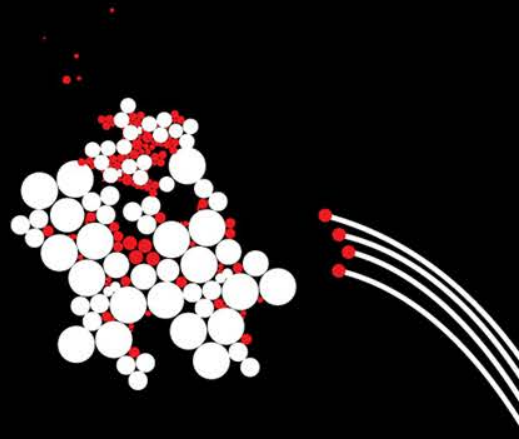
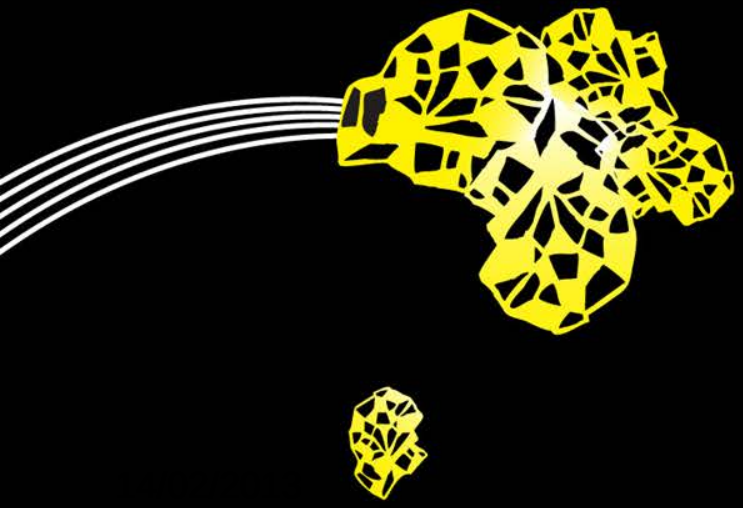
UNIVERSITY OF TWENTE.



Searching for the Fundamentals of Tissue Engineering

Ana Barradas

14th February 2013



Tissue Engineering… in words

- *Tissue Engineering is an interdisciplinary field that applies the principles of engineering and life sciences towards the development of biological substitutes that restore, maintain or improve tissue function.*

Langer and Vacanti; Tissue Engineering; Science; 1993

Tissue Engineering… in words

General Strategies for the creation of new tissues:

1. Isolated cells

1. Growth Factors

2. Cells placed on or within matrices

ClinicalTrials.gov (U.S.A.)

1	Unknown †	Allogeneic Bone Marrow Mesenchymal Stem Cells Transplantation in Patients With Liver Failure Caused by Hepatitis B Virus (HBV) **Condition:** Liver Failure **Interventions:** Other: Group 1; Other: Group 2; Other: Group 3
2	Recruiting	Autologous Bone Marrow Mesenchymal Stem Cell Transplantation for Chronic Stroke **Condition:** Stroke **Intervention:** Genetic: intracerebral stem cell transplantation
3	Recruiting	The Use of Autologous Bone Marrow Mesenchymal Stem Cells in the Treatment of Articular Cartilage Defects **Conditions:** Degenerative Arthritis; Chondral Defects; Osteochondral Defects **Interventions:** Procedure: Bone Marrow Aspiration; Procedure: Bone marrow mesenchymal stem cell implantation
4	Unknown †	Autologous Bone Marrow Mesenchymal Stem Cells Transplantation Via Hepatic Artery in Patients With Liver Cirrhosis **Condition:** Liver Cirrhosis **Interventions:** Procedure: Hepatic artery infusion; Procedure: Conserved Therapy
5	Completed	Autologous Transplantation of Mesenchymal Stem Cells (MSCs) and Scaffold in Full-thickness Articular Cartilage **Condition:** Knee Osteoarthritis **Intervention:** Biological: Bone marrow derived mesenchymal stem cells
6	Recruiting	Mesenchymal Stem Cells in the Treatment of Relapsed/Refractory Severe Acquired Aplastic Anemia **Condition:** Aplastic Anemia **Intervention:** Biological: Intravenous bone marrow mesenchymal stem cells infusion

Tissue Engineering… in words

General Strategies for the creation of new tissues:

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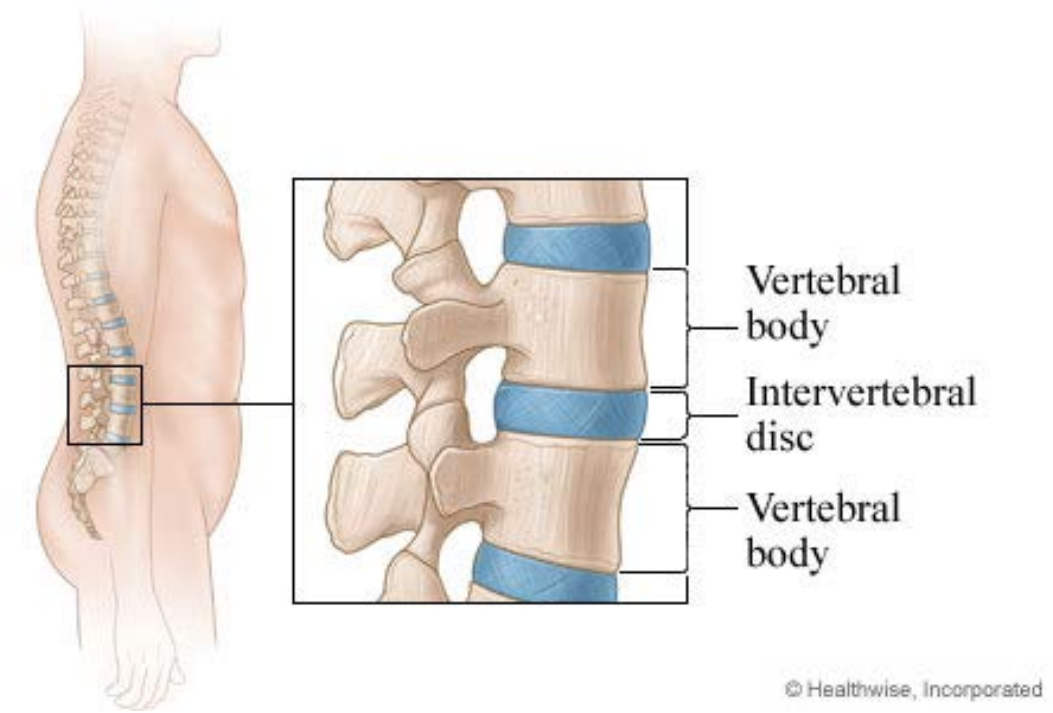
3. Cells placed on or within matrices

Langer and Vacanti; Tissue Engineering; Science; 1993c

INFUSE® Bone Graft



INFUSE® Bone Graft

Medtronic

Tissue Engineering… in words

General Strategies for the creation of new tissues:

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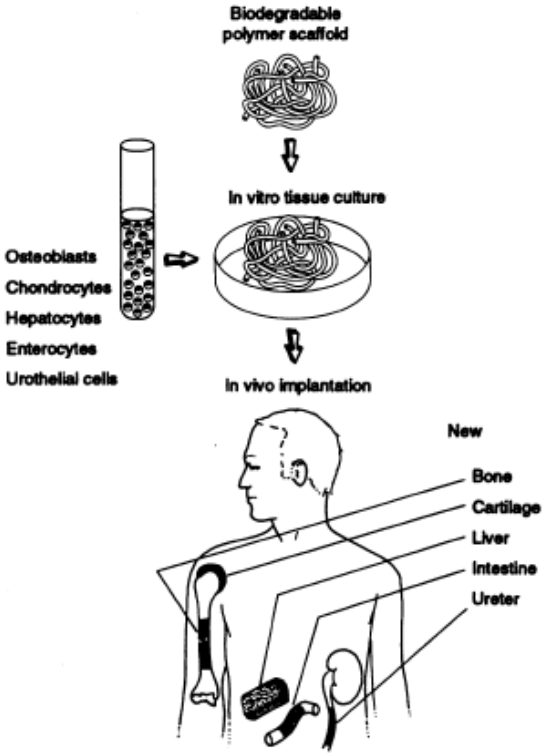
Cells placed on or within matrices



Langer and Vacanti; Tissue Engineering; Science; 1993

But does it really work?

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Page last updated at 23:02 GMT, Monday, 3 April 2006 00:02 UK

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Lab-grown bladders 'a milestone'

US scientists have successfully implanted bladders grown in the laboratory from patients' own cells into people with bladder disease.

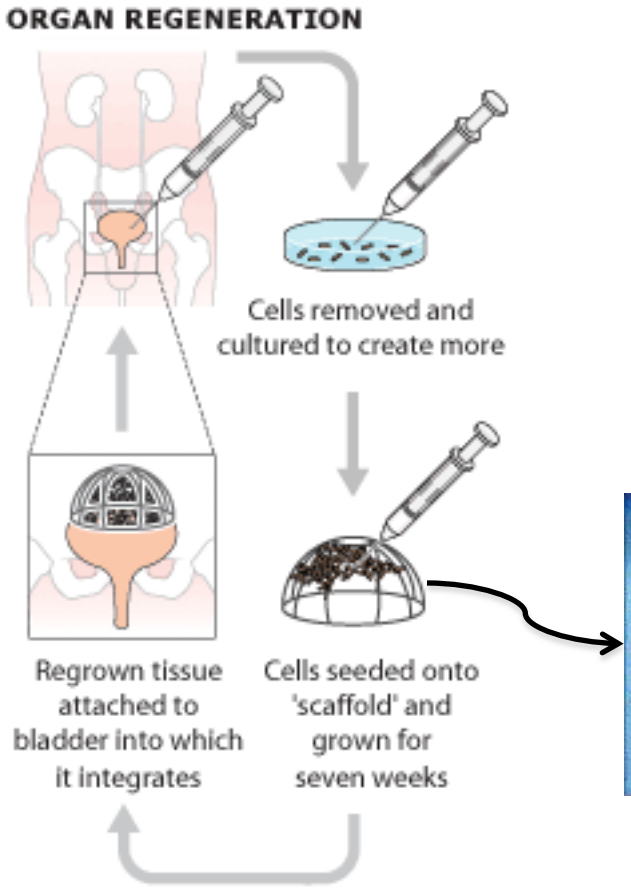
The bladders were grown from patients' own cells

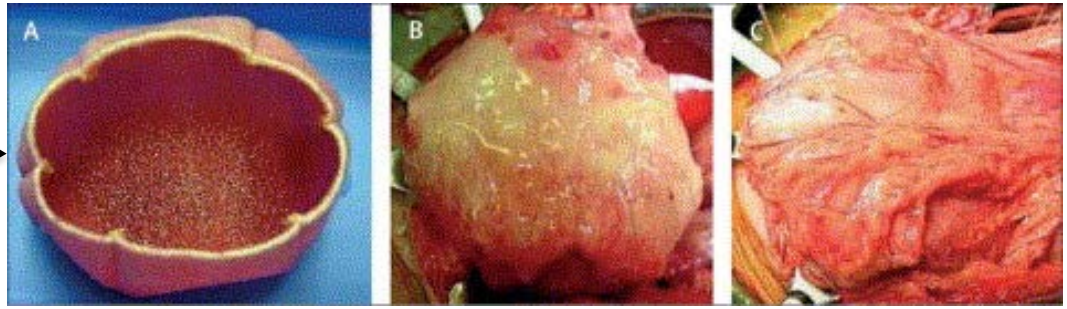
The researchers, from North Carolina's Wake Forest University, have carried out seven transplants, and in some the organ is working well years later.

The achievement, details of which have been published online by The Lancet, is being described as a "milestone".

The team is now working to grow organs including hearts using the technique.

Tissue Engineered Bladder





A. Atala et. Al.; The Lancet; 2006

Tissue Engineered Trachea

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7 July 2011 Last updated at 16:03 GMT

Surgeons carry out first synthetic windpipe transplant

By Michelle Roberts
Health reporter, BBC News, in Stockholm

Surgeons in Sweden have carried out the world's first synthetic organ transplant.

Scientists in London created an artificial windpipe which was then coated in stem cells from the patient.

Crucially, the technique does not need a donor, and there is no risk of the organ being rejected. The surgeons stress a windpipe can also be made within days.

The replacement windpipe was grown in the lab

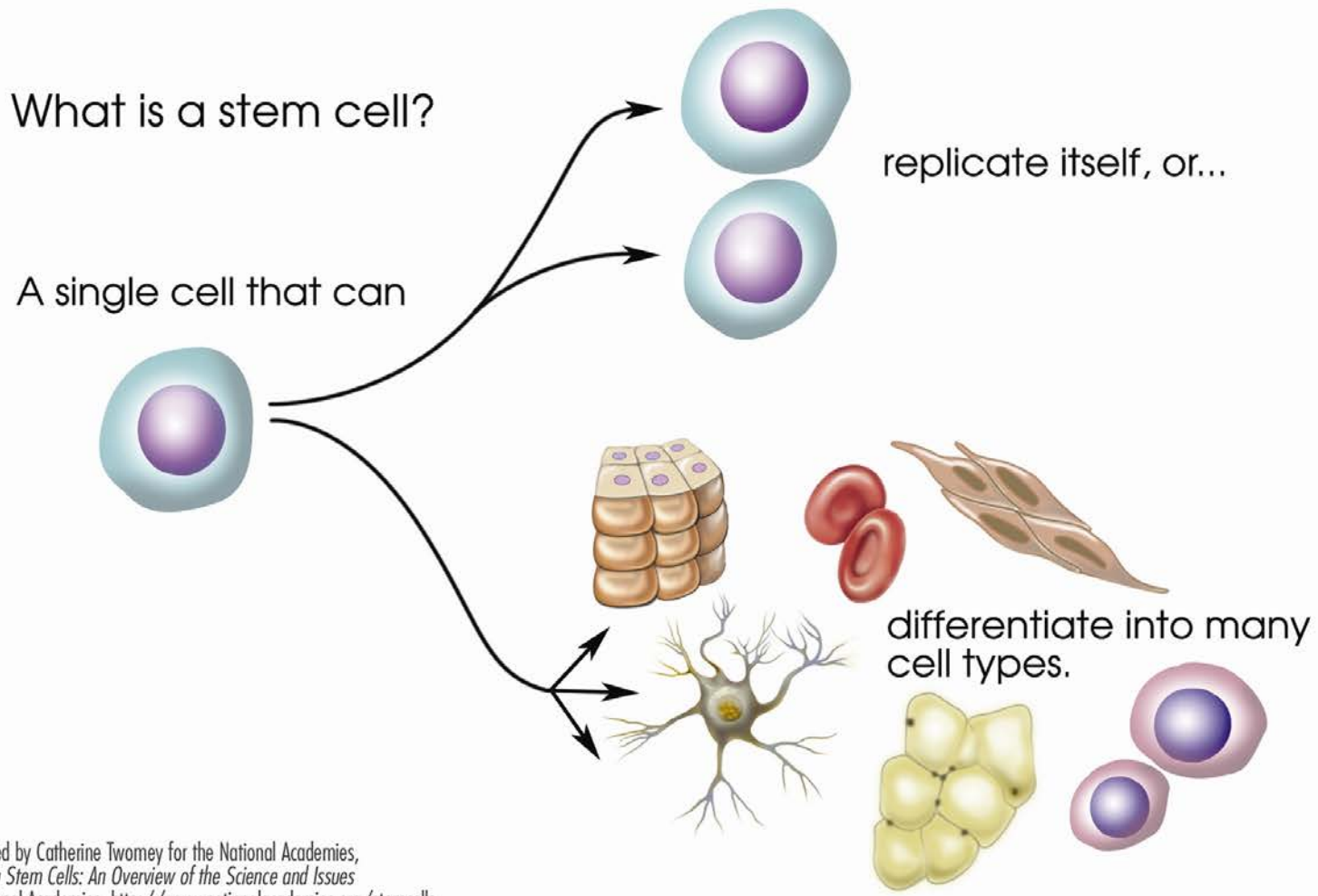

Image prepared by Catherine Twomey for the National Academies,
Understanding Stem Cells: An Overview of the Science and Issues
from the National Academies, http://www.nationalacademies.org/stemcells.
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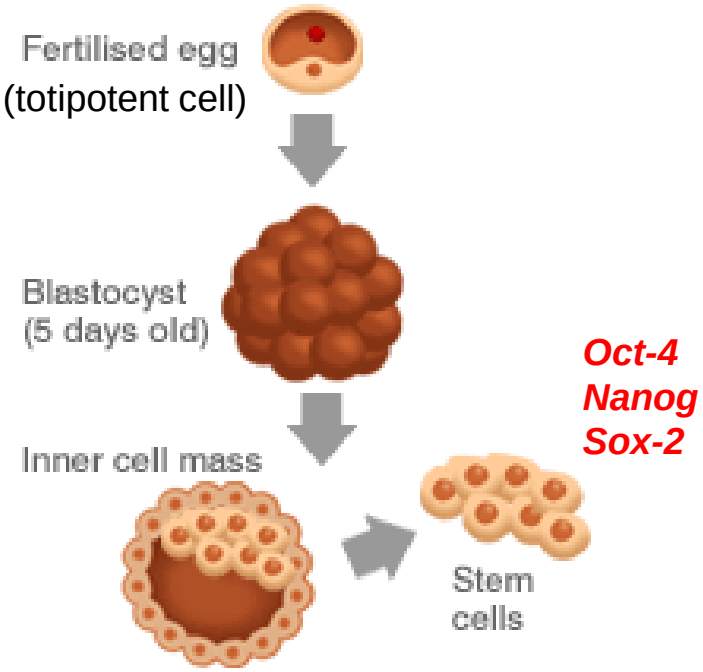
Embryonic stem cells



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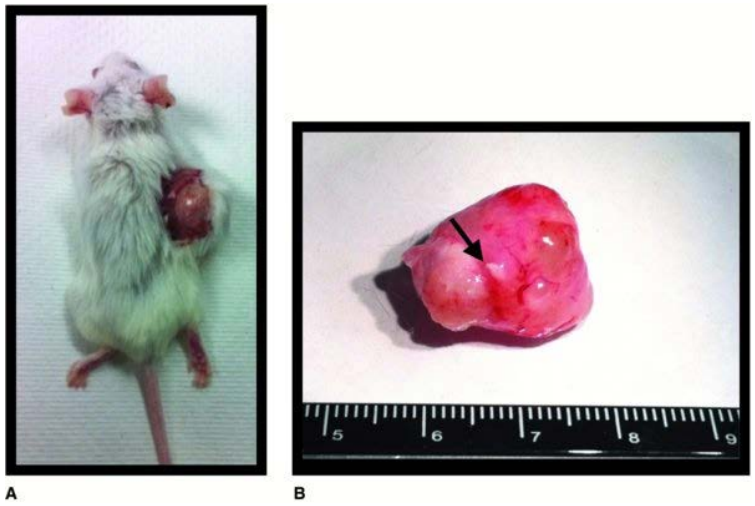
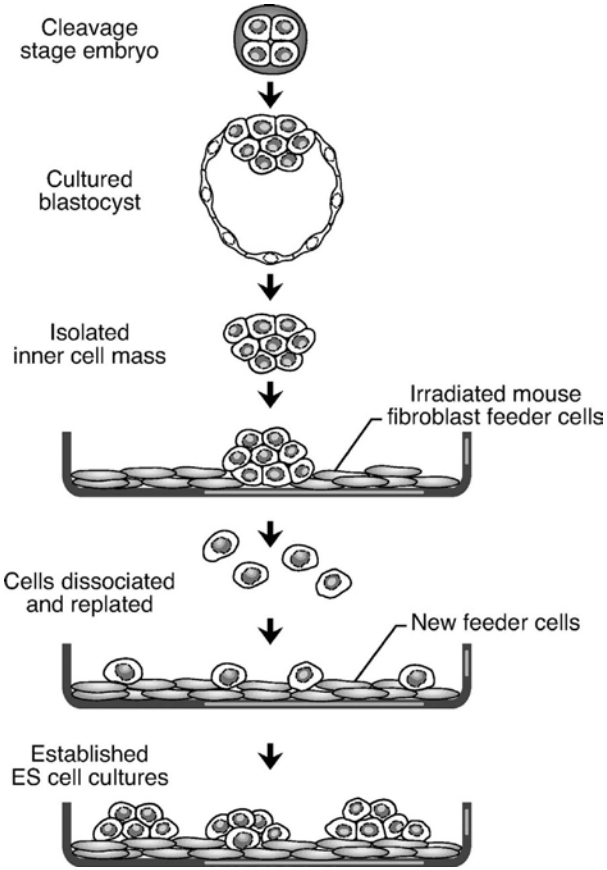


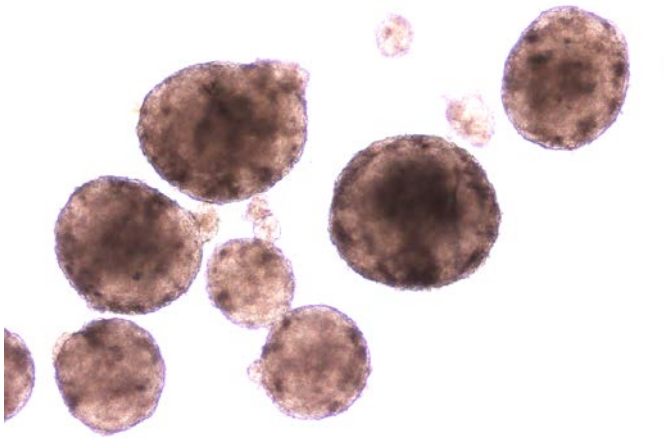
http://news.bbc.co.uk/2/hi/americas/7929690.stm

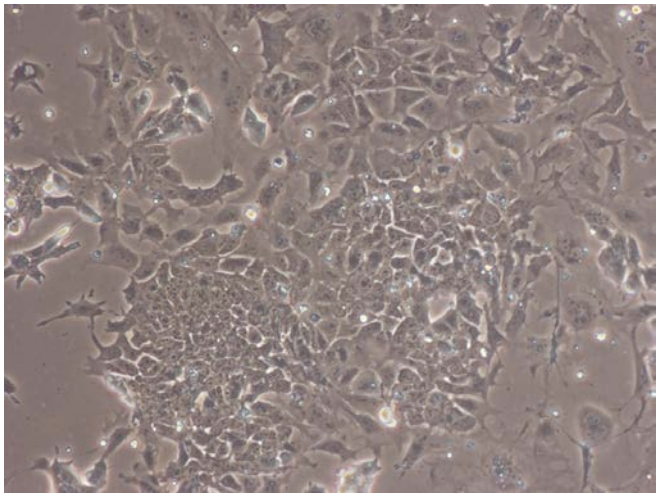
http://www.stembook.org/sites/default/files/protocols

Embryonic stem cells



J.S. Odorico, et. Al.; Stem Cells; 2001





Embryonic Stem Cells

1. When implanted, ESC often remain pluripotent (teratoma formation)

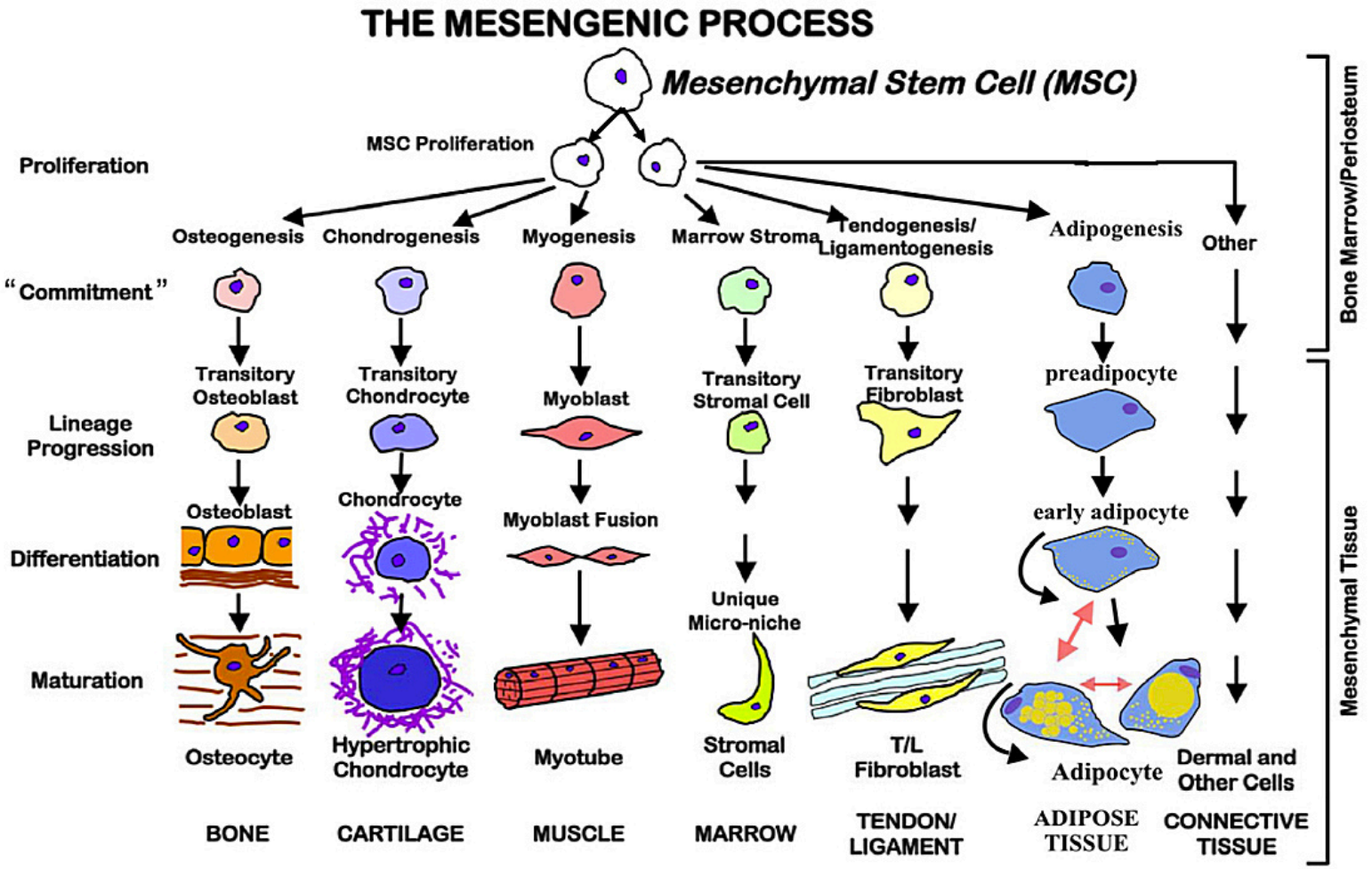
2. Need of feeder layers to support their culture

3. Ethical debate over the destruction of an embryo

Adult Stem Cells

- Hematopoietic stem cells
- Mesenchymal stem cell (MSC)
  - Multipotent
  - Human bone marrow, blood, fat, liver, brain, muscle, pancreas, umbilical cord blood, …
  - Functional assay: Colony Forming Unit-Fibroblast
  - Express (at least 95% population): CD105, CD73, CD90 and lack expression of (less than 2%) CD45, CD34, CD14, CD79a, HLA class II

Adult Stem Cells



T.L. Bonfield, et. Al.; Discovery Medicine; 2010

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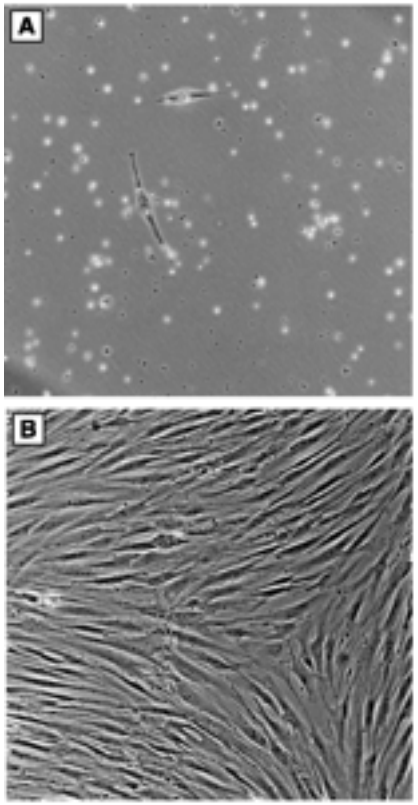
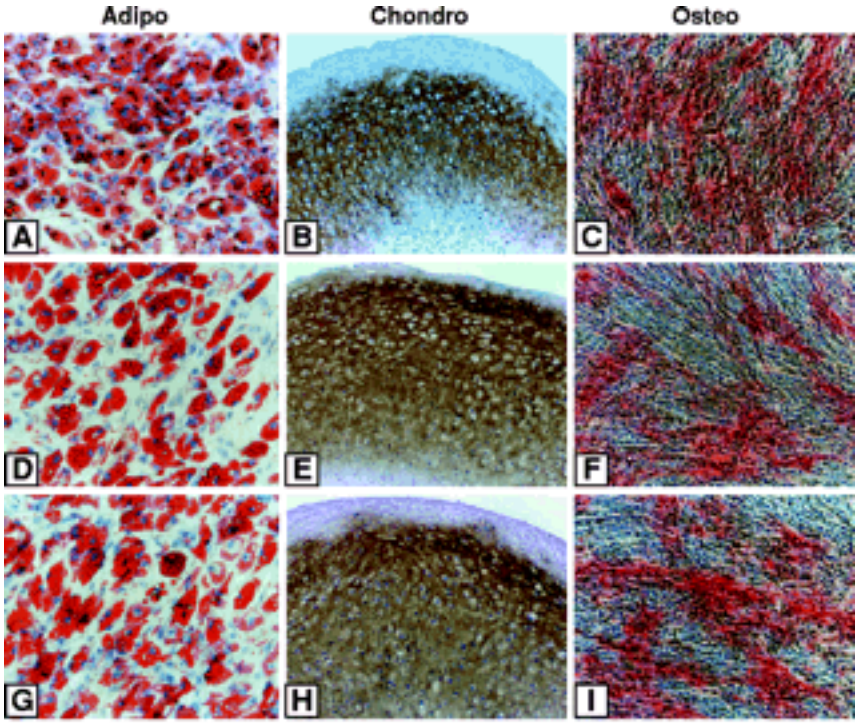
MSC (functional assay)





M.F. Pittenger, et.al.; Science; 1999

Adult Stem Cells

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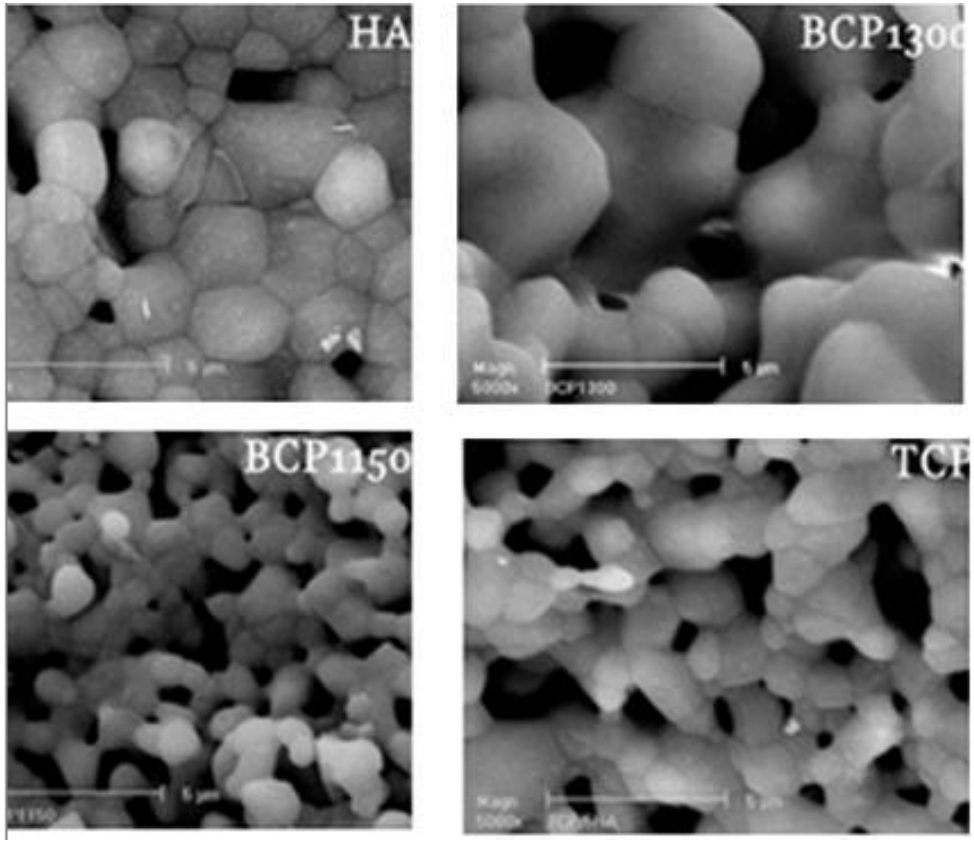
Mesenchymal Stem Cells

1. Can be obtained from adults (no ethical issues) and from the same patient prior to surgery

2. Easily expandable *in vitro*

3. Secrete immune-modulatory factors (immune reaction less likely)

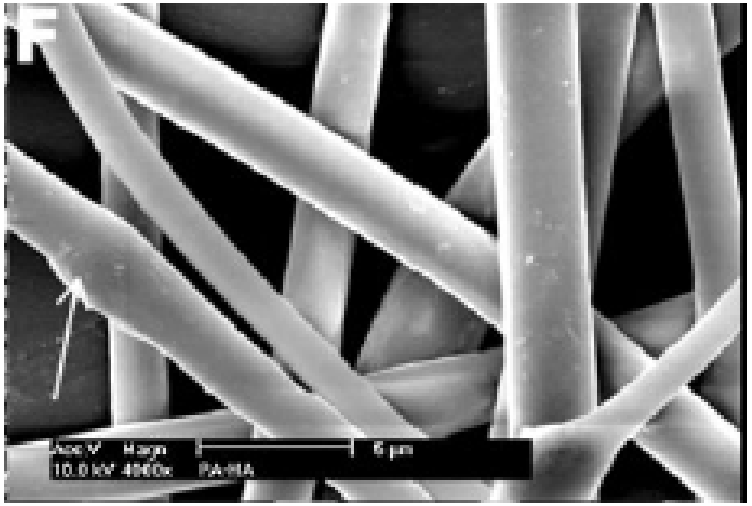
Tissue Engineering Scaffolds



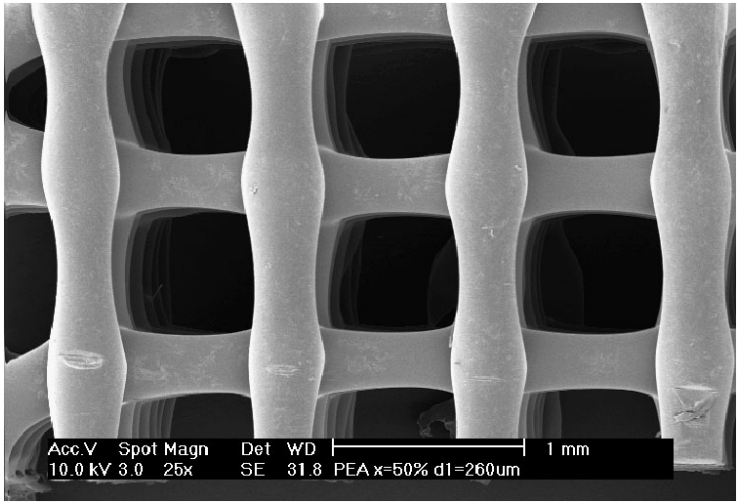
H. Yuan, et. Al.; PNAS; 2010

Tissue Engineering Scaffolds-Controlling 3D architecture

Electrospun scaffolds



3D fibre deposition technique

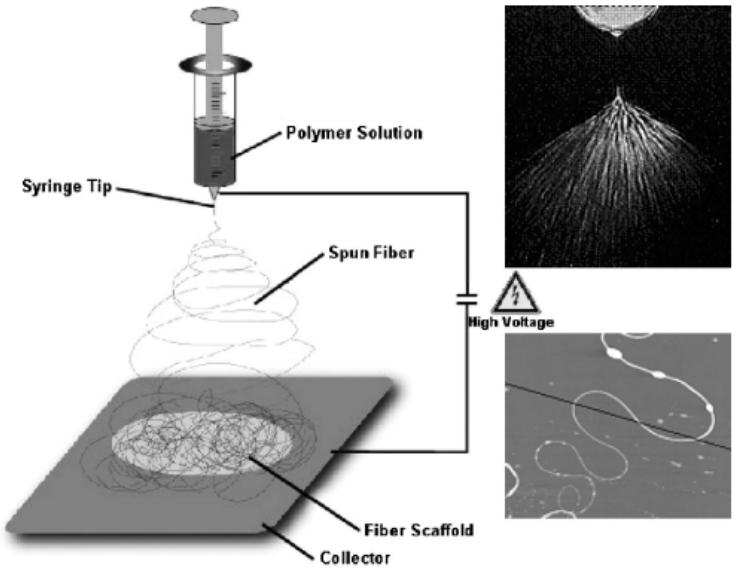


A. Nandakumar, et. Al.; Macromolecular Bioscience.; 2010

L. Moroni, et. Al.; J. Biomater. Sci. Polymer Edn.; 2008

Tissue Engineering Scaffolds-Controlling 3D architecture

Electrospun scaffolds



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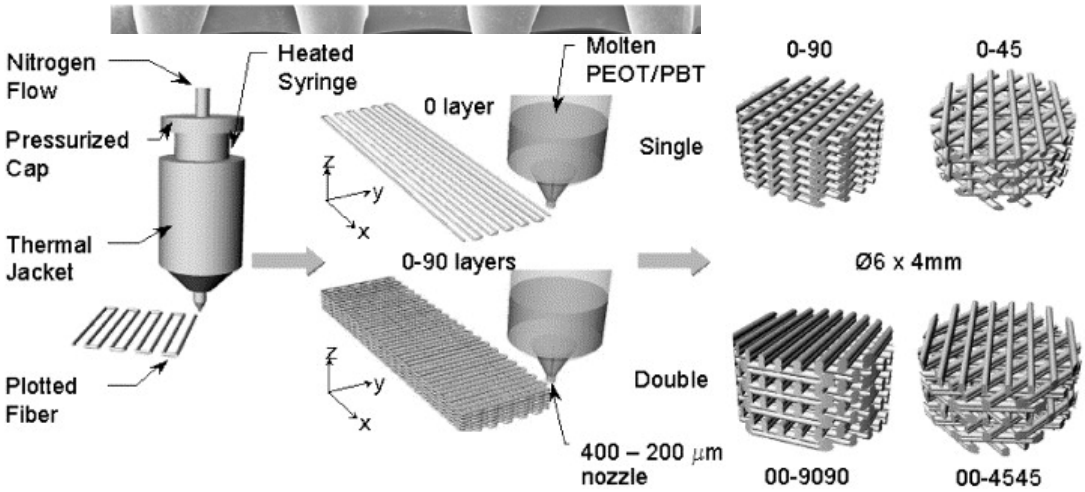
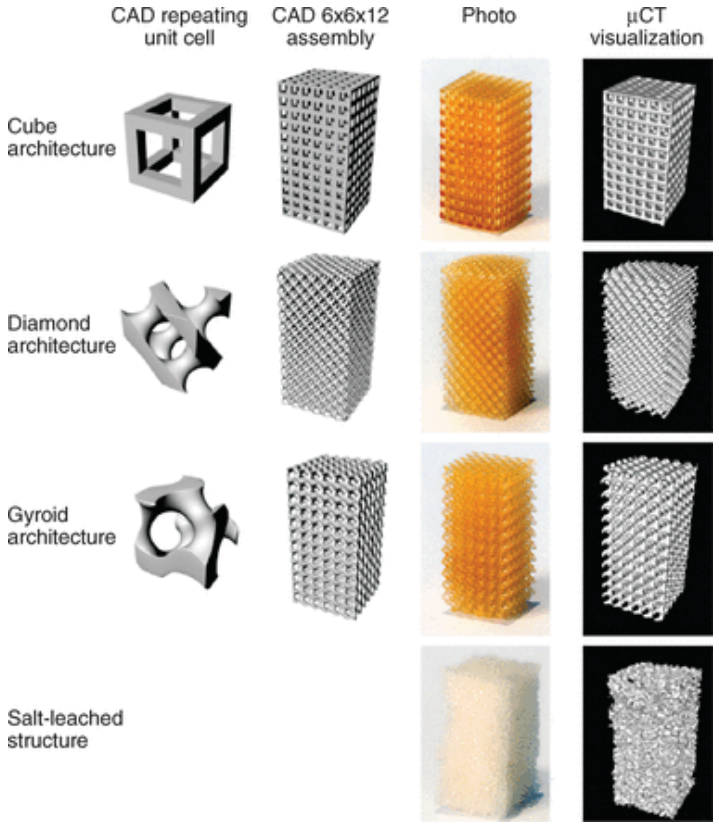


A. Nandakumar, et. Al.; J. Biomater. Sci. Polymer Edn; 2008

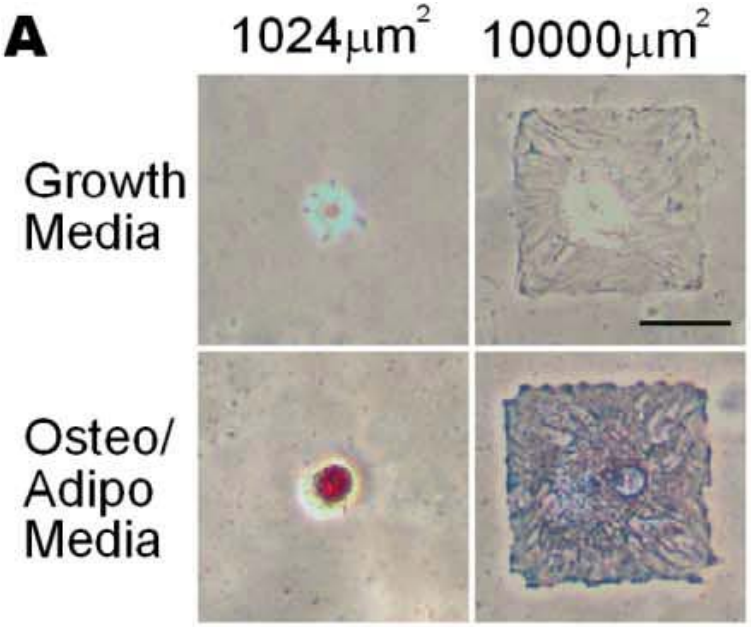
L. Moroni, et. Al.;Biomaterials; 2006

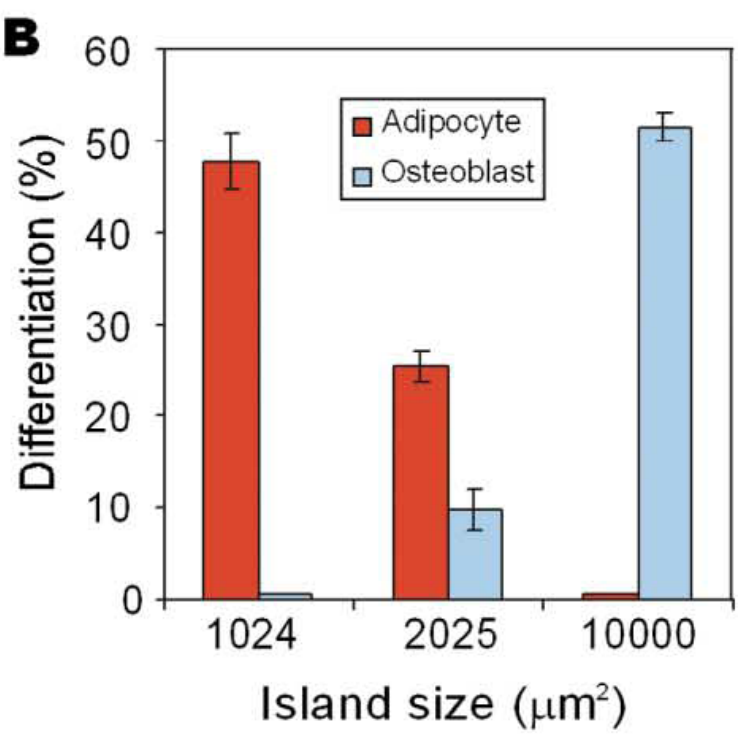
Tissue Engineering Scaffolds-Controlling 3D architectures



F.P.W. Melchels; Biomaterials; 2010

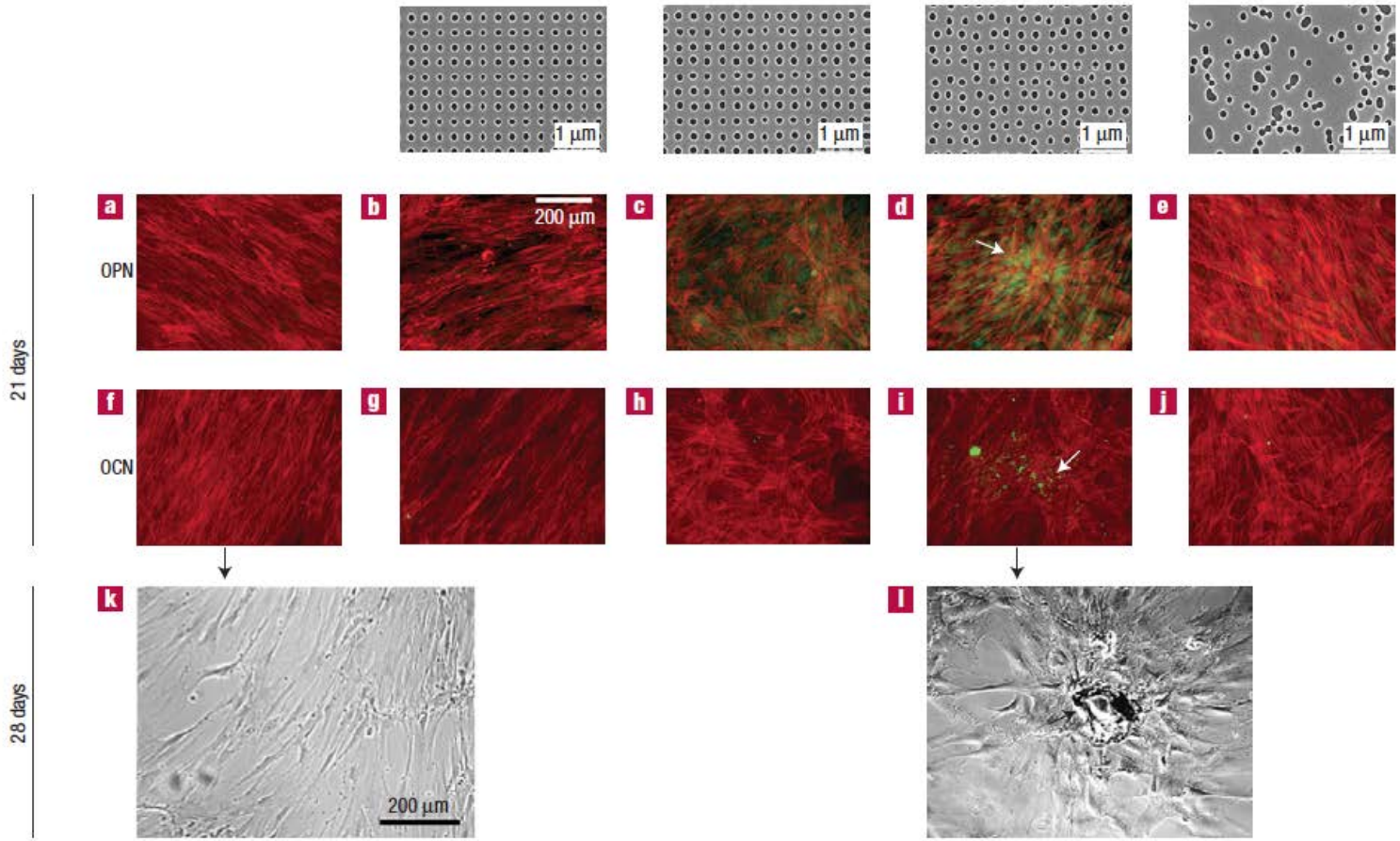
Controlling Cell Function through surface properties





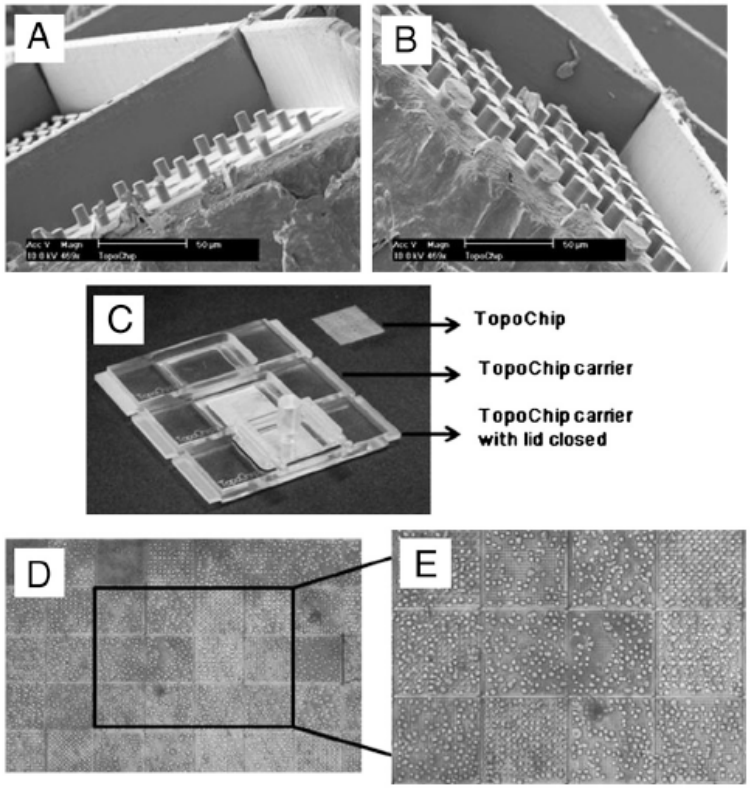
McBeath, et. Al.; Cell; 2004

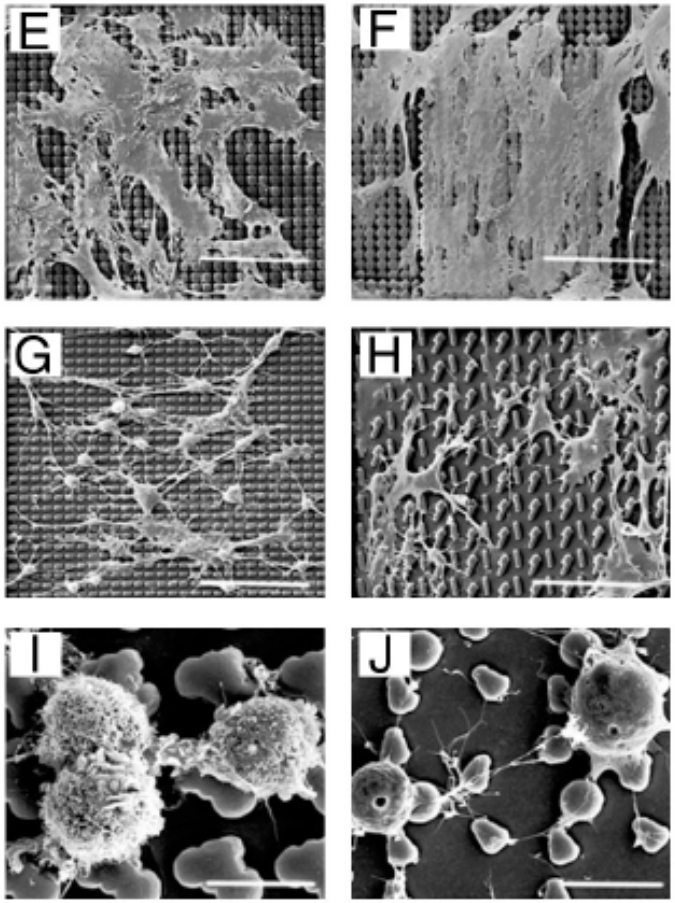
Controlling Cell Function through surface properties



M.J. Dalby, et. Al.; Nature Materials; 2007

Controlling Cell Function through surface properties





2,176 randomly designed topographies

H. Unadkat, et. Al.; PNAS; 2011

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Lattrop, the Netherlands, 14-15 November 2013

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- Molly Stevens (Imperial College, UK)
- Shulamit Levenberg (Technion, Israel)
- Christine Mummery (Leiden University Medical Center, Netherlands)
- Katarina Le Blanc (Karolinska Institutet, Sweden)
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