

# Tissue engineering using nonwoven: Limitations and futuristic thoughts

Dr. Sourabh Ghosh

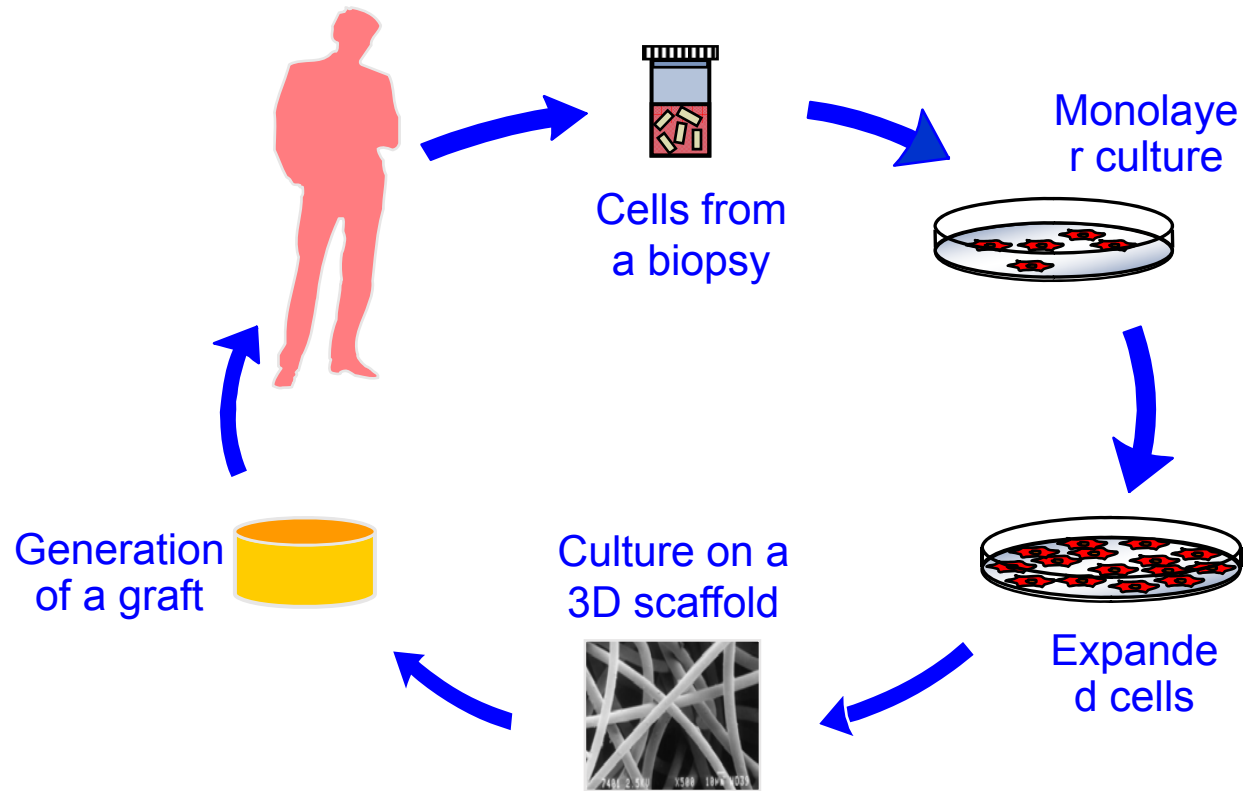
Professor

Department of Textile and Fibre Engineering

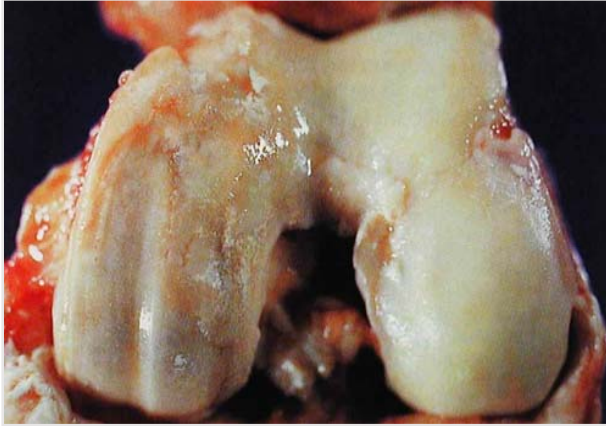
Institute Chair Professor

Indian Institute of Technology (IIT) Delhi

# Basic principles of Tissue engineering



# Articular cartilage



Load transmission,  
shock absorption,  
maintenance of functional  
integrity of the joint

**No blood vessels**

**No nerves**

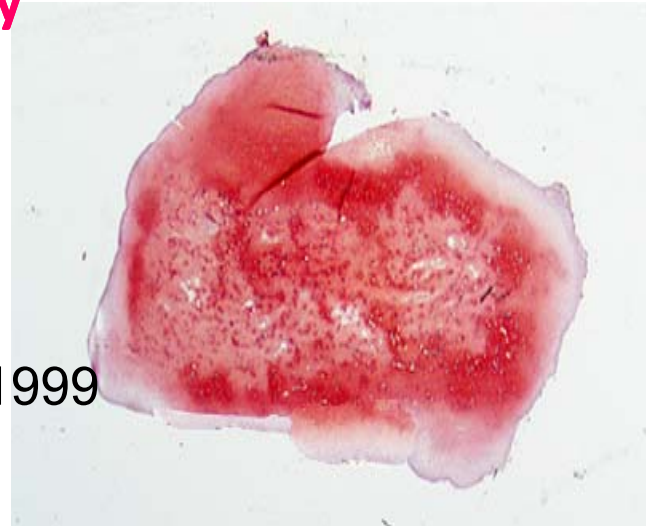
**Cells of low mitotic activity**

**Thickness ONLY : ~ 0.5 to 3  
mm**

**Very poor regeneration capacity**



Ann Biomed Eng , 1999  
PNAS , 1997





'bioactive' scaffolds

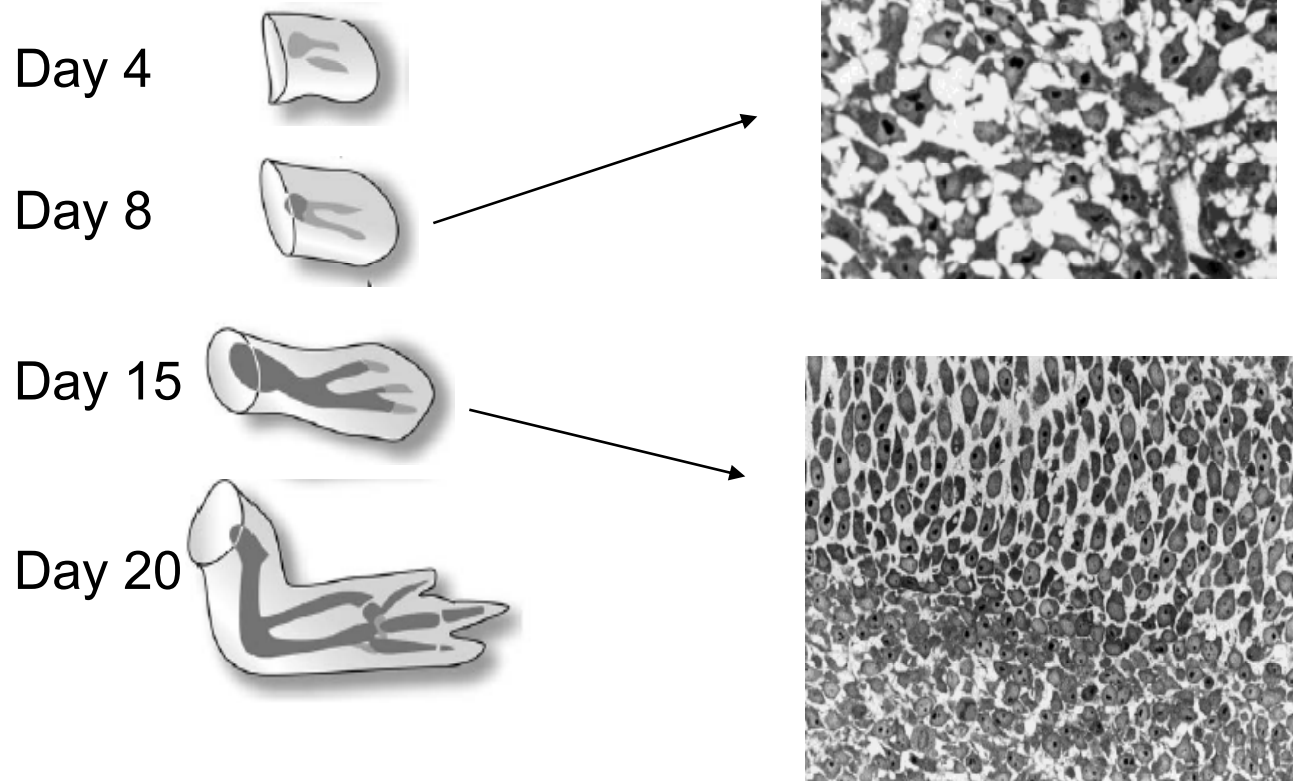
should provide environmental signals to the cells

to better control proliferation  
enhance the synthesis of ECM  
assembly of a functional neo-tissue.

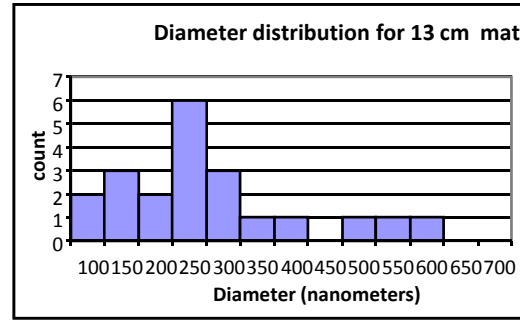
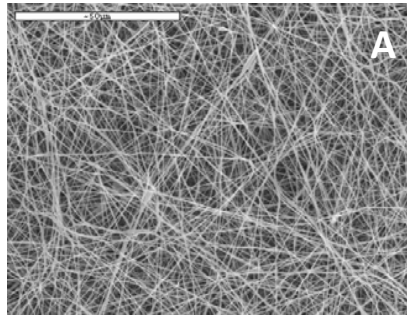
PLA  
Hyalograft-C



## Mesenchymal condensation during tissue formation

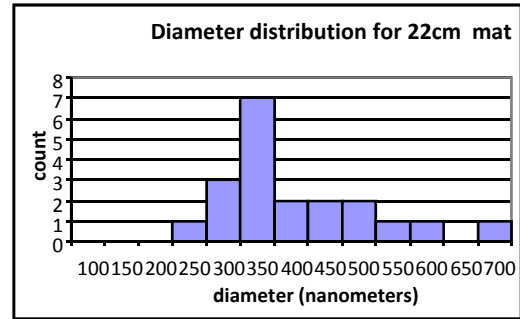
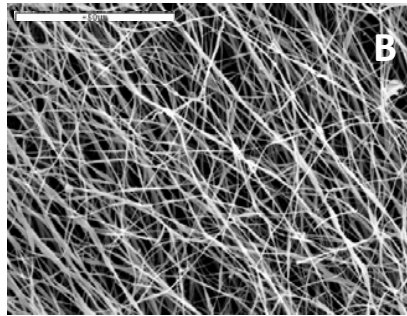


# Electrospun Silk matrix



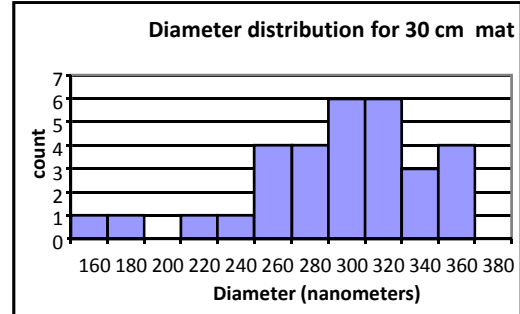
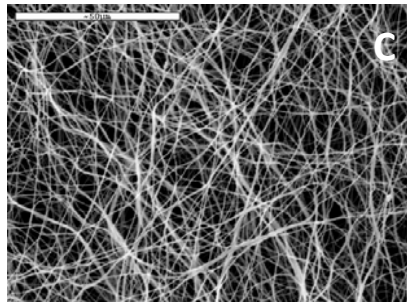
**13 cm mat**

Std dev= 47.8  
Counts = 30



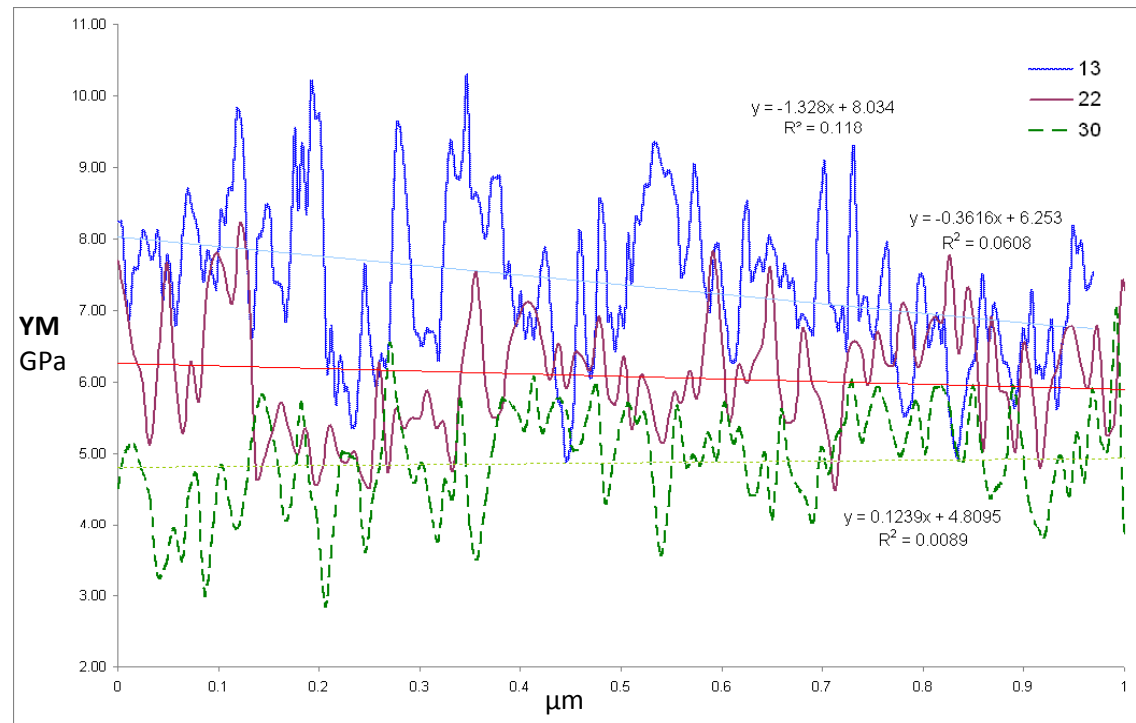
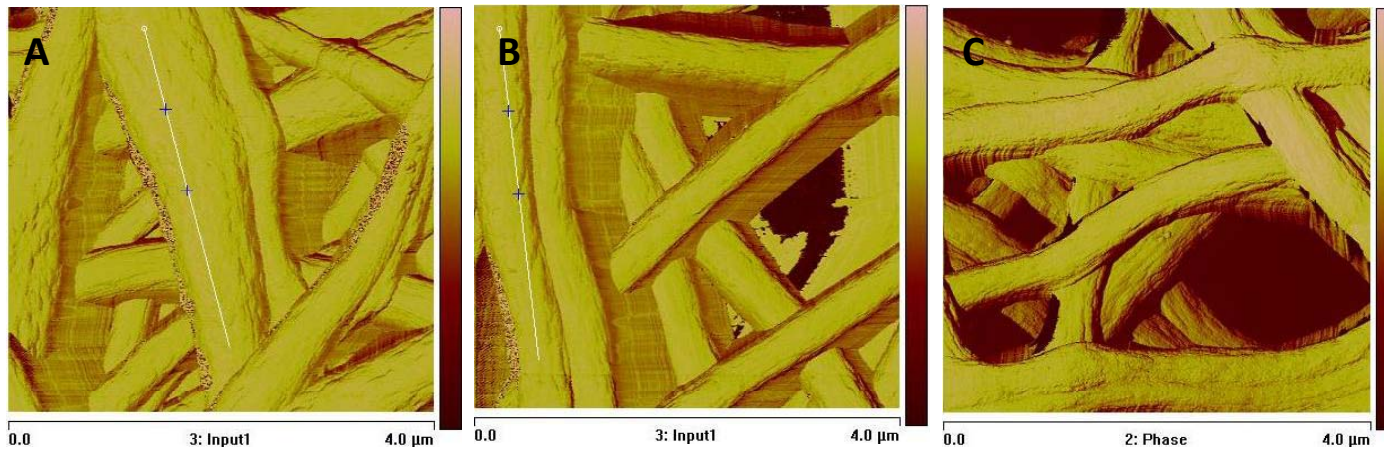
**22 cm mat**

Std dev= 102.9  
Counts = 30

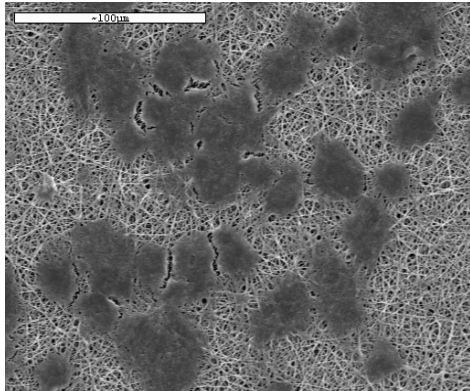


**30 cm mat**

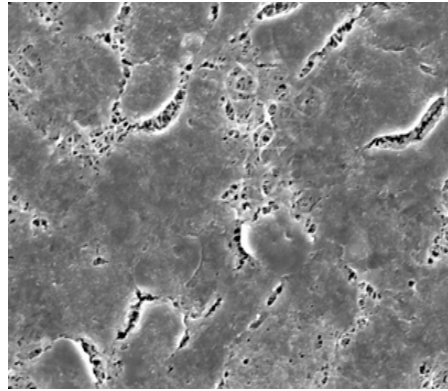
Std dev= 139.1  
Counts = 30



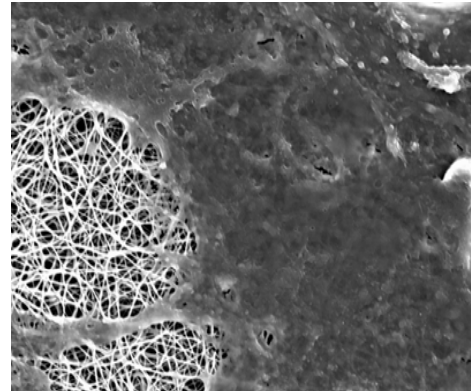
# Stem cells can sense difference in matrix stiffness



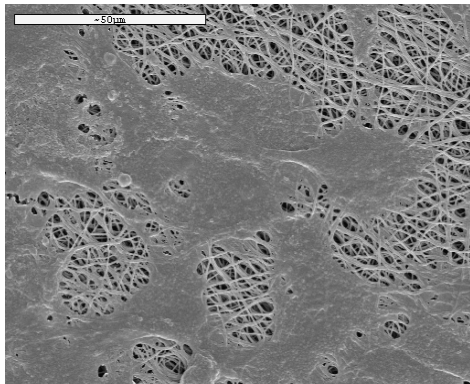
Stiffest electrospg matrix- day 1



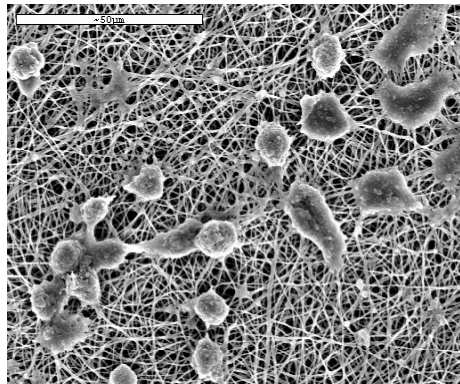
day 5



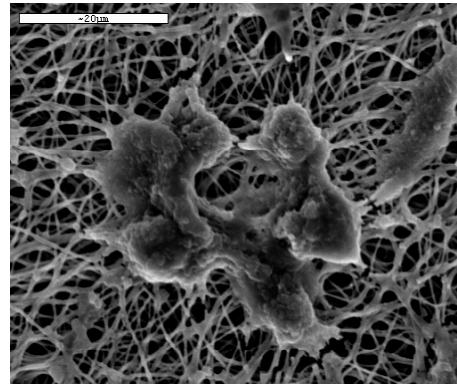
day 10



loose electrospg matrix- day 1

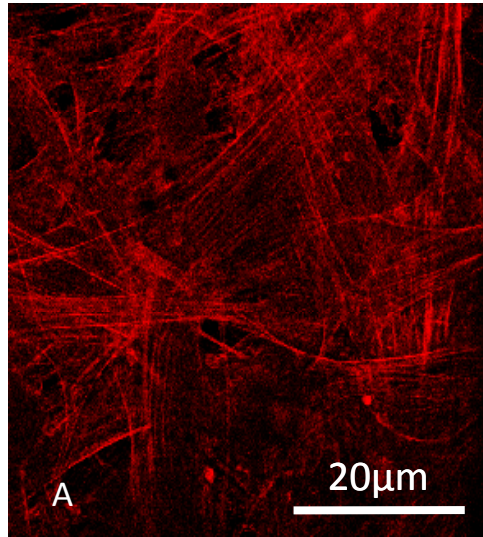


day 5

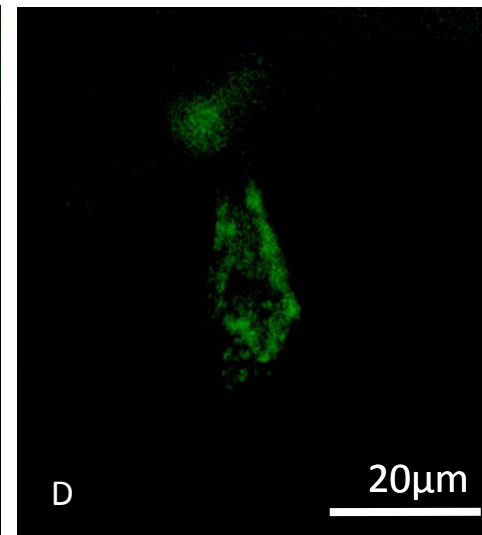
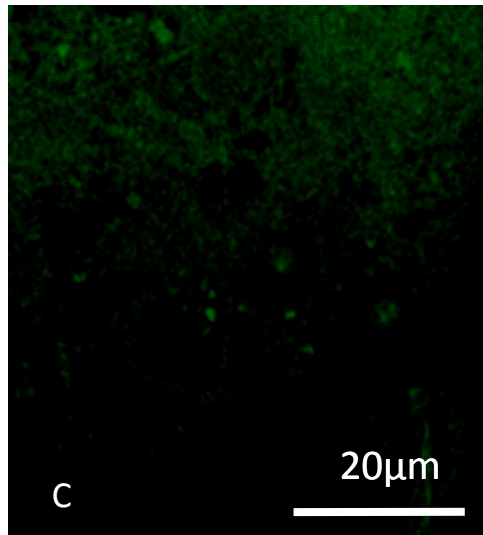
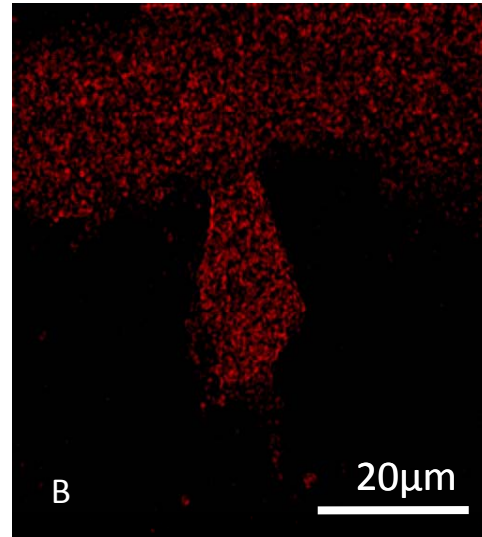


day 10

13 cm

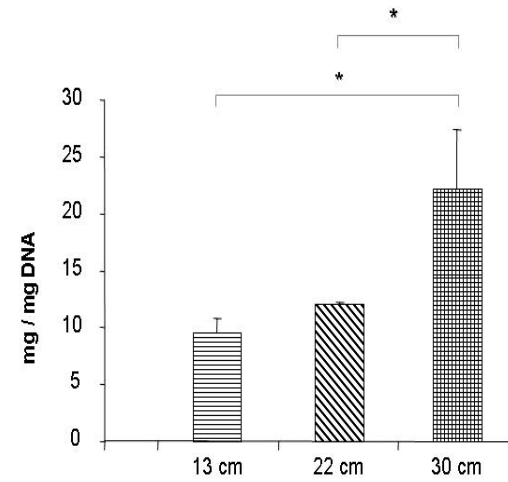


30 cm



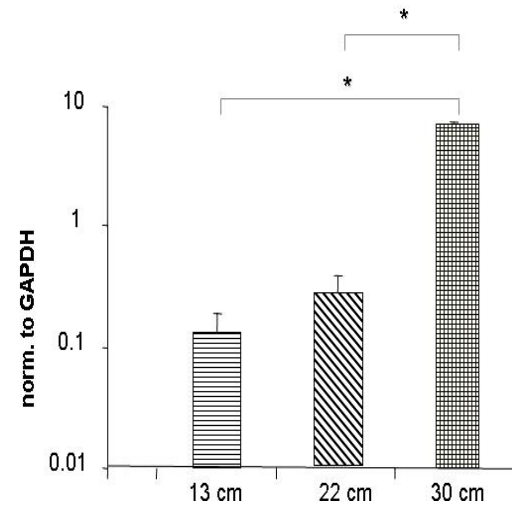
A

GAG accumulation

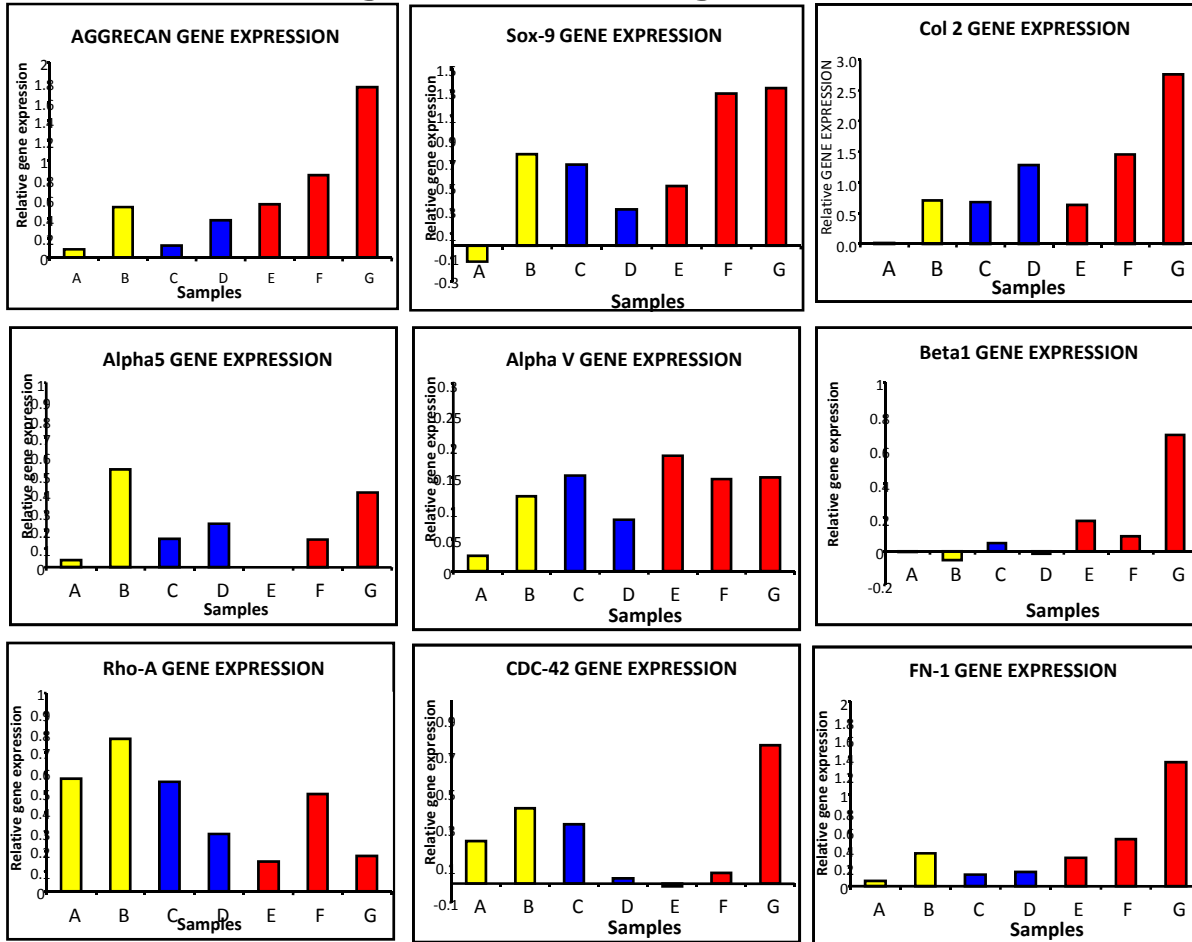


B

Collagen type II mRNA

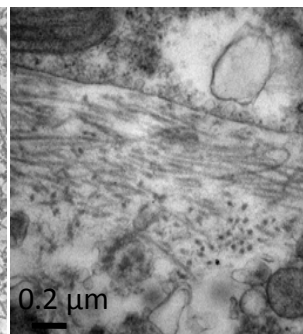
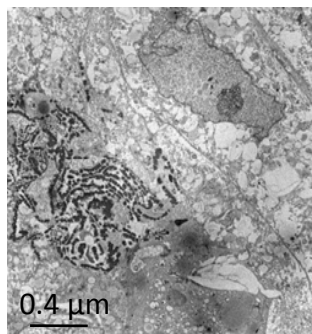
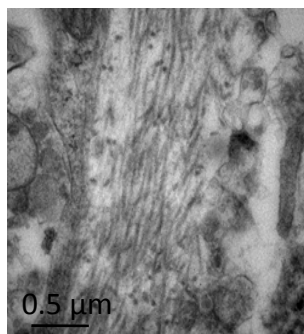
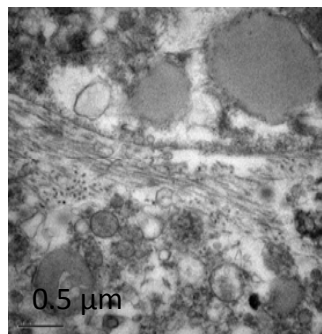
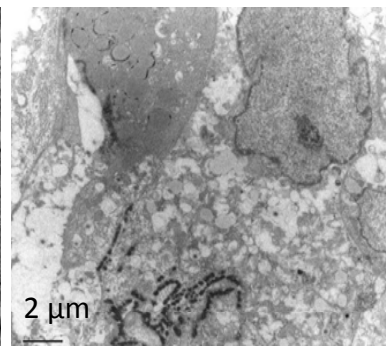
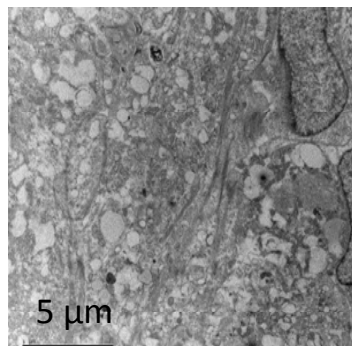
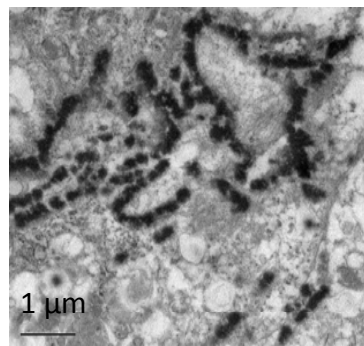
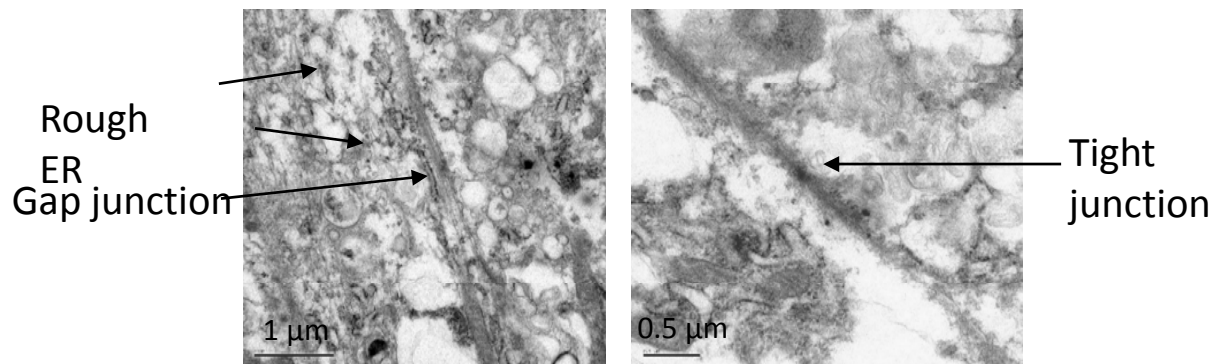


# Cartilage specific gene expression

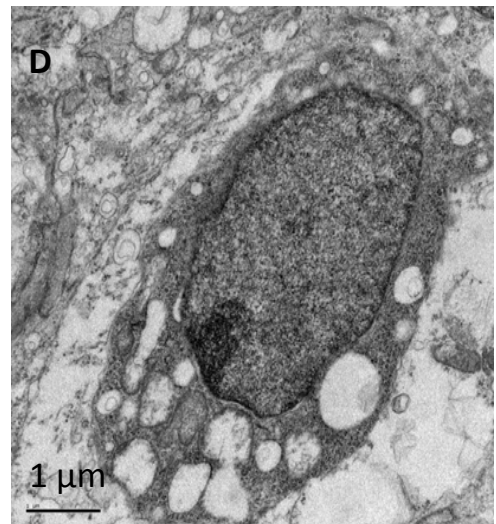
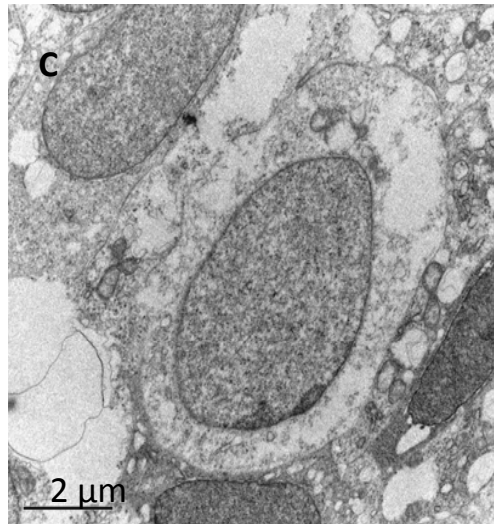
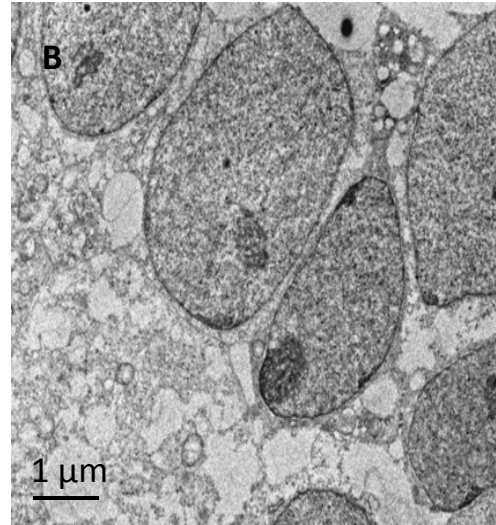
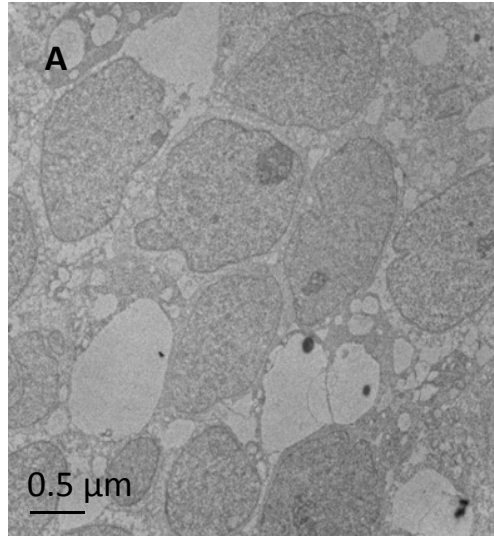


A=13-DAY5 : B= 13-DAY21 : C= 22-DAY5 : D= 22-DAY21 : E= 30-DAY5 : F= 30-DAY14 : G= 30-DAY21

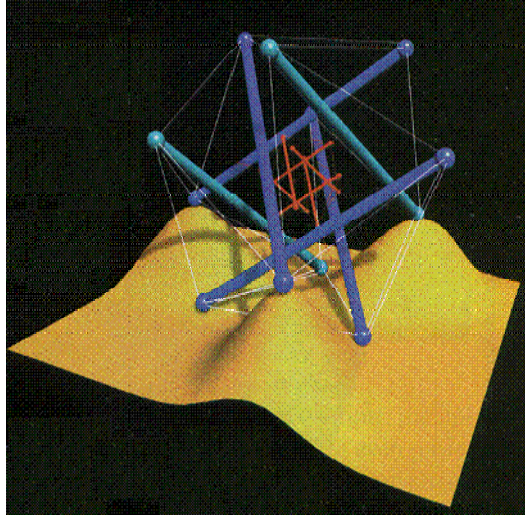
# TEM pictures of hMSCs grown over flexible nanofibrous mats



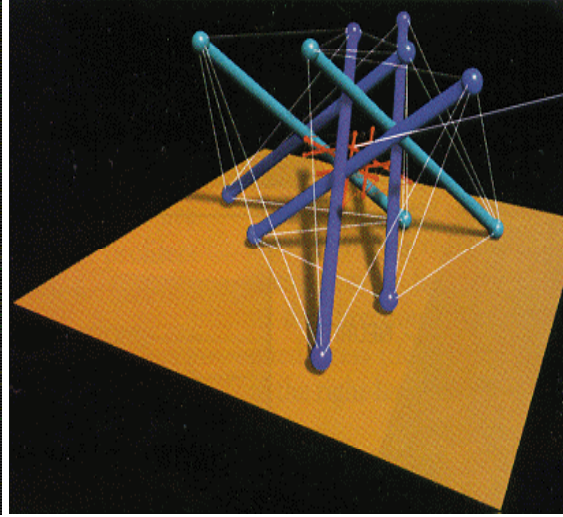
# TEM pictures of human embryonic stem cells on flexible mat



# Prof Donald Ingber's tensegrity model



on flexible-puckering surface –  
Rounded cell morphology  
rounded nucleus

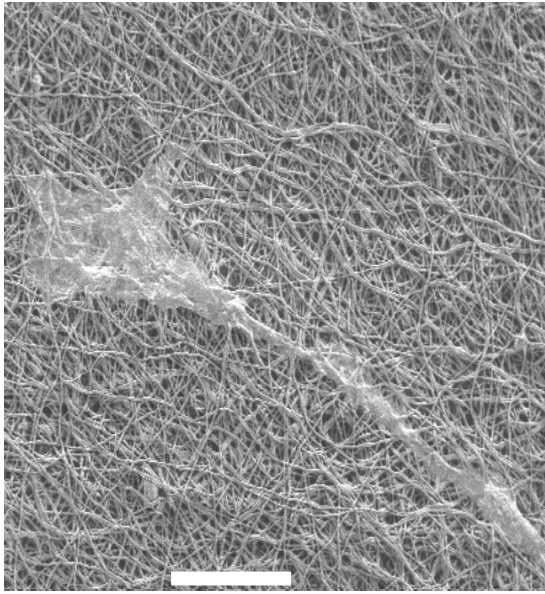


on rigid surface –  
flattened nucleus



Fig from, D Ingber, **Cellular mechanotransduction**

∩: putting all the pieces together again, FASEB J, Vol. 20 , 2006



Day 1

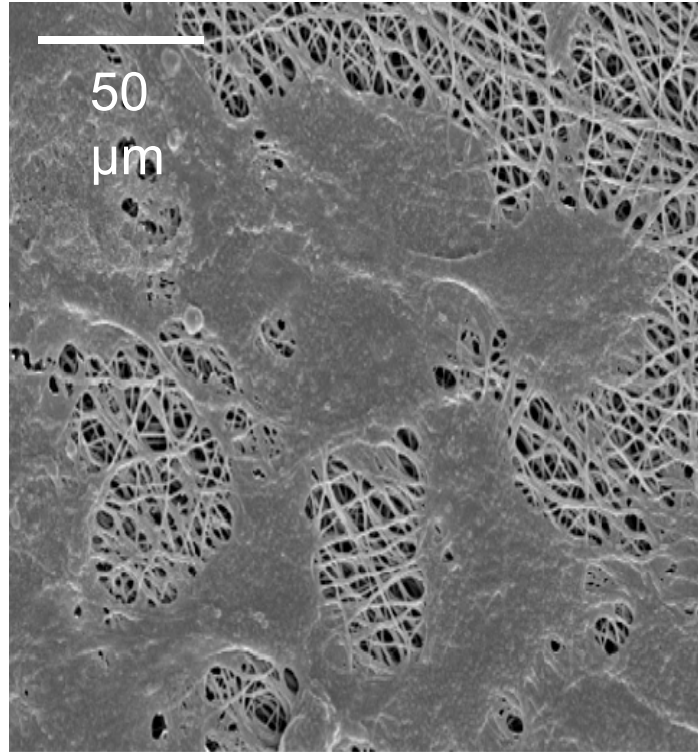
## Limitations:

Poor cell infiltration

Inadequate mechanical properties

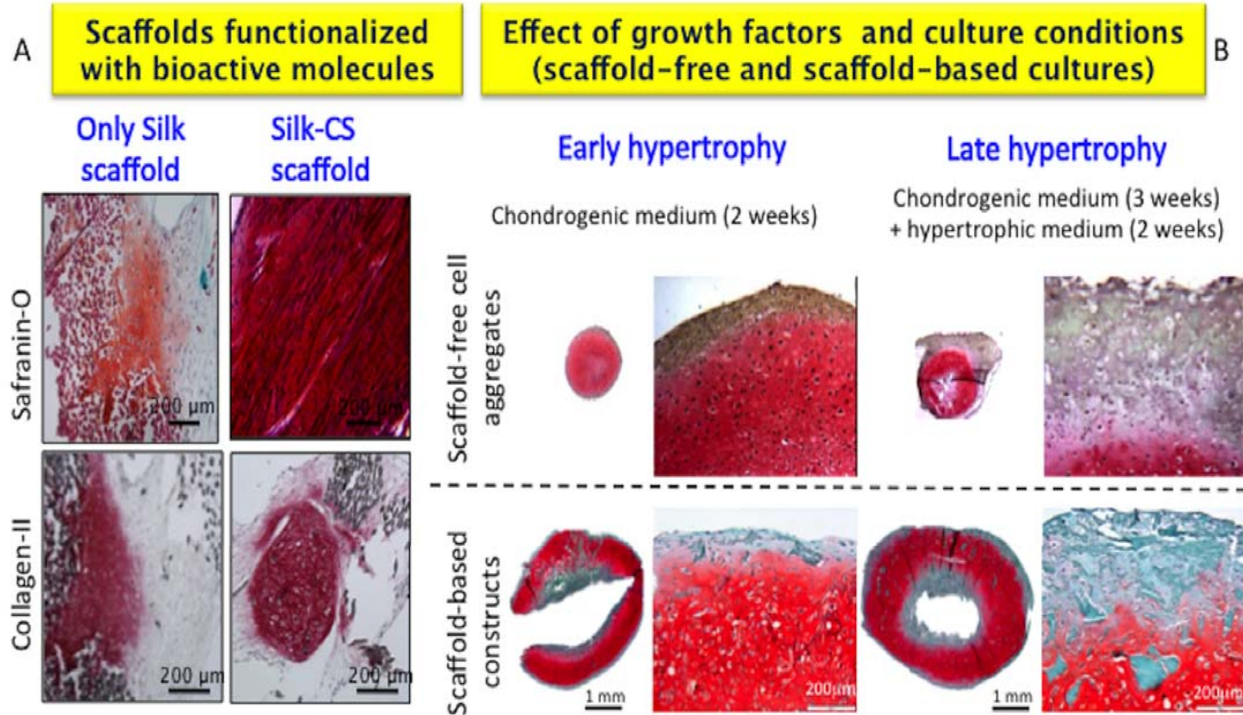
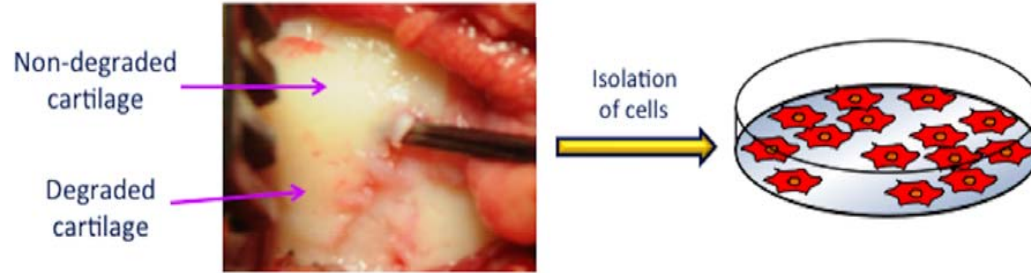
Inconvenient handling issues

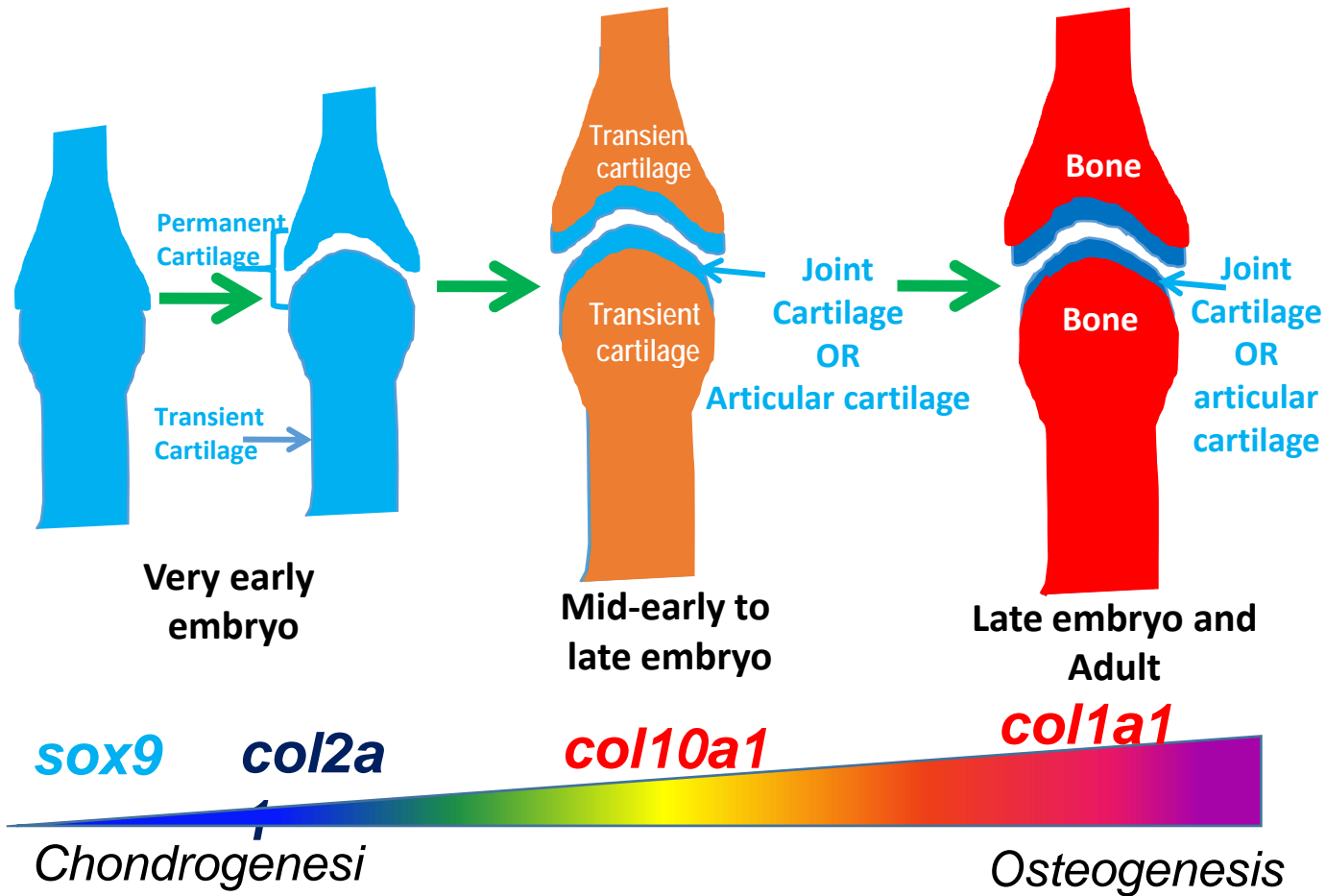
Scale up



Day 14

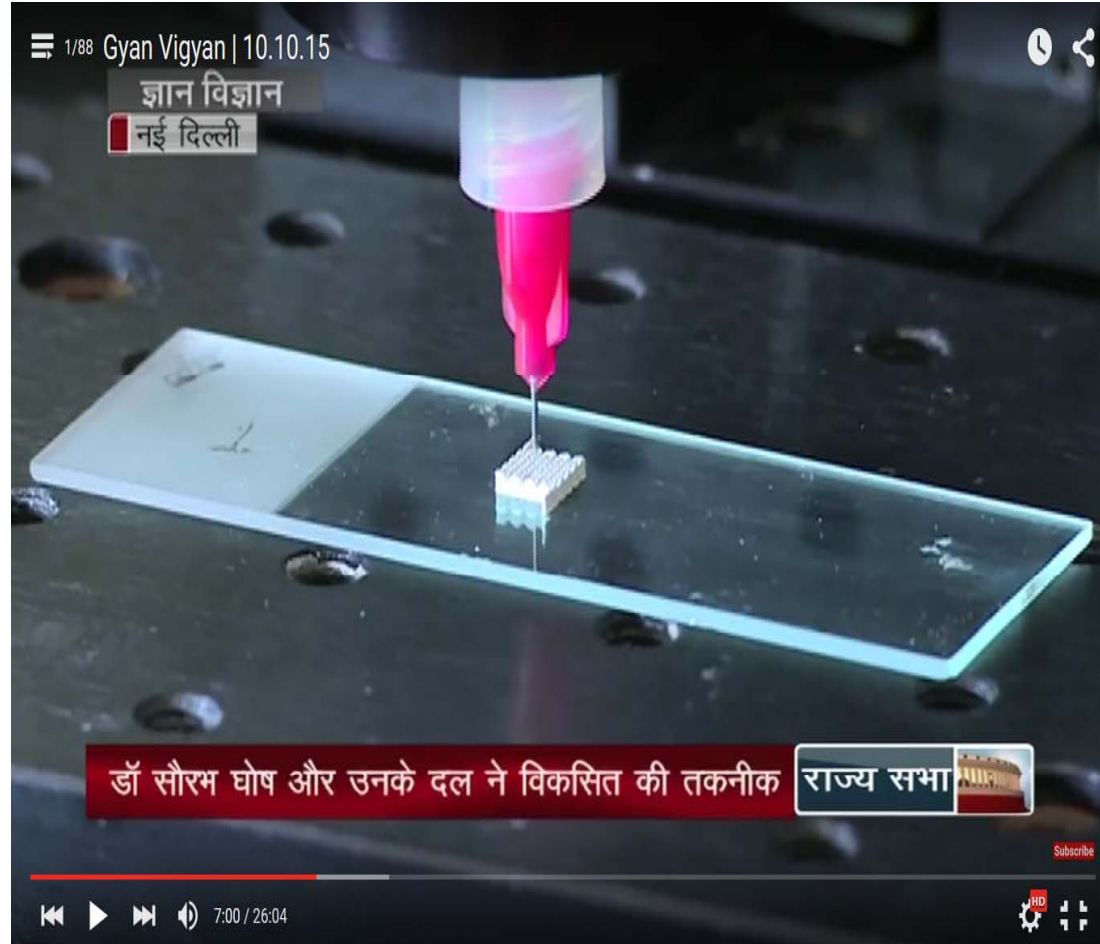
# Unstable cellular phenotypes





<sup>S</sup>  
**Transient cartilage** cells undergo **hypertrophy**, **angiogenesis** and eventual replacement by **conversion to bone** while **joint cartilage** does not.

# 3D bioprinting

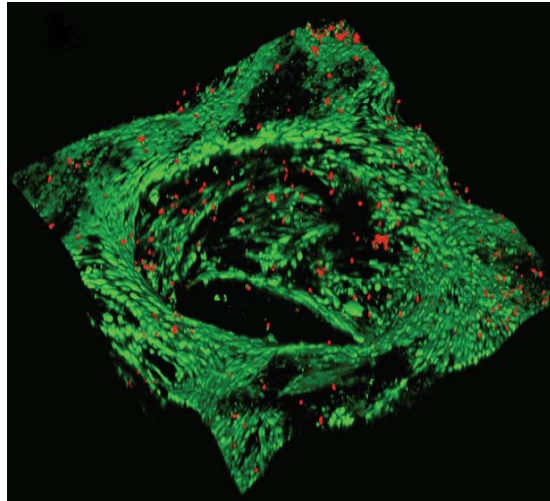


BMSCs cultured in 3D bioprinted construct **in absence of TGF- $\beta$ 1 resist hypertrophic differentiation** and undergo articular cartilage differentiation.

Bioprinting, 2017

silk-gelatin bioink: direct negative regulatory role of on **IHH signaling pathway**

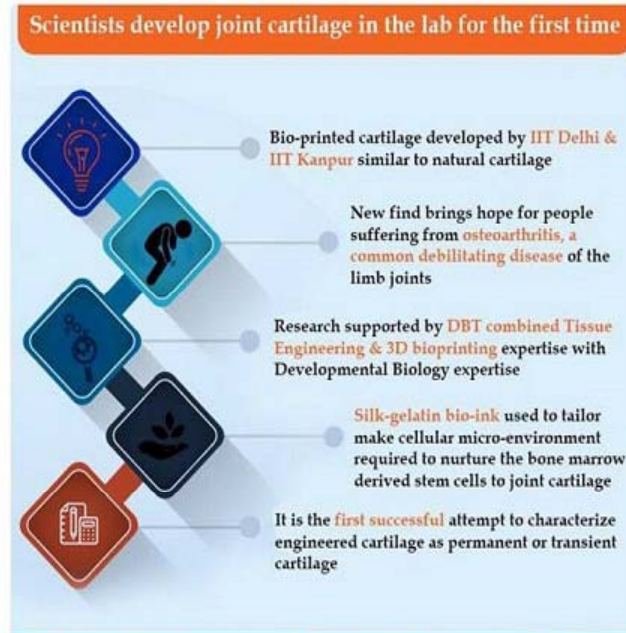
**Massive upregulation of Wnt signaling pathway** in minimizing hypertrophy during chondrogenic differentiation of BMSC





**Dr. Harsh Vardhan** @drharshvardhan · 11h

IITs Delhi & Kanpur collaborate to produce 3D bioprinted joint cartilage - a step closer to osteoarthritis regenerative therapy. @DBTIndia



**Soumya Swaminathan**

@doctorsoumya

Director-General, Indian Council of Medical Research, tweeting in personal capacity

New Delhi,

icmr.nic.in

Joined October 2014

153 Photos and videos



**Soumya Swaminathan**

@doctorsoumya

Follow

Arthritis is a common degenerative disease affecting millions - this could potentially be useful. @MoHFW\_INDIA @DBTIndia @ICMRDELHI

**R. Prasad** @RPrasad12

Indian researchers develop 3D bioprinted cartilage @doctorsoumya @ICMRDELHI @IndiaDST @RajivdSt journo diary.com/2017/05/27/3d-... via @RPrasad12

Retweets 12 Likes 17



5:49 PM - 27 May 2017

2 12 17

## Media coverage:

**28<sup>th</sup> May, 2017:** The Hindu highlighted our work on 3D bioprinted cartilage;

<http://www.thehindu.com/todays-paper/tp-features/tp-sci-tech-and-agri/indian-researchers-develop-3d-bioprinted-cartilage/article18592836.ece>

**11-12th June, 2017:** NDTV highlighted this work on 3D bioprinted cartilage;

<http://doctor.ndtv.com/bones-joints/knee-cartilage-recreated-by-iit-delhi-team-1711471>;

**4th June, 2017:** The Asomiya Pratidin highlighted this work on 3D bioprinted cartilage; <http://web.iitd.ac.in/~sghosh08/media.php>

**30<sup>th</sup> May, 2017:** [3dprint.com](http://3dprint.com/);

<https://3dprint.com/176176/3d-bioprinted-knee-cartilage>

**29<sup>th</sup> May, 2017:** [3ders.org](http://3ders.org/);

<http://www.3ders.org/articles/20170529-iit-delhi-3d-bioprinted-knee-cartilage-india-first-lab-grown-printed-tissue.html>

**30<sup>th</sup> May, 2017:** [thebetterindia.com](http://thebetterindia.com/);

<http://www.thebetterindia.com/102746/iit-delhi-3d-bioprinted-cartilage/>

**1<sup>st</sup> May, 2017:** [indiatoday](http://indiatoday.com/)

<http://indiatoday.intoday.in/story/3d-printed-cartilage-may-help-treat-osteoarthritis/1/942737.html>

**25<sup>th</sup> June, 2016:** [indianexpress.com](http://indianexpress.com/);

<http://indianexpress.com/article/technology/science/scientists-develop-new-bio-ink-for-3d-printing-2874908>

**30<sup>th</sup> May, 2017:** [3dprintingindustry.com](http://3dprintingindustry.com/);

<https://3dprintingindustry.com/news/indian-institute-technologies-3d-printed-silk-cartilage-helps-activate-organ-growth-114508/>

**3<sup>rd</sup> May, 2017:** [iascurrentaffairswb.wordpress.com](http://iascurrentaffairswb.wordpress.com/);

<https://iascurrentaffairswb.wordpress.com/2017/05/03/3d-printed-cartilage-to-treat-osteoarthritis-current-affairs-cor-civil-service>

**30th May, 2017:** [www.fashionatingworld.com](http://www.fashionatingworld.com/);

<https://www.fashionatingworld.com/new1-2/3d-bioprinted-knee-cartilage-with-printed-tissue-developed>

**DBT website;** <http://www.dbtindia.nic.in/scientists-develop-joint-cartilage-in-the-lab-for-the-first-time/>

## Intertwinement of nanofibrous scaffold matrix compliance, cell shape, cytoskeletal mechanics, and developmental processes

1. Nanofibrous scaffold matrix compliance... human embryonic stem cells and adult mesenchymal stem cells
2. Lack of cell infiltration
3. Effect of matrix chemistry: controlling cellular signaling and phenotype



सत्यमेव जयते

Department of  
Science and Technology

Indo-USA  
Indo-Switzerland  
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Indo-Korea  
Indo-Egypt  
Indo-Poland  
Indo-Italy

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Indo-US Science and Technology Forum