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Growing new body parts

Daniel J. Kelly[1,2,3,4]

[1] Trinity Centre for Bioengineering, Trinity Biomedical Sciences Institute, Trinity College Dublin, Dublin, Ireland.

[2] Department of Mechanical and Manufacturing Engineering, School of Engineering, Trinity College Dublin, Dublin, Ireland.

[3] Department of Anatomy, Royal College of Surgeons in Ireland, Dublin, Ireland.

[4] Advanced Materials and Bioengineering Research Centre (AMBER), Royal College of Surgeons in Ireland and Trinity College Dublin, Dublin, Ireland.

@dannykelly1978

The organ donor shortage

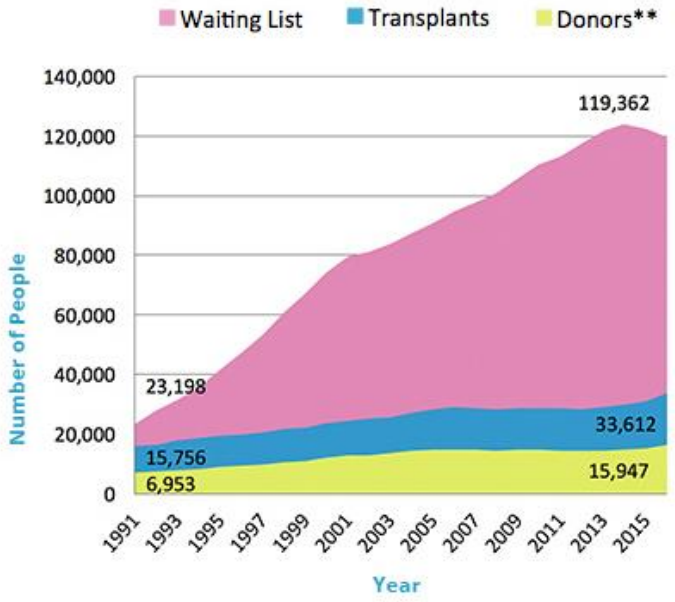
116,000+ Number of men, women and children on the national transplant waiting list as of August 2017.

33,611 transplants were performed in 2016.

20 people die each day waiting for a transplant.

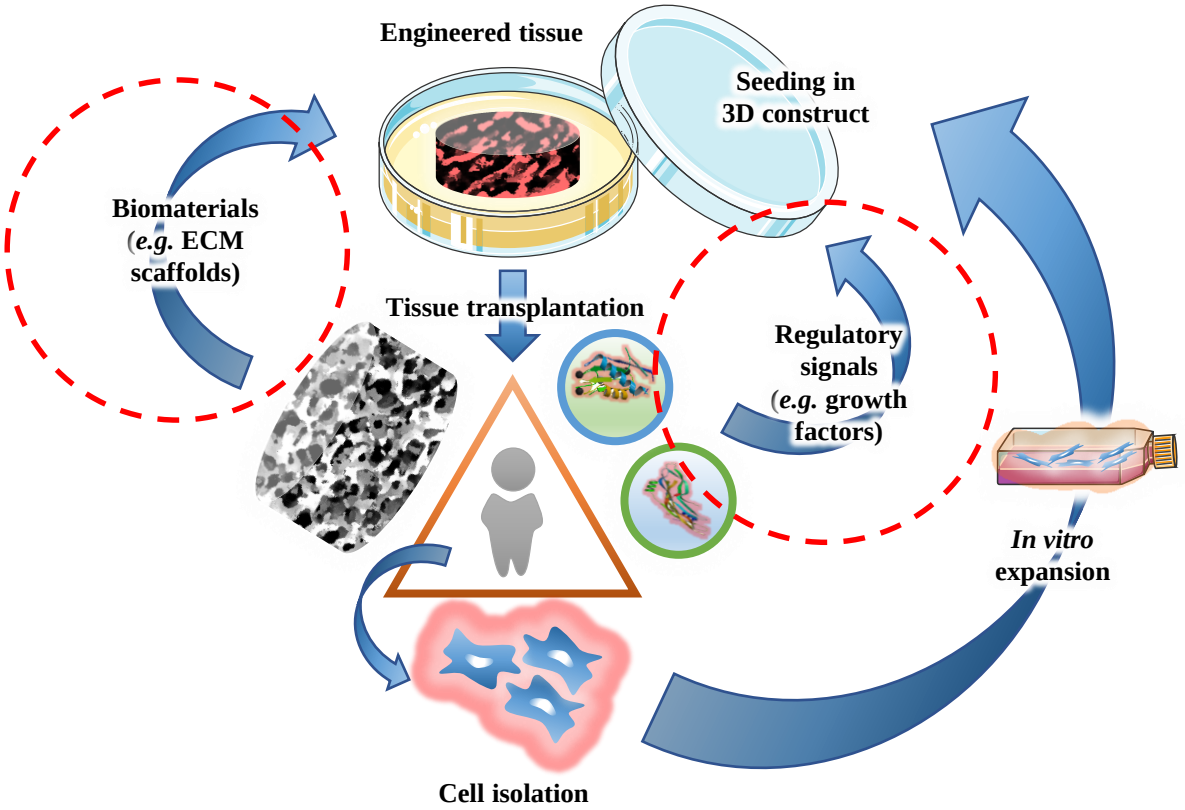
every 10 minutes another person is added to the waiting list.

only 3 in 1,000 people die in a way that allows for organ donation.




Google

What is Tissue Engineering?

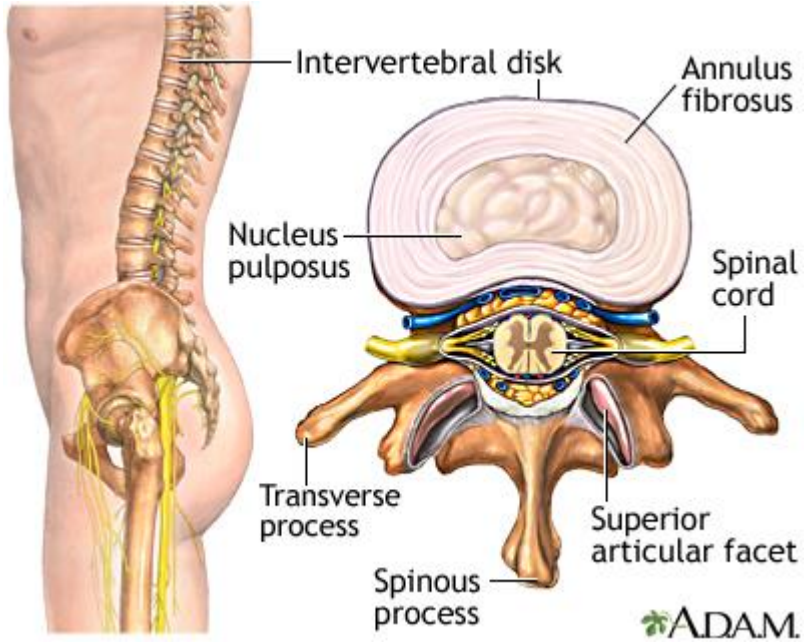


Outline of Talk

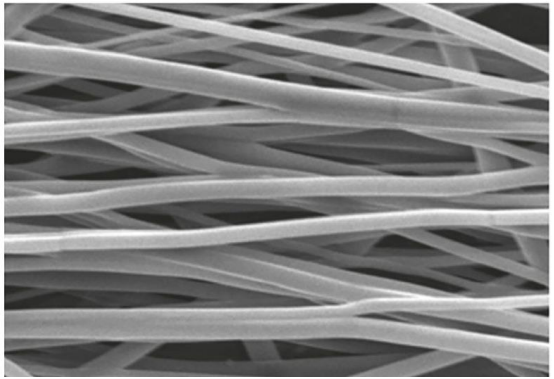
- **An example – a tissue-engineered intervertebral disc (IVD)**
- **What is 3D bioprinting and what can it actually do?**
- **What are we doing in my lab?**
  - Bone organ engineering, cartilage regeneration, printing new joints.
- **The future of 3D bioprinting**

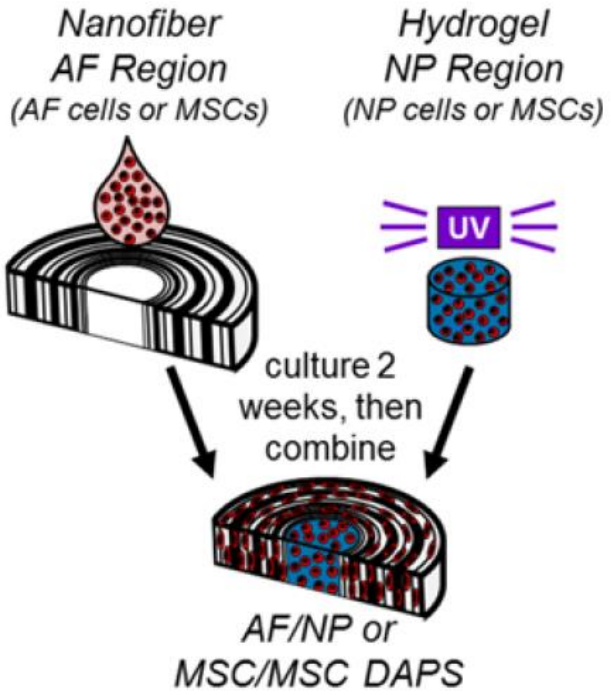
The intervertebral disc

- Back and neck pain are ubiquitous in modern society, affecting about two-thirds of adults at some point in their lives.
- Degeneration of the intervertebral disc (IVD) is frequently associated with back pain.
- Spinal fusion (which involves removing the IVD to restore disc space height) is problematic, warranting new strategies.



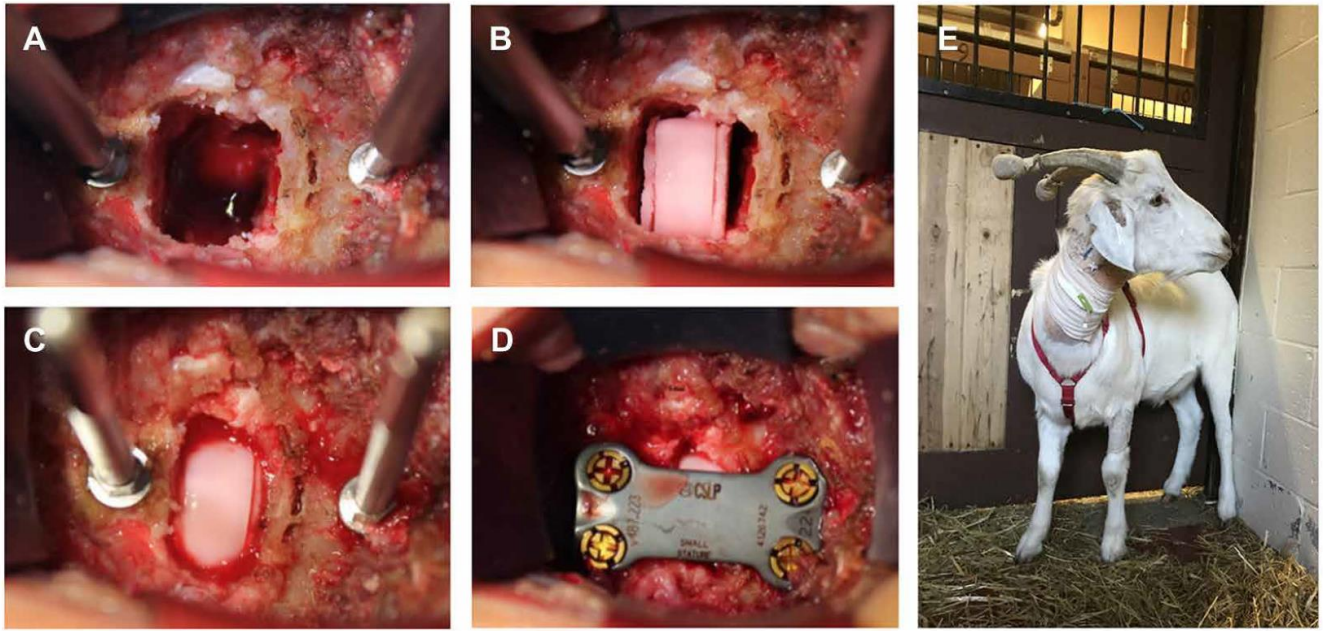
A tissue-engineered intervertebral disc





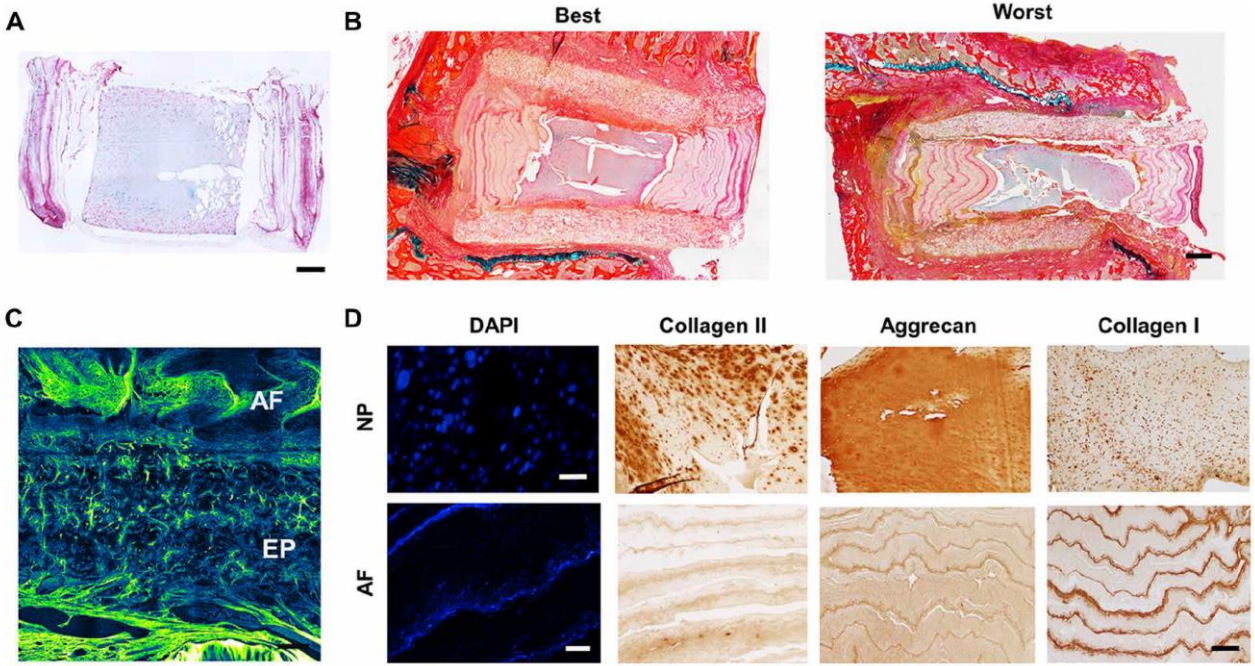
Gullbrand et al., 2018

A tissue-engineered intervertebral disc (IVD)



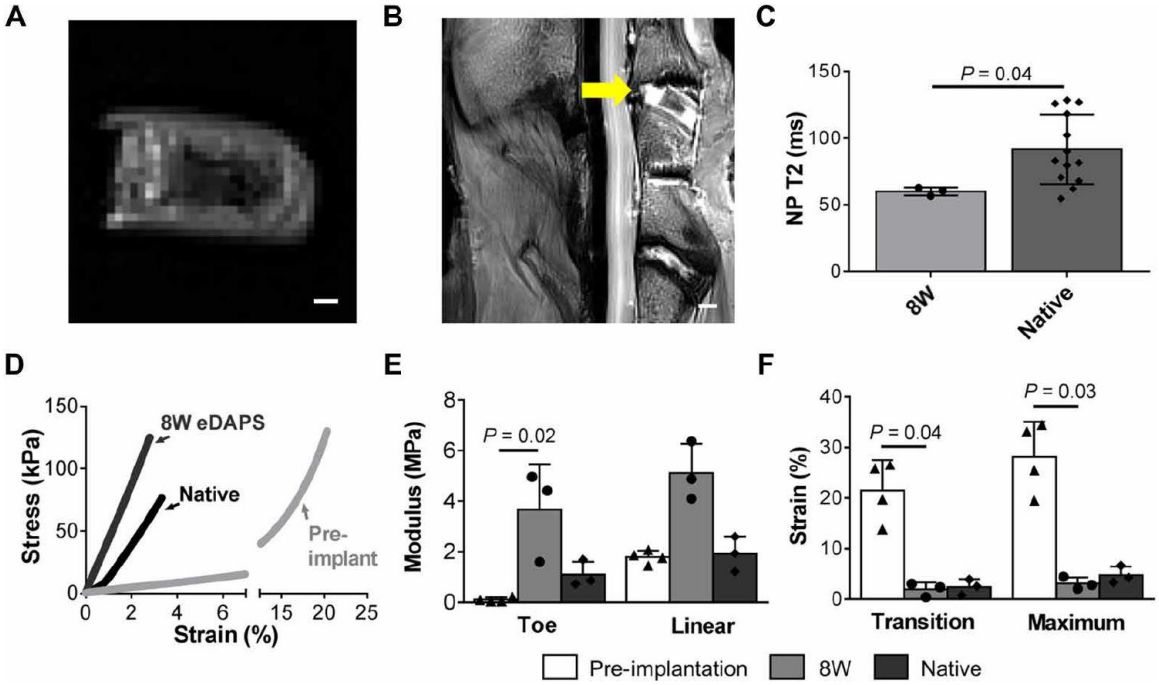
Gullbrand et al., 2018

Tissue-engineered IVDs compositionally and functionally mature after implantation



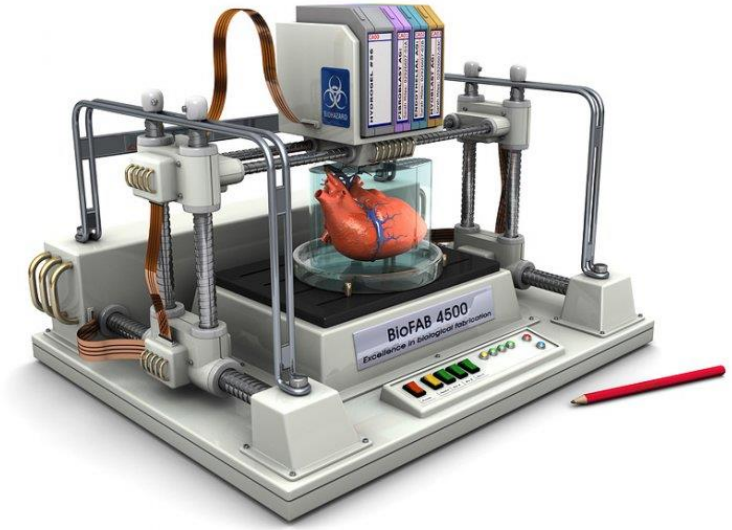
Gullbrand et al., 2018

Tissue-engineered IVDs compositionally and functionally mature after implantation

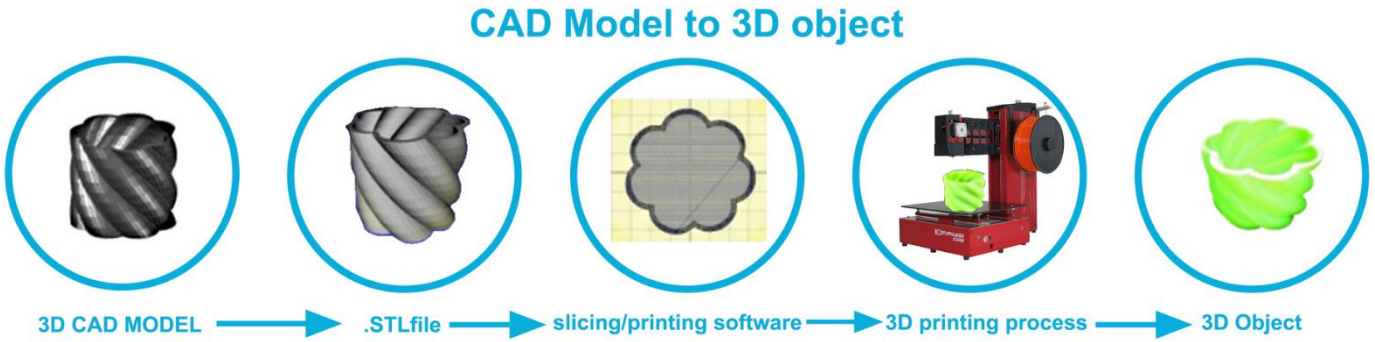


Gullbrand et al., 2018

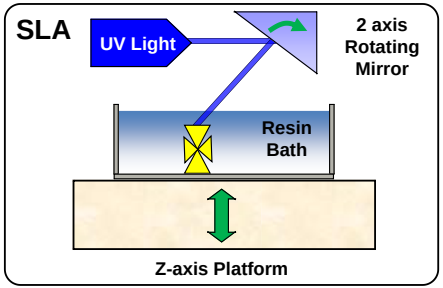
What is 3D bioprinting and what can it actually do?



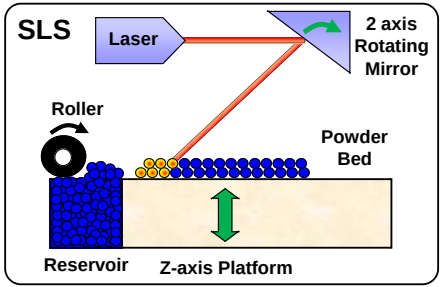
What is 3D printing?



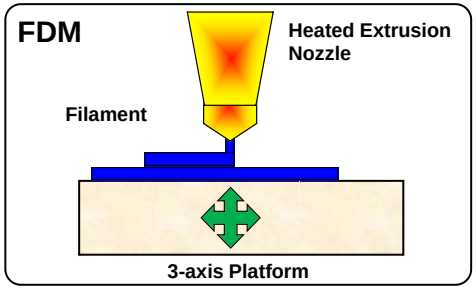
3D printing hardware



Stereolithography Apparatus (SLA)

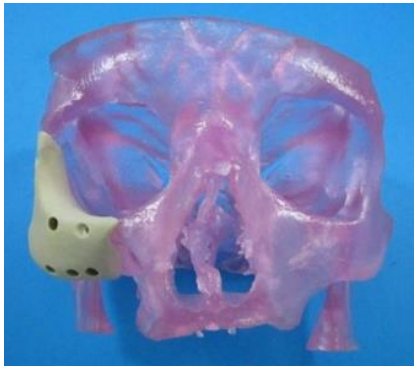


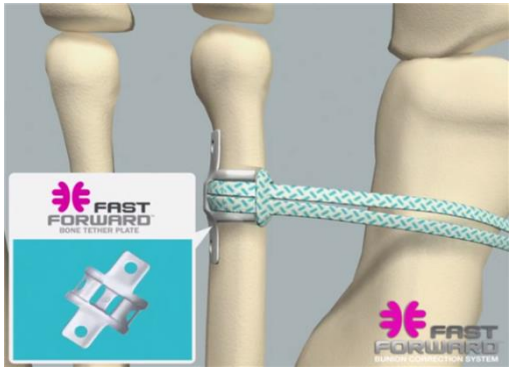
Selective Laser Sintering (SLS)



Fused Deposition Modelling (FDM)

3D printing of medical devices

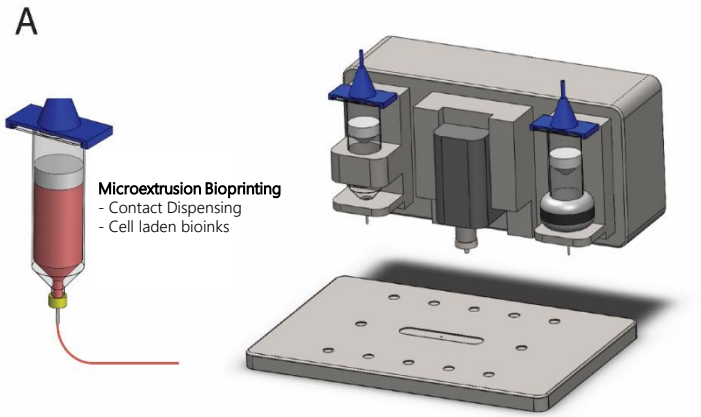


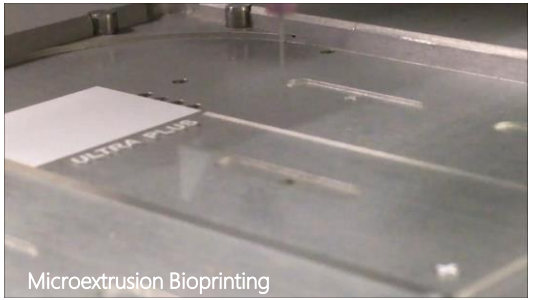


The science behind 3D bioprinting

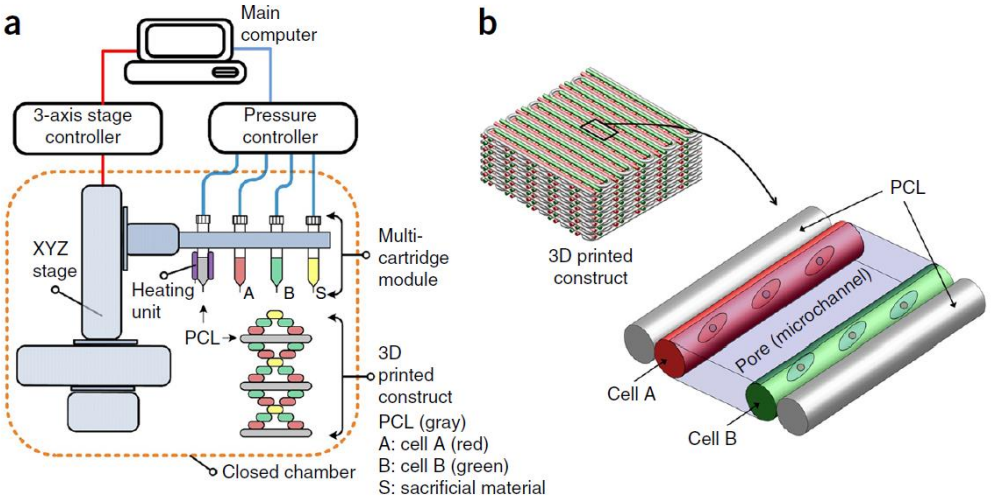
Murphy & Atala (2014)

Bioprinting: Hardware



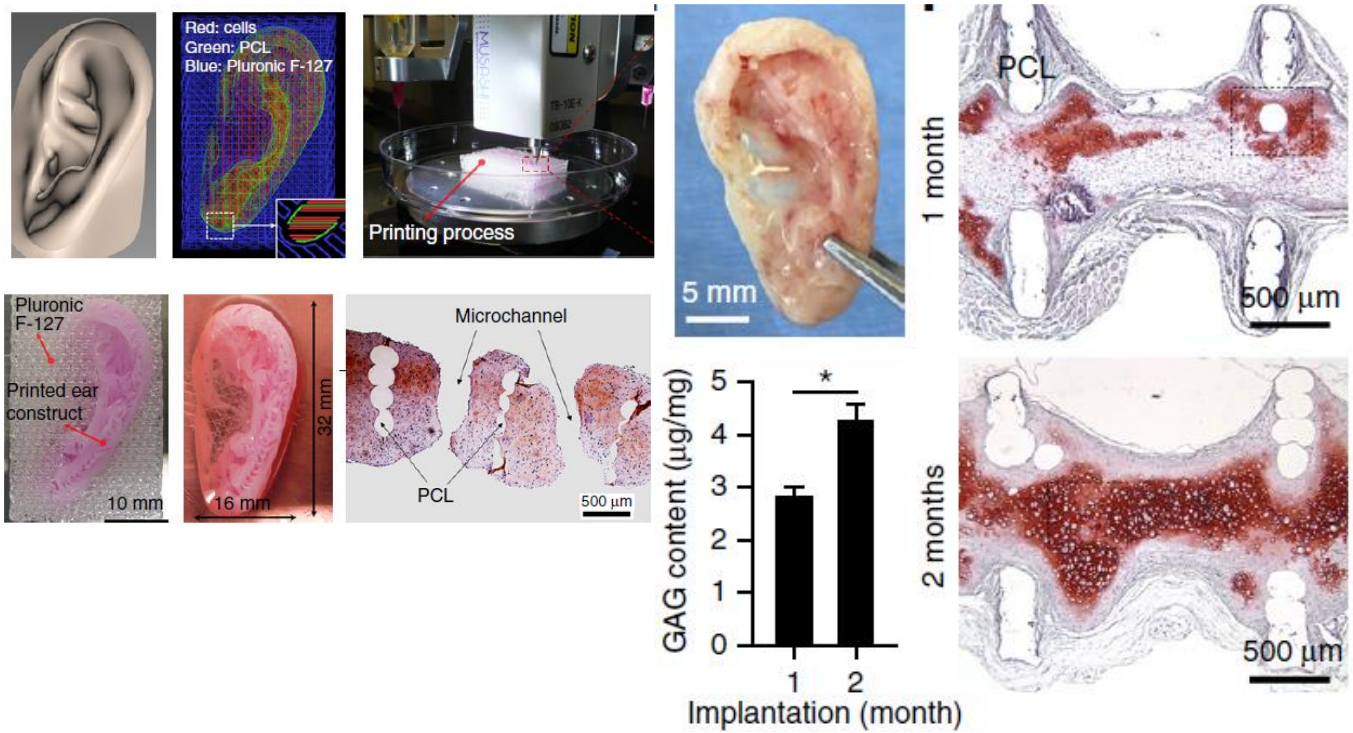


Bioprinting – what can it actually do?



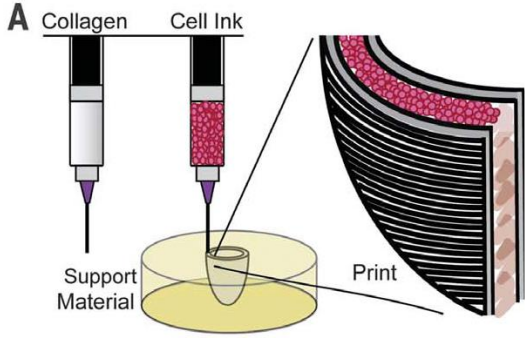
Kang et al., Nature Biotechnology, 2016

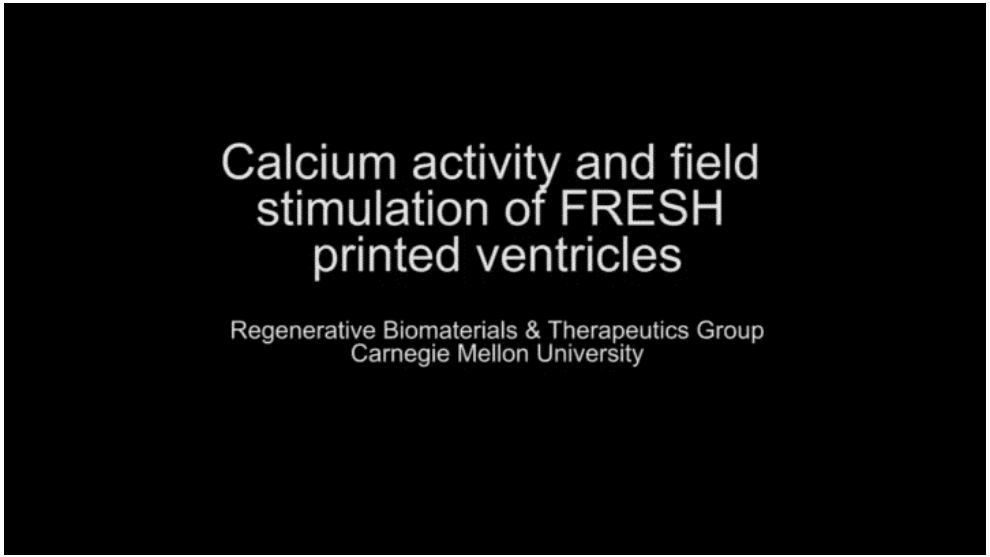
Bioprinting Ear Cartilage



Kang et al., Nature Biotechnology, 2016

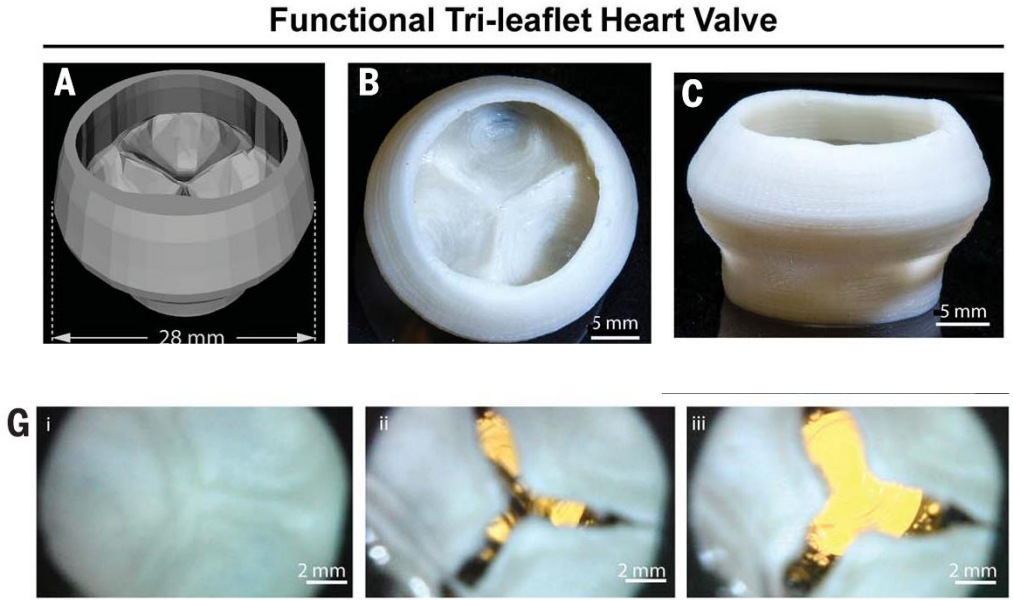
Bioprinting components of the human heart





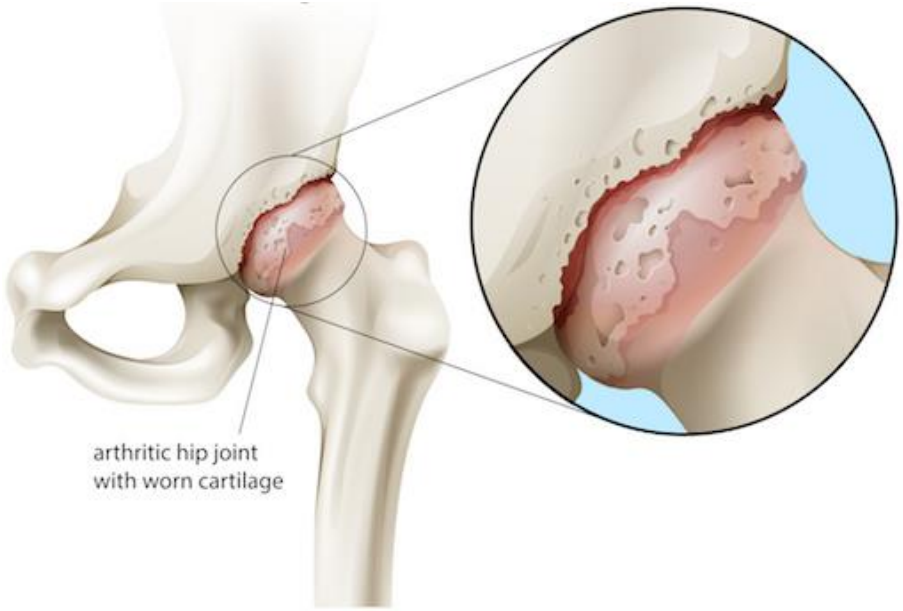
Lee et al., Science, 2019

Bioprinting components of the human heart

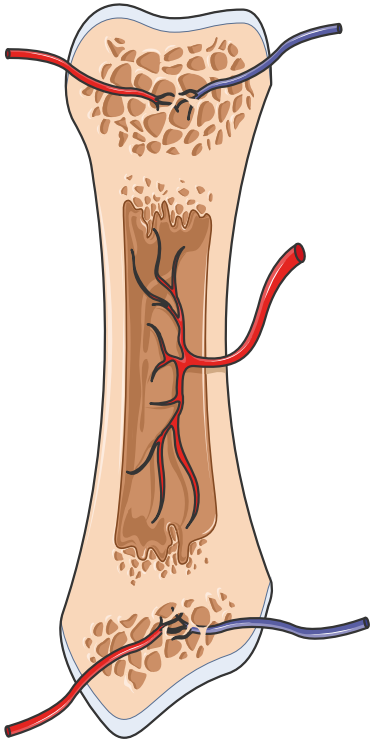


Lee et al., Science, 2019

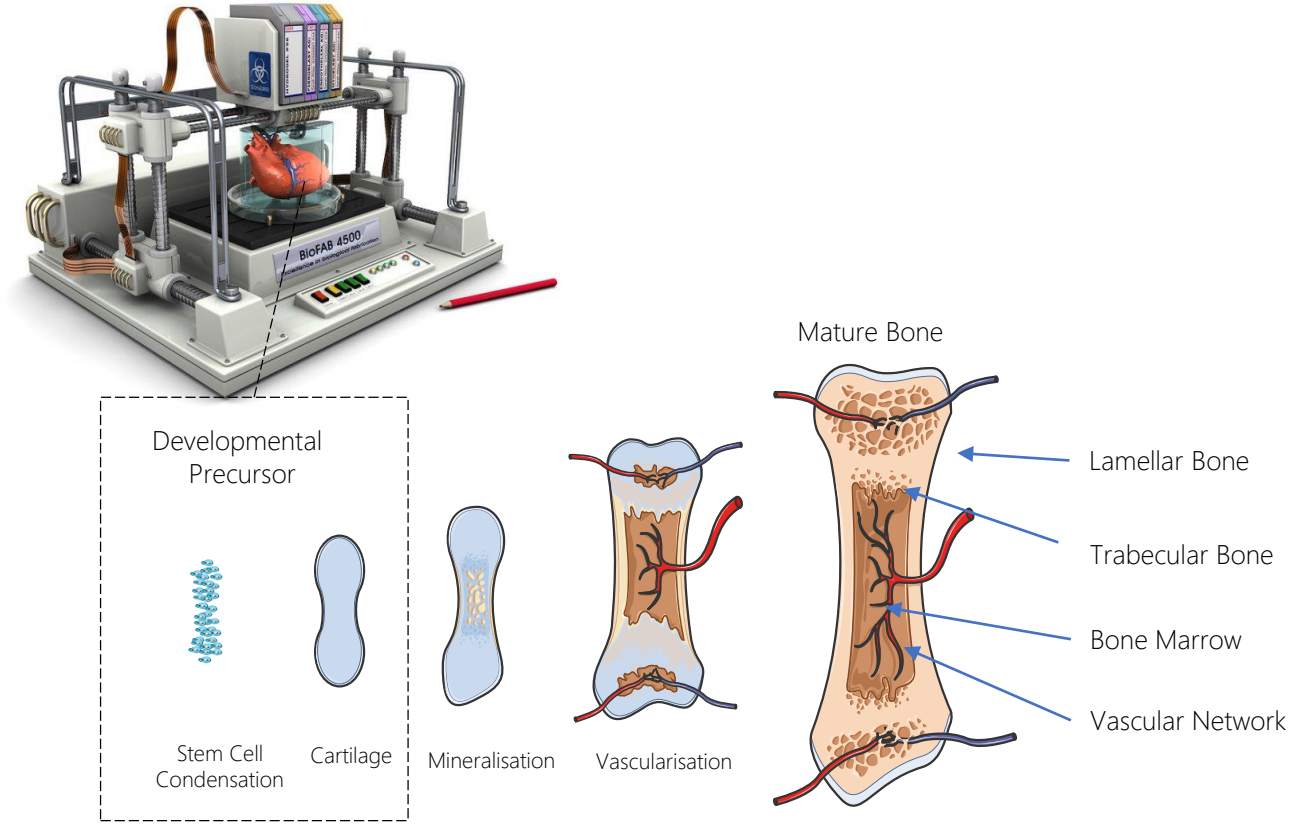
What are we doing in my lab?



The challenge for tissue engineers

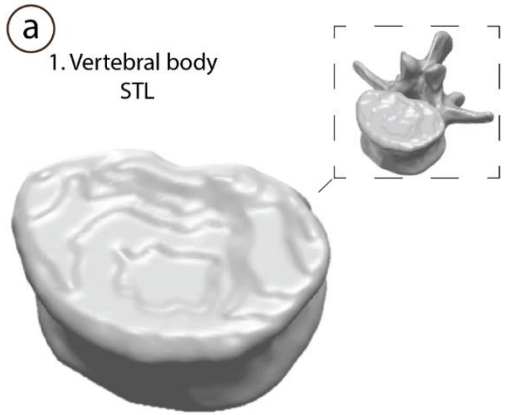


3D Bioprinting for Bone and Joint Regeneration



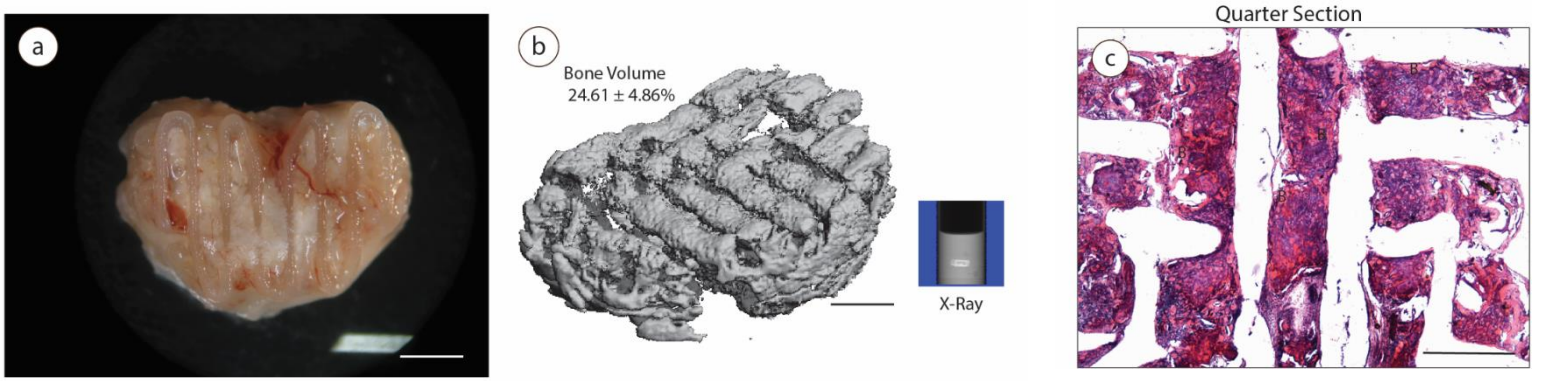
Endochondral Bone Tissue Engineering – Huang+ 2006; Scotti+ 2010; Farrell+ 2011.

Bioprinting for Whole Bone Organ Engineering



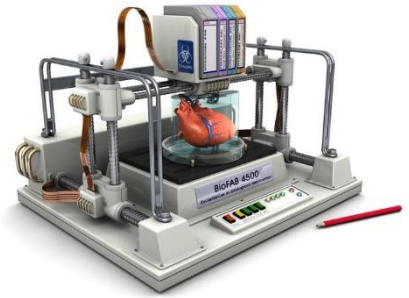
Daly + 2016.

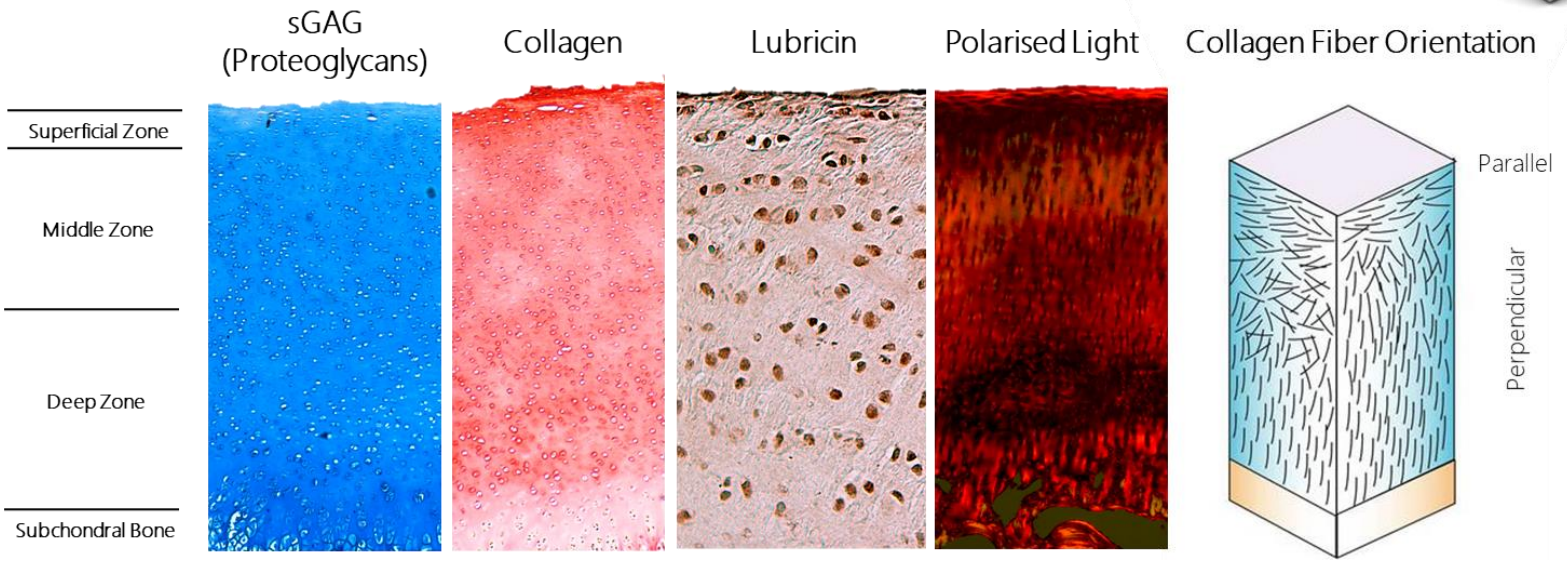
Bioprinting for Whole Bone Organ Engineering



Daly + *Advanced HealthCare Materials* 2016.

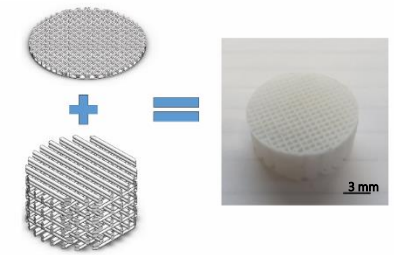
Can we bioprint articular cartilage to biologically resurface diseased joints?

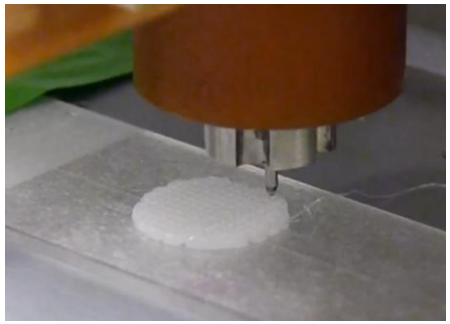




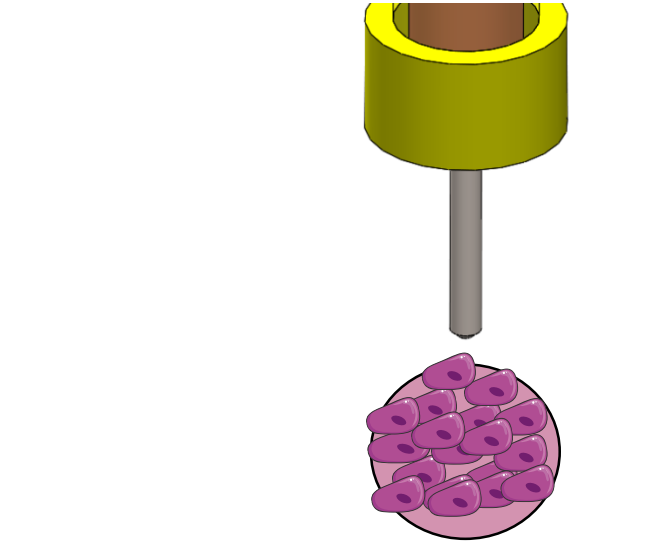
Bioprinting strategy

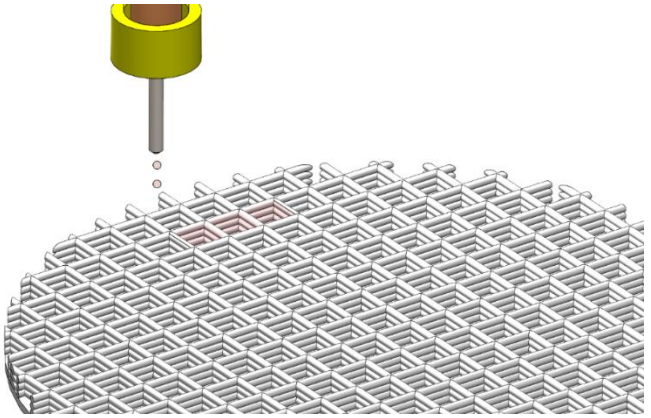
Step 1: Fused Deposition Modelling
(PCL framework)

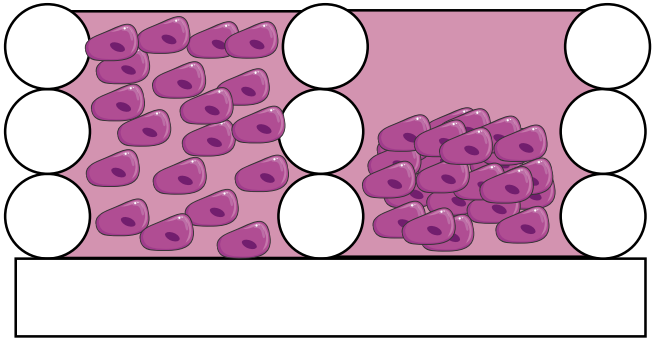




Daly + Biomaterials, 2019.

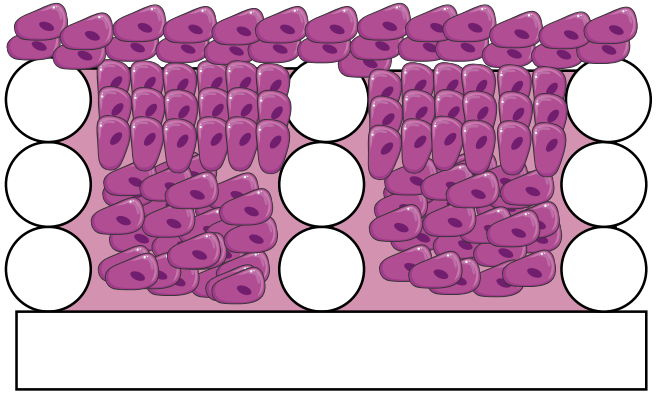






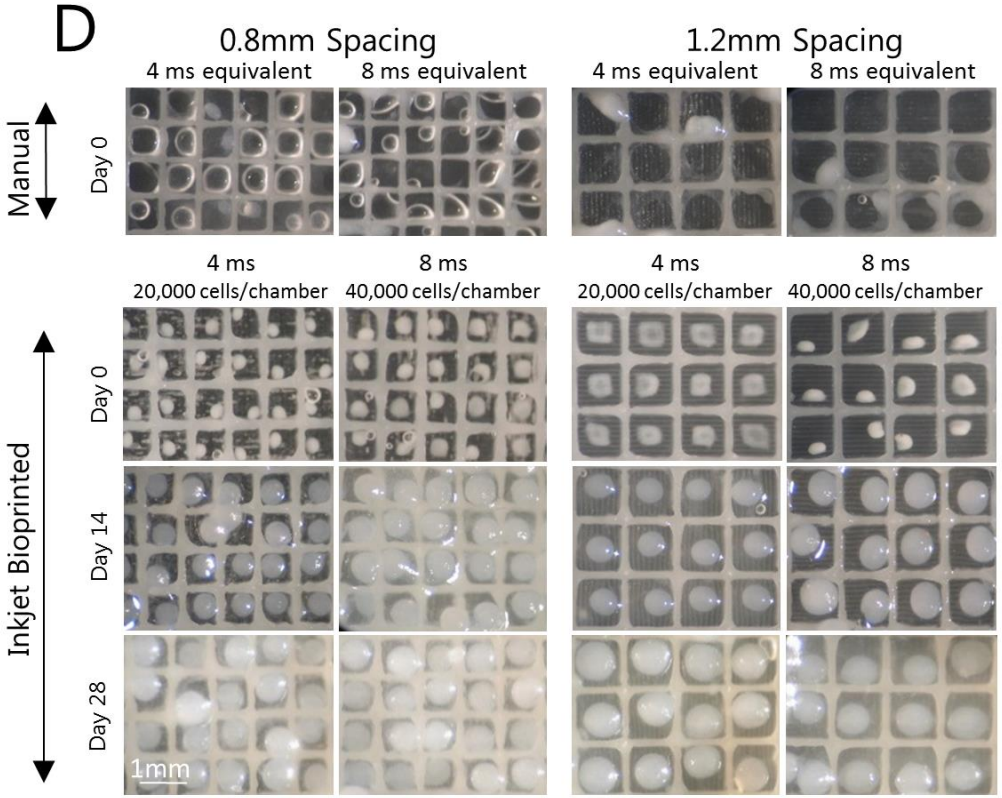
Inkjet Printing of Confined Chambers

Meshing of Condensation



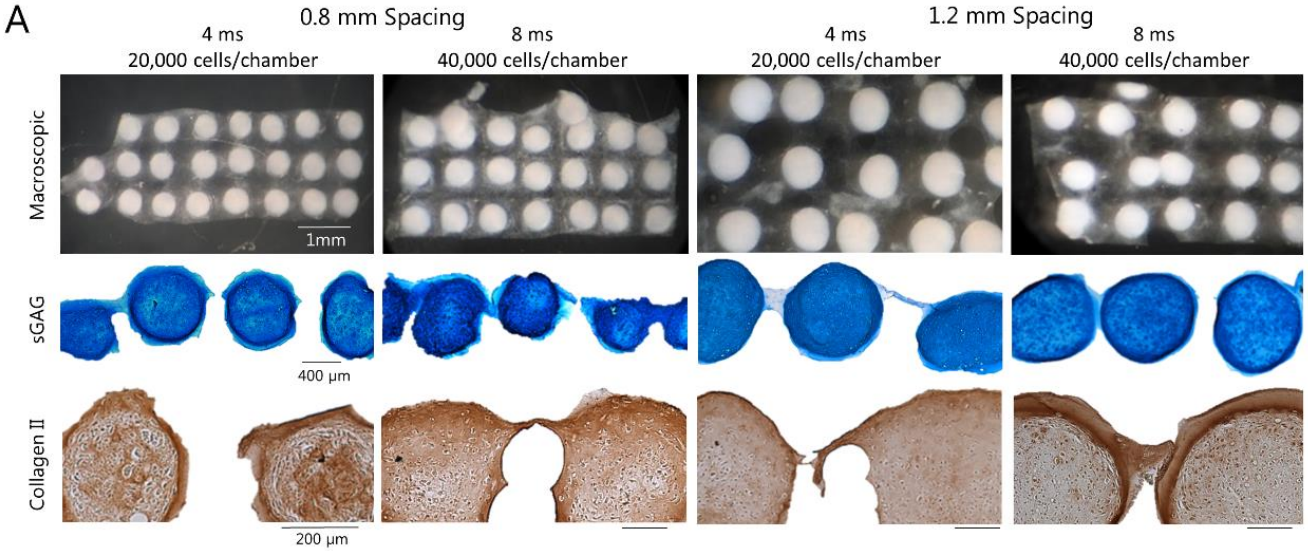
Directed Growth?

Inkjet printing of cellular condensations



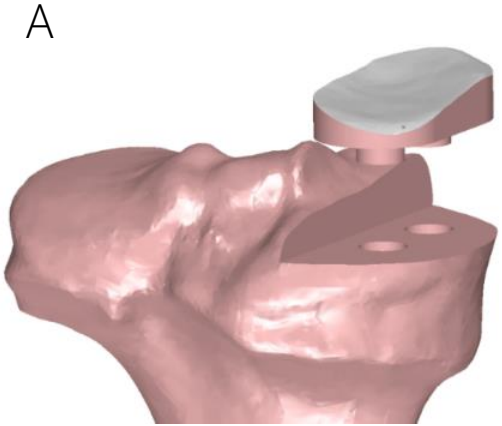
Daly + Biomaterials, 2019

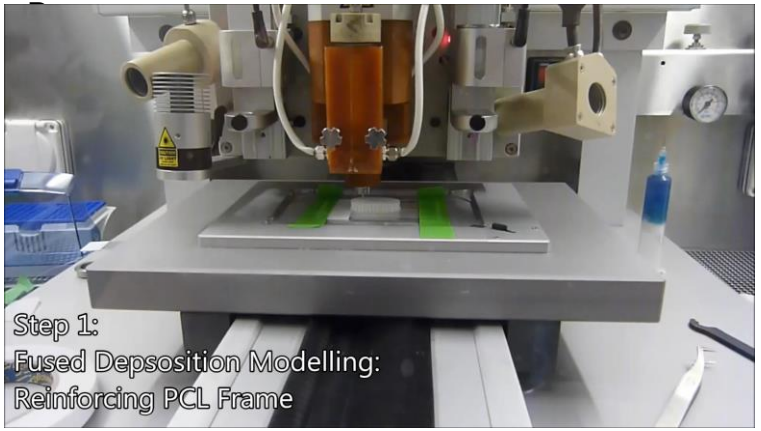
Inkjet printing of cellular condensations

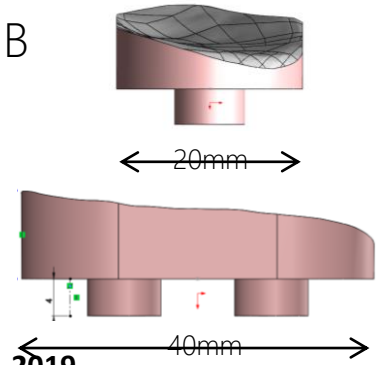


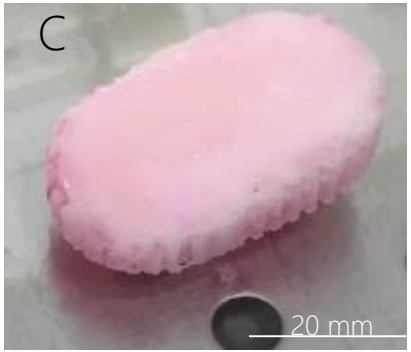
Daly + Biomaterials, 2019.

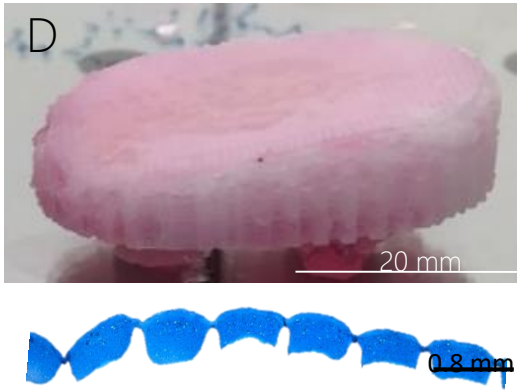
Bioprinting for Biological Joint Resurfacing





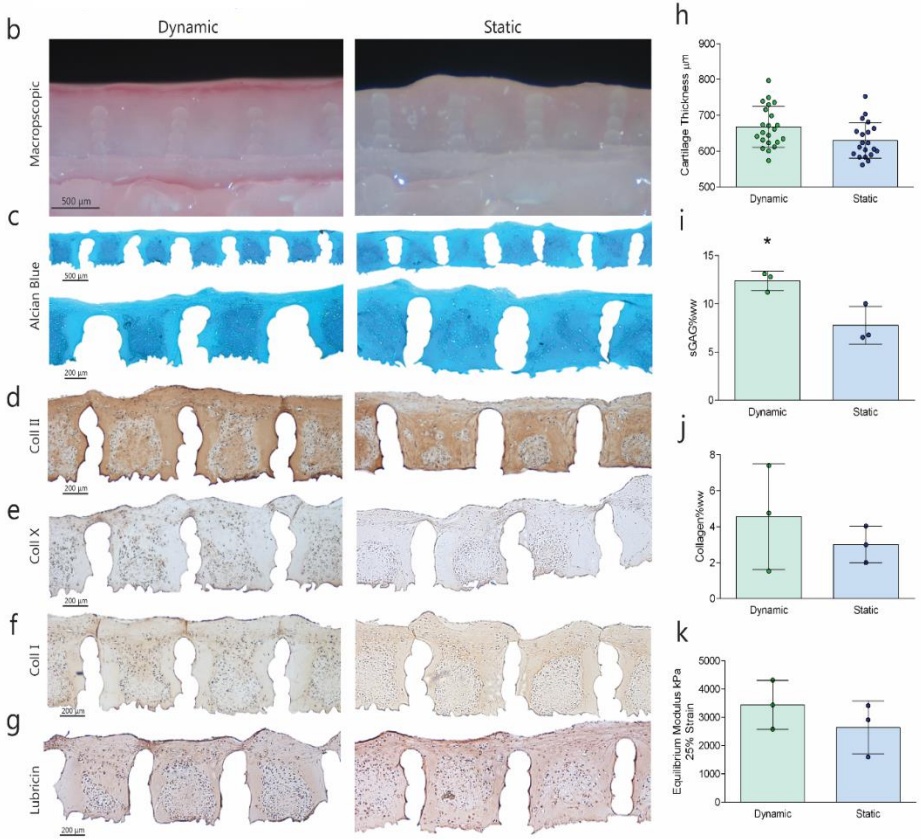


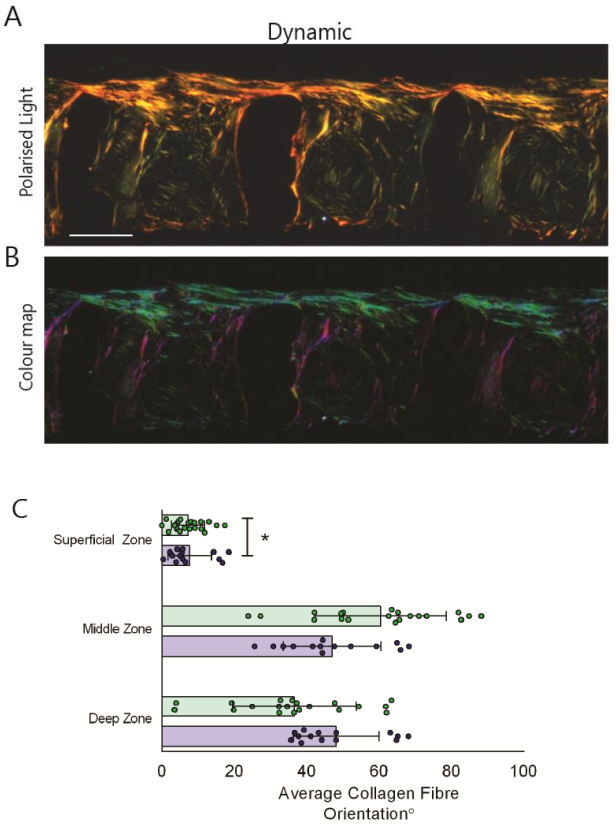




Daly + Biomaterials, 2019.

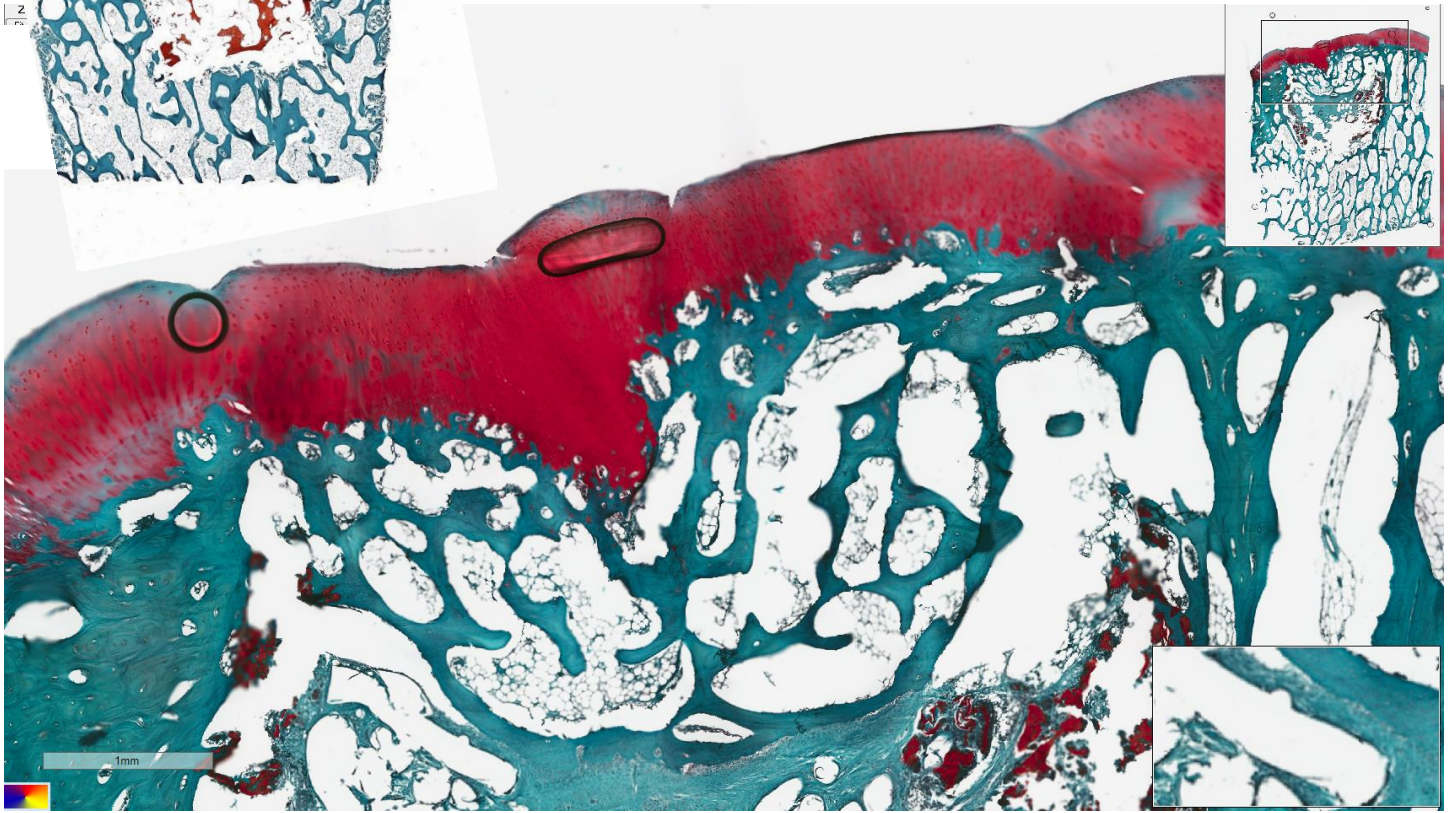
Printed cartilage development



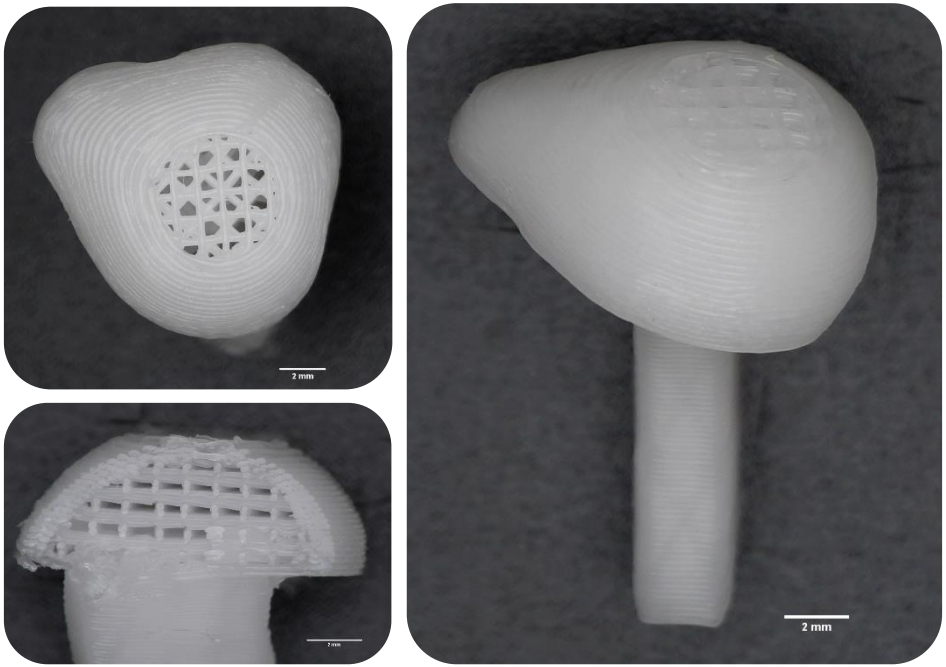


Daly + Biomaterials, 2019.

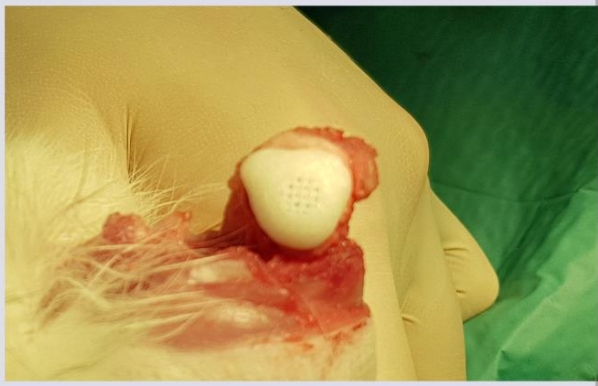
Osteochondral defect repair



Bioprinting implants for joint regeneration



Cadaver



Pilot

Xenotransplantation: A viable alternative to bioprinting of human organs?

- **Challenge**
  - Pig organs normally provoke a violent immune response upon implantation.
- **Gene-editing tools such as CRISPR:**
  - Eliminate immune-provoking sugars from the surface of pig cells
  - Introduce human genes that regulate blood coagulation to prevent dangerous clots
  - Snip out viral sequences that some fear could infect a human host
- **Raises new ethical questions**

Impact of Bioprinting

- When Hull originally invented SLA (1986), he said it would take between 25 and 30 years before the technology would find its way into the home. In many cases, bioprinting will likely take even longer to reach the clinic.
- Short-term impact of bioprinting
  - 3D-bioprinted tissue models for research, drug discovery and toxicology.
- Long-term impact of bioprinting
  - Tissues and organs on demand - will dramatically change medicine for the better.
  - Likely first clinical targets - Skin, cartilage, vascular grafts.

Acknowledgements

Current Lab Members:

- Dr David Browe
- Dr Fiona Freeman
- Dr Stanislas Von Euw
- Dr Bin Wang
- Dr Kevin Behan
- Dr Kian Eichholz
- Dr Alexander Dufour
- Dr Rajesh Lakshmanan
- Pedro Diaz Payno
- Paola Aprile
- Jessica Nulty
- Anna McDermott
- Romain Florentin
- Rossana Schipani
- Olwyn Mahon
- Stefan Scheurer
- Ian Whelan
- Ross Burdis
- Pierluca Pitacco
- Inês Gonçalves
- Xavier Barceló Gallostra
- Sarah Deegan
- Angelica Federici

Past Lab Members:

- Dr Conor Buckley
- Dr Eric Meyer
- Dr Mathew Haugh
- Dr Rajalakshmanan Eswaramoorthy
- Dr Grainne Cunniffe
- Dr Binulal Sathy
- Dr Swetha Rathan
- Dr Adam O'Reilly
- Dr Lu Luo
- Dr Henrique Almeida
- Dr Tariq Mesallati
- Dr Alanna Gannon
- Dr Eamon Sheehy
- Dr Andrew Steward
- Dr Darren Burke
- Dr Thomas Nagel
- Dr Stephen Thorpe
- Dr Eoghan Maher
- Dr Tatiana Vinardel
- Dr Michael Early
- Dr Sara Romanazzo
- Dr Simon Carroll
- Dr Alan Irvine
- Dr Rukmani Sridharan
- Dr Andrew Daly
- Dr Tomas Gonzalez Fernandez
- Dr Susan Critchley
- Dr Dinorath Olvera
- Bruce McKee
- Edoardo Dell'Amico
- Peter Kearney
- Johnnie Chu

Acknowledgements

- Collaborators:
  - Prof. Fergal O'Brien (Royal College of Surgeons in Ireland)
  - Prof Cathal Moran (Trinity College Dublin)
  - Prof. Ed Lavelle (Trinity College Dublin)
  - Prof Aishling Dunne (Trinity College Dublin)
  - Prof. Paula Murphy (Trinity College Dublin)
  - Prof. Conor Buckley (Trinity College Dublin)
  - Prof. David Hoey (Trinity College Dublin)
  - Prof. Pieter Brama (University College Dublin)
  - Dr. Garry Duffy (Royal College of Surgeons in Ireland)
  - Prof. Kevin Mulhall, (Consultant Orthopaedic Surgeon, Mater University Hospital).
  - Dr. Mary Murphy (NUI Galway)
  - Dr Laoise McNamara (NUI Galway)
  - Prof. Dennis McGonagle (University of Leeds)
  - Prof. Chris Jacobs (Columbia University)
  - Prof. Diane Wagner (University of Notre Dame)
  - Prof. Kurt Hankenson (University of Pennsylvania School of Veterinary Medicine)
  - Prof. Miguel Angel Martınez (University of Zaragoza)
  - Prof. Tammy Donahue (Colorado State University)
  - Prof. Nicholas Dunne (Dublin City University)
  - Dr. Helen McCarthy (Queens University Belfast)
  - Prof. Eben Alsberg (Case Western Reserve University)
  - Prof Joel Boerckel (University of Notre Dame)
  - Prof Rossana Thiré (Centro de Tecnologia – UFRJ)

- Lab funding:
  - Science Foundation Ireland (12/IA/1554; 12/US/I2489; 17/SP/4721).
  - European Research Council (JointPrint; ERC-2014-CoG-647004; StemRepair; #258463; ANCHOR #779909).
  - Enterprise Ireland (CF/2014/4325)
  - H2020 (Carbon ITN).
  - Irish Research Council (GOIPG/2015/3186)
  - Johnson and Johnson Services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