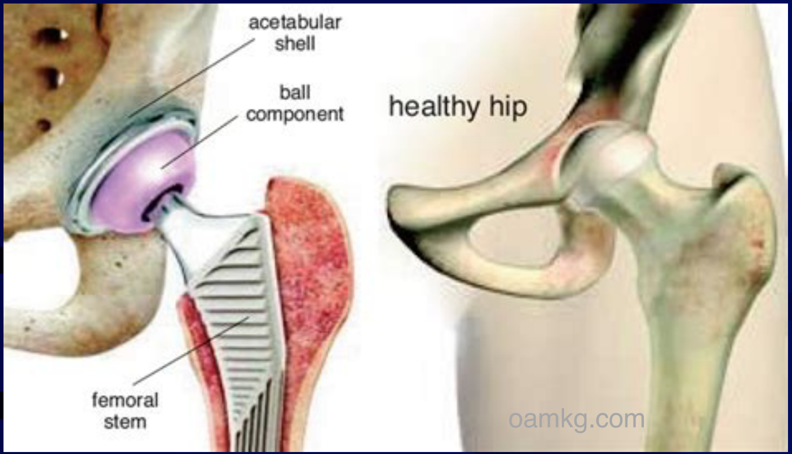
Topics

- Orthopedic Implant Registries
- Cartilage and Joint Tissue Engineering
- Biologics and Cell Therapies

Surgeons Address Joint Structural Issues



- Arthroscopy
- Total Joint Replacement
  - Total Hip
  - Total Knee
  - Total Shoulder
- TMJ Replacement
  - Small Bearing Surface
  - Near critical structures
    - Facial nerve
    - Dural Space

Total Hip Replacement
“Operation of the Century” (20^{th})

- 1891 Gluck: Ivory/Nickel
- 1950’s John Charnley ”low friction arthroplasty”
  - Polytetrafluorethylene (Teflon)
    - 1^{st} 100 did great ≈ 1 year
    - Many failures by 2 years
  - 1962, high molecular weight polyethylene
    - 81% survivorship at 25 years

Sir John Charnley
Father of Modern Joint Replacement

Joint Replacement Issues

- Bone Fixation
- Infection
- Mechanical Failure
  - Material properties
  - Implant Design
  - Surgical Technique
- Wear Debris
  - Bone loss
  - Tissue Reaction

Age > 65
Severe Arthritis
"Bone on Bone"

Issues are greater concern for younger patients.

Joint Replacement Registries
31 national registries

- 1975 Sweden
- 1999 Australia
- 1999 New Zealand
- 2003 United Kingdom
- 2012 United States
  - 2009 AAOS AJRR
  - Kaiser Registry 2001

Implant Performance
Clinical Outcomes

Metal/Metal Replacements
Registry Data: more early failures
2010 UK Medical Device Alert
UK Registered patients recalled for monitoring
2011 FDA postmarket surveillance ("522" Studies)

American Joint Replacement Registry

Improving orthopaedic care through data.

Partnership with Professional Society

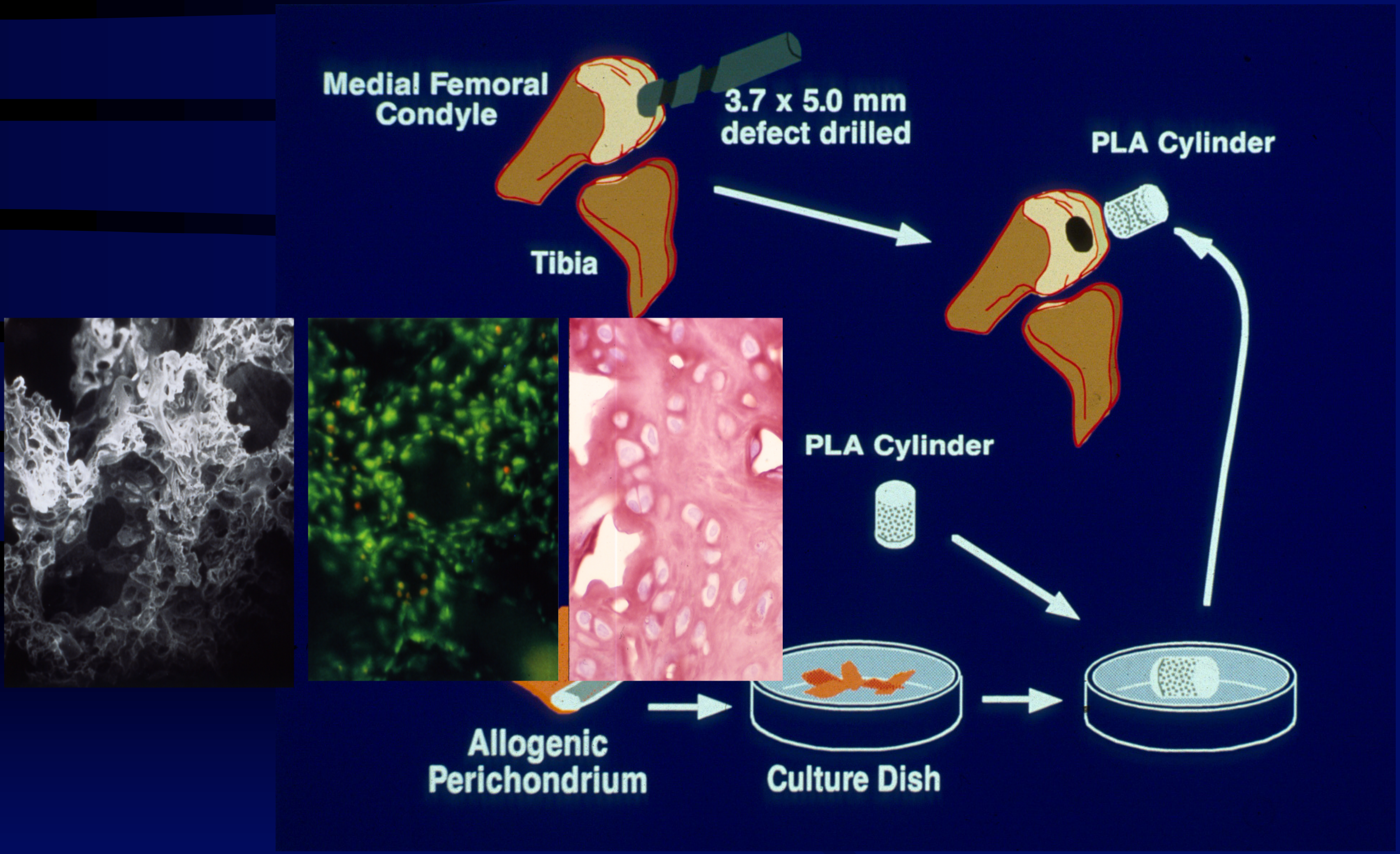
Voluntary

ajrr.net

Cartilage Tissue Engineering

- 1991 Vacanti et al.
  - Chondrocytes + PGA
- 1994 Wakitani et al
  - BMSC + collagen
- 1995 Chu et al
  - MSC+PLA/biphasic osteochondral scaffold

Cartilage Tissue Engineering For Joint Repair



Chu et al, J Biomed Materials 1995

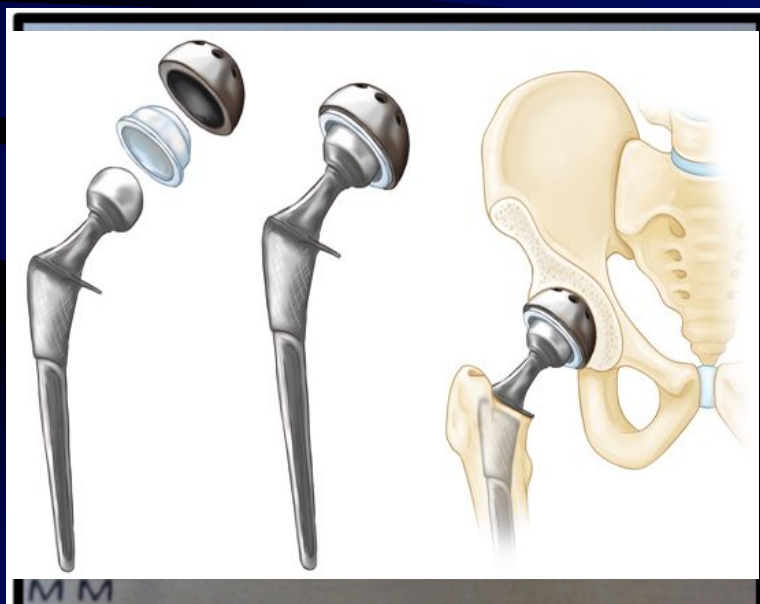
PNAS

Anatomically shaped tissue-engineered cartilage with tunable and inducible anticytokine delivery for biological joint resurfacing

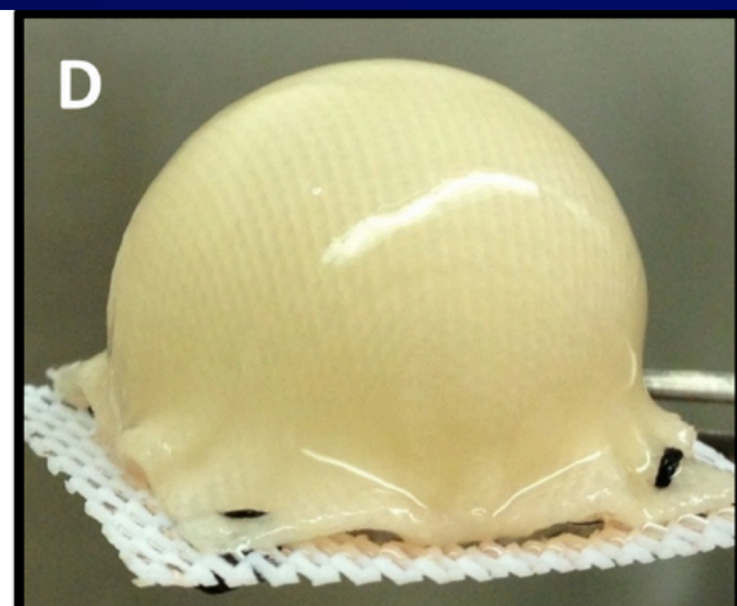
Author(s): Franklin T. Moutos, Katherine A. Glass, Sarah A. Compton, Alison K. Ross, Charles A. Gersbach, Farshid Guilak and Bradley T. Estes

Source: *Proceedings of the National Academy of Sciences of the United States of America*, Vol. 113, No. 31 (August 2, 2016), pp. E4513-E4522

Published by: National Academy of Sciences



Poly(ε-caprolactone)



adipose derived stem cells cultured for 38 days

Cellular Rejuvenation

Lee *et al. Stem Cell Research & Therapy* (2017) 8:244
DOI 10.1186/s13287-017-0696-x

Stem Cell Research & Therapy

RESEARCH **Open Access**

CrossMark

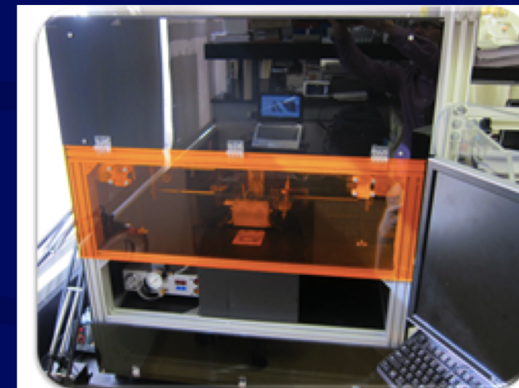
Human iPSC-derived chondrocytes mimic juvenile chondrocyte function for the dual advantage of increased proliferation and resistance to IL-1β

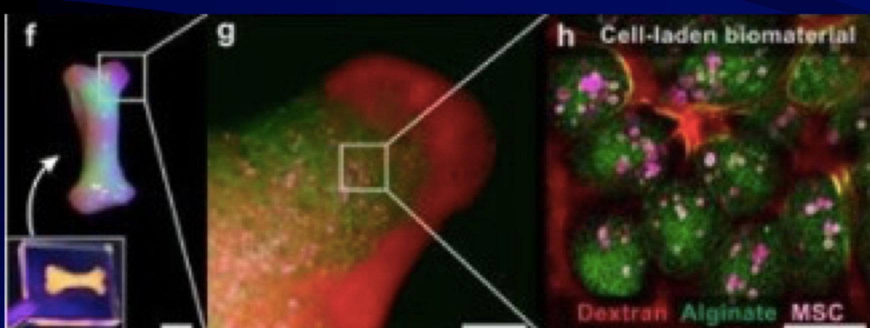
Jieun Lee[1], Piera Smeriglio[1], Constance R. Chu[1,2] and Nidhi Bhutani[1*]

- Human adult skin cells
- Reprogrammed to an embryonic stem cell state
- Differentiated into “youthful” cartilage cells

3D Printing with Living Cells

Using 3D printing, researchers can create scaffolds to repair/replace bone tissue. Shown here: a 3D printed skull. Photo Credit: © The University of Nottingham





"in-air microfluidics"
University of Twente

TechConnect
INNOVATION
AWARD
2018

Bioprinting of Hybrid
Tissue Engineering Constructs
Peter Yang, PhD
Stanford Orthopedic Surgery

From Bench to Bedside?

- Safety
- Durability
- Efficacy
- Scale-up
- Manufacturing
- Regulatory Approvals

Treatments may potentially avoid FDA regulation if:

- Cells, tissues or blood products come from the person being treated
- Aren’t being used in a fashion different from its normal purpose
- Are “minimally manipulated”

OrthoBiologics

- Exponential Growth
- Platelet Rich Plasma (PRP)
- Cell Therapies
  - Bone Marrow
  - Fat
  - Etc
- Indications with Data
  - Knee Osteoarthritis
  - ‘Tennis Elbow’

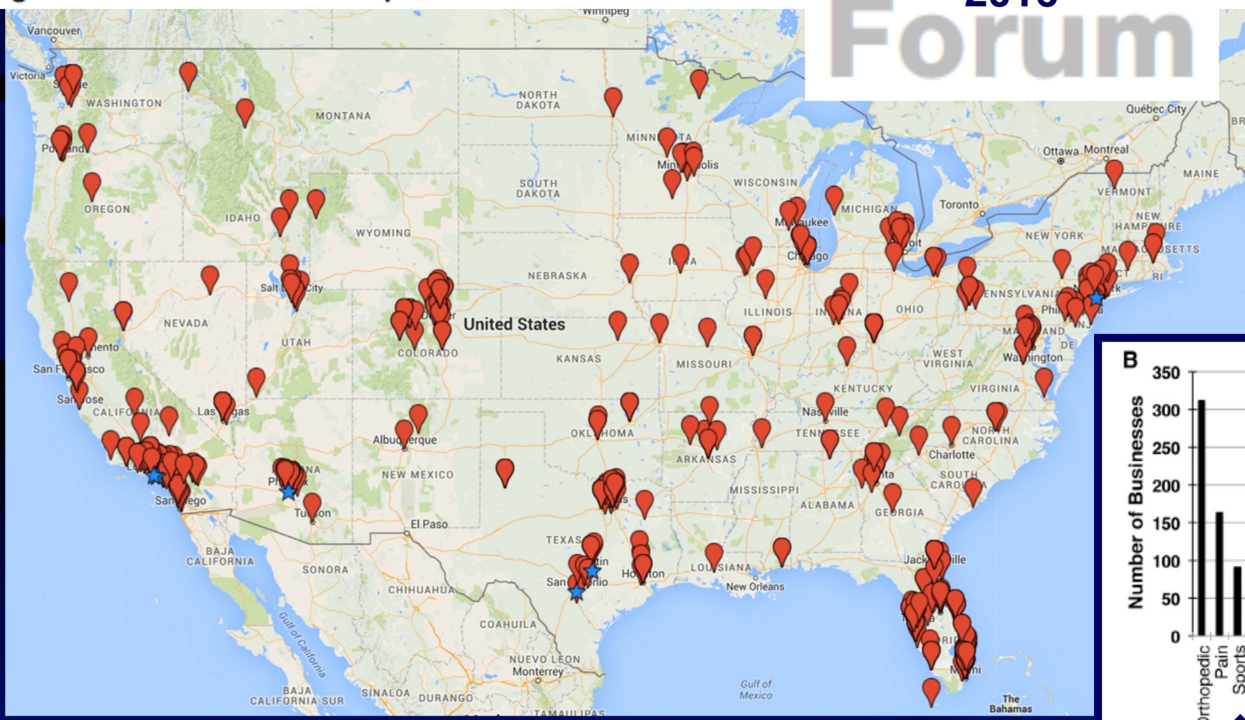
Will the PRP/Cells Work the Same?

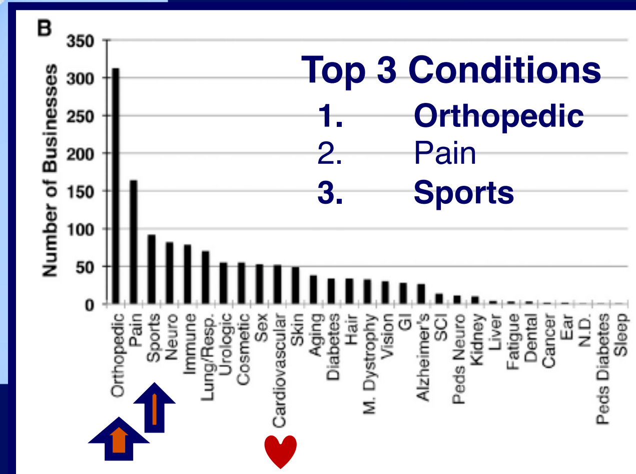
Unproven treatments are being marketed as ‘Stem Cell’ therapies

Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry

Leigh Turner[1,*] and Paul Knoepfler[2,3,*]

Cell Stem Cell
2016
Forum





AAOS/NIH U13 Symposium

AAOS
AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

Optimizing Clinical Use of Biologics in Orthopaedic Surgery

February 15-17, 2018

Stanford University
Li Ka Shing Learning and Knowledge Center

Program Chair: Constance Chu, MD
Co-Chairs: William Maloney, MD; Jeremy Mao, DDS, PhD; Scott Rodeo, MD; and Rocky Tuan, PhD
NIAMS Collaborator: Fei Wang, PhD

Presented with Support From

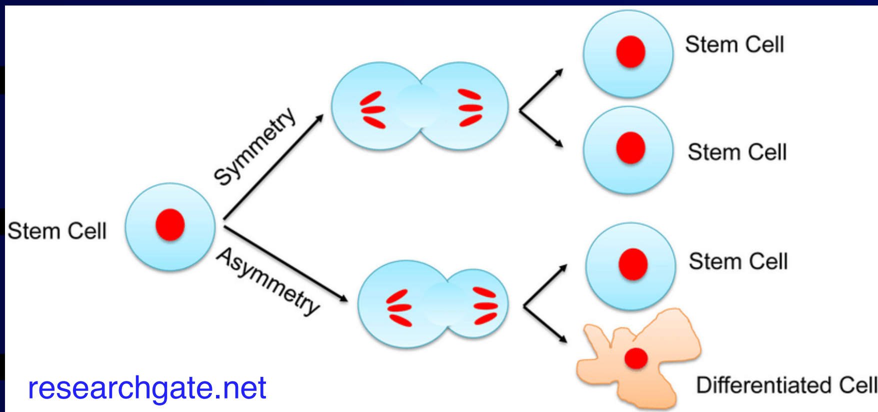
NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases

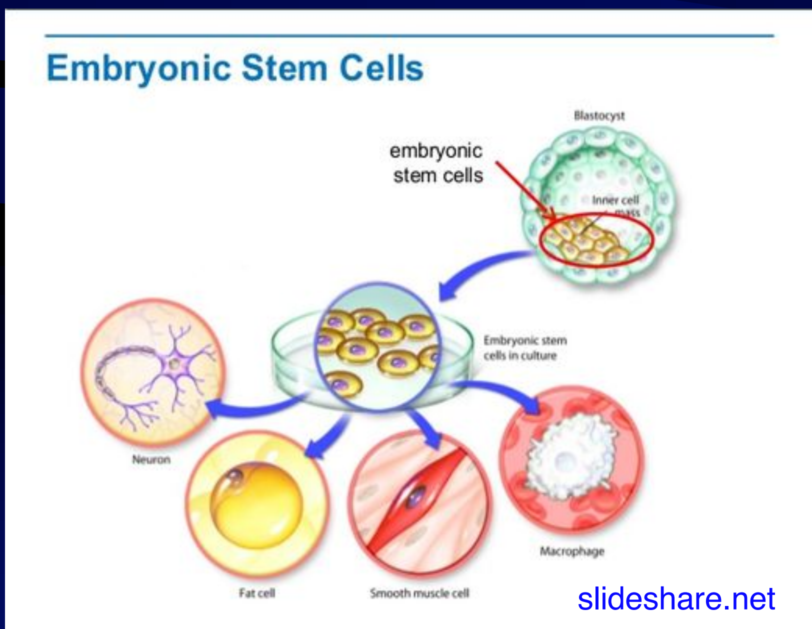
February 15-17, 2018
Stanford University

Symposium Goals

- Establish a clear, collective impact agenda for the clinical evaluation and use of biologics in orthopedics
- Develop a Guidance Document on clinically meaningful endpoints and outcome metrics for common orthopedic problems.

What is a ‘Stem Cell’?





- Capable of self-renewal for long periods of time (asymmetric division)
- Unspecialized
- Can give rise to specialized cell types

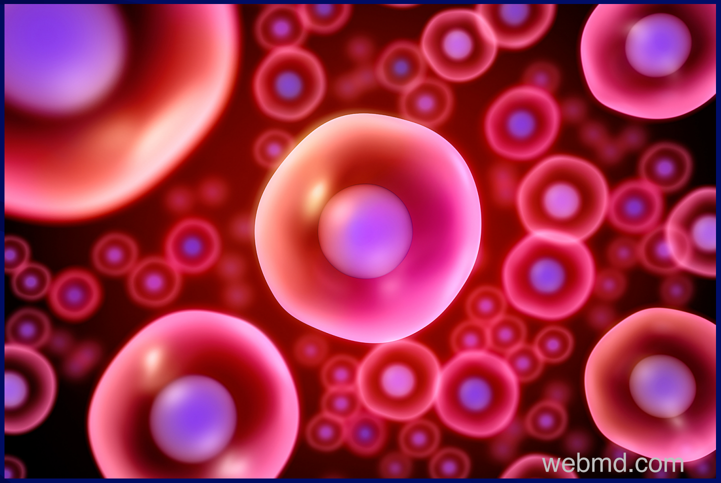
stemcells.nih.gov

Central Issue: Terminology

- Minimally manipulated cell preparations (MMCP)
  - No standards, uncharacterized, and widely used.
  - Contain few putative stem cells (0.01 to 0.001%)

MMCP

are not



Stem Cells

MMCP are not Stem Cells

The work group recommended that minimally manipulated cell products be referred to as cell therapies and that the untested and uncharacterized nature of these treatments be clearly communicated within the profession, to patients, and to the public.

Facilitating Evidence-Based Evaluation of Biologics

Osteoarthritis is a ‘Serious Condition’

- Japanese Accelerated Pathway (no safety concerns)
  - Conditional Approval of 7 Years
  - Post-market observational studies

Establish Registries for Post-market assessment

Optimizing Clinical Use of Biologics in Orthopaedic Surgery: Consensus Recommendations From the 2018 AAOS/NIH U-13 Conference

Chu, Constance R.; Rodeo, Scott; Bhutani, Nidhi; More

JAAOS - Journal of the American Academy of Orthopaedic Surgeons. 27(2):e50-e63, January 15, 2019.

https://journals.lww.com/jaaos/Fulltext/2019/01150/Optimizing_Clinical_Use_of_Biologics_in.3.aspx

jaaos.org