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Bacterial Synthesis of Polymers and their Biomedical Applications

Tissue Regenerating Plastics from Bacteria

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POLITECNICO DI TORINO 1859 1906

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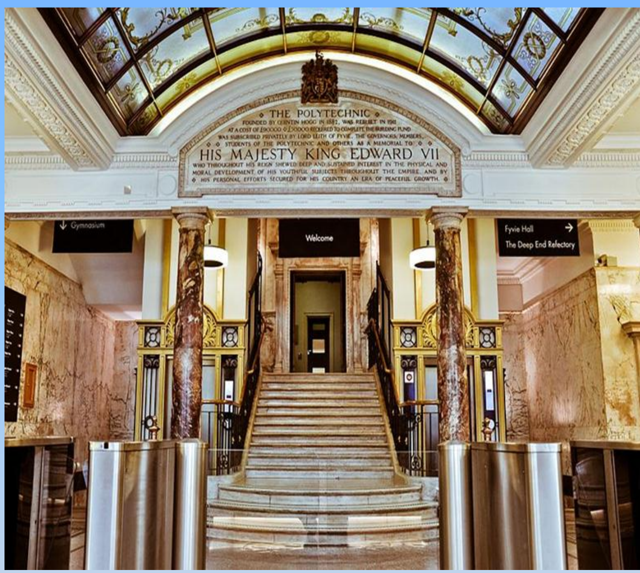

Regent Street, UoW

New Cavendish Street, UoW

ICTEM, Imperial College

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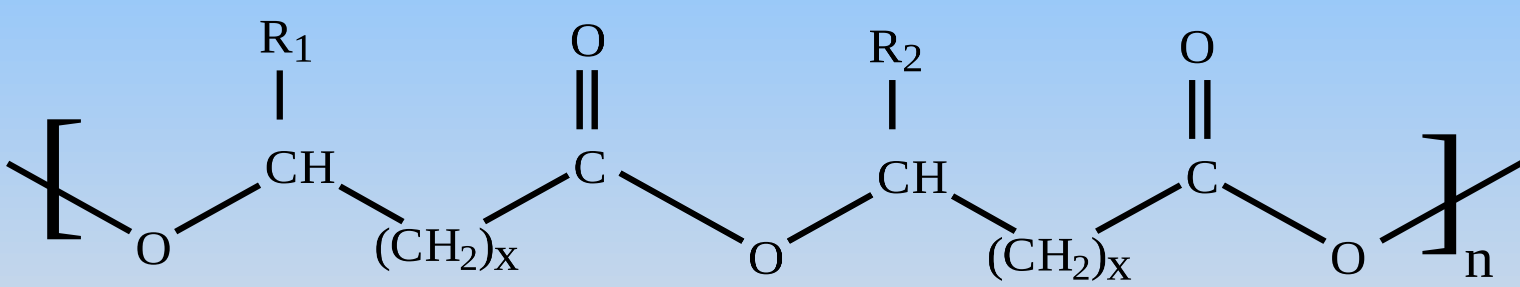
Polyhydroxyalkanoates, the biodegradable and biocompatible plastic from bacteria

Polyhydroxyalkanoates are water-insoluble storage polymers which are polyesters of 3-, 4-, 5- and 6-hydroxyalkanoic acids produced by a variety of bacterial species under nutrient-limiting conditions. They are biodegradable and biocompatible, exhibit thermoplastic properties and can be produced from renewable carbon sources. Hence, there has been considerable interest in the commercial exploitation of PHAs.

Philip *et al*., 2007, JCTB, 82 (3):233-247
Akarayonye *et al*., 2010, JCTB, Volume 85 (6): 732-743
Keshavarz *et al*., 2010, Current Opinion in Microbiology 13 (3): pp. 321-326

The general structure of Polyhydroxyalkanoates



R_1/ R_2 = alkyl groups (C_1-C_{13})
x = 1,2,3,4

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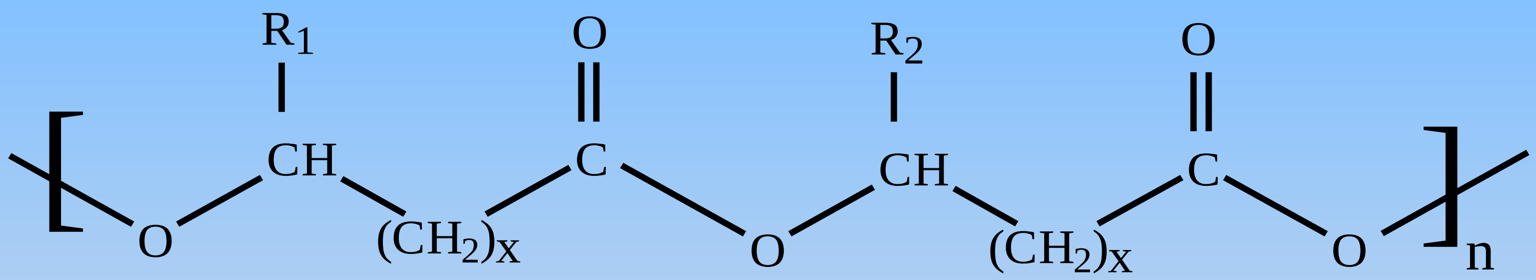
SCL and MCL Polyhydroxyalkanoates



Total Carbon chain length in monomer = 4-5;**SCL PHAs**
Total Carbon chain length in monomer =6-14;**MCL PHAs**

SCL-PHAs- Thermoplastics
MCL-PHAs-Elastomerics

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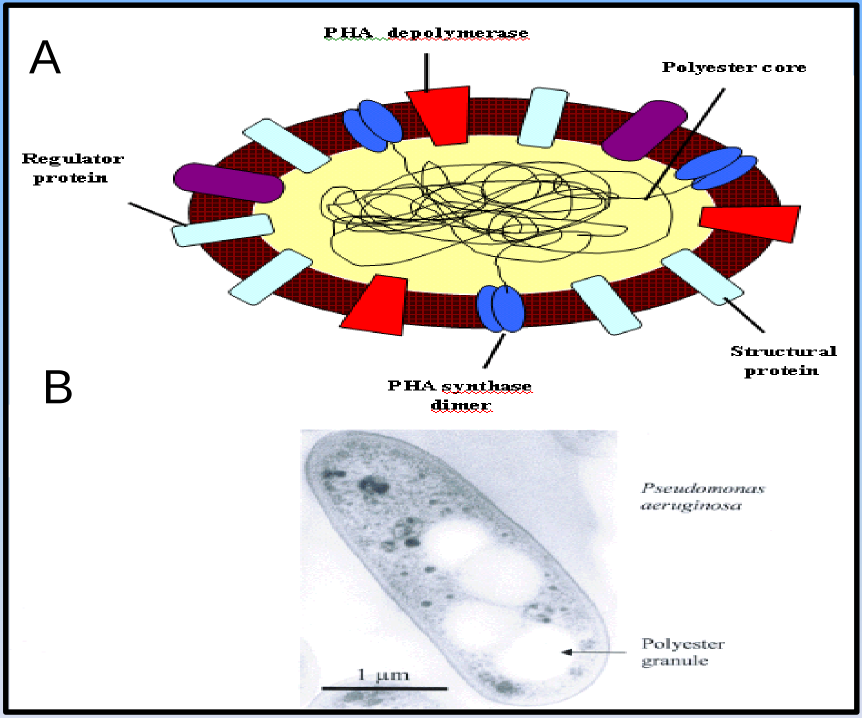
Properties of SCL and MCL Polyhydroxyalkanoates

Type of PHA	Melting Temp (^{o}C)	Glass Transition Temp (^{o}C)	Young's Modulus (GPa)	Elongation at break (%)	Tensile strength (MPa)
P(3HB)	171	2.7	3.5	1	40
P(3HB-co-20%3HV)	145	-1	1.2	3.84	32
P(4HB)	60	50	0.149	1000	104
P(3HB-co-16%4HB)	152	8	ND	444	26
P(3HO-co-18%3HHx)	61	35	0.008	400	9
P(3HB-co-3HHx)	120	-2	0.5	850	21

Polyhydroxyalkanoates as inclusions in bacteria



Roy *et al*., 2015, “Polyhydroxyalkanoates (PHAs) based Blends, Composites and Nanocomposites” edited by Ipsita Roy and Visakh P.M. published by Royal Society of Chemistry, ISBN: 978-1-84973-946-7

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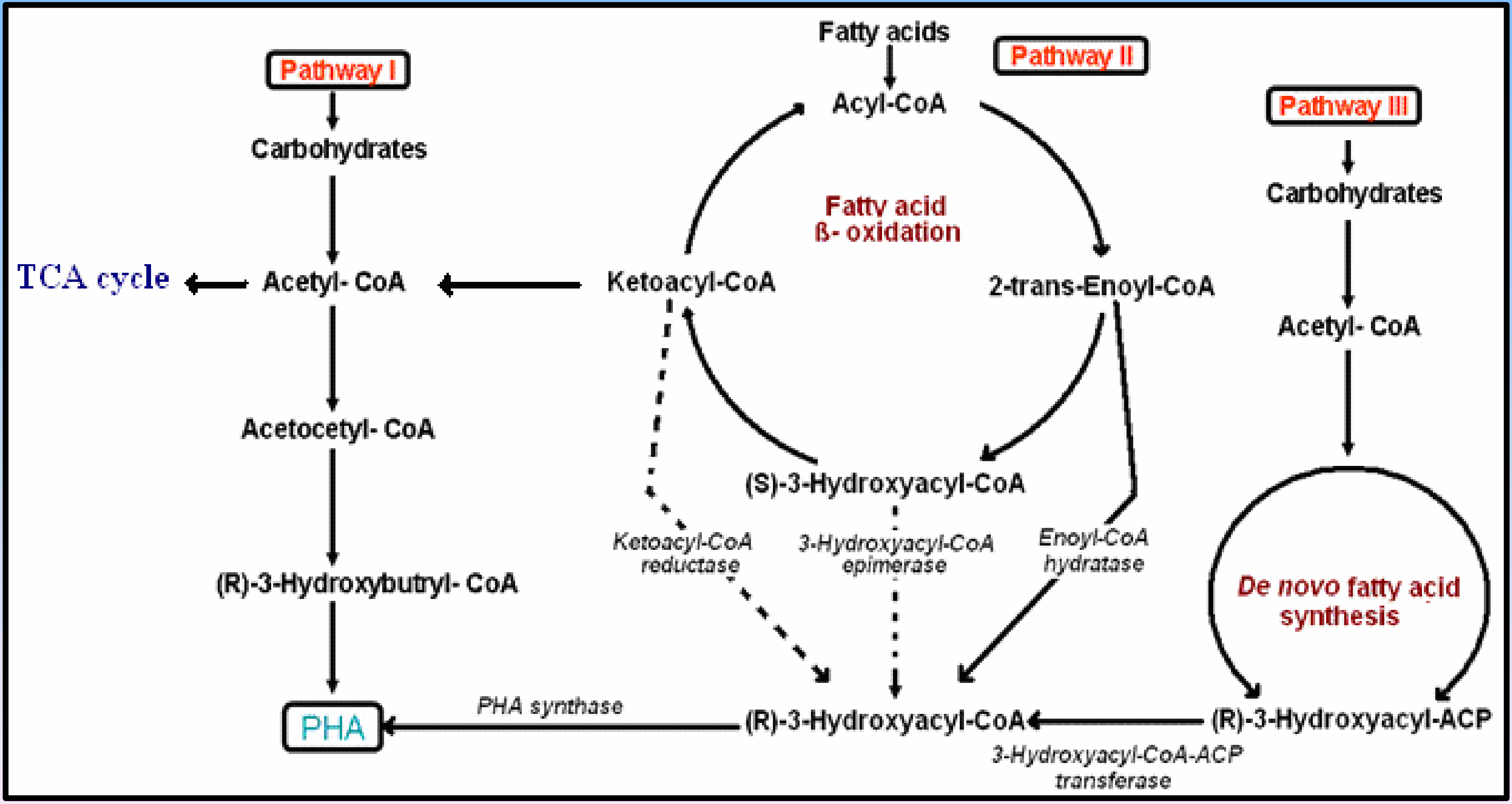
Metabolic Pathways involved in PHA Biosynthesis



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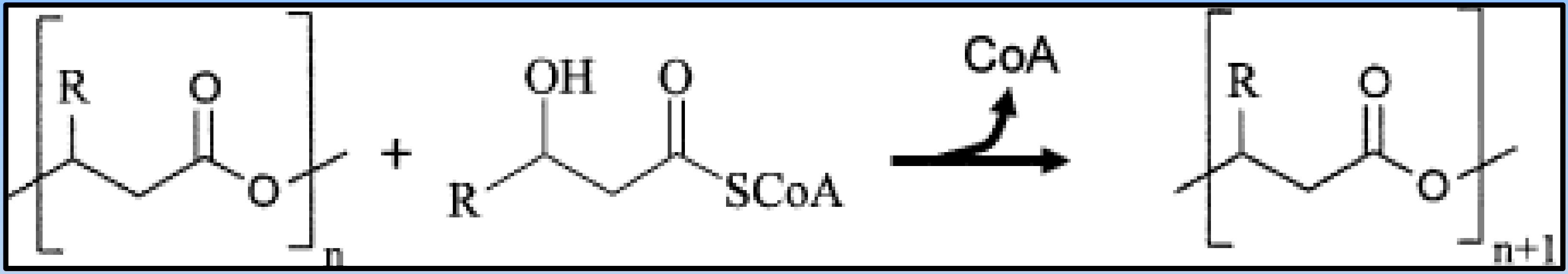
Polyhydroxyalkanoate Synthases, the enzymes involved in PHA Biosynthesis



PHA synthases catalyse the stereo-selective conversion of (*R*)-3-hydroxyacyl-CoA substrates to PHAs with the concomitant release of CoA

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Production of SCL-Polyhydroxyalkanoates using *Bacillus cereus* SPV, a Gram positive bacteria

Valappil *et al*., 2007, Journal of Biotechnology, Volume 127(3), 475-487

Valappil *et al*., 2008, Journal of Applied Microbiology Jun; 104(6):1624-35

Philip *et al*., 2009, Biomacromolecules 10(4): 691 – 699

Akarayonye *et al*., 2010, Biotechnology Journal 7(2) 293-303

PHA biosynthesis in *Bacillus cereus* SPV

- *Bacillus cereus* SPV up to **80% dcw of PHA**
- It is capable of **using a range of different carbon sources** for PHA production including, glucose, fructose, sucrose, gluconate, a range of alkanoic acids and plant oils
- The polymer produced is lipopolysaccharide-free and hence **non-immunogenic**, a great advantage for medical applications.

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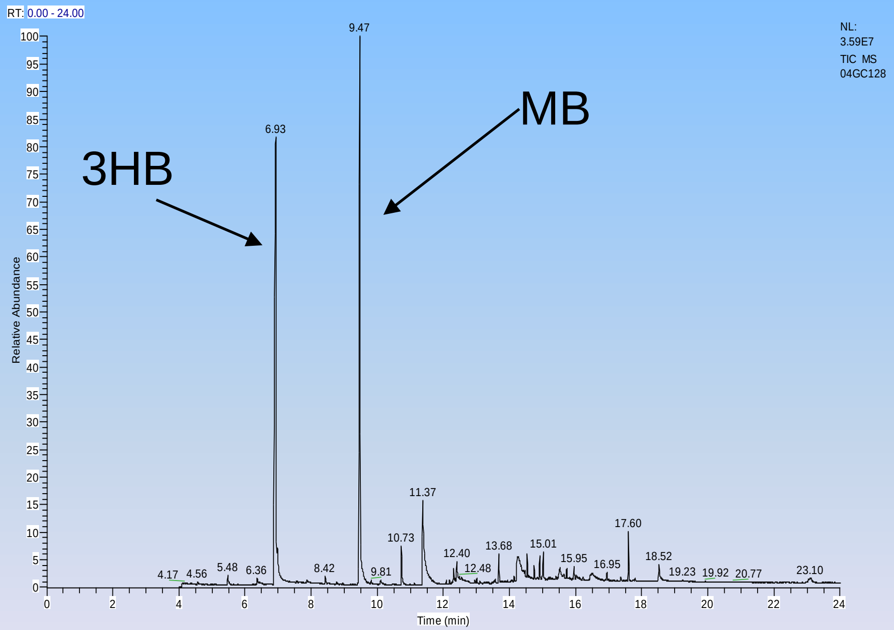
PHAs produced by *Bacillus cereus* SPV using carbohydrates

Carbon source	Dry cell weight (g/litre)	PHA concentration (g/litre)	3HB fraction (mol%)	3HV fraction (mol%)	4HB fraction (mol%)	PHA yield (% dry cell weight)
Glucose	2.143	0.814	100	0	0	38.00
Fructose	1.242	0.500	82	0	18	40.25
Sucrose	1.666	0.640	97	0	3	38.40
Gluconate	1.943	0.814	57	6.5	36.5	41.90

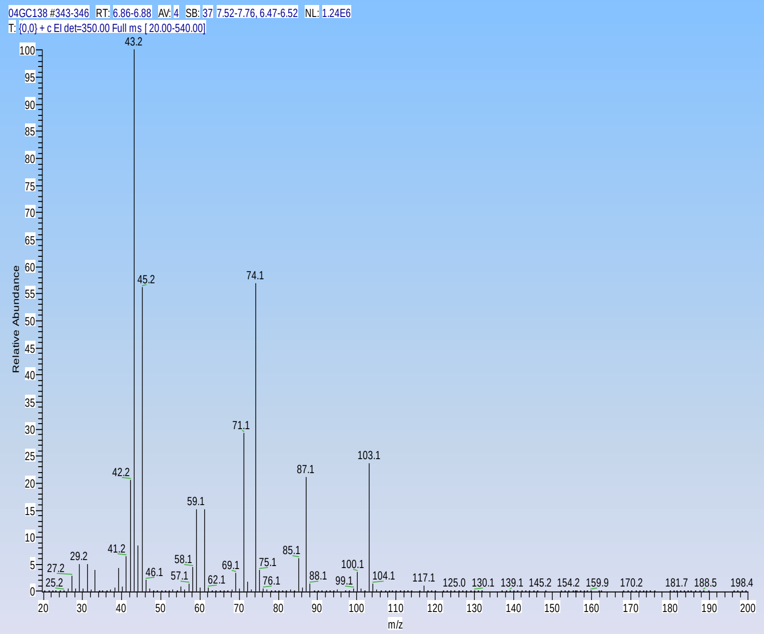
Valappil *et al*., 2007, Journal of Biotechnology, Volume 127(3), 475-487

P(3HB) production by *Bacillus cereus* SPV using glucose

(Yield:38% dcw)



The GC chromatogram
of the methanolysed polymer



Mass spectrum of the methyl ester
of 3-hydroxybutyrate

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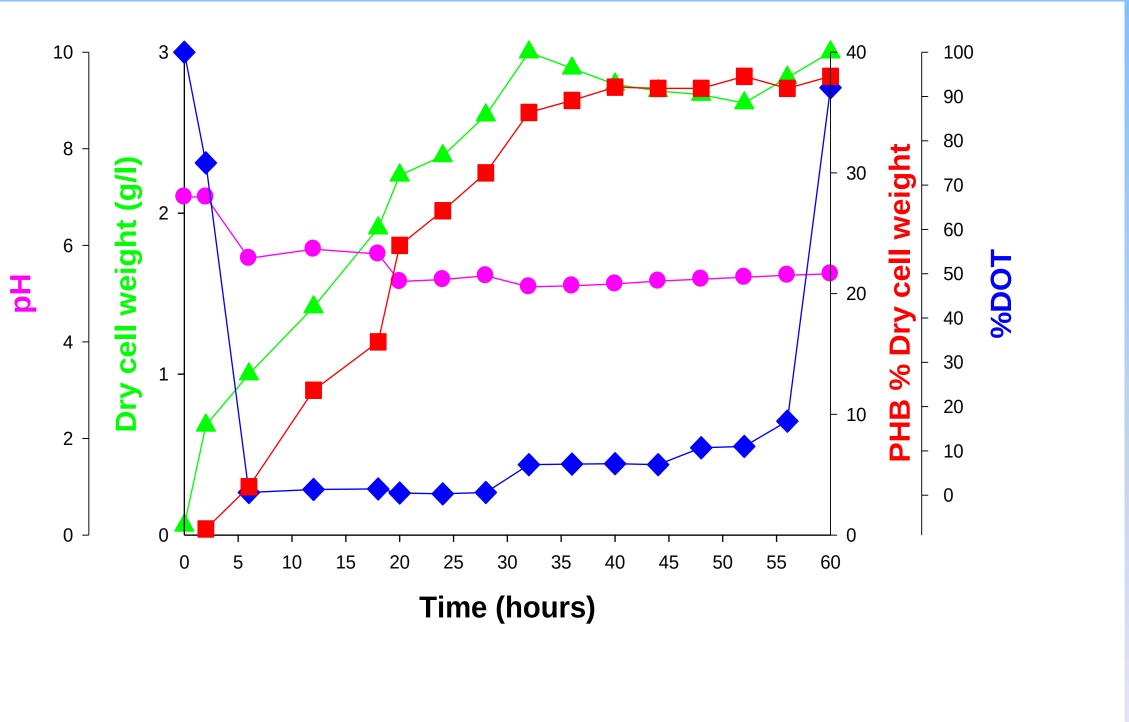
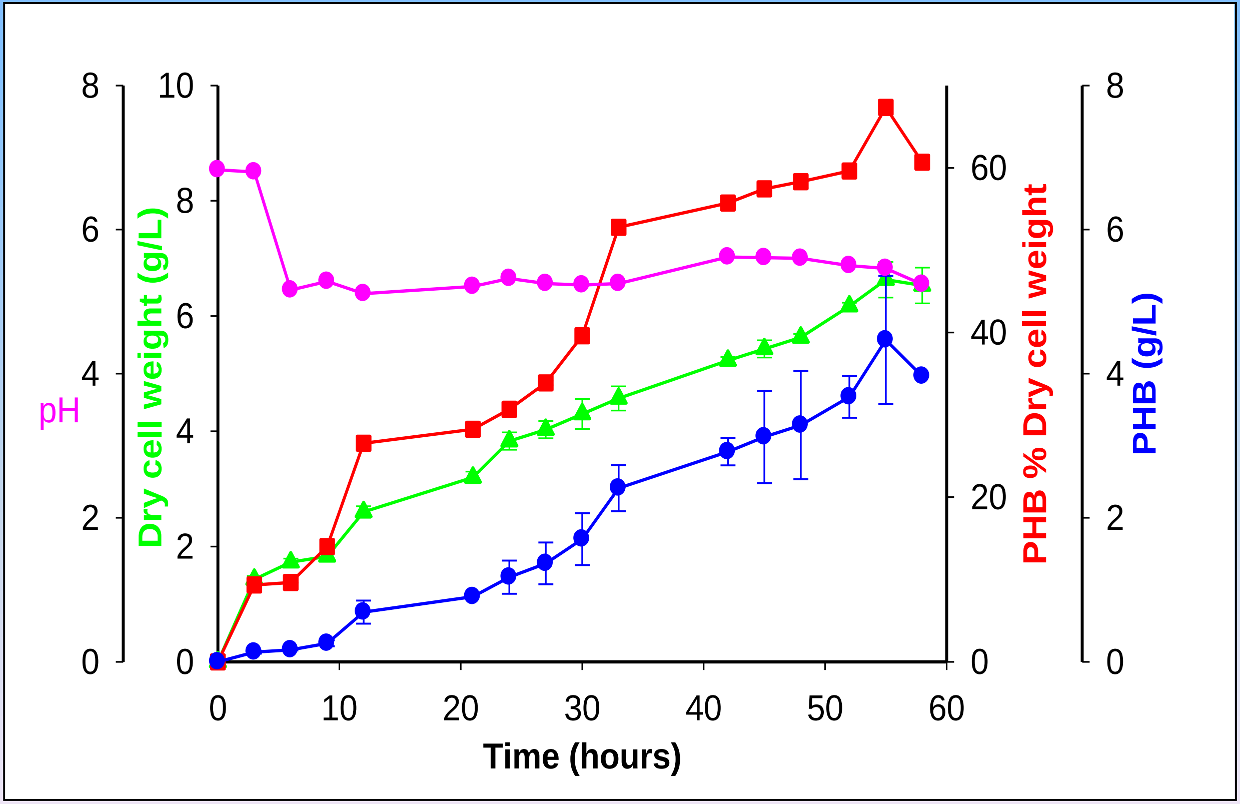
Large scale production of P(3HB) using fed batch fermentation in Kannan and Rehacek medium (Yield 38% dcw)



GLUCOSE as the main Carbon Source

Valappil *et al*., 2007, Journal of Biotechnology, 132; 251-258

Large scale production of P(3HB) using batch fermentation in modified G medium, MGM (Yield 67% dcw)



MOLASSES
as the main
Carbon Source
(cheap C source!)

Akaraonye *et al*., 2012, Biotechnology Journal **7(2)** 293-303

Material and Thermal Properties of the P(3HB) produced

Type of PHA	Melting Temp (°C)	Glass Transition Temp (°C)	Young's Modulus (GPa)	Elongation at break (%)	Tensile strength (MPa)
P(3HB)	169	1.9	1.7	3.8	25.7

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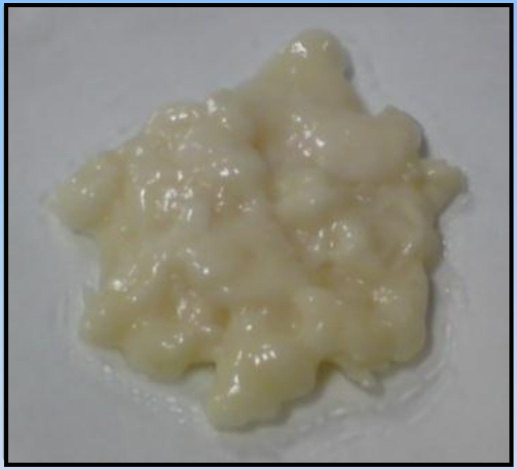
Production of MCL-Polyhydroxyalkanoates using *Pseudomonas mendocina*, a Gram negative bacteria



Rai *et al*., 2011, Material Science Engineering (Reviews) 72(3) 29-47

Rai *et al*., 2011, Biomacromolecules, 12 (6), pp 2126–2136

Rai *et al*., 2011, Journal of Applied Polymer Science, 122, (6), 3606-3617

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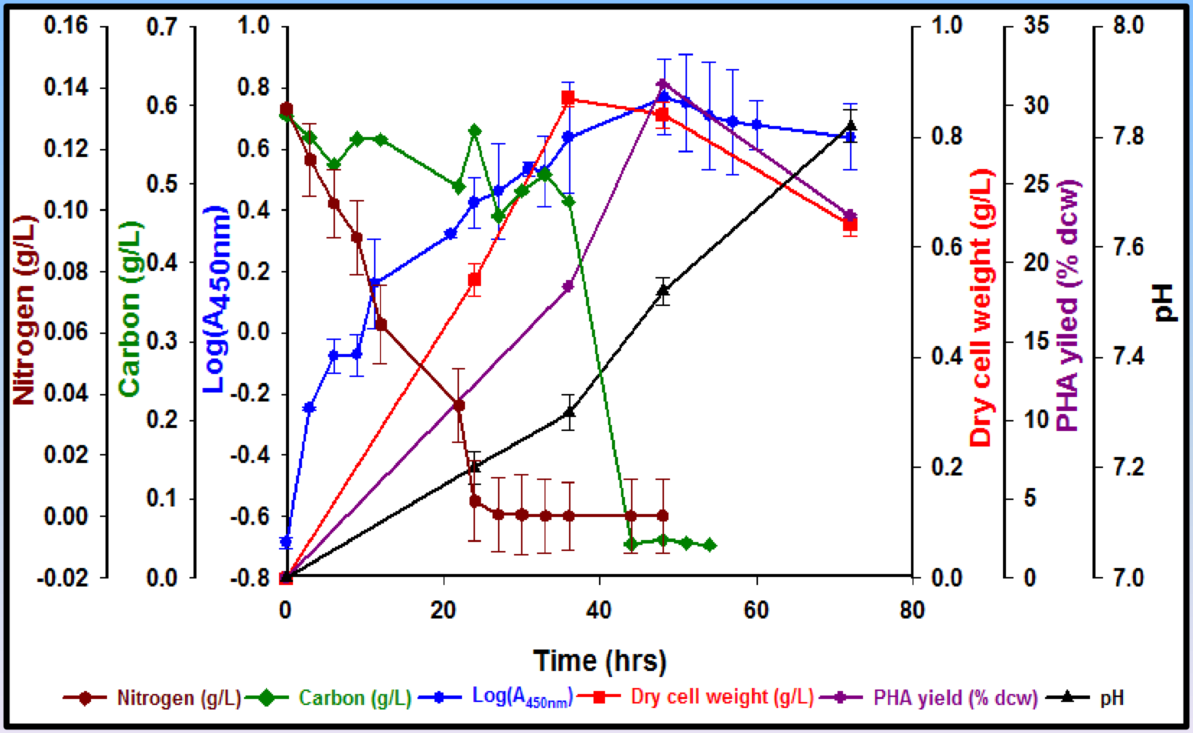
Large scale production of P(3HO) using batch fermentation in MSM media

(Yield 31% dcw)



SODIUM OCTANOATE as the main Carbon Source

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Material and Thermal Properties of the P(3HO) produced

Type of PHA	Melting Temp (^oC)	Glass Transition Temp (^oC)	Young's Modulus (MPa)	Elongation at break (%)	Tensile strength (MPa)
P(3HO)	42	-38	0.8	1200	8.6

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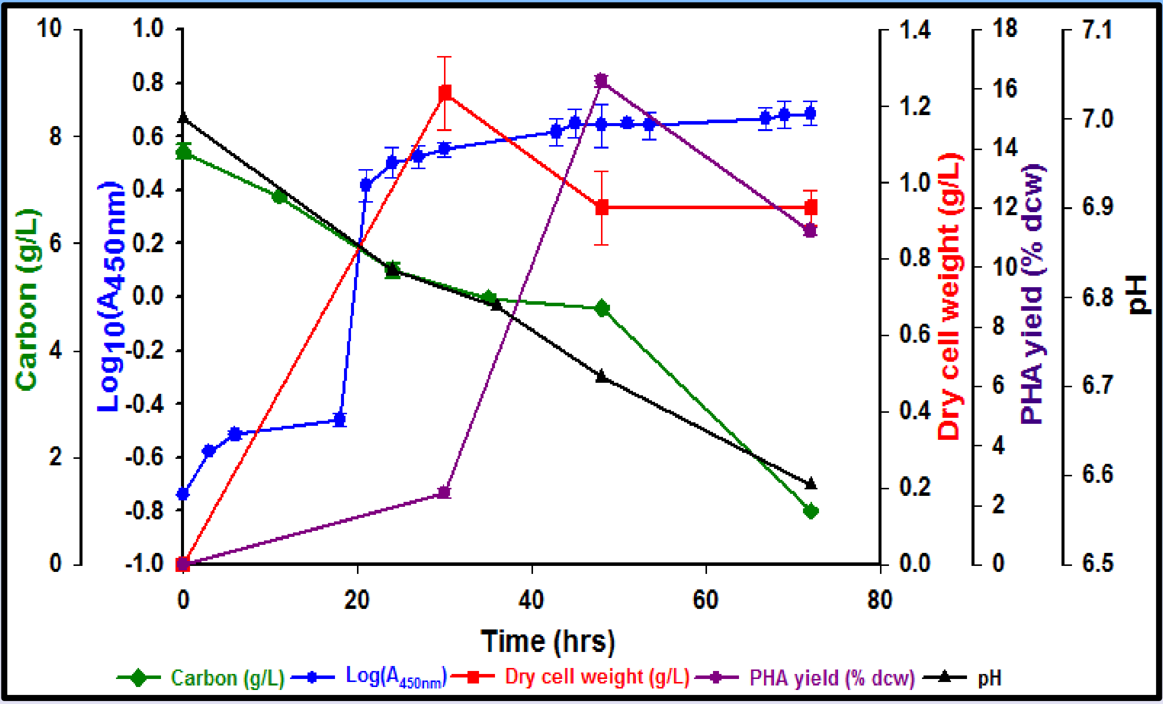
Large scale production of P(3HO-3HHx-3HD) using batch fermentation in MSM media

(Yield 15% dcw)



GLUCOSE as the main Carbon Source

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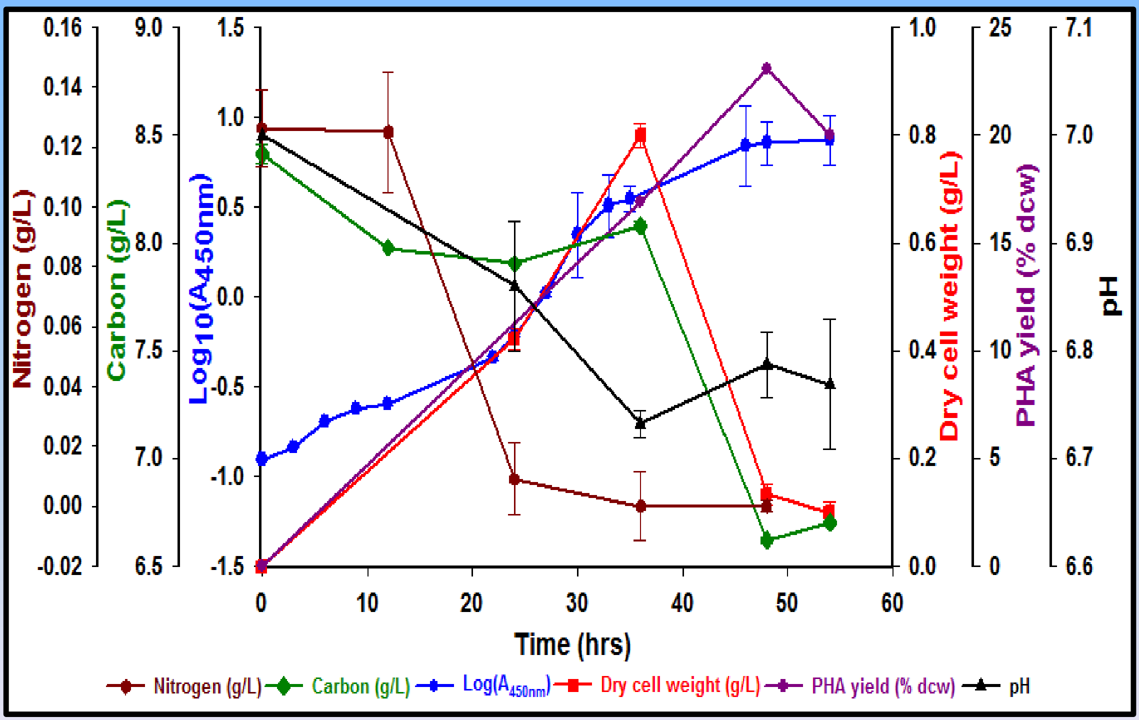
Large scale production of P(3HO-3HB) using batch fermentation in MSM media

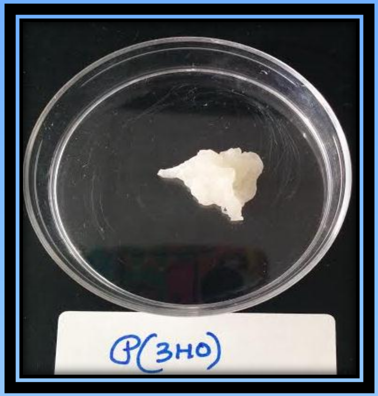
(Yield 23% dcw)

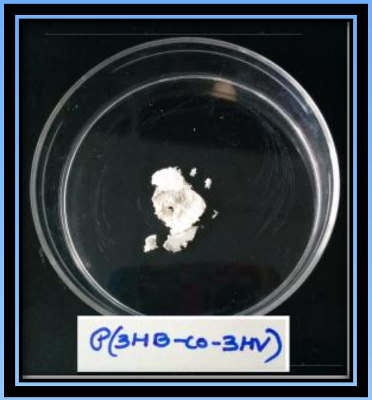


SUCROSE as the main Carbon Source

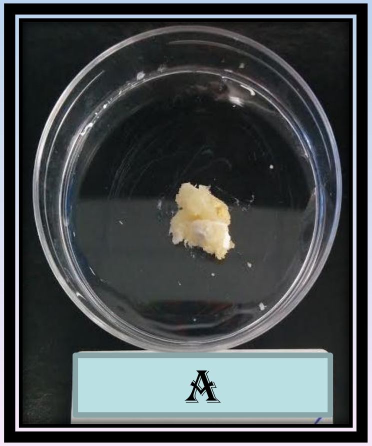
An SCL-MCL COPOLYMER!

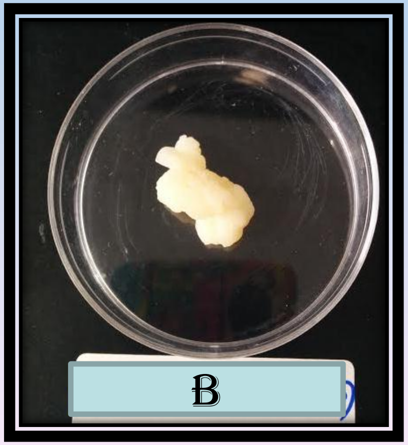
Production of a range of SCL-PHAs and MCL-PHAs

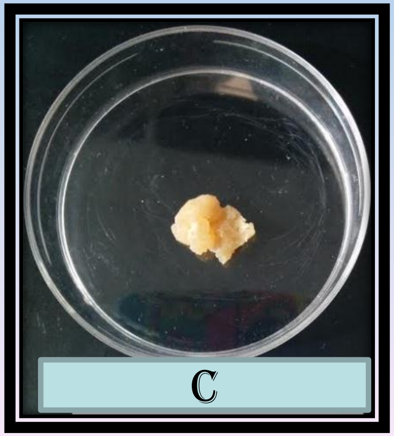


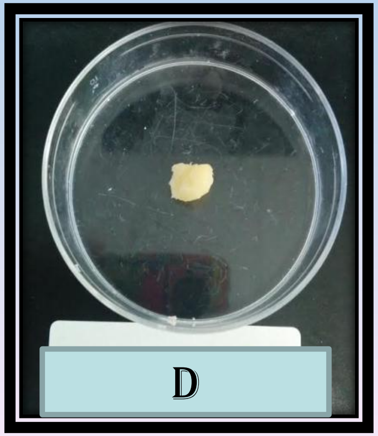


Polyhydroxyalkanoates produced using a range of different carbon sources









PHAs
The new emerging medical materials!

Valappil *et al*., 2006; *Expert Review in Medical Devices* **3(6):** 853-868
Rai *et al*., 2010; Material Science Engineering (Reviews) **72(3)**:29-47
Dubey *et al*., 2014 Novel cardiac patch development using biopolymers and biocomposites; ISBN13: 9780841229907

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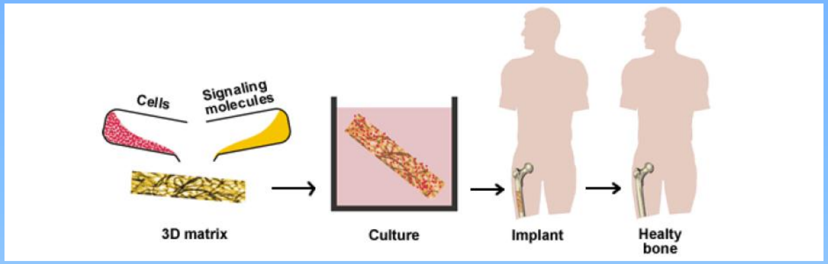
Regulatory Body Approval of Polyhydroxyalkanoates for Medical Applications

❖ **Apr 2, 2007** Tepha, Inc. Receives **FDA Clearance** for TephaFLEX® Absorbable Suture product for marketing in the U.S. TephaFLEX® is the first medical device derived from PHAs developed by Tepha and the MIT.

❖ **May 1, 2009** Tepha, Inc. announced that its corporate partner, Aesculap AG, has received a **CE Mark** and is launching its MonoMax monofilament absorbable suture for general surgical indications in Europe. The product is made with TephaFLEX® fibre.

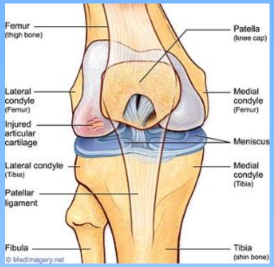
Medical applications of PHAs being explored in my Group

Bone tissue engineering

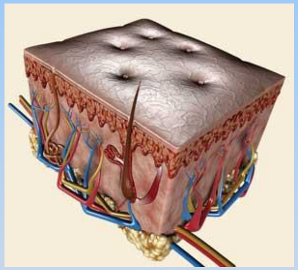


P(3HB) and P(3HB)/Bioglass® composites

Cartilage Tissue Engineering

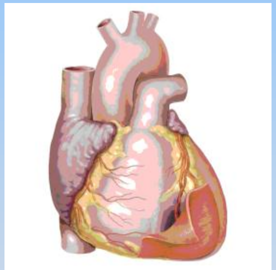


P(3HB)/MFC composites



Skin Tissue Engineering/ Wound Healing

P(3HO)/NanoBioglass Composites



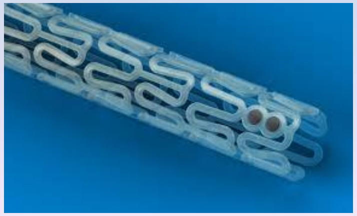
Cardiac Tissue Engineering

P(3HO) and P(3HN-co-3HP)

Drug Delivery

P(3HB)/P(3HB-co3HV)

Medical Device Development:



Biodegradable Drug Eluting Stents

SCL/MCL PHAs

Biodegradable Nerve Conduits

SCL/MCL PHAs

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EPSRC
Pioneering research and skills

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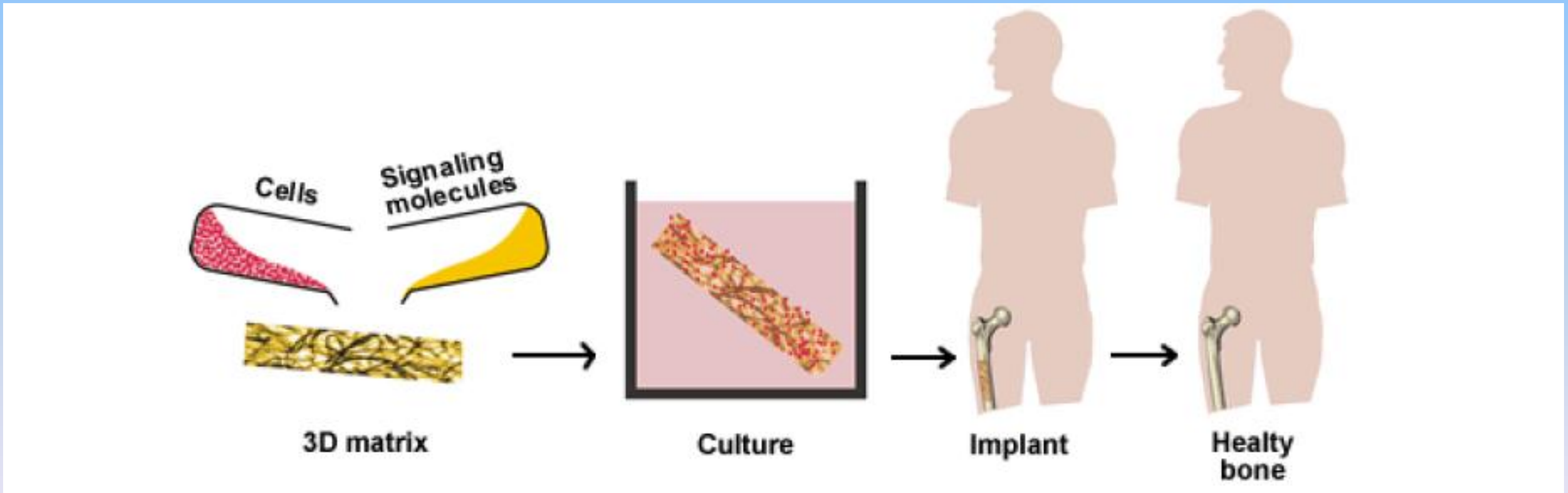
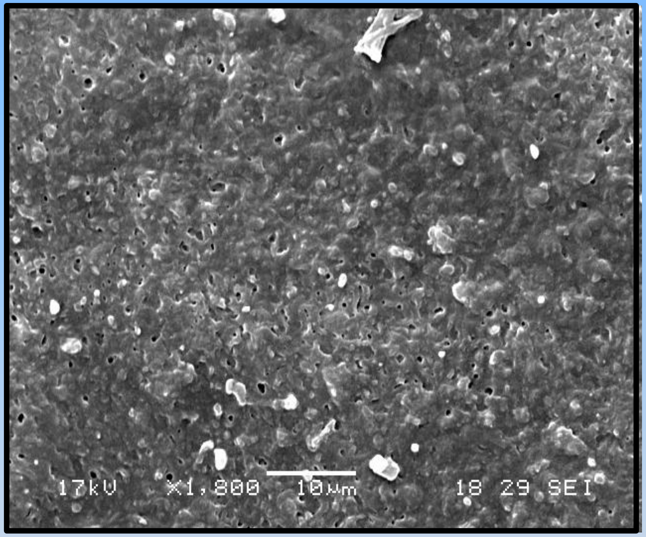
Bone tissue engineering

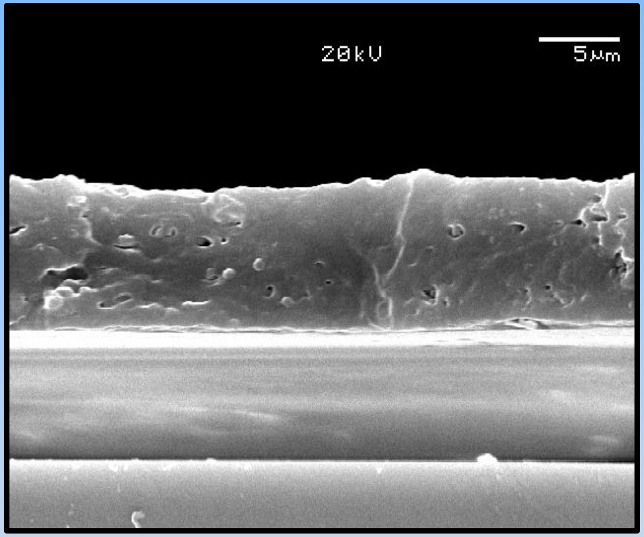


In collaboration with Imperial College London

Production of P(3HB)/Bioglass® composites

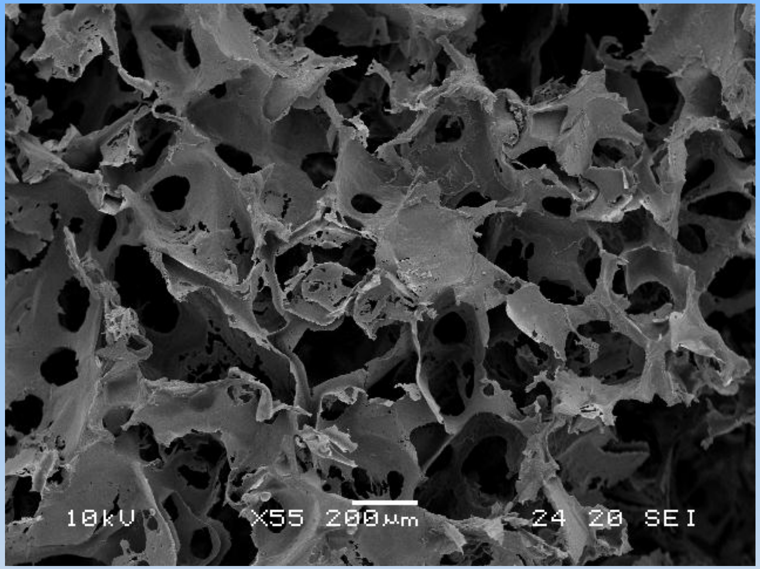


P(3HB)/20 wt% Bioglass® film



Cross section of a P(3HB)/20 wt% Bioglass® film

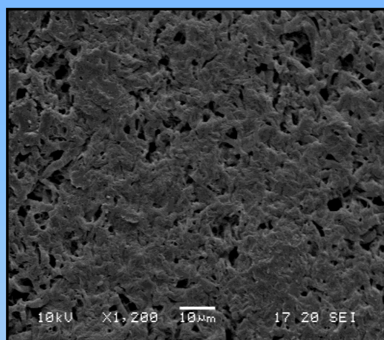
Production of 3D-scaffolds using P(3HB)/Bioglass® composites



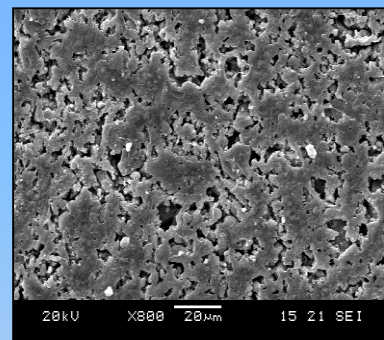
- ❖**Bioglass® is osteoproductive, osteoconductive and osteoinductive**
- ❖**Increased Young's Modulus**
- ❖**Increased Hydrophilicity**

Akaraonye *et al*., unpublished data

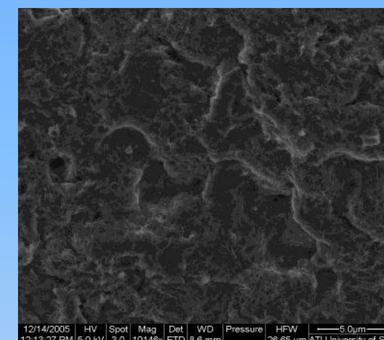
Production of PHA/Bioglass®/CNT composites



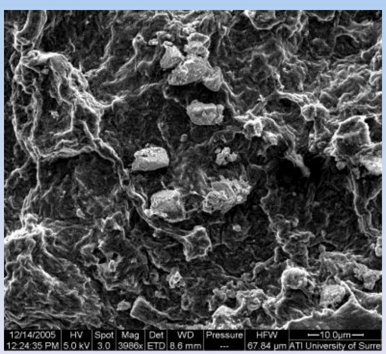
P(3HB)



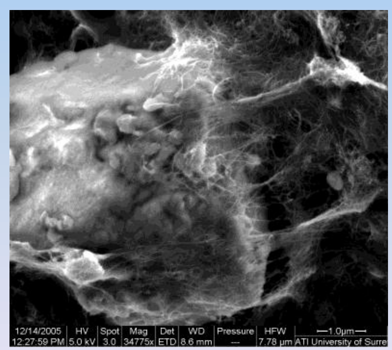
P(3HB)/Bioglass® 40wt%



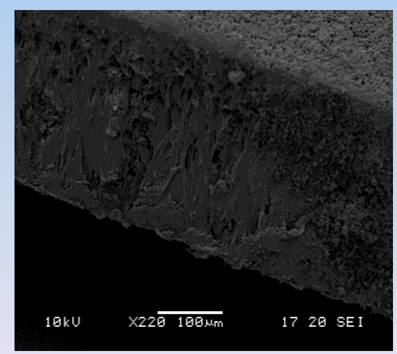
P(3HB)/CNT 2wt%



P(3HB)/CNT 4wt%

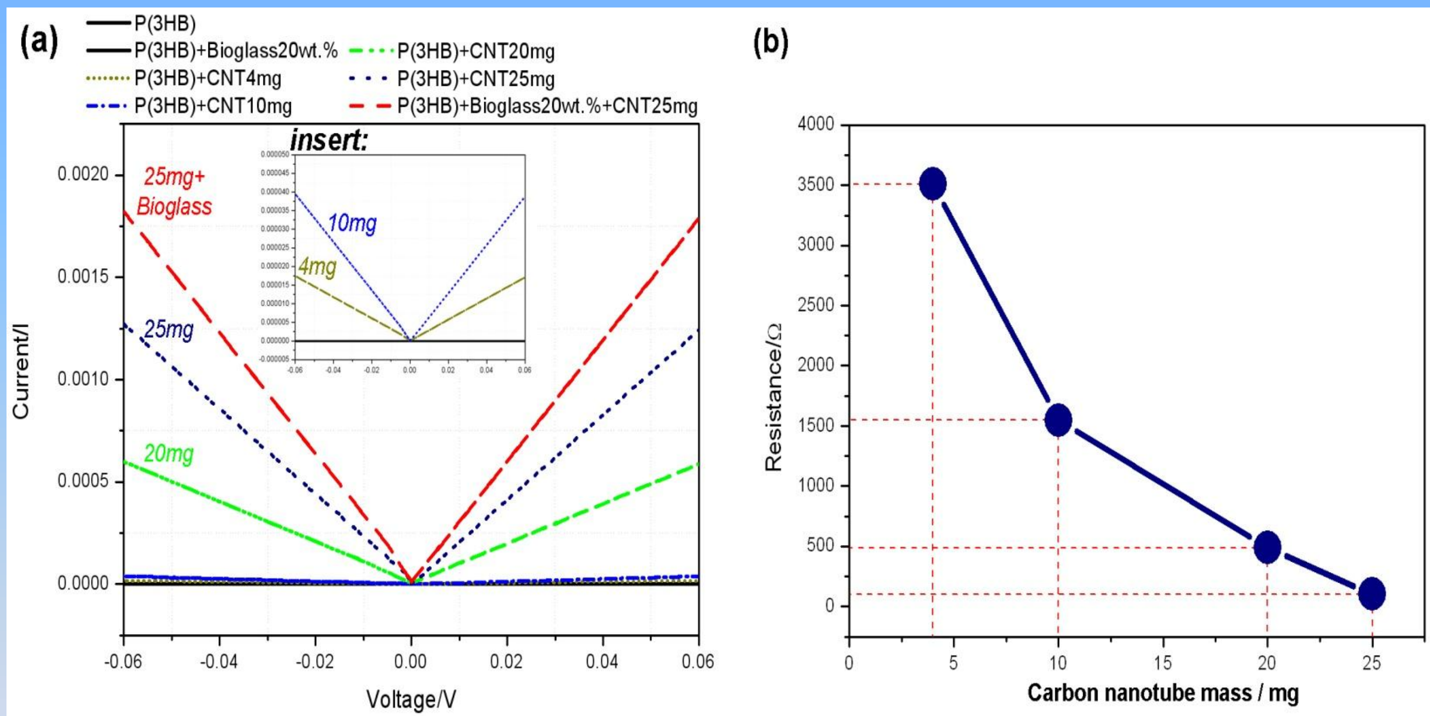


P(3HB)/CNT 7wt%



P(3HB)/Bioglass® 20wt%/CNT 8wt%

Electrical Properties of PHA/Bioglass®/CNT scaffolds

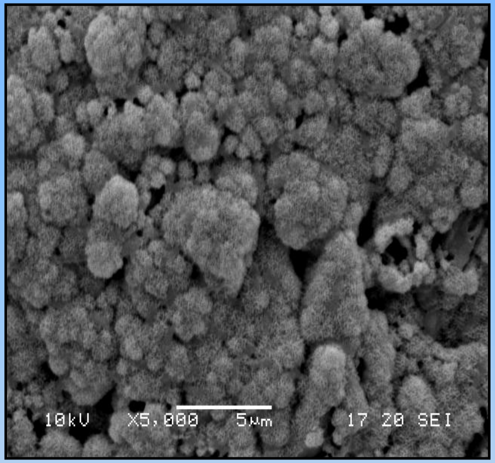


Four-point current-voltage measurements on P(3HB) and P(3HB)-based composites

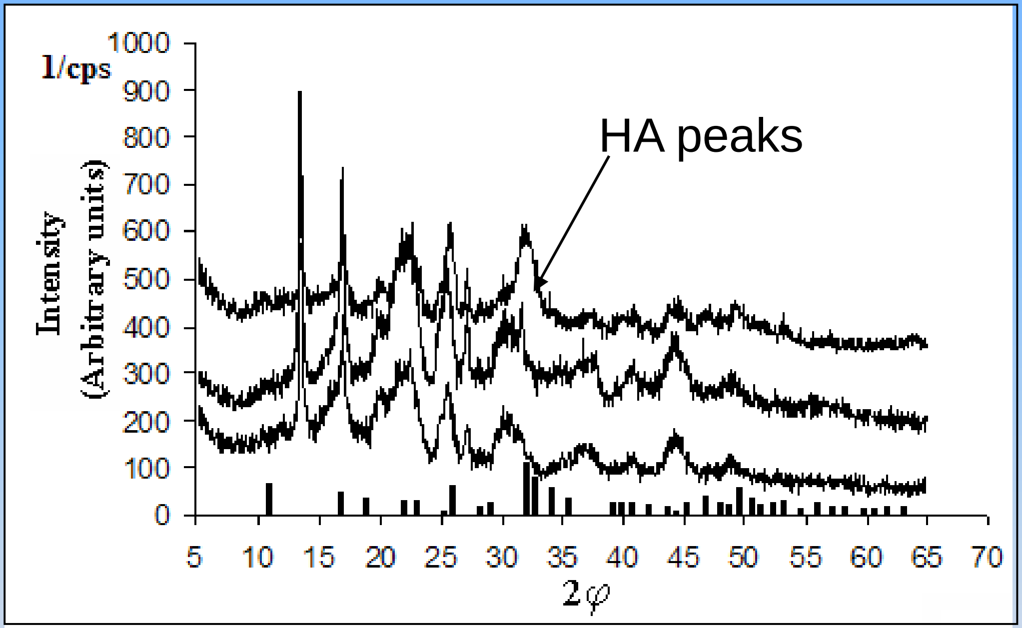
Graph showing the decrease in electrical resistance as a function of carbon nanotube content.

S.K.Misra *et al*., 2007 Nanotechnology 18(7) doi:10.1088/0957-4484/18/7/075701

Acellular bioactivity of PHA/Bioglass®/CNT scaffolds



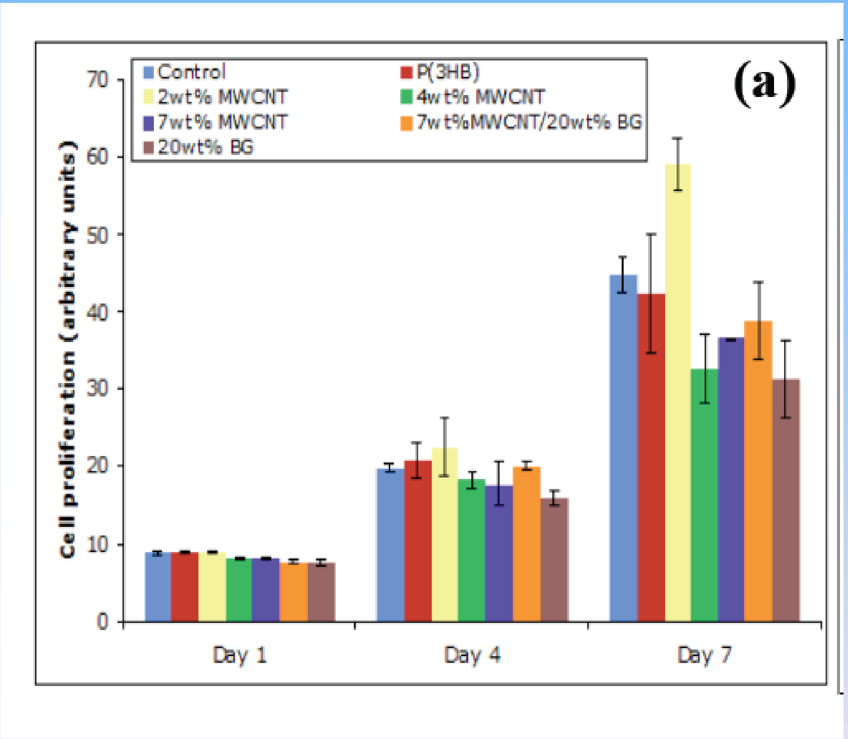
SEM micrograph of the composite showing the formation of hydroxyapatite on the surface of the composite after two months of immersion in SBF

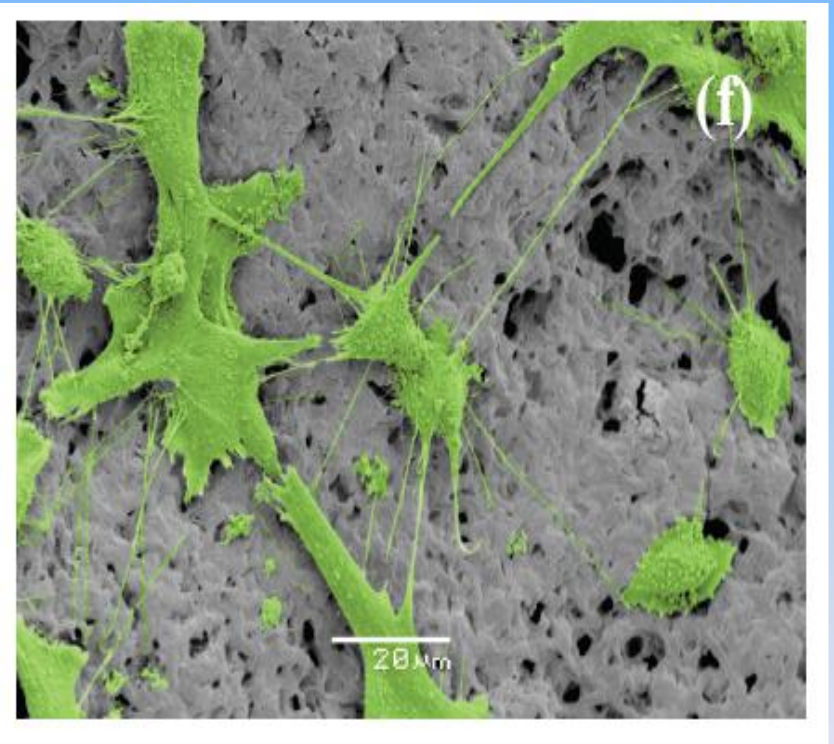


XRD patterns of (a) P(3HB) (b) P(3HB)/Bioglass®/CNT composite (c) P(3HB)/Bioglass®/CNT composite immersed in SBF for two months, showing the emergence of hydroxyapatite peaks marked by the arrow and the indicators.

S.K.Misra *et al*., 2007 Nanotechnology 18(7) doi:10.1088/0957-4484/18/7/075701

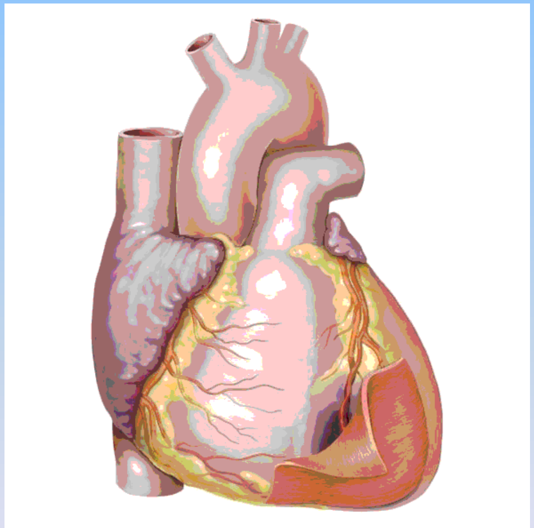
Cellular bioactivity of PHA/Bioglass®/CNT scaffolds





S.K.Misra *et al*., 2009 *Acta Biomaterilia* 6 (3): pp. 735-742.

Cardiac tissue engineering



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British Heart Foundation

Three BHF Funded

National Centres for Cardiovascular Regenerative Medicine

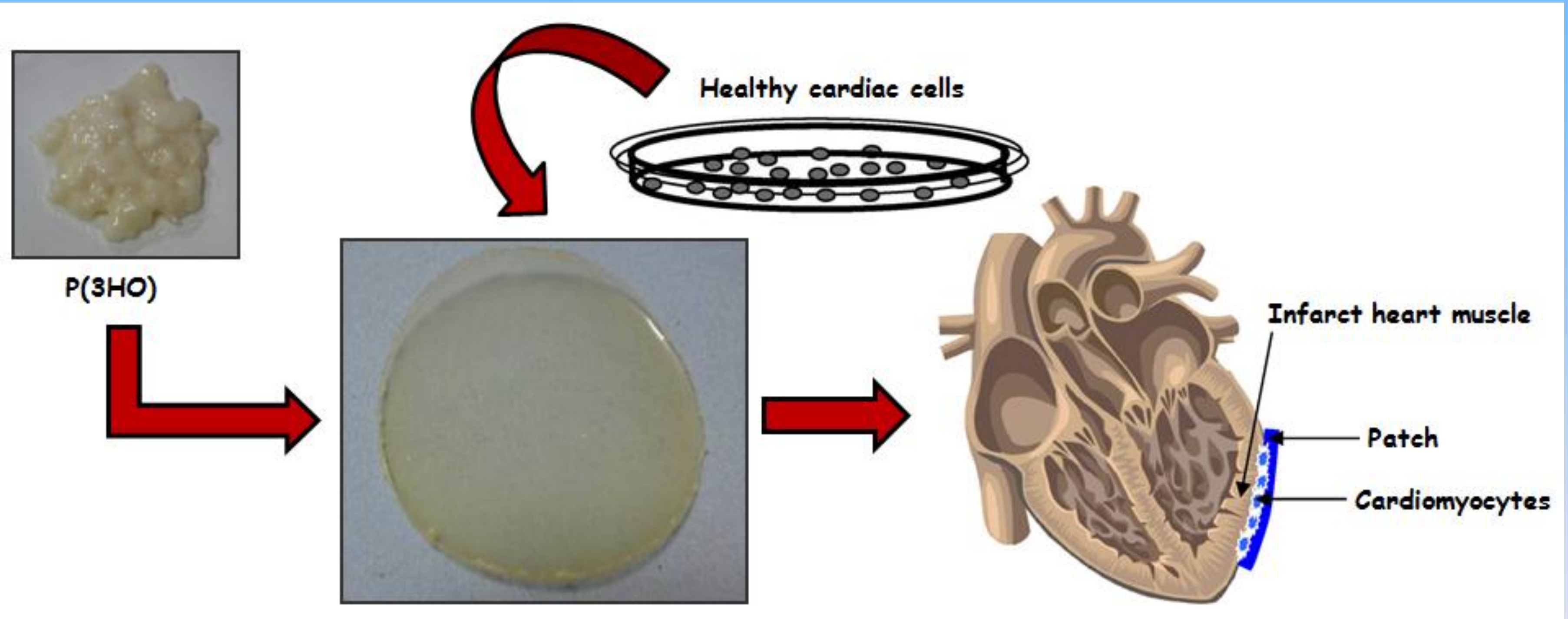
The **Centre at Imperial College London** is led by Professor Sian Harding

Includes: Universities of Westminster, Nottingham, Glasgow and UKE Hamburg.

“Our aim is to reverse the decline in function of the damaged heart by creating fresh muscle in combination with new materials.”

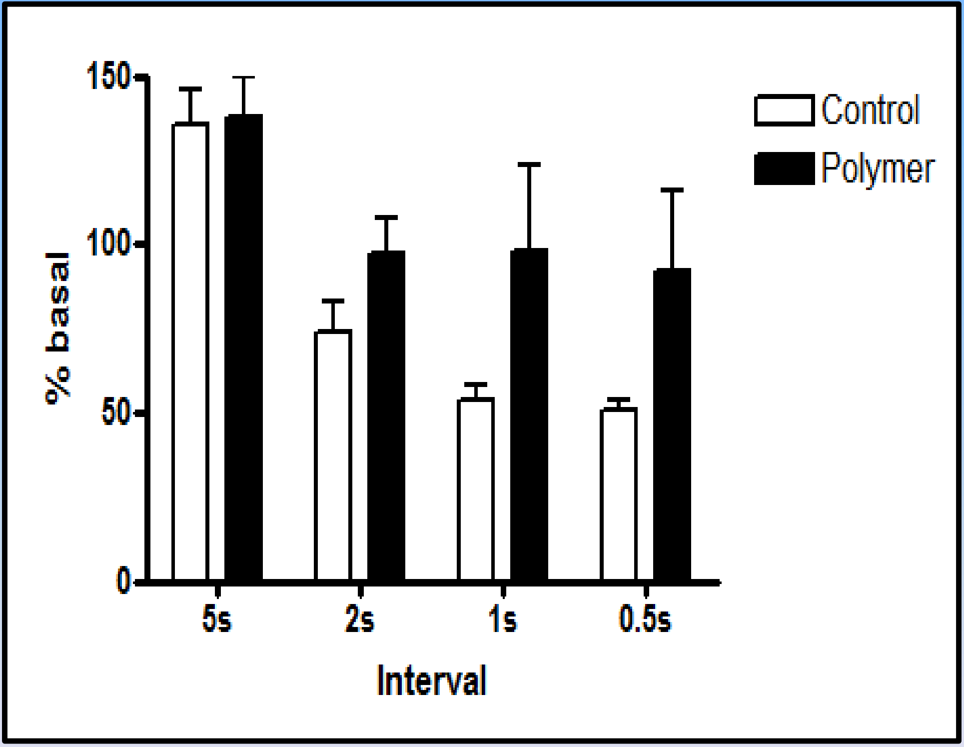
BHF CARDIOVASCULAR REGENERATIVE MEDICINE CENTRE

Cardiac tissue engineering using P(3HO)



Cardiac patches

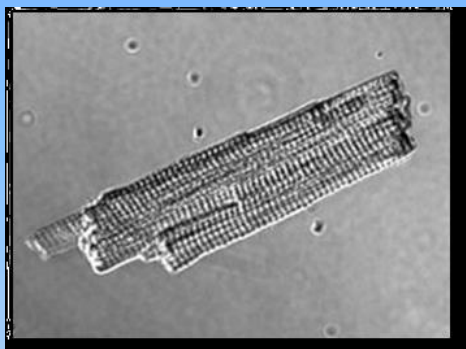
Biocompatibility of the P(3HO) patches

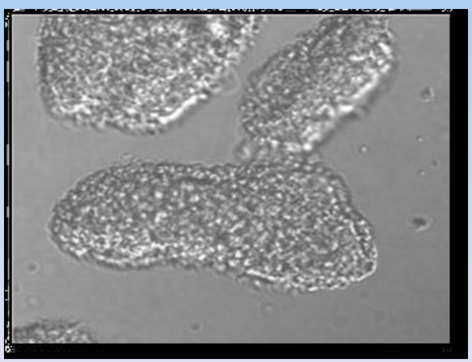


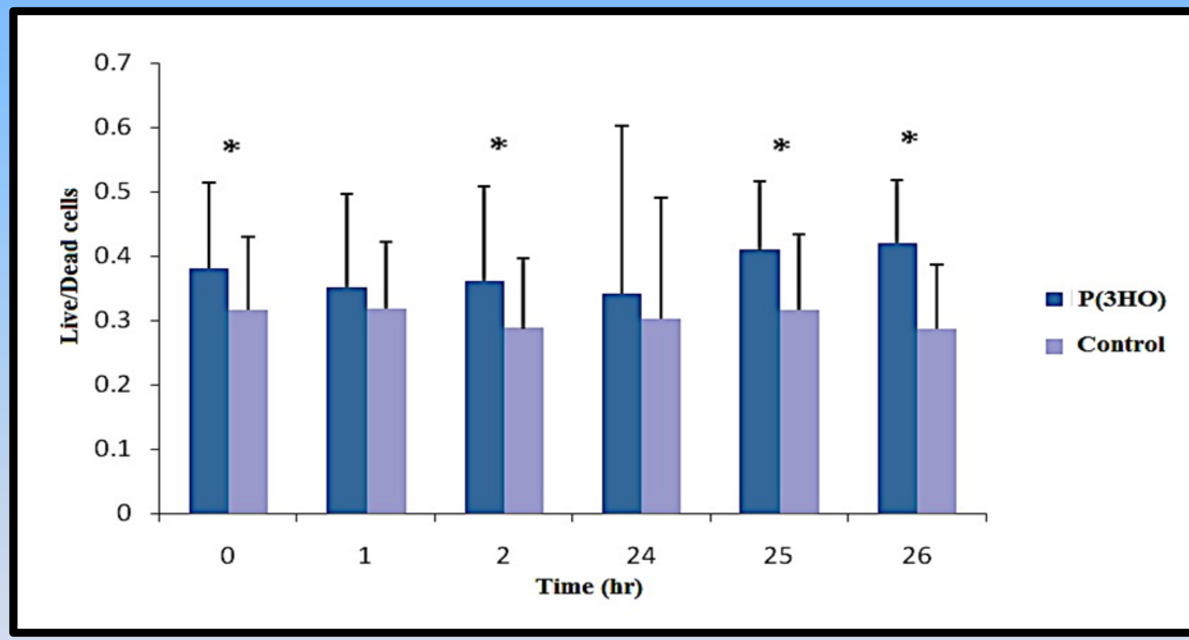
Contraction amplitude (as a percentage of basal) of adult ventricular cardiomyocytes stimulated to beat at different intervals on glass. Differences between control and polymer are not significantly different.

Bagdadi *et al*., 2013, unpublished data

Cardiomyocyte viability on P(3HO)



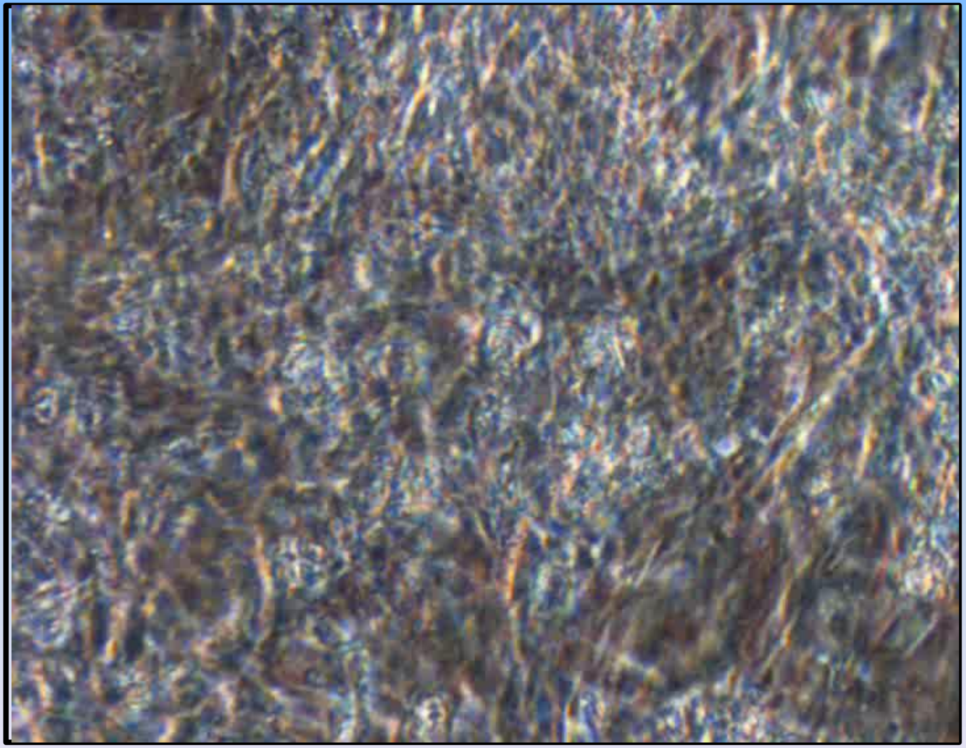




Live/dead rat cardiomyocytes seeded on the P(3HO) film

Bagdadi *et al*., 2013,unpublished data

Cardiomyocytes beating on P(3HO)



Dubey *et al*., 2014,unpublished data

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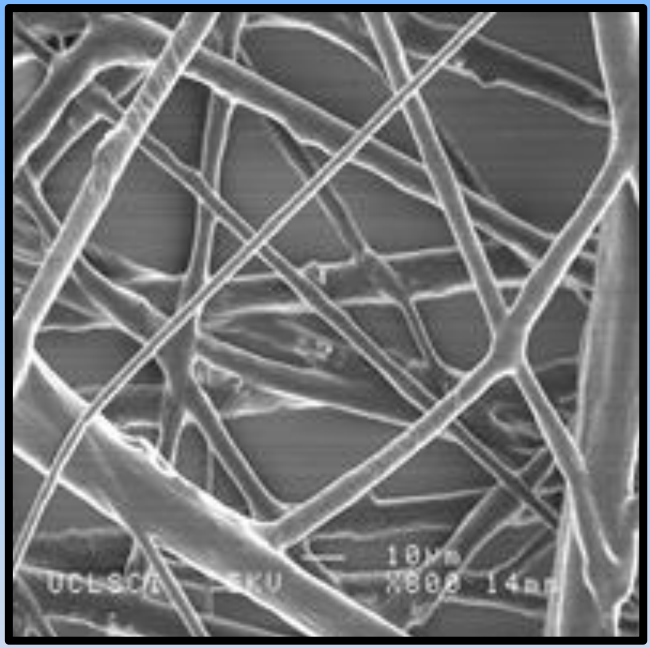
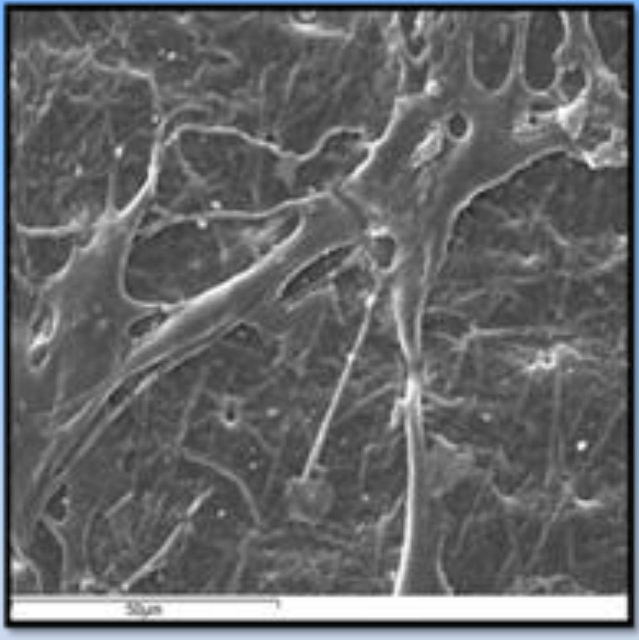
P(3HO) cardiac patches with topography



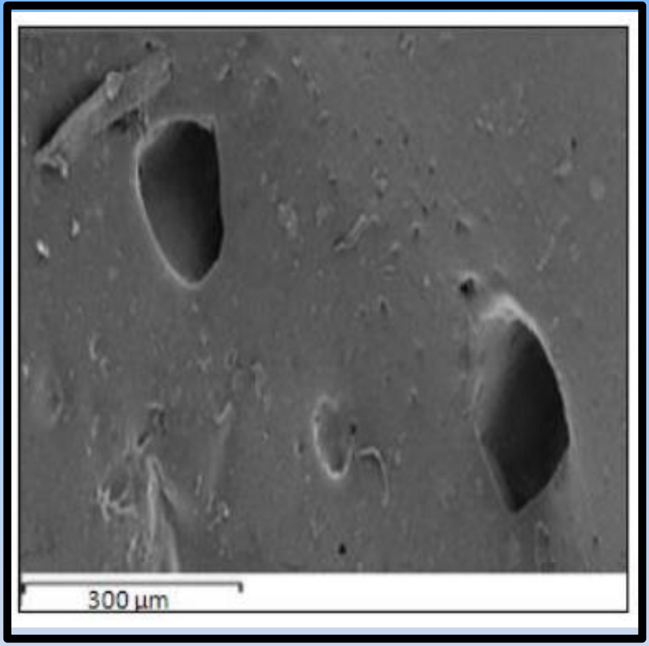
Fibres of P(3HO)



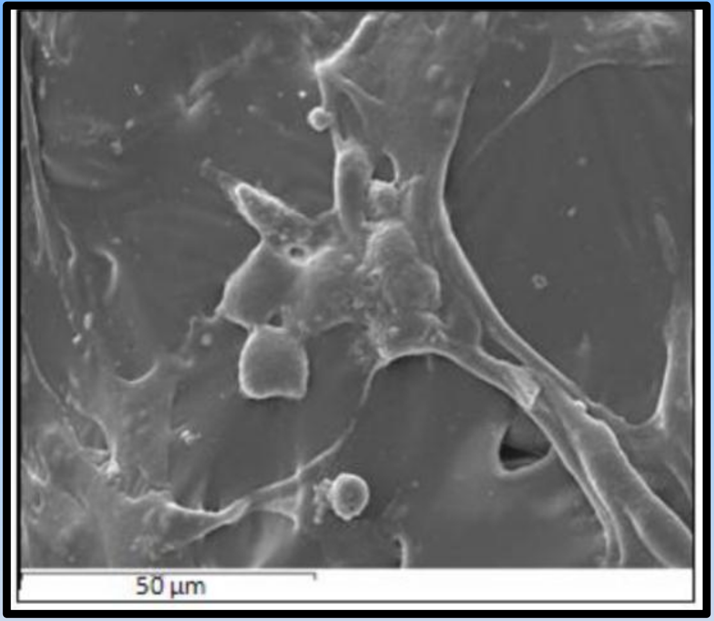
Proliferating C2CL2 cells

Bagdadi *et al*., 2013, unpublished data

P(3HO) cardiac patches with pores



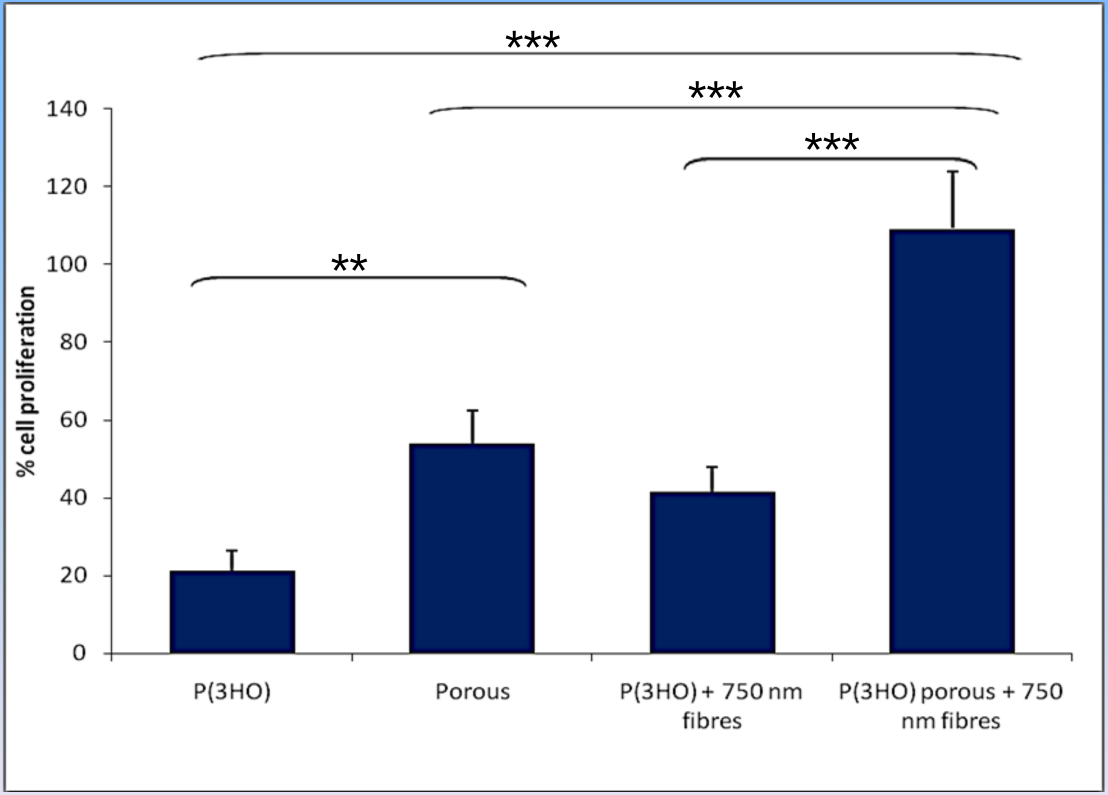
Porous P(3HO) patches



Proliferating C2C12 cells

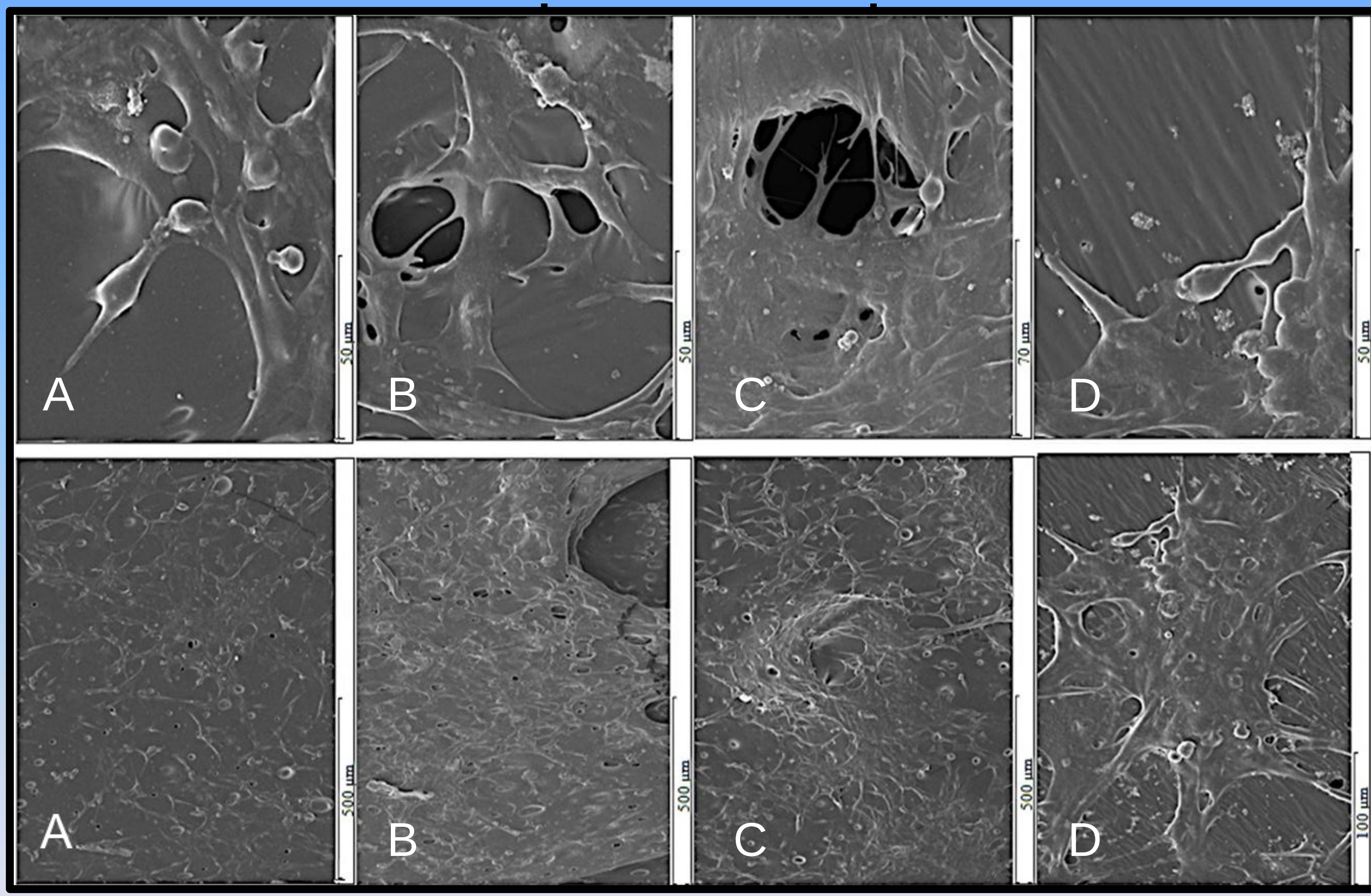
Bagdadi *et al*., 2013, unpublished data

P(3HO) cardiac patches with topography and porosity



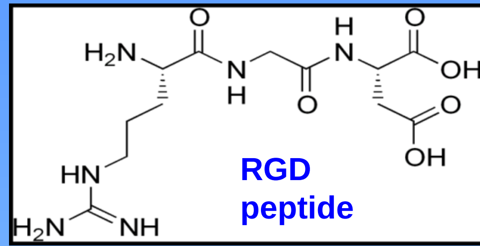
Bagdadi *et al*., 2013, unpublished data
(in collaboration with Professor Mohan Edirisinghe)

P(3HO) cardiac patches with porosity

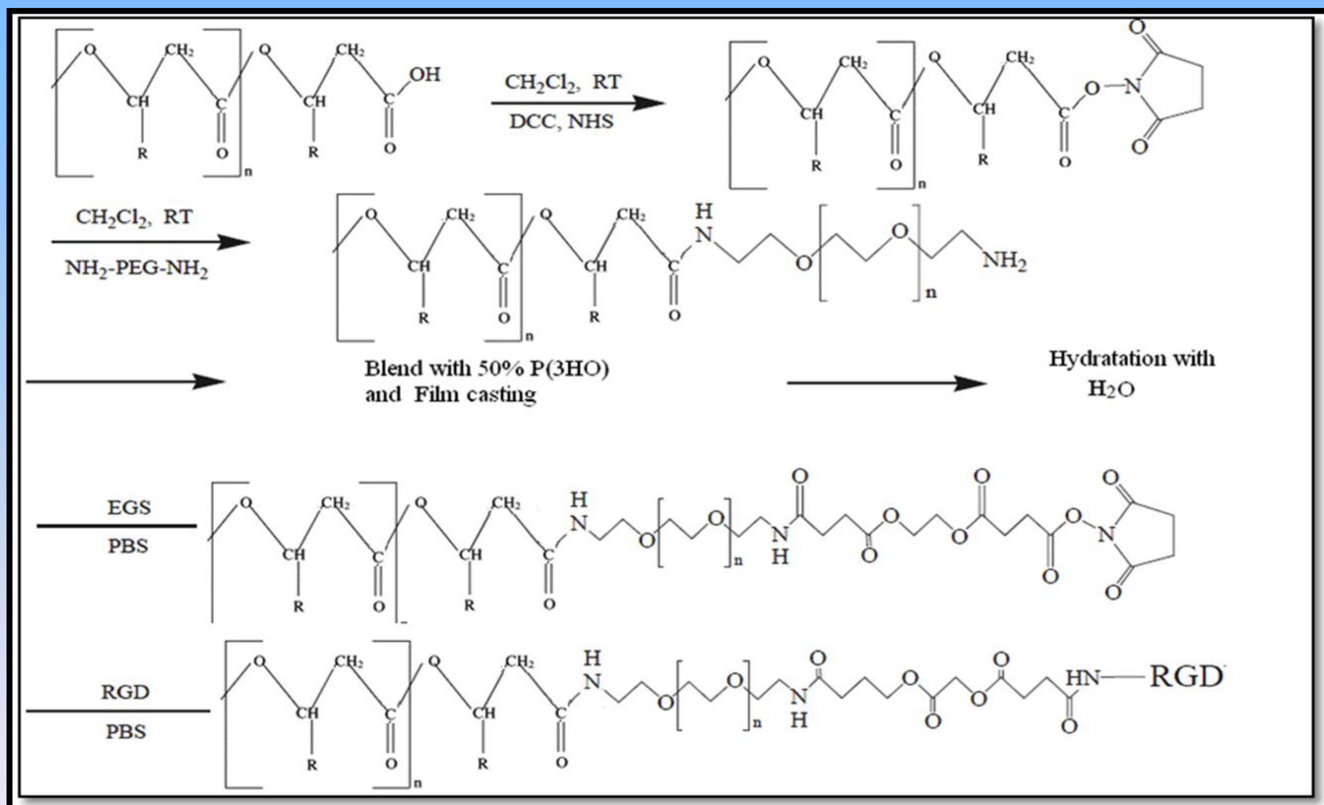


SEM images of C2C12 myocyte growth
A: neat; B: porous; C: neat with fibres; D porous with fibres

Bagdadi *et al*., 2013, unpublished data



RGD immobilisation on P(3HO) cardiac patches



Synthetic scheme of the RGD peptide immobilization

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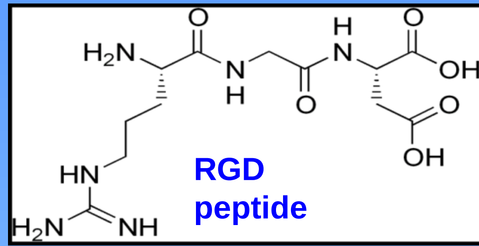
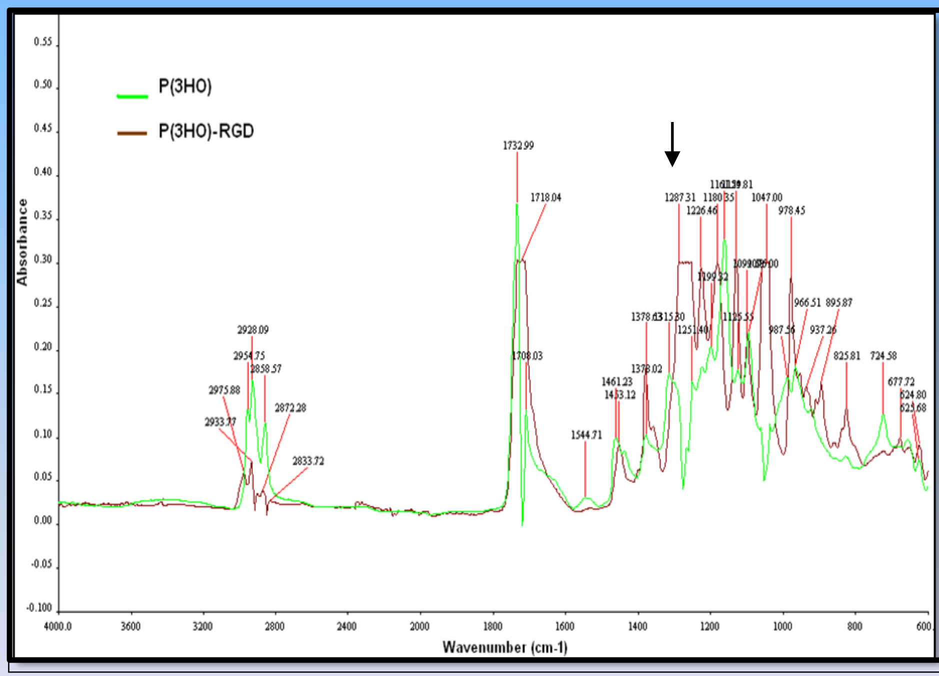
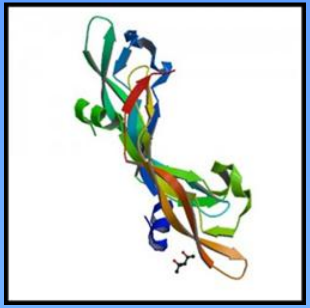


RGD immobilisation on P(3HO) cardiac patches

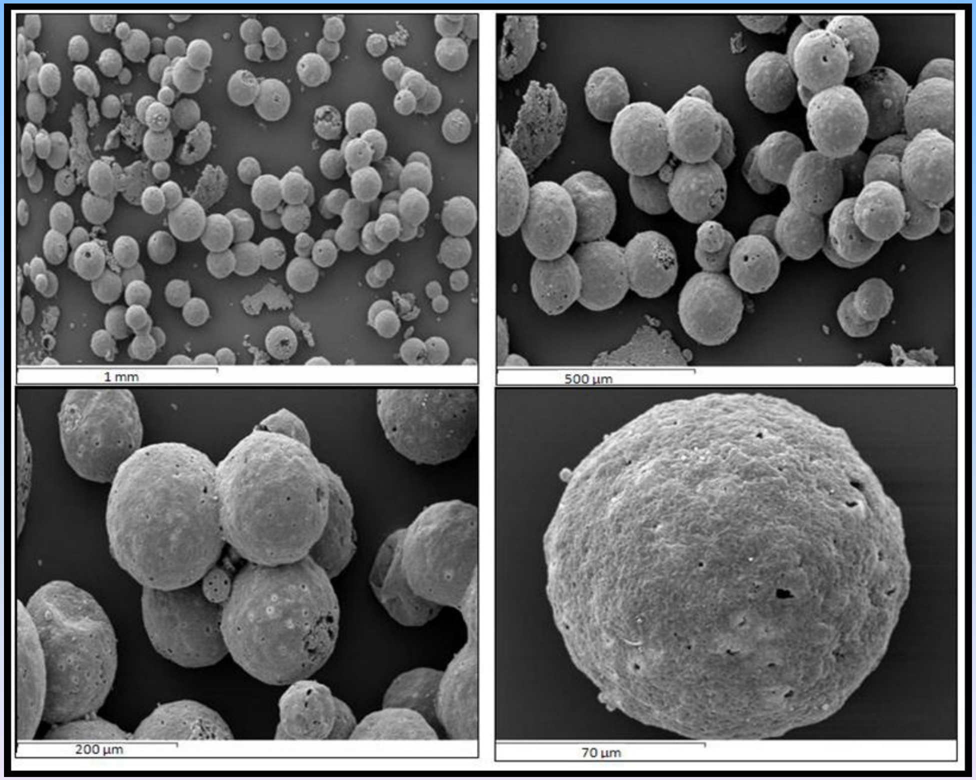


FTIR spectra of P(3HO) polymer vs. P(3HO)-RGD

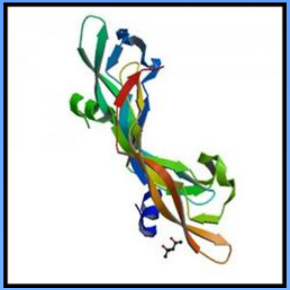
(The arrow at 1200 cm^{-1} indicates the C-N bond)



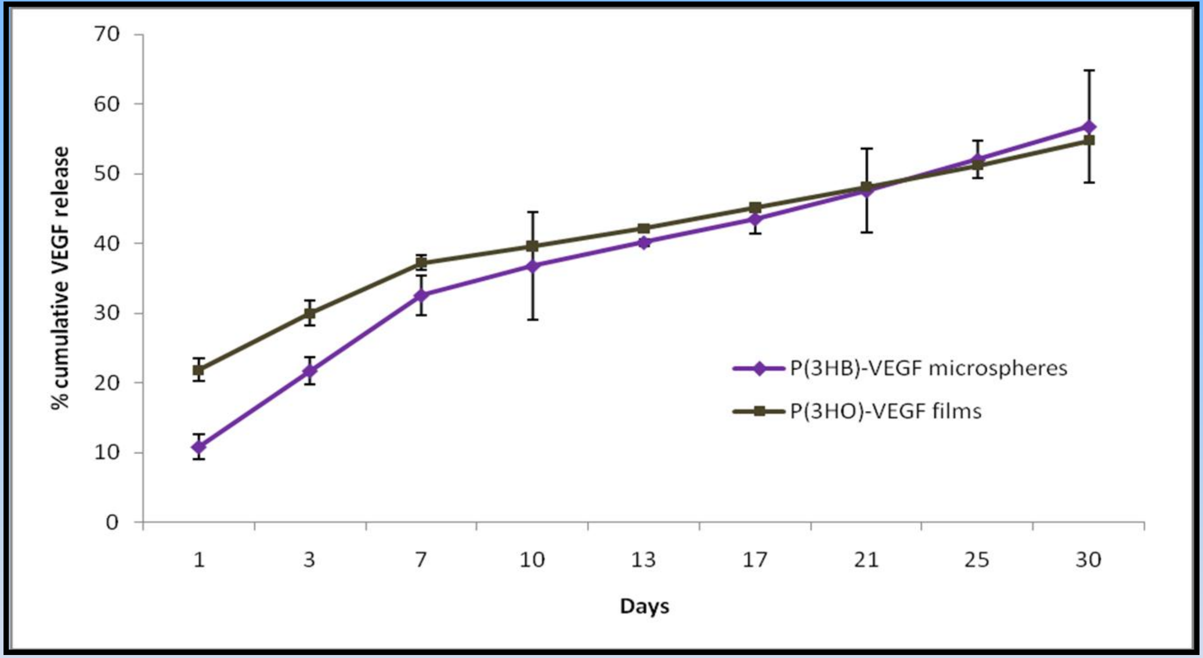
VEGF encapsulation in P(3HB) microspheres



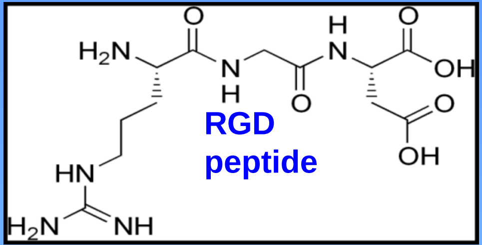
SEM images of P(3HB) microspheres, containing VEGF



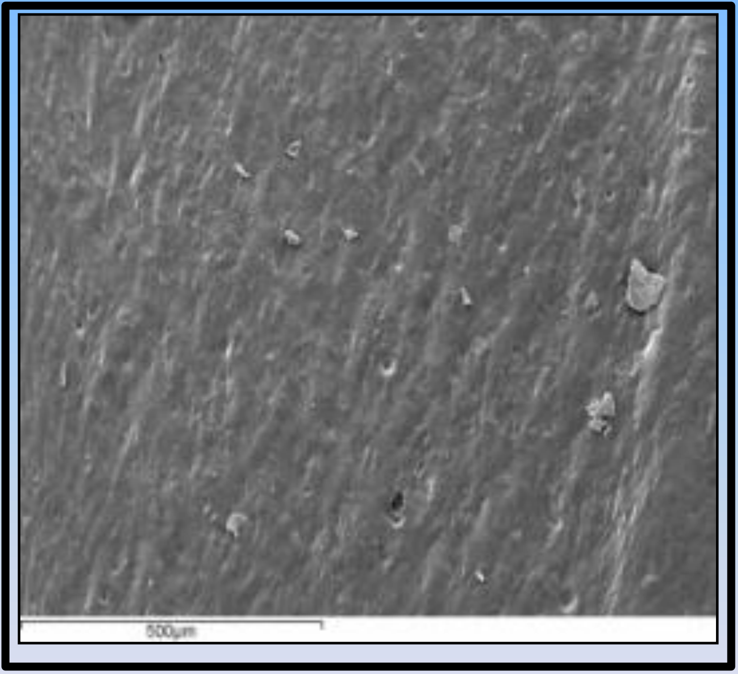
VEGF encapsulation



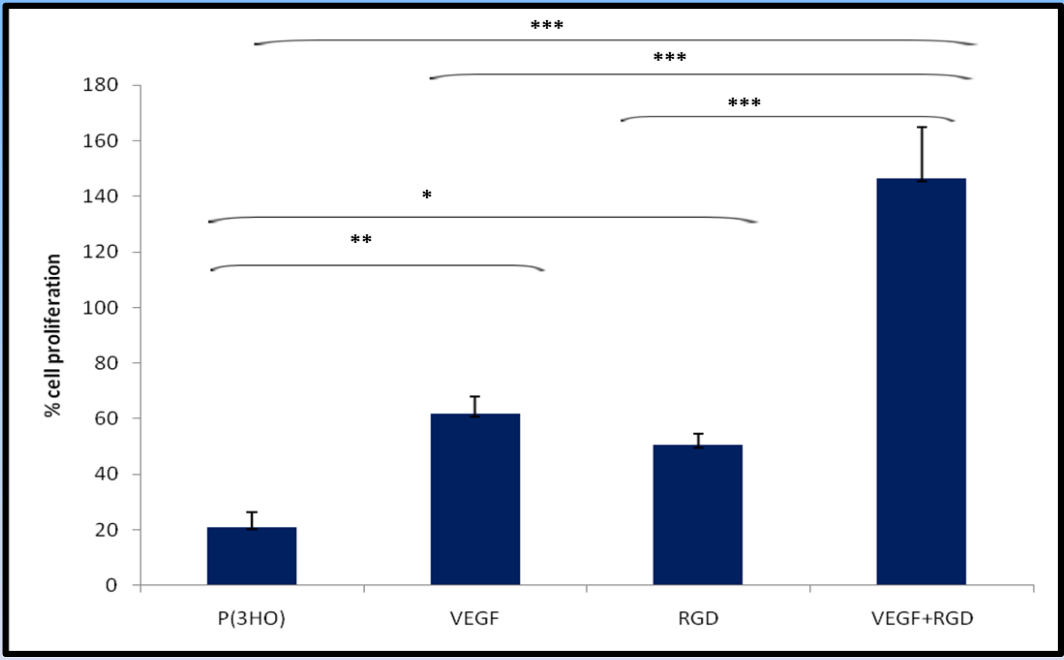
Release profile of VEGF from P(3HB) microspheres and P(3HO) films



P(3HO) cardiac patches with RGD peptide and VEGF



SEM images of RGD and VEGF containing P(3HO) film



% Cell proliferation of C2C12 cell line at 24 hr

Bagdadi *et al*., 2013, unpublished data

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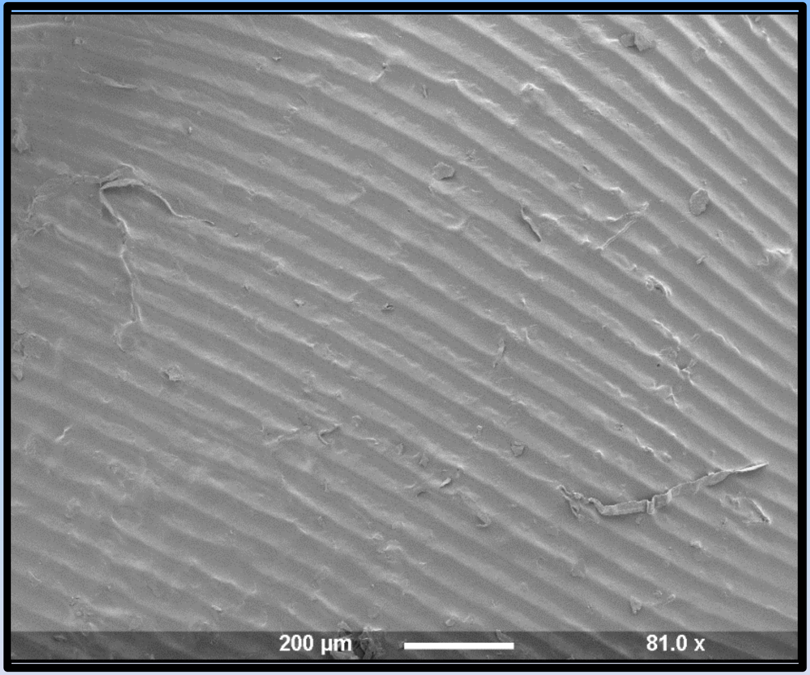
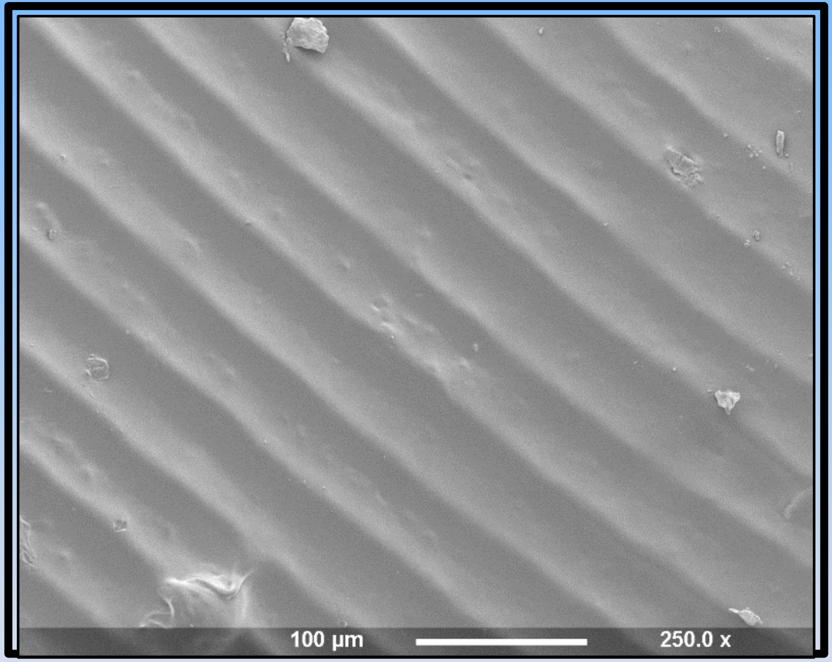
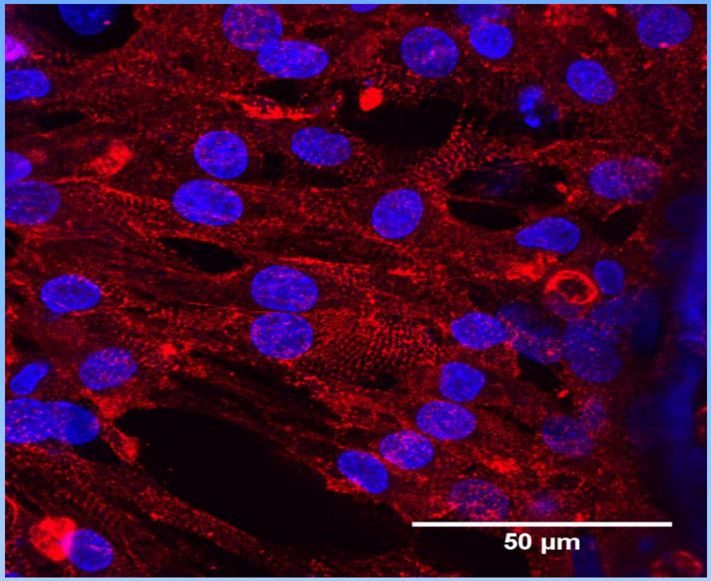
Laser Micro-patterned P(3HO)

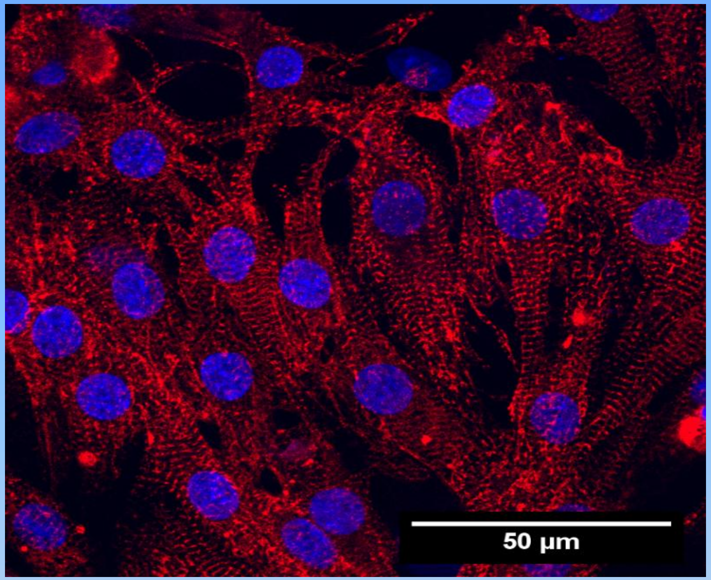




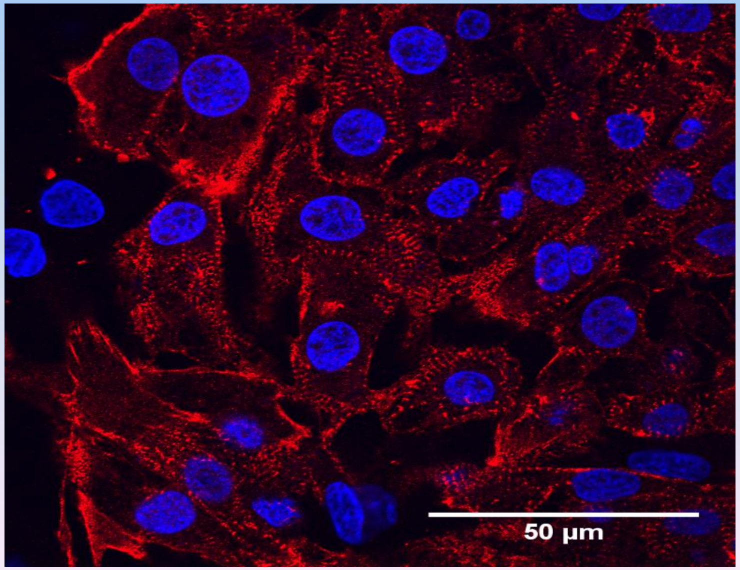
Dubey *et al*., 2015, unpublished data

Laser Micro-patterned P(3HO)





Patterned P(3HO) construct



Unpatterned P(3HO) construct

Dubey *et al*., 2015, unpublished data

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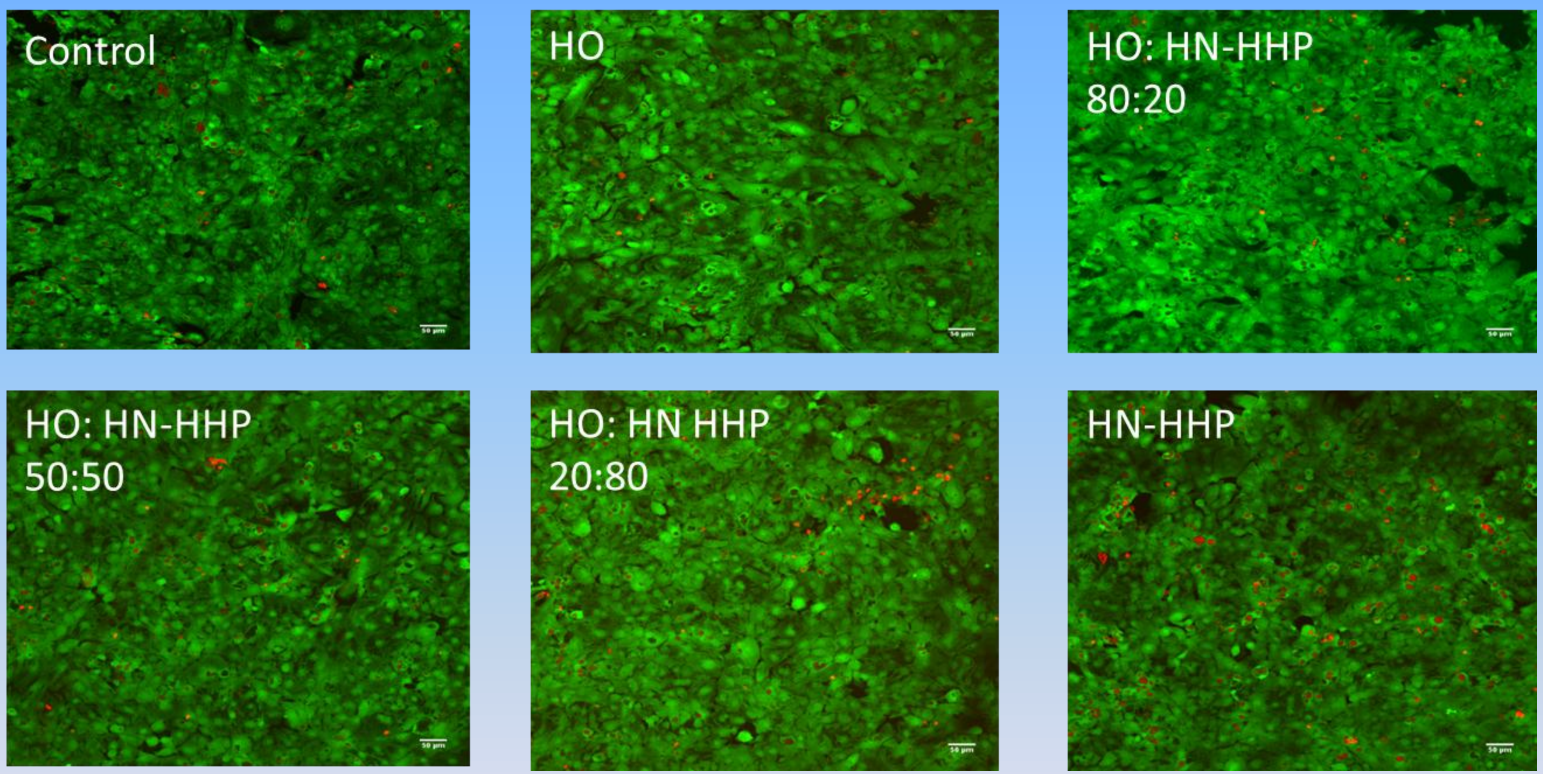
hiPSC-CM on P(3HO)/P(3HN-co-3HHP) blends

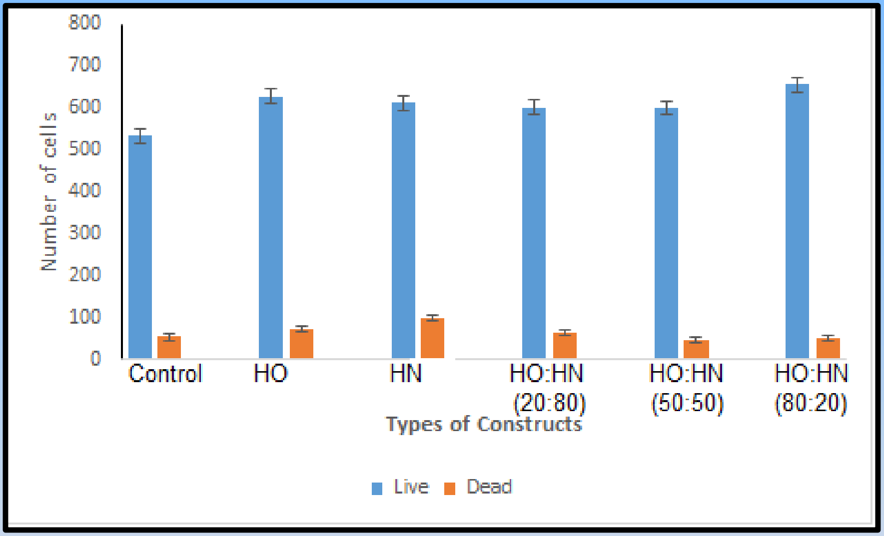


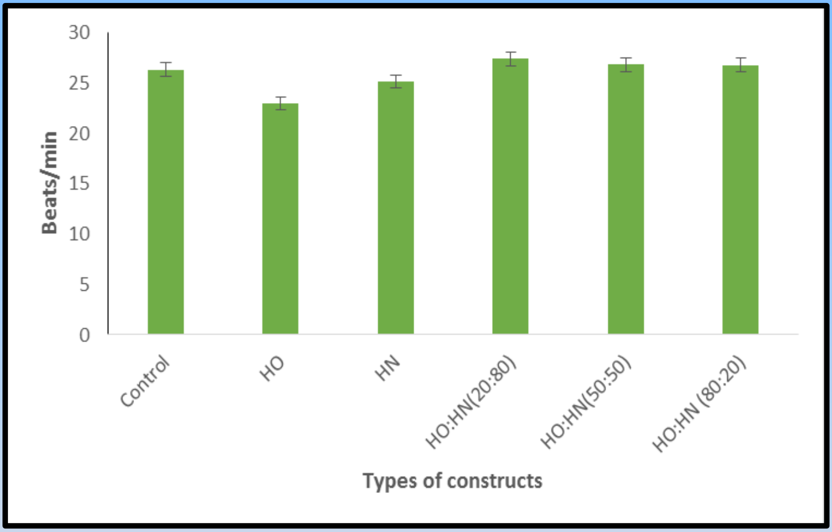
Live (green) and dead (red) hiPSC-CM cells as grown on control, P(3HO), P(3HO):P(3HN-3HHP)[20:80], P(3HO):P(3HN-3HHP) [50:50], P(3HO):P(3HN-3HHP)[80:20].

Dubey and Humphrey *et al*., 2014, unpublished data

(In collaboration with Professor Harding and Professor Terracciano)

hiPSC-CM on P(3HO)/P(3HN-co-3HHP) blends



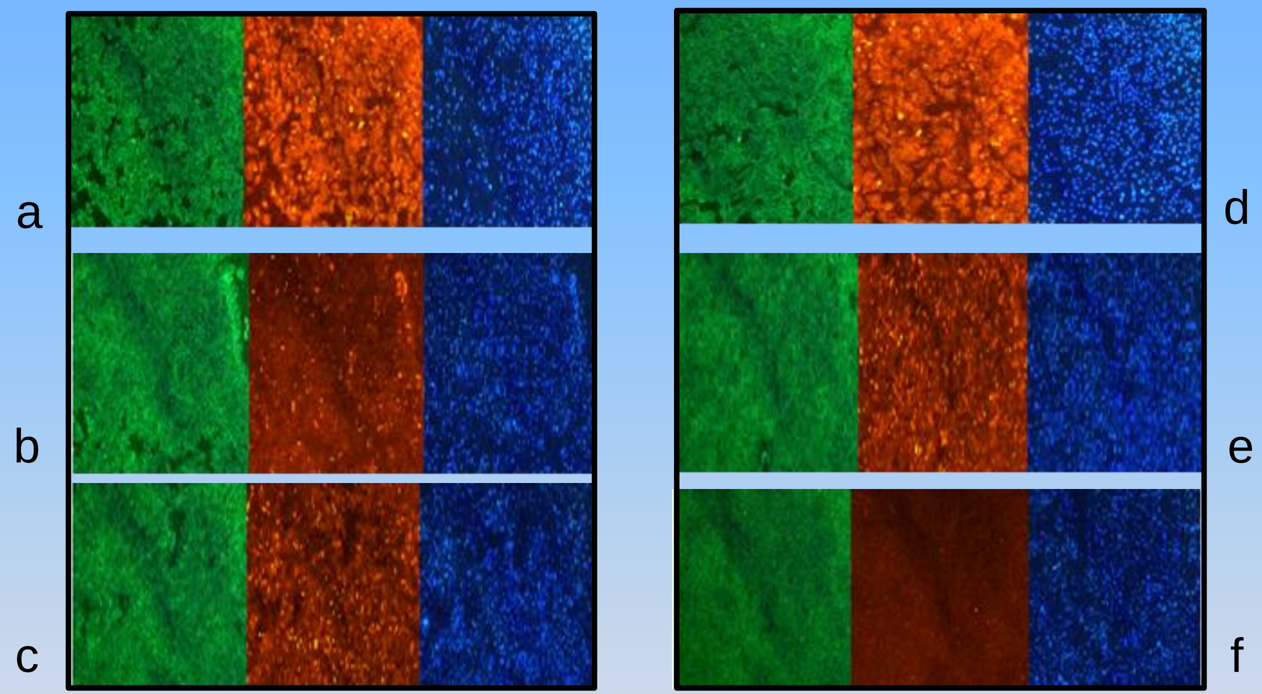


Live/Dead Assay

Beat Rate Measurement

Dubey and Humphrey *et al*., 2014, unpublished data
(In collaboration with Professor Harding and Professor Terracciano)

hiPSC-CM on P(3HO)/P(3HN-co-3HHP) blends



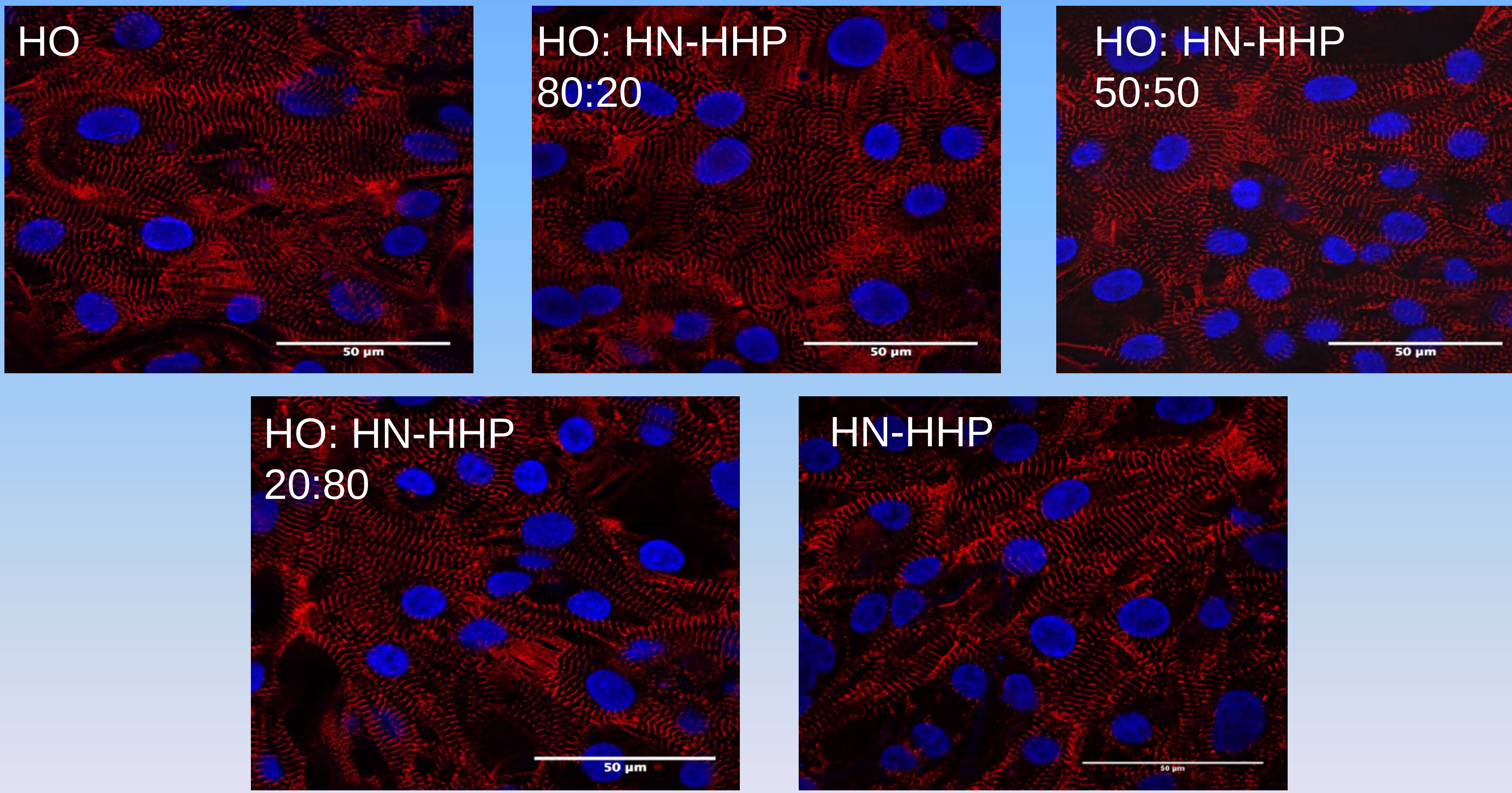
Immunofluorescence detection

F-actin (green), Myosin heavy chain (MHC) (red) and nuclei (blue)

*(*a) gelatin control (b)P(3HO) scaffolds (c) P(3HN-co-3HP) scaffolds. (d) P(3HO)/P(3HN-co-3HP) blend (80:20) (e) P(3HO)/P(3N-co-3HP) blend (50:50) (f) P(3HO)/P(3N-co-3HP) blend (20:80).

Dubey and Humphrey *et al*., 2014, unpublished data

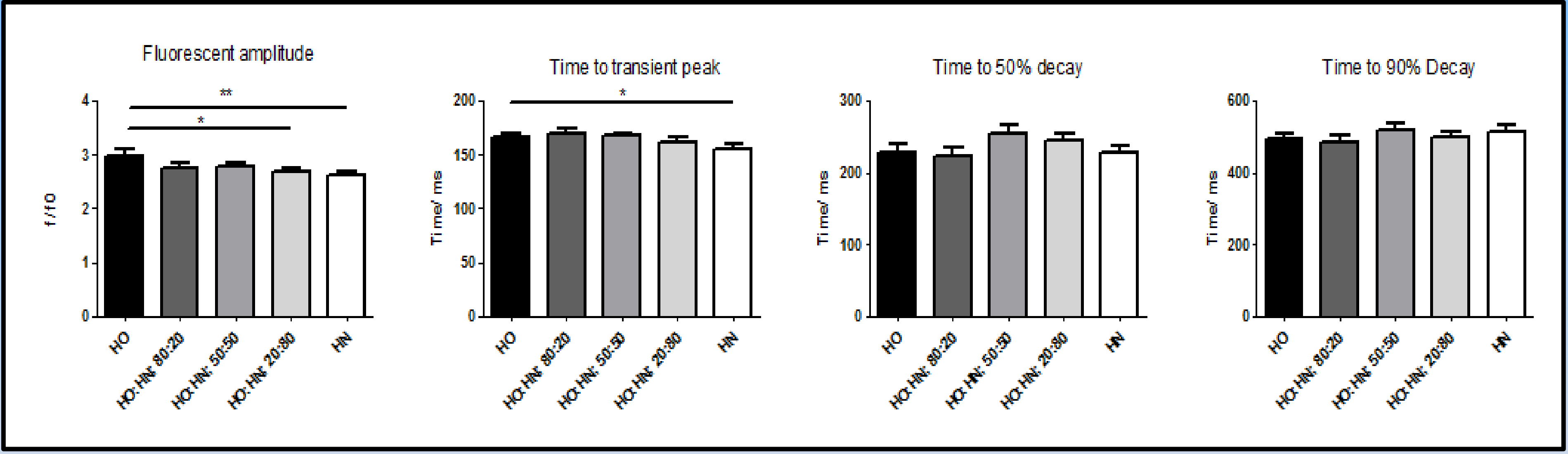
hiPSC-CM on P(3HO)/P(3HN-co-3HHP) blends



Sarcomere and nuclei staining

Dubey and Humphrey *et al*., 2014, unpublished data

Calcium transients of hiPSC-CMs on P(3HO)/P(3HN-co-3HHP) blends



n=6 constructs (5 areas each), 3 experiments

Humphrey and Dubey *et al.*, 2014, unpublished data
(In collaboration with Professor Harding and Professor Terracciano)

Cartilage tissue engineering

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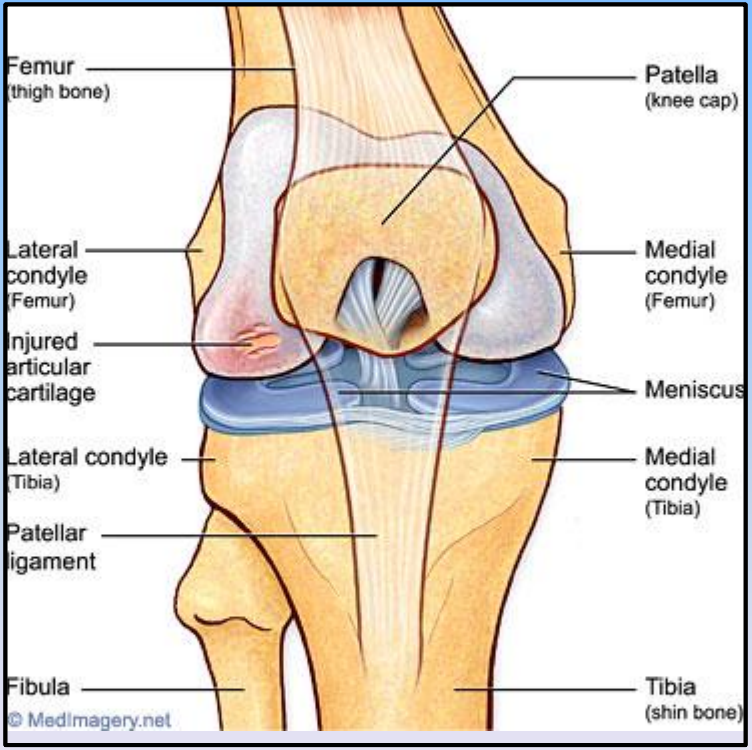
P(3HB)/MFC composites for cartilage tissue engineering



Cartilage is prone to loss and degeneration due to age and injury, especially sports related injuries. Hence, in this work we aimed towards the development of novel materials for cartilage tissue engineering

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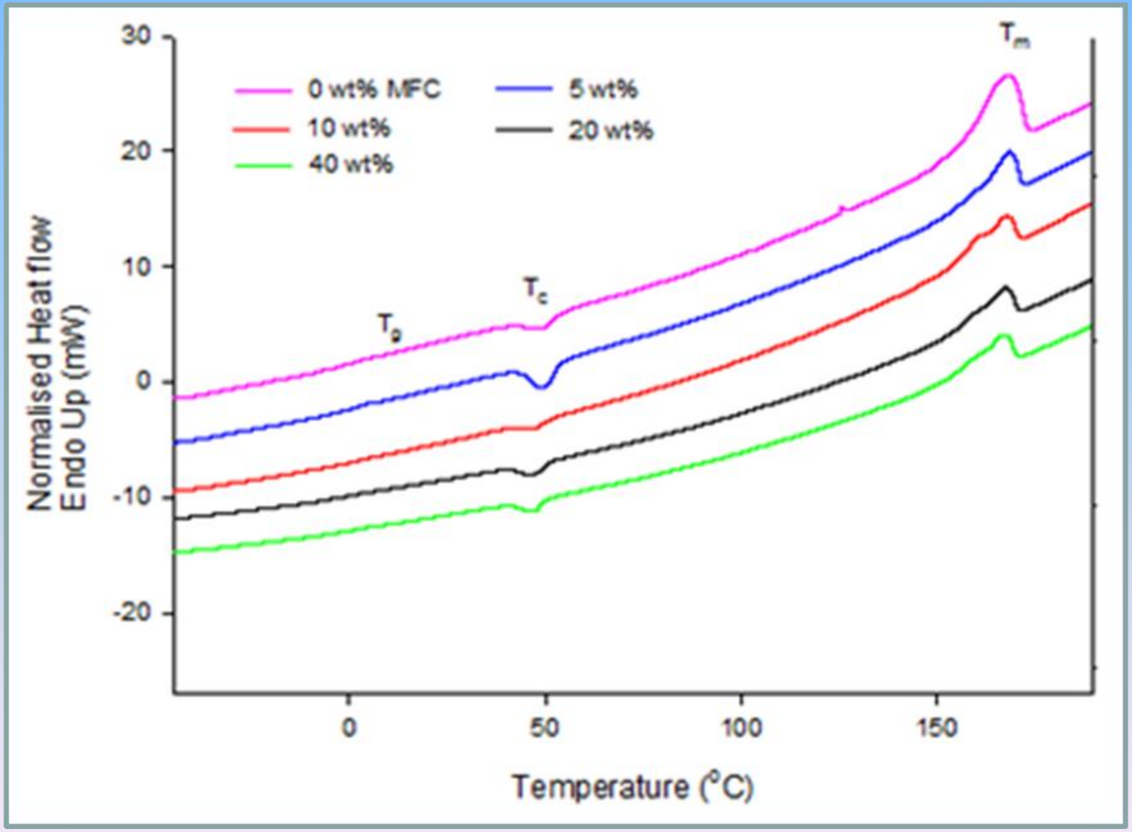
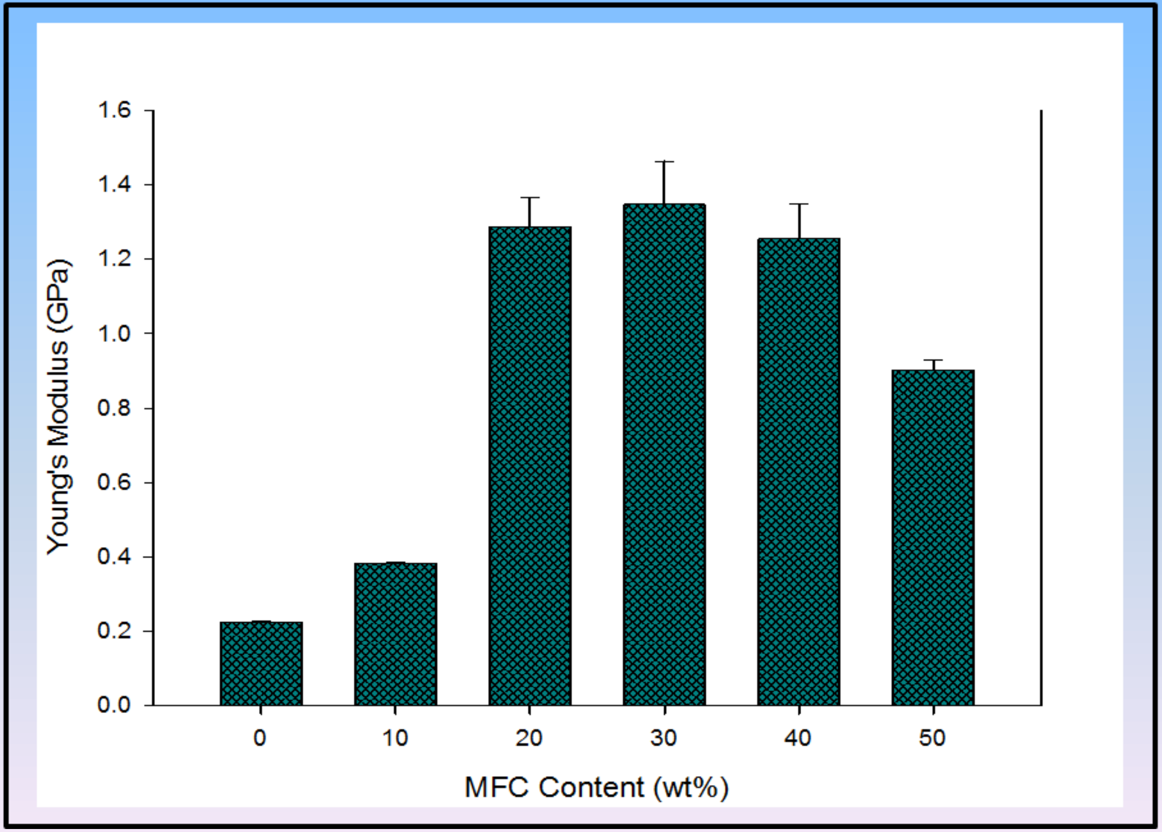
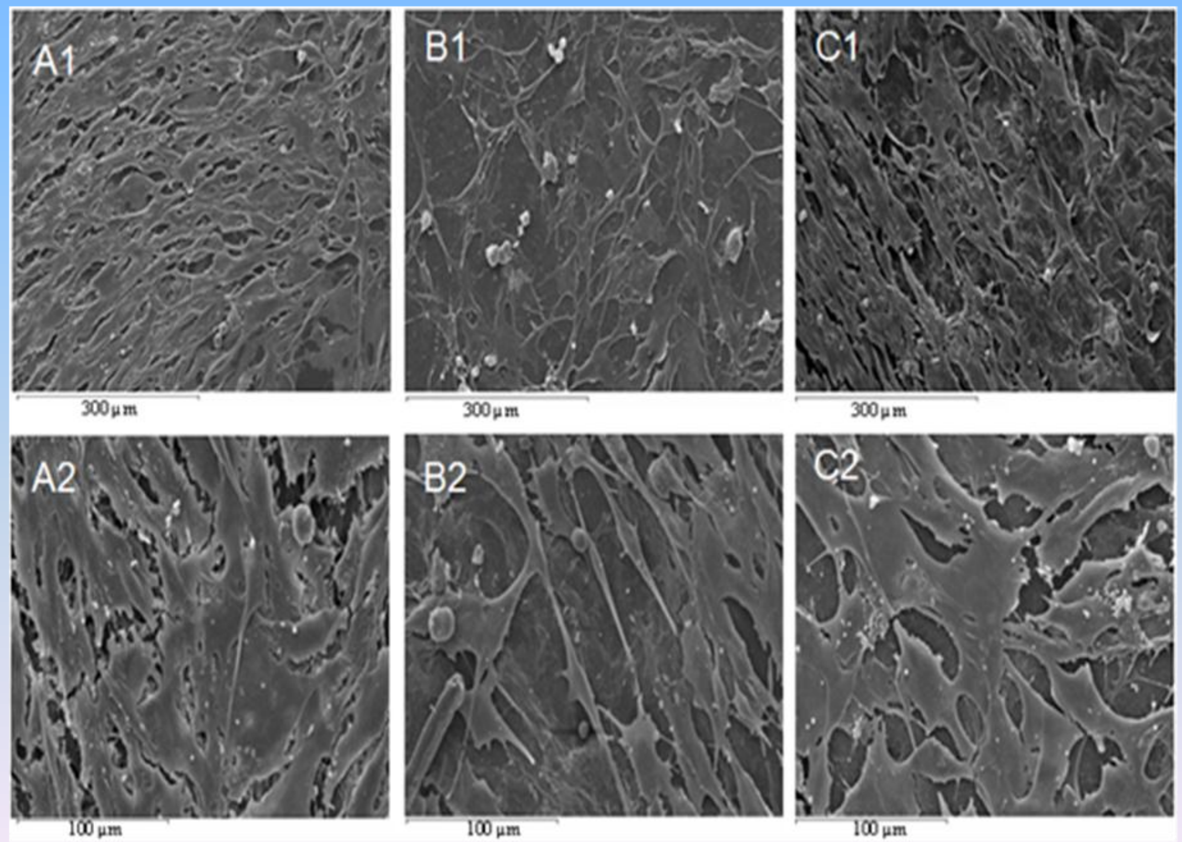
Thermal properties of the P(3HB)/MFC composites



Mechanical properties of the P(3HB)/MFC composites



Biocompatibility of the P(3HB)/MFC composites



Murine ATDC-5 cell line proliferation (7 days)

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Drug delivery

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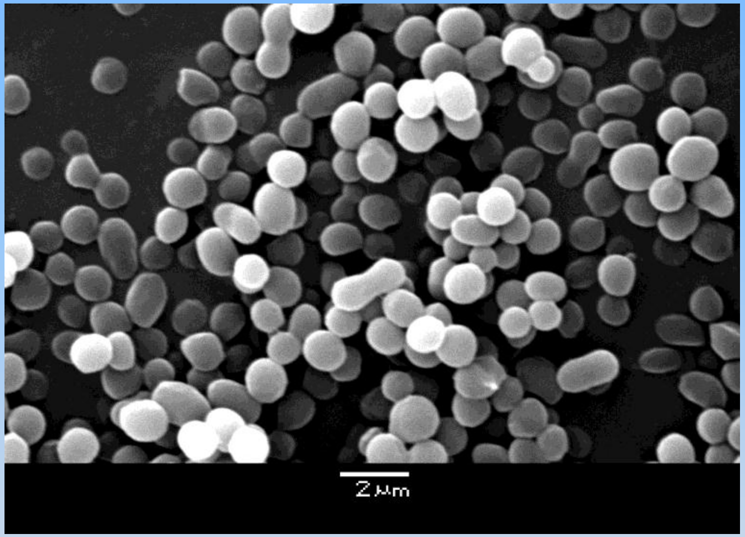
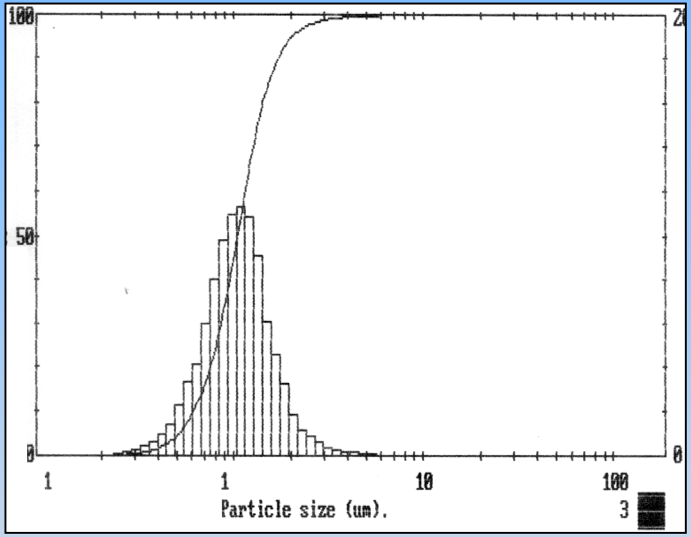
P(3HB) microspheres for drug delivery





SEM image P(3HB) microspheres ***Particle size distribution analysis***

Francis *et al*., Acta Biomaterialia, 2010, **6**: 2773-2776

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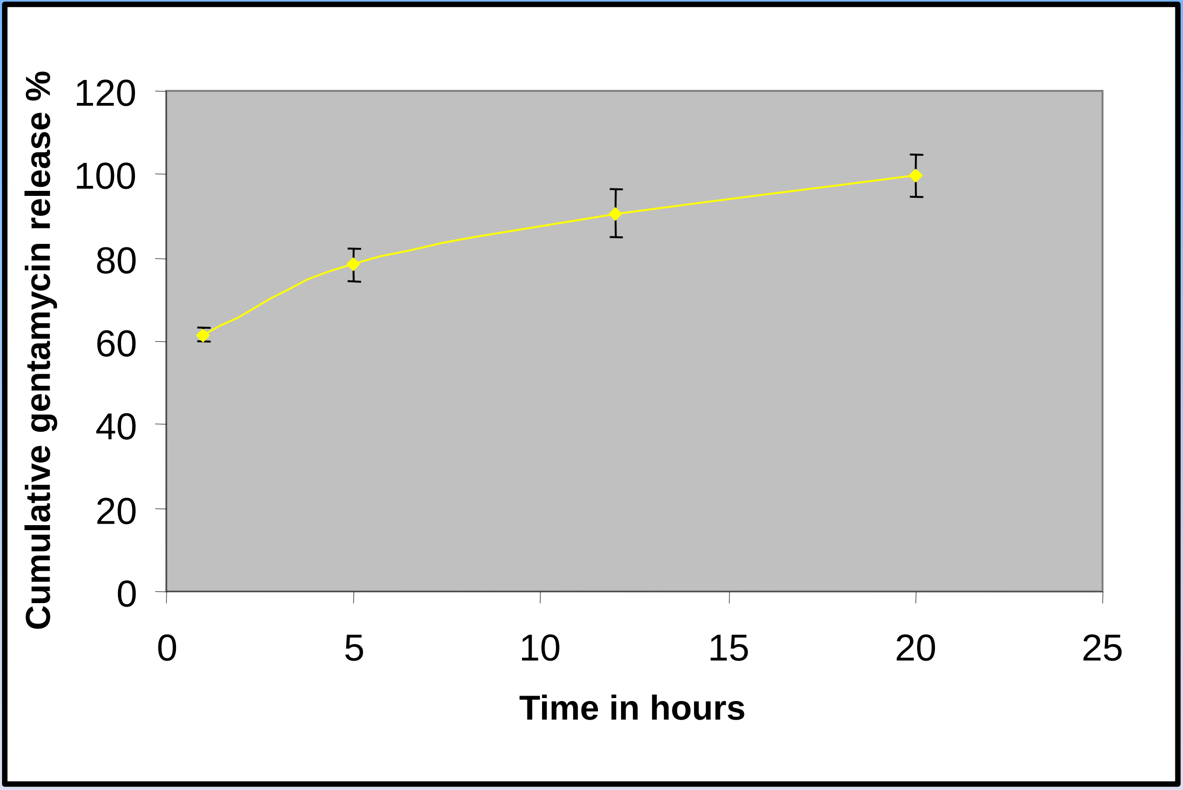
P(3HB) microspheres for drug delivery



Gentamycin release kinetics

Francis *et al.*, Acta Biomaterialia, 2010, 6: 2773-2776

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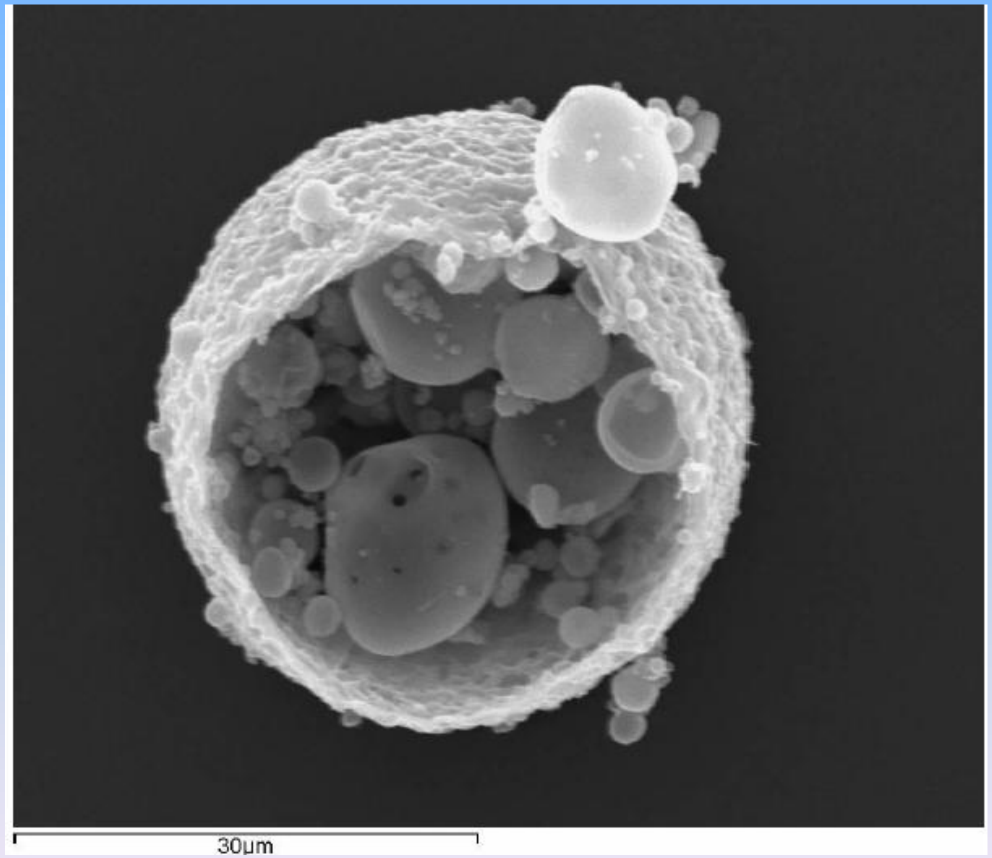
P(3HB) microspheres/ bacterial cellulose spheres for multiple drug delivery



Akaraonye *et al*., unpublished data

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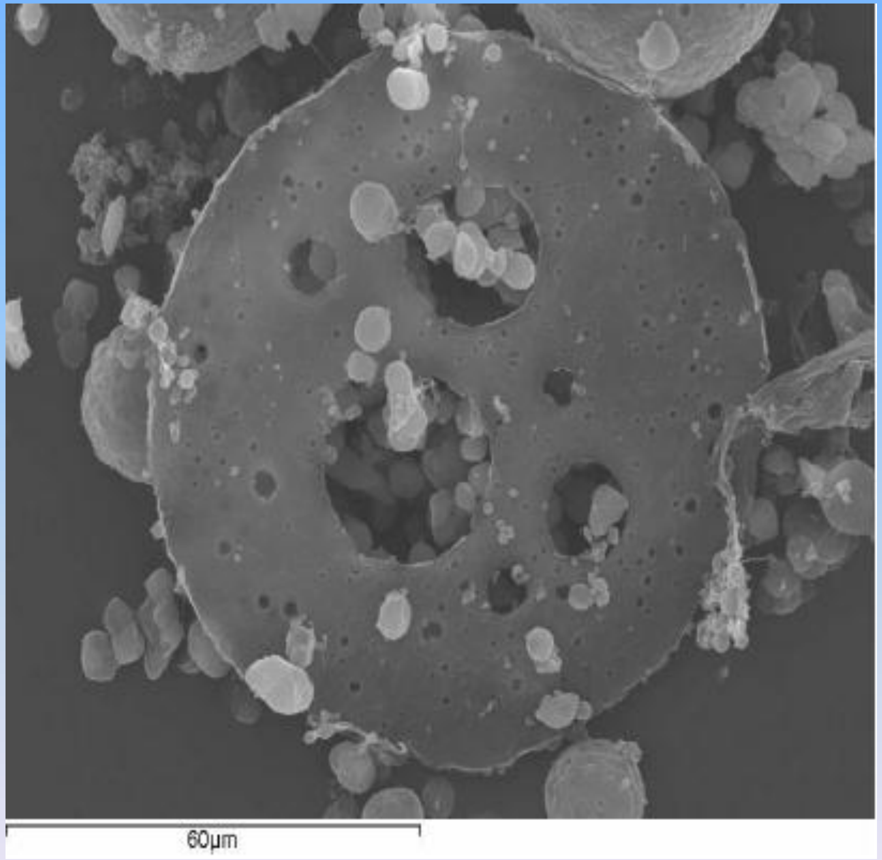
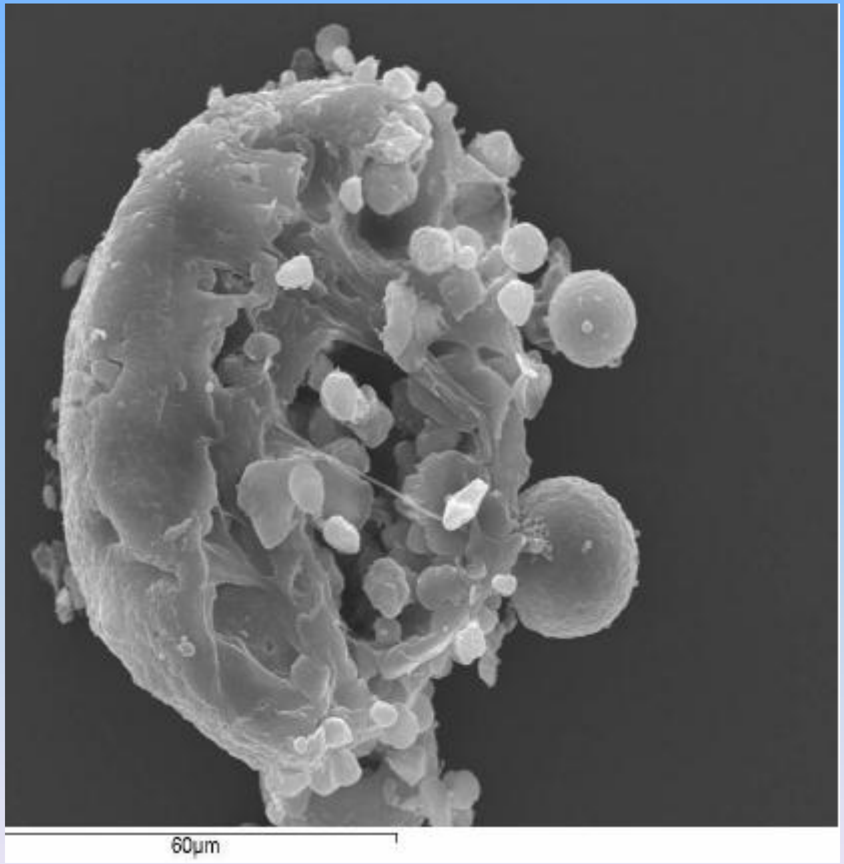
P(3HB) microspheres/ bacterial cellulose spheres for multiple drug delivery



Cross sectional area of a composite sphere



Degradation of a composite sphere

Akaraonye *et al*., unpublished data

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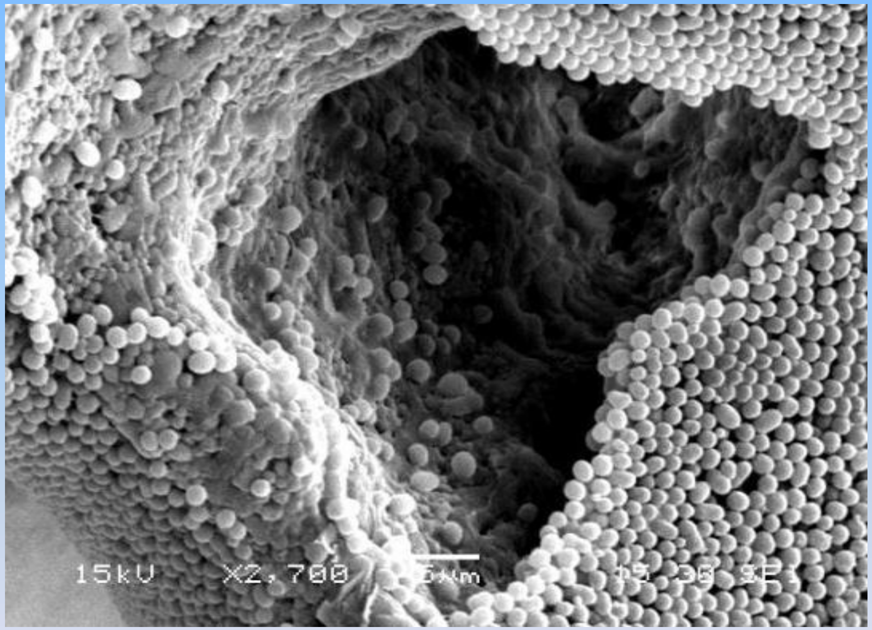
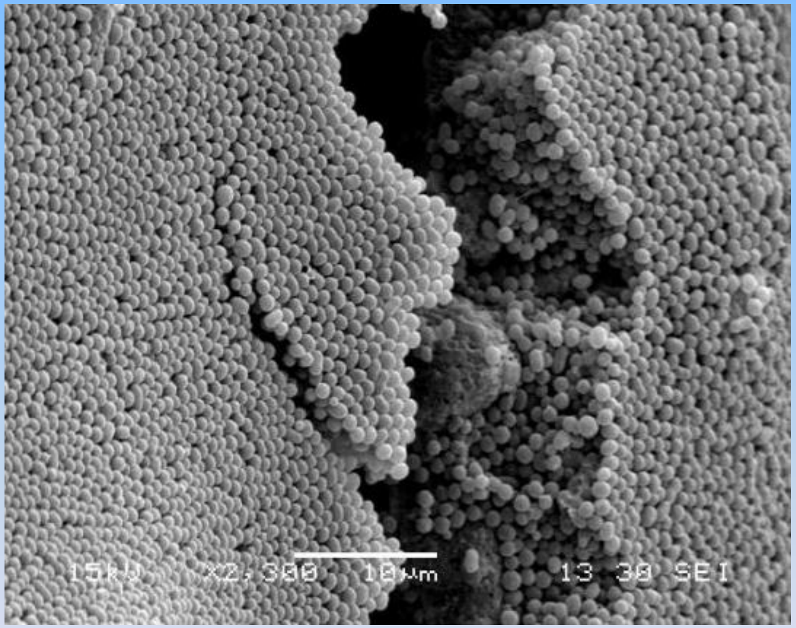
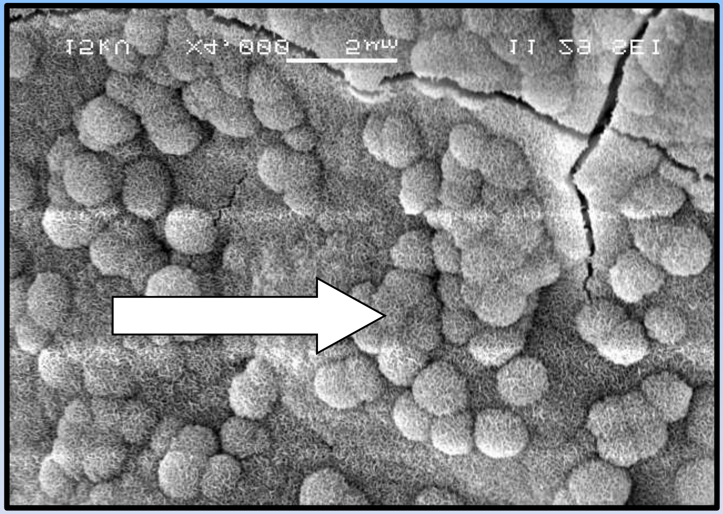
Drug delivery via P(3HB) microsphere coated Bioglass® scaffold



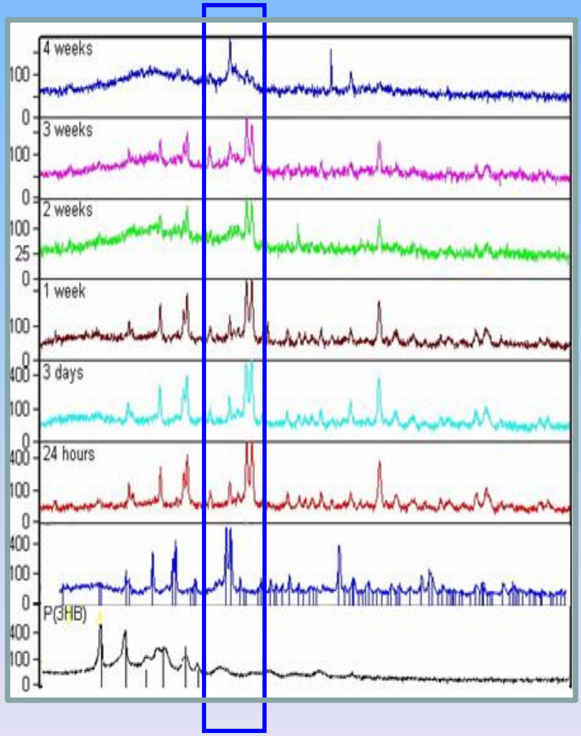


Microspheres loaded with gentamycin

Bioactivity measurements of the P(3HB)microsphere coated composite scaffold



Evidence of hydroxyapatite formation



XRD analysis

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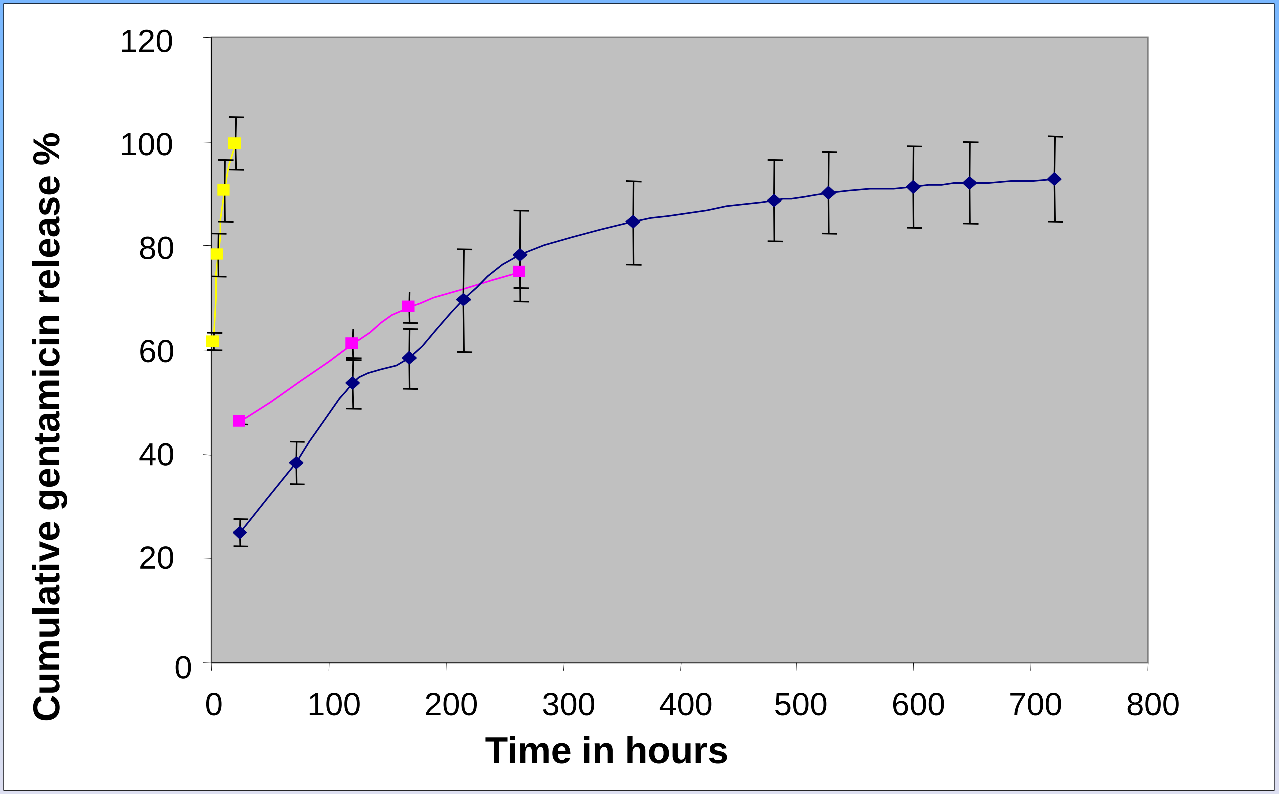
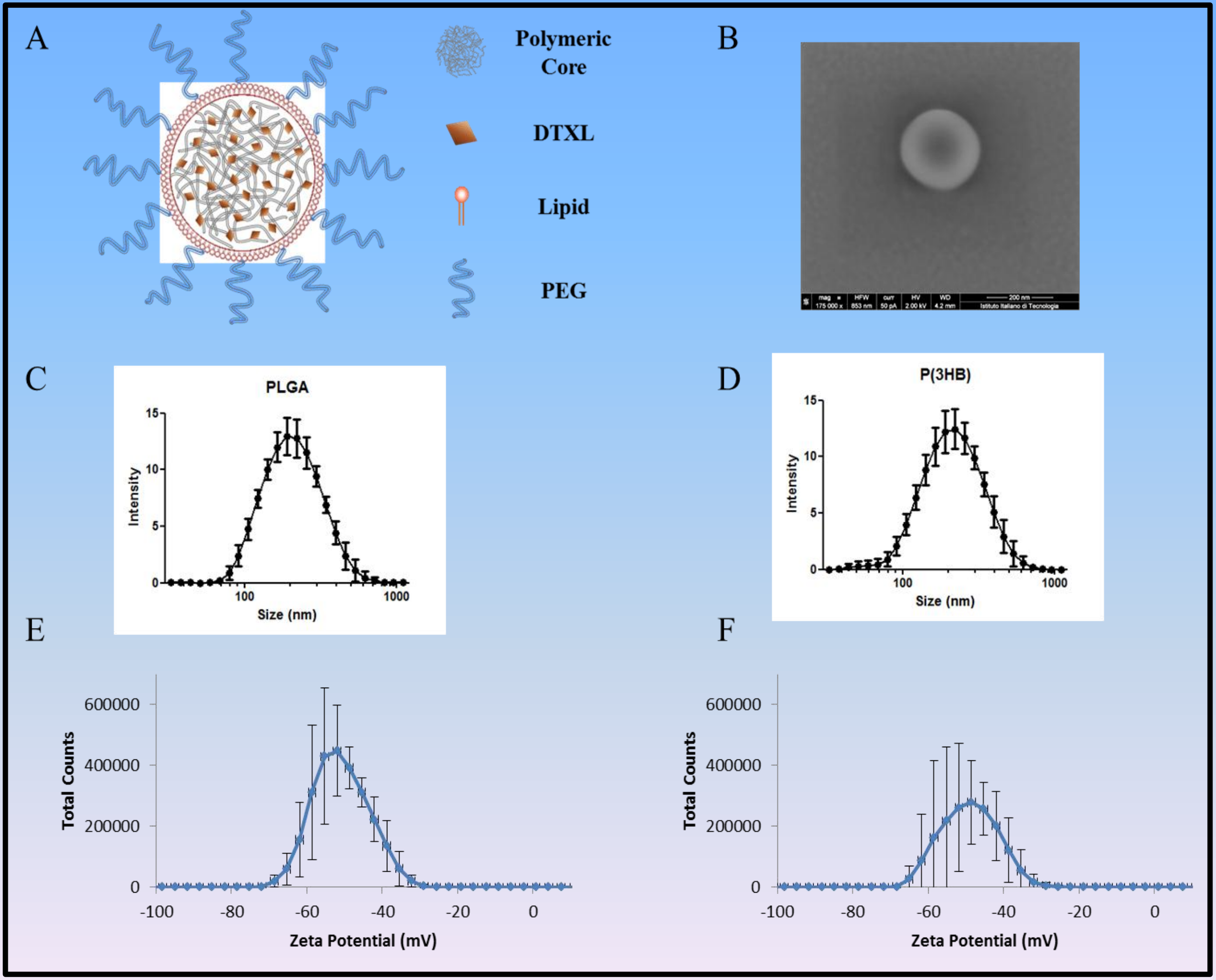
Comparison of Gentamycin release kinetics

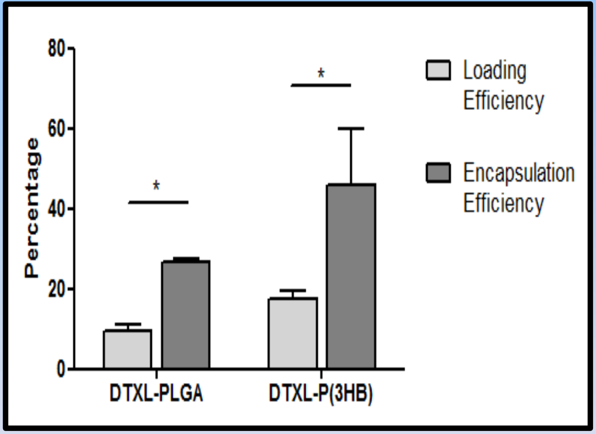


Francis *et al*., Acta Biomaterialia, 2010, **6**: 2773-2776

Spherical Polymeric Nanoconstructs with P(3HB)

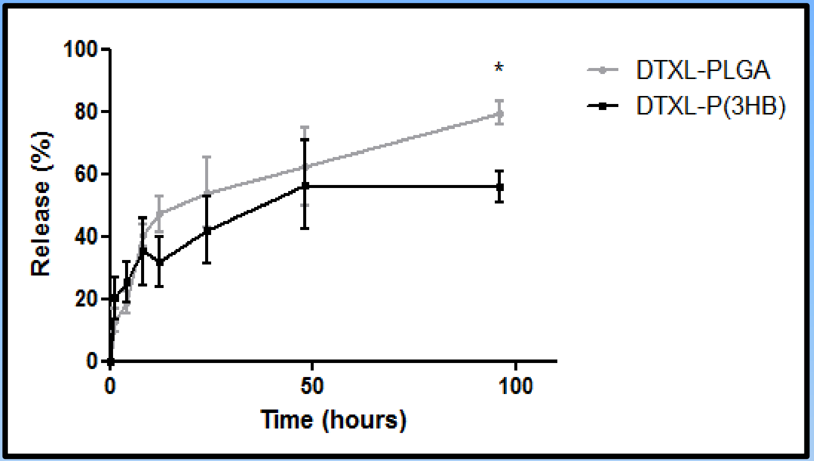


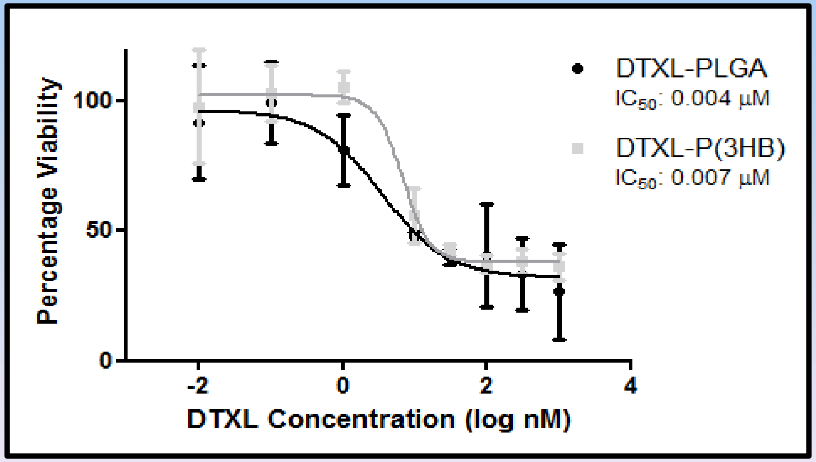
In Collaboration
with Dr. Paolo Decuzzi
IIT, Genoa

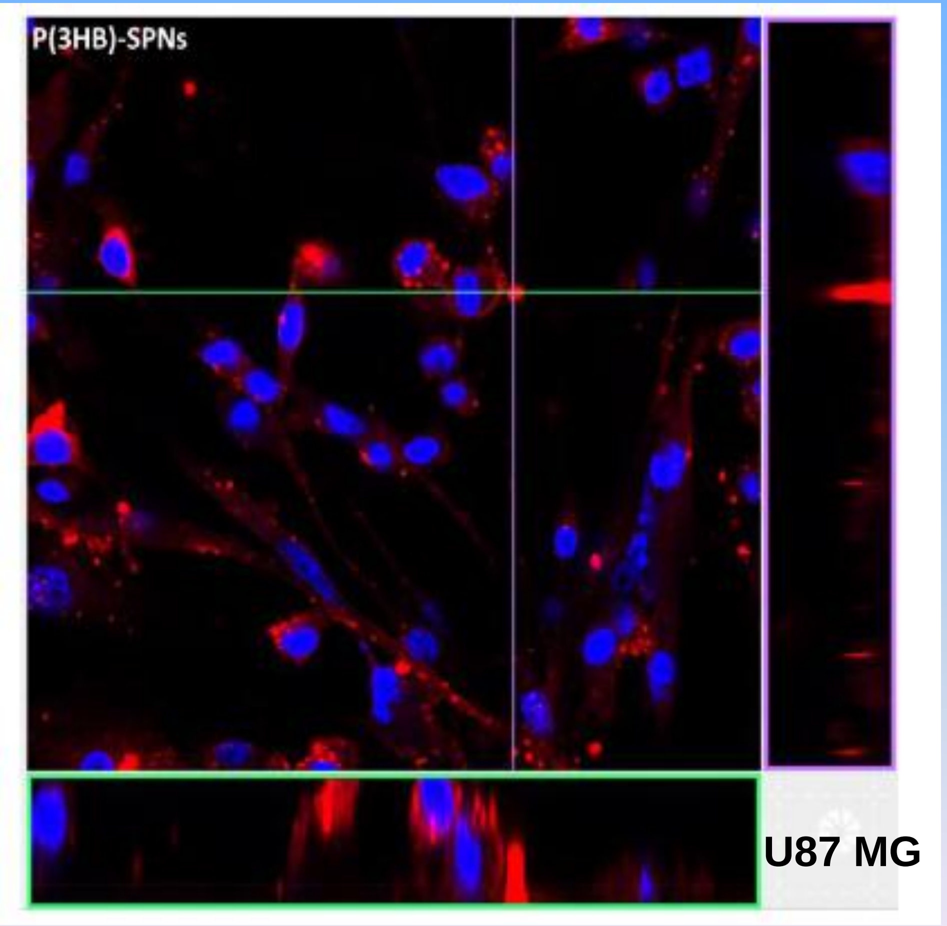


Di Mascolo *et al*., 2015 accepted in Polymer International

Spherical Polymeric Nanoconstructs with P(3HB)







Di Mascolo *et al*., 2015 accepted in Polymer International

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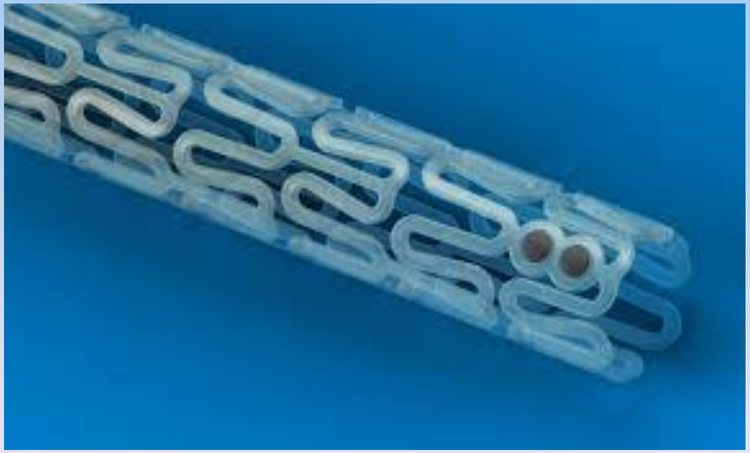
MEDICAL DEVICE DEVELOPMENT USING POLYHYDROXYALKANOATES



Biodegradable drug eluting stents

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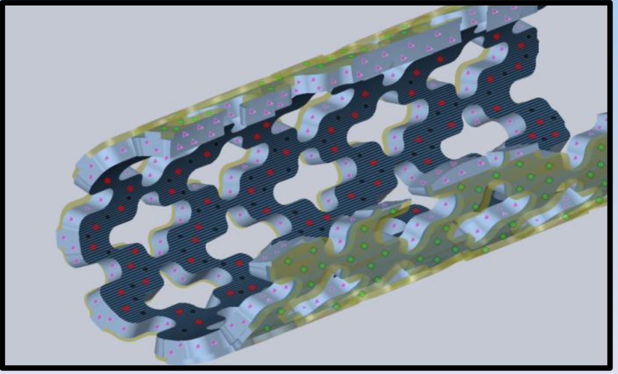
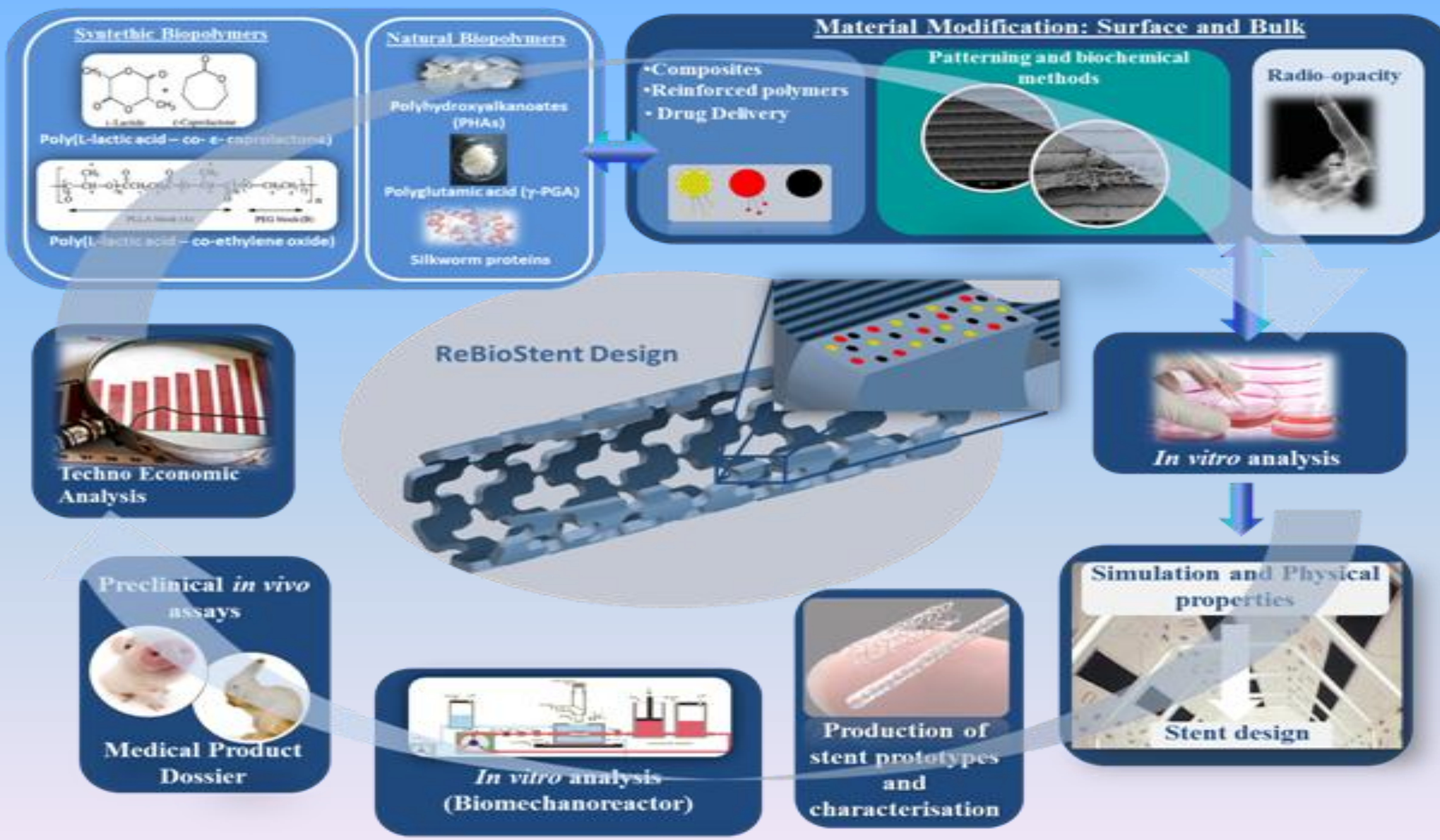
Drug eluting biodegradable stents using Polyhydroxyalkanoates

❖Coronary artery disease is caused by the blockage of arteries due to hardening of the cholesterol, fats and other components of the blood leading to abnormal blood flow. Routinely, tubular structures called stents are used to recover the shape of such blocked arteries. Although the use of such cardiovascular stents is widespread, **currently, an ideal stent that recovers the arterial shape without any adverse effects does not exist.** The most common unwanted responses include **inflammation**, **in stent restenosis** and **thrombosis.**

Reinforced Bioresorbable Biomaterials for Therapeutic Drug Eluting Stents



http://rebiostent.eu/; Scientific Coordinator: Dr Ipsita Roy, University of Westminster



http://rebiostent.eu/; Scientific Coordinator: Dr Ipsita Roy, University of Westminster

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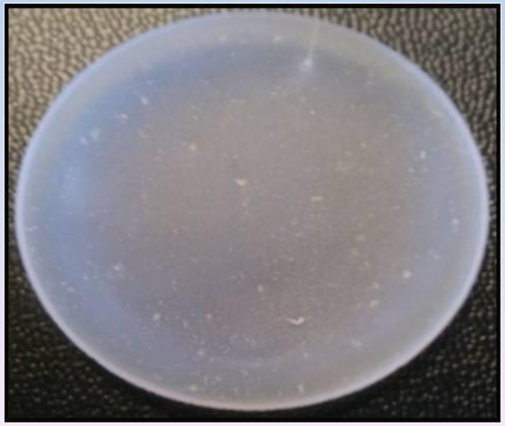
Drug eluting biodegradable stents using P(3HB) and P(3HO) blends

+



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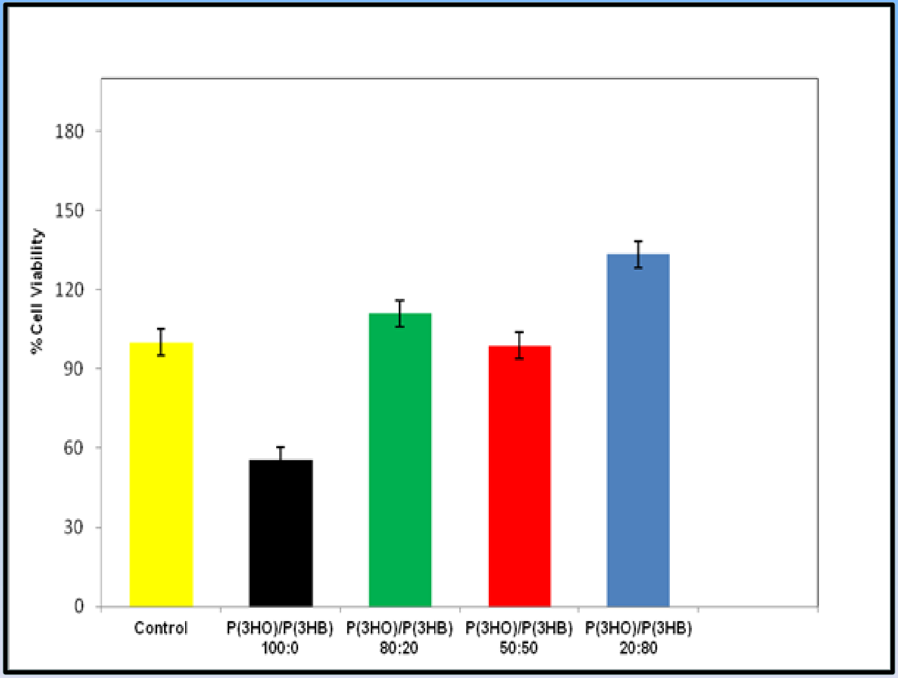
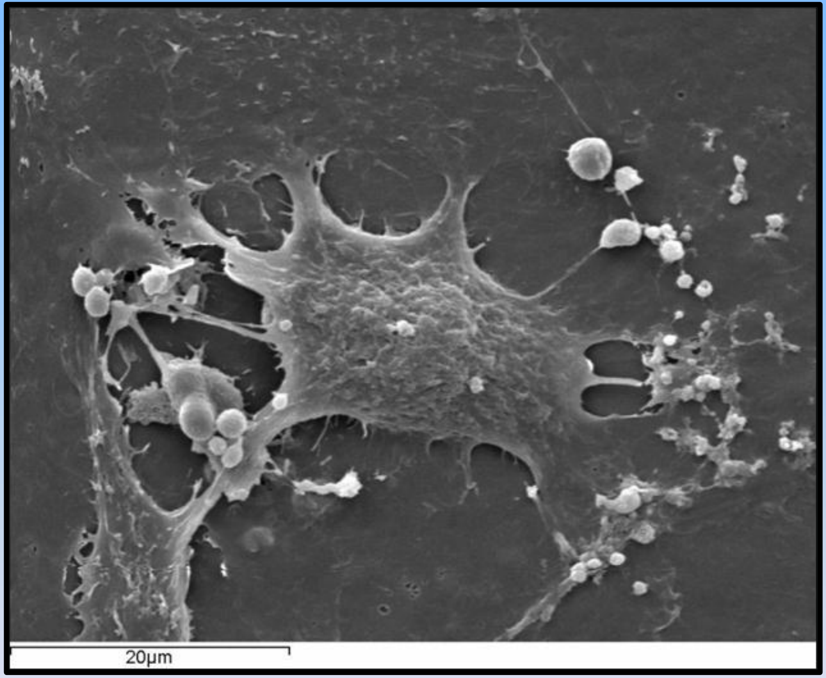
Mechanical Properties of the P(3HB) and P(3HO) blends

P(3HB)/P(3HO) blend films	Young's modulus (MPa)	Tensile Strength (MPa)	Elongation at break (%)
P(3HO) Neat	7.0	1.8	204
P(3HB)/P(3HO) 20:80	46.2	6.0	58.9
P(3HB)/P(3HO) 50:50	78.4	7.5	22.9
P(3HB)/P(3HO) 80:20	86.1	7.8	10.1

Basnett *et al*. 2013, Reactive and Functional Polymers, 73:1340–1348

Biocompatibility of the P(3HB) and P(3HO) blends





Proliferation of seeded HMEC-1 cells

Basnett *et al*., Reactive and Functional Polymers, 73:1340–1348

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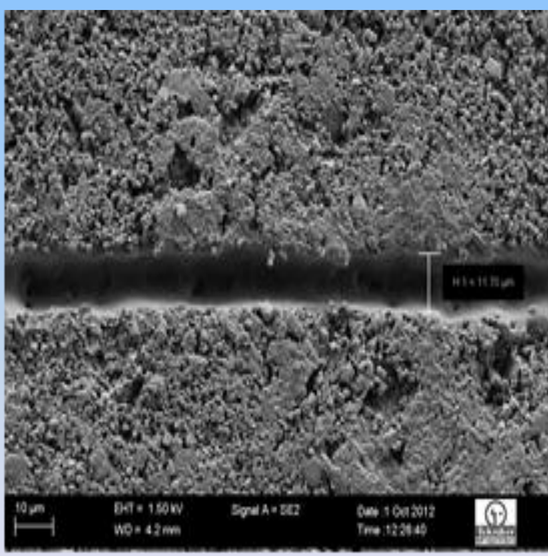
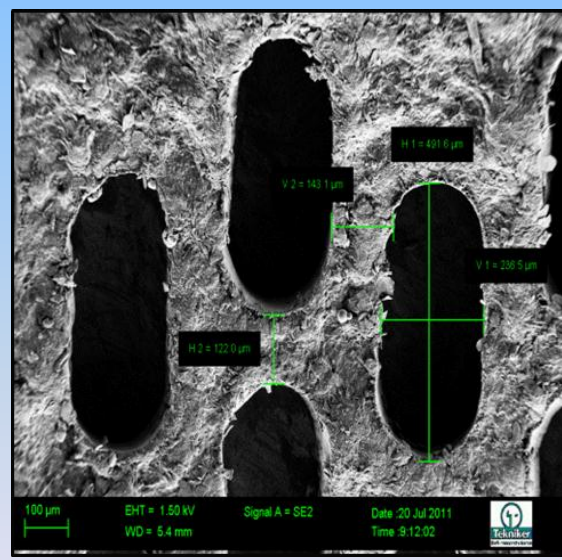
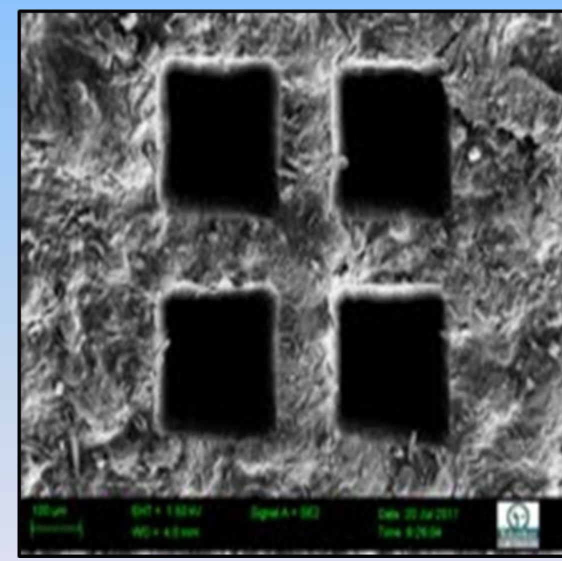
Laser micropatterning of the P(3HB) and P(3HO) blends







Basnett *et al*., unpublished data

Peripheral Nerve Tissue Engineering

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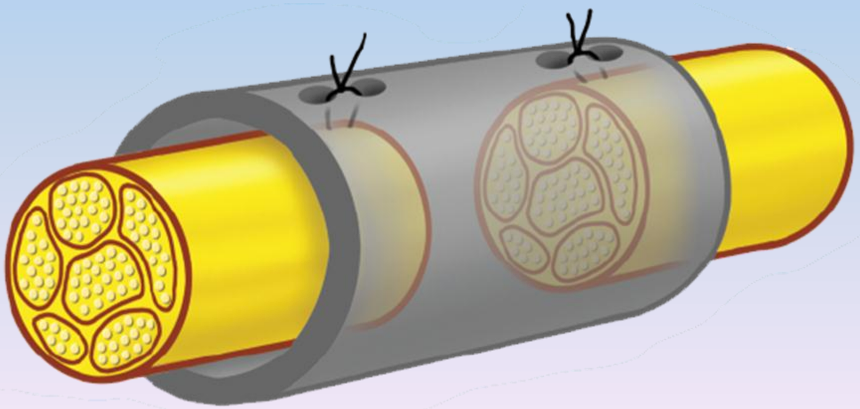
Peripheral Nerve injury affects 2.8% of trauma patients, many of whom suffer life-long disability. For injuries resulting in gaps more than 5mm treatment is using autologous nerve graft repair. This Has several limitations including donor site morbidity, scar tissue Invasion, scarcity of donor nerves, inadequate return of function and aberrant regeneration. Currently there are several clinically approved artificial nerve guidance conduits. We aim to produce second generation nerve guidance conduits using PHAs



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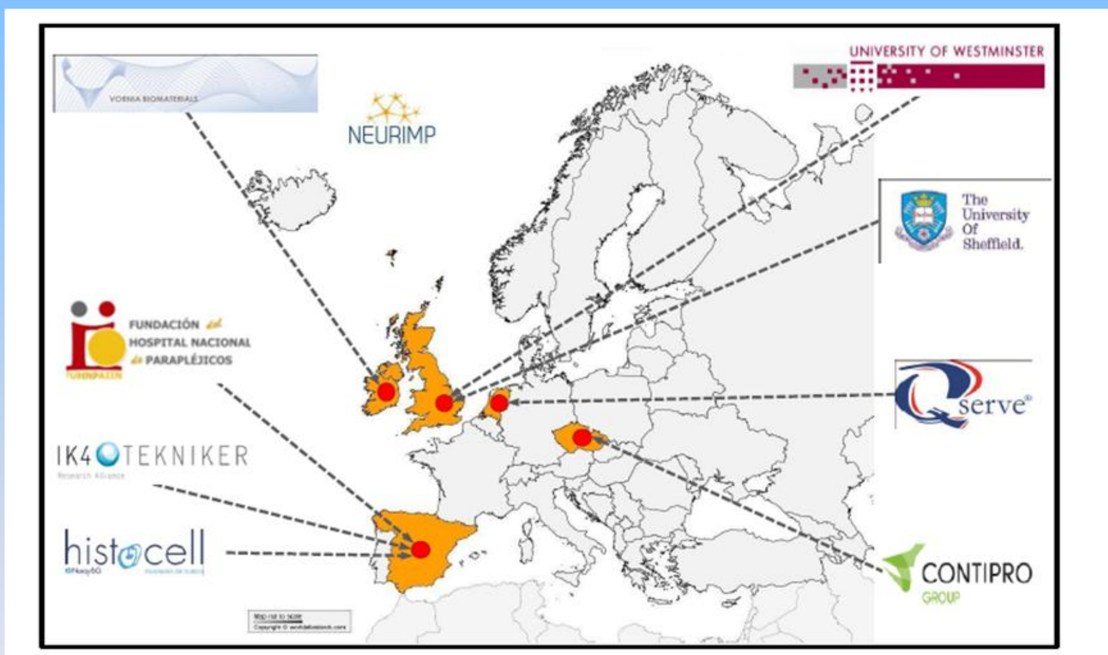
SEVENTH FRAMEWORK PROGRAMME

Novel combination of biopolymers and manufacturing technologies for production of a peripheral nerve implant containing an internal aligned channels array



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Scientific Coordinator: Dr Santos Merino, Tekniker

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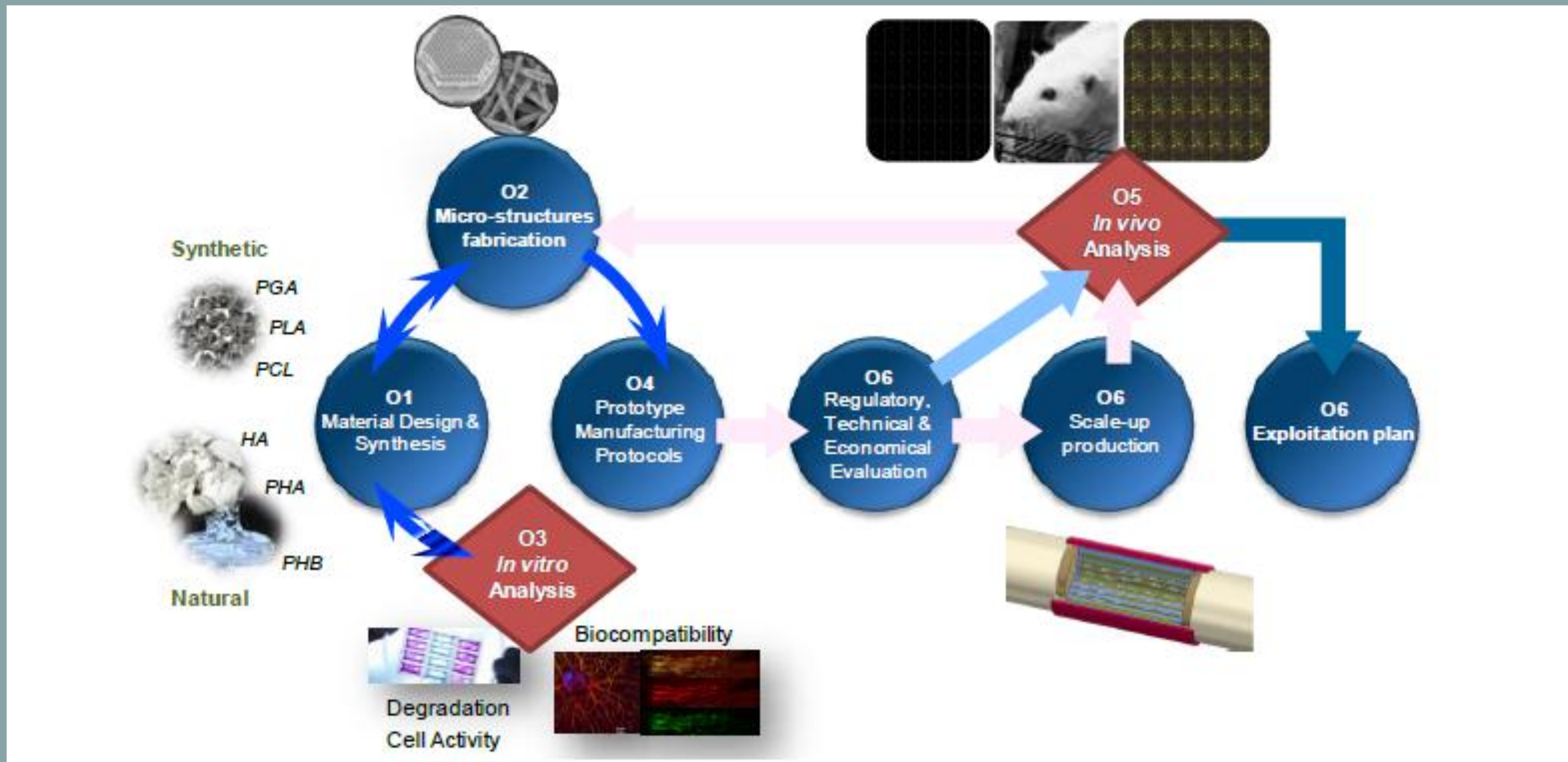

www.neurimp.eu/ Dr Santos Merino,Tekniker

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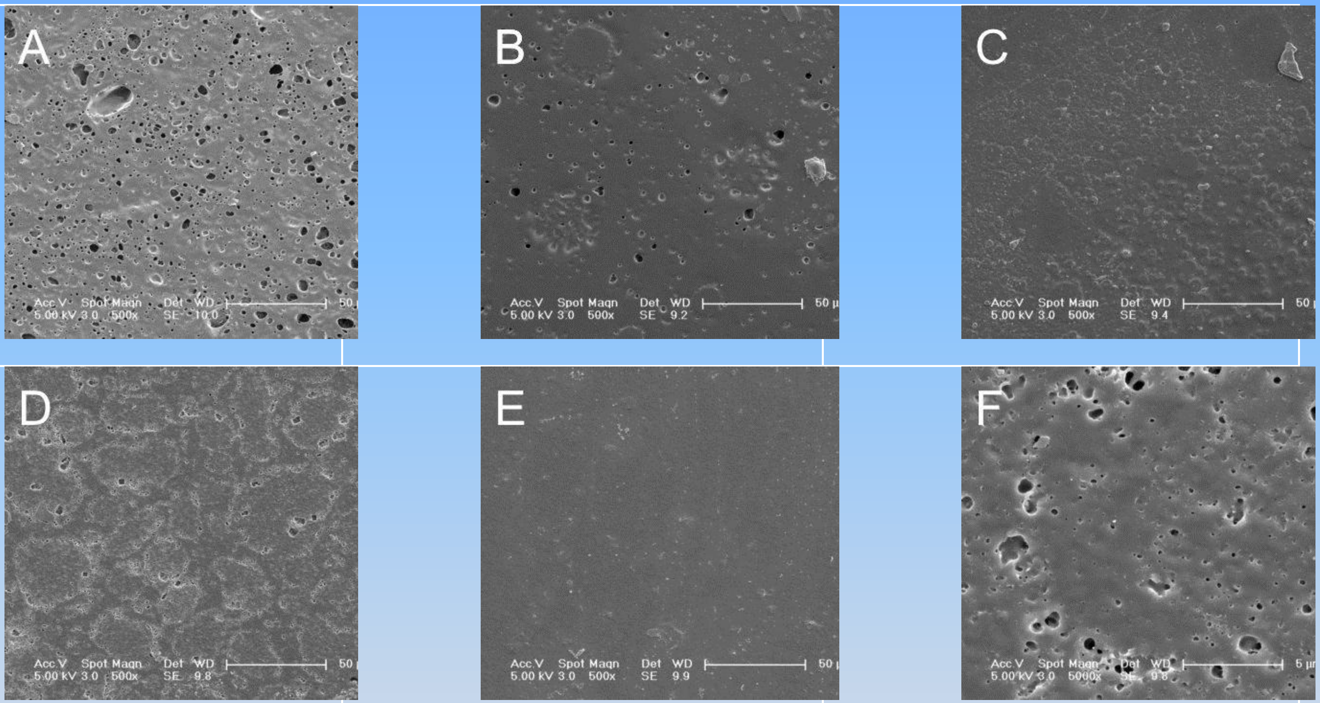
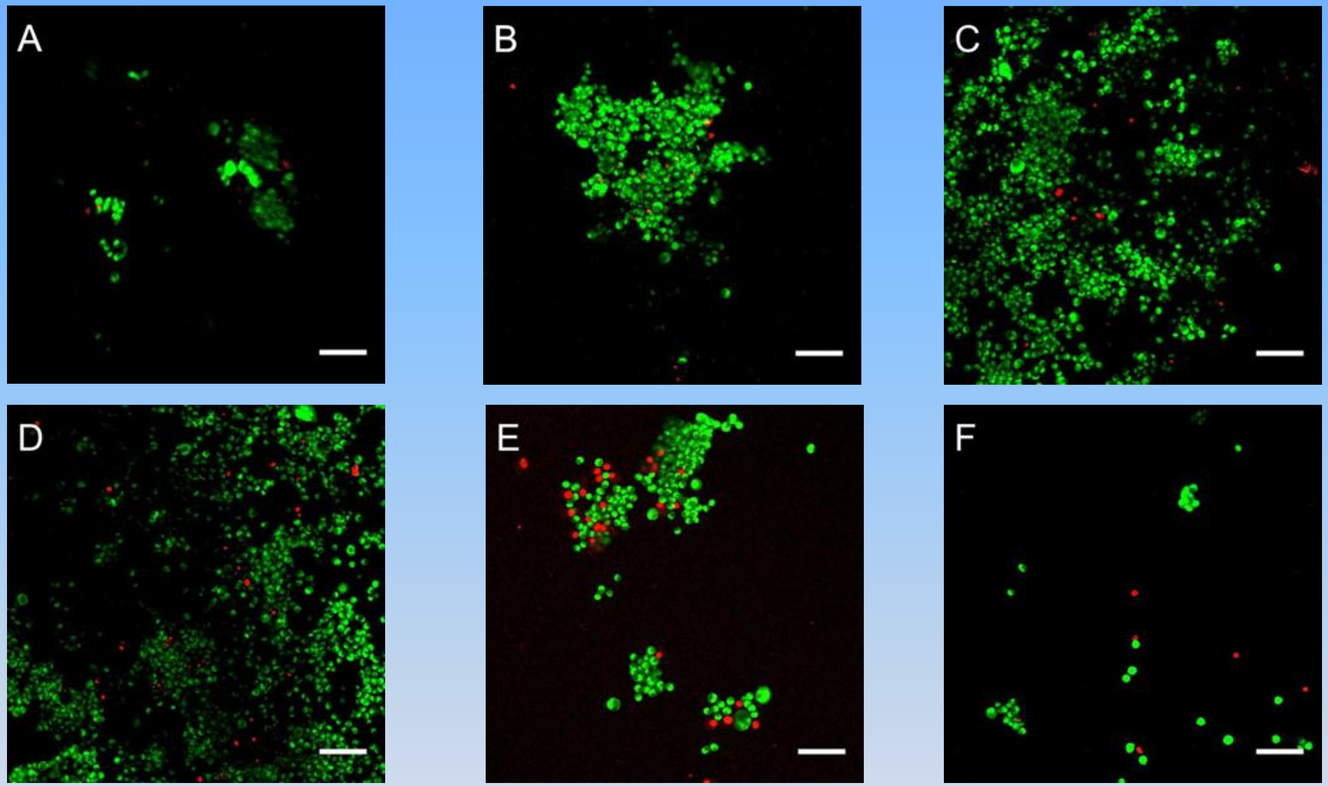
P(3HB)/P(3HO) blends for Nerve Tissue Engineering



SEM images of P(3HB)/P(3HO) Blends

(A) P(3HO)/P(3HB) 100:0; (B) P(3HO)/P(3HB) 75:25; (C) P(3HO)/P(3HB) 50:50; (D) P(3HO)/P(3HB) 25:75 and (E) P(3HB) (F) PCL 500x

P(3HB)/P(3HO) blends for Nerve Tissue Engineering

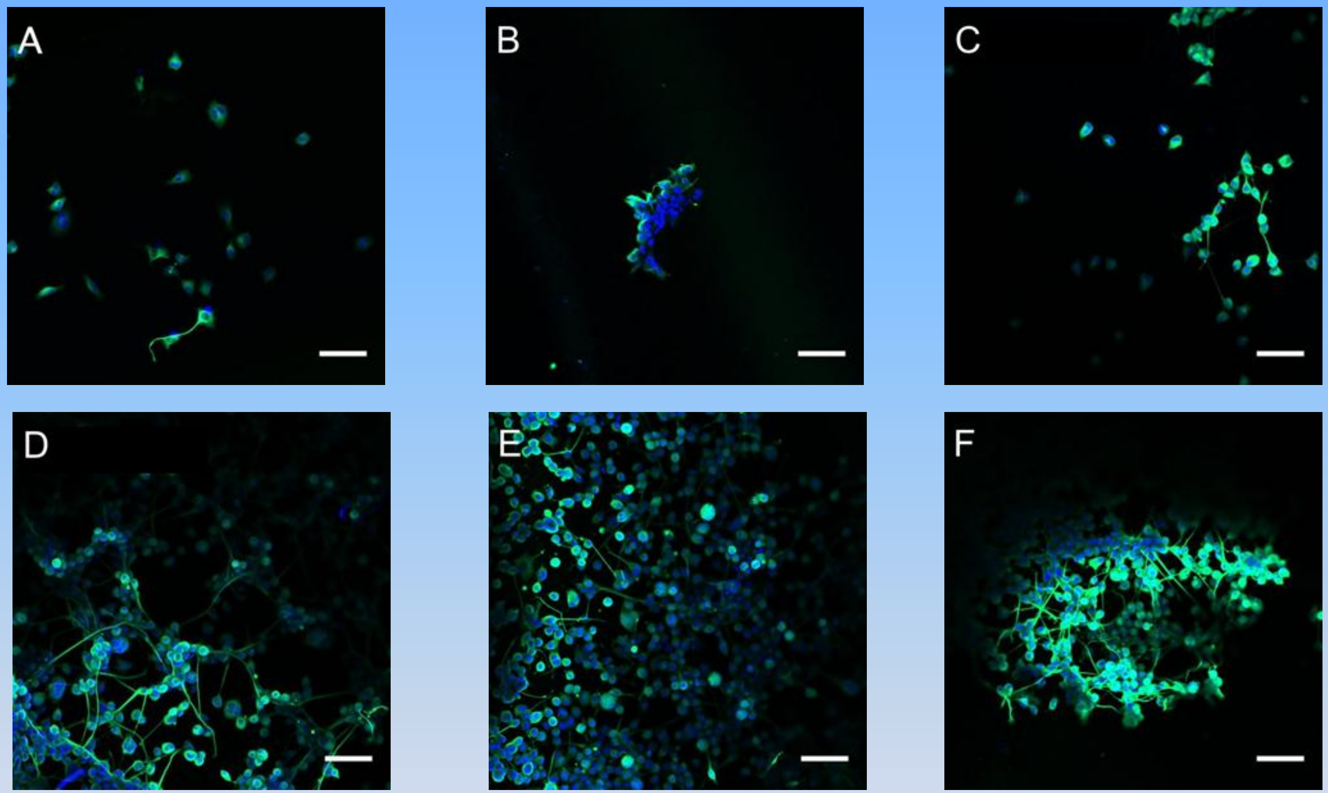


In collaboration with Professor John Haycock, University of Sheffield, UK

Confocal microscopy images of NG108-15 neuronal cells stained with propidium iodide (red) and Syto-9 (green)

(A) P(3HO)/P(3HB) 100:0; (B) P(3HO)/P(3HB) 75:25; (C) P(3HO)/P(3HB) 50:50; (D) P(3HO)/P(3HB) 25:75; and (E) P(3HB) (F) PCL

P(3HB)/P(3HO) blends for Nerve Tissue Engineering

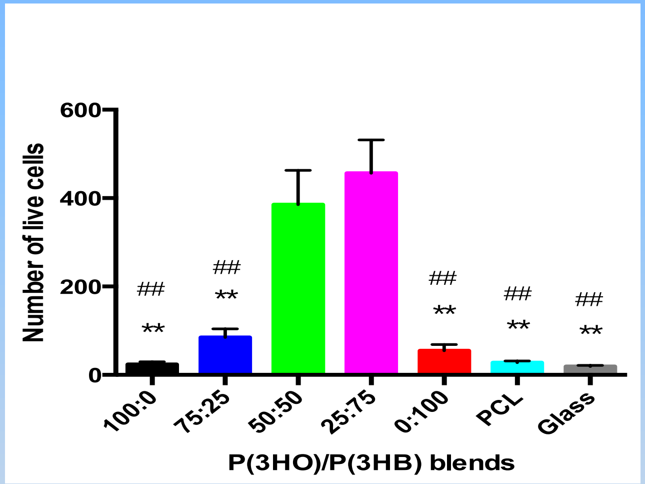


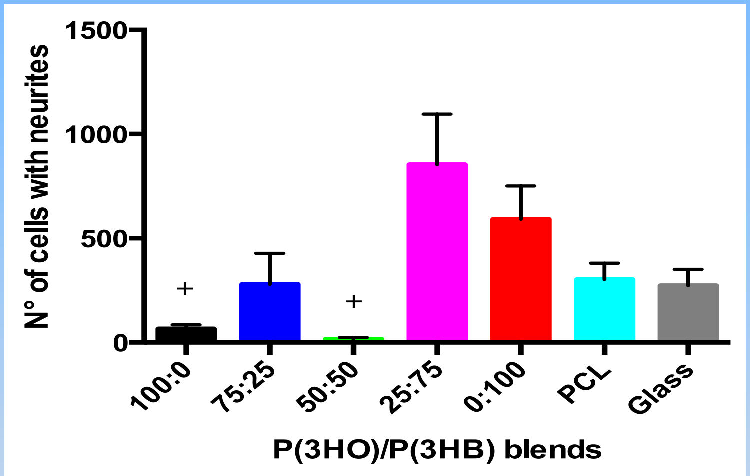
In collaboration with Professor John Haycock, University of Sheffield, UK

Confocal microscopy images of NG108-15 neuronal cells stained with labelled for beta-III tubulin (neurite growth)

(A) P(3HO)/P(3HB) 100:0; (B) P(3HO)/P(3HB) 75:25; (C) P(3HO)/P(3HB) 50:50; (D) P(3HO)/P(3HB) 25:75; and (E) P(3HB) (F) PCL

P(3HB)/P(3HO) blends for Nerve Tissue Engineering





Confocal microscopy images of NG108-15 neuronal cells stained with labelled for beta-III tubulin (neurite growth)

(A) Growth of NG-108-15 cells on PHAs (B) Cells with neurites on PHAs

In collaboration with Professor John Haycock, University of Sheffield, UK

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HyMedPoly

“**Drug-Free Antibacterial Hybrid Biopolymers for Medical Applications**”,
Horizon 2020 Research and Innovation Programme
Marie Sklodowska-Curie Grant for European Industrial Doctorate

Horizon 2020
European Union Funding
for Research & Innovation

Conclusions

- Polyhydroxyalkanoates (PHAs) are an emerging class of biodegradable and biocompatible polymers of natural origin with huge potential in biomedical applications.
- PHAs are currently being produced using Gram negative bacteria. We have pioneered the use of Gram positive bacteria, especially, *Bacillus* sp for the production of SCL-PHAs.
- *Bacillus cereus* SPV has been successfully used for the production of SCL-PHAs and in large scale. Cheap carbon sources have also been explored.
- *Psuedomonas mendocina*, a relatively unexplored bacteria has been successfully used for the production of a range of MCL-PHAs and in large scale.
- The PHAs produced have been used in hard and soft tissue engineering, drug delivery, wound healing, stent and nerve conduit development.

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Key scientists:

Dr.S.P.Valappil (polymer production from *Bacillus cereus* SPV)
Dr. Ranjana Rai (polymer production from *Pseudomonas mendocina* and its applications in soft tissue engineering and wound healing)
Dr. Akarayonye Everest (polymer production from *Bacillus cereus* SPV, composite work and drug delivery work)
Dr. Lydia Francis (drug delivery work and wound healing)
Dr. DeCheng Meng (drug delivery work)
Dr. Superb Misra (the composite work using Bioglass® and CNT for hard tissue engineering)
Dr. Pooja Basnett (polymer production and biodegradable stent work)
Dr. Andrea Bagdadi (polymer production and cardiac patch work)
Dr. Rinat Nigmatullin (polymer characterisation)
Ms. Prachi Dubey (polymer production and cardiac patch work)
Ms. Lorena Lizzarraga (polymer production and nerve tissue engineering work)

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Dr. I. Quintana, Tekniker, Spain

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Funding Bodies

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SEVENTH FRAMEWORK PROGRAMME

British Heart Foundation

WestFocus Knowledge Exchange

EPSRC Pioneering research and skills

NEURIMP

ReBioStent

Horizon 2020 European Union Funding for Research & Innovation

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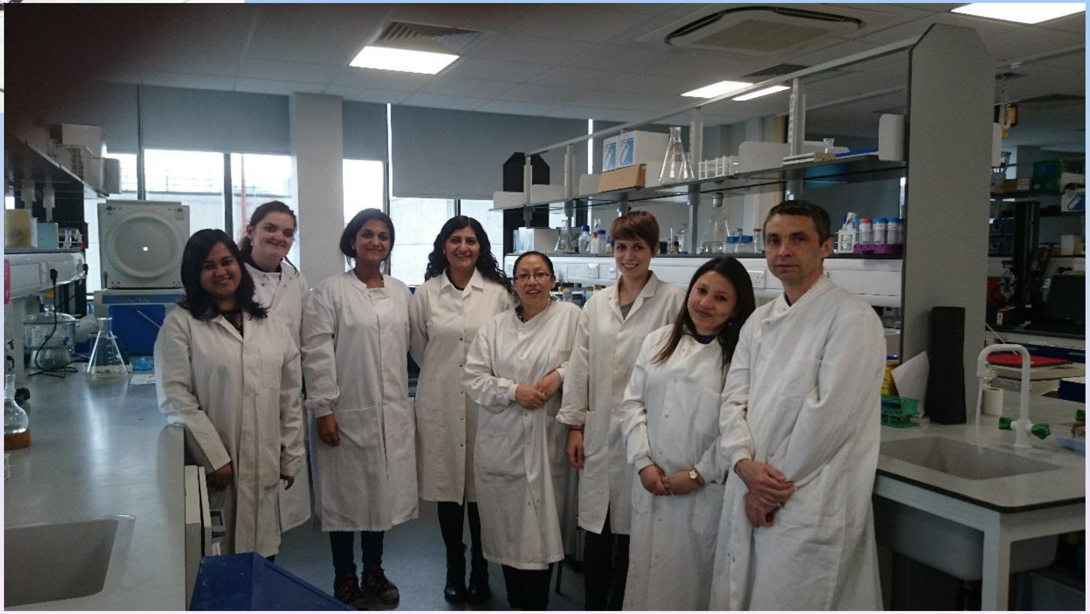

My Group!

Thanks for your attention!