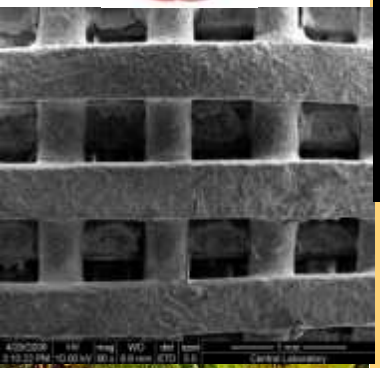
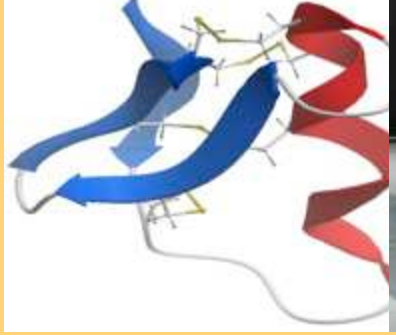




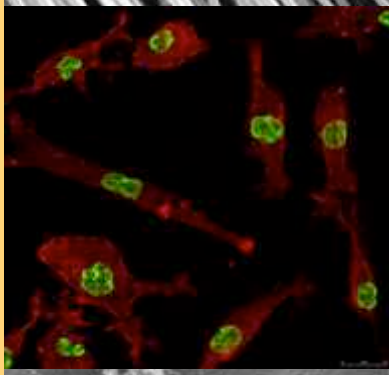
BIOMATEN

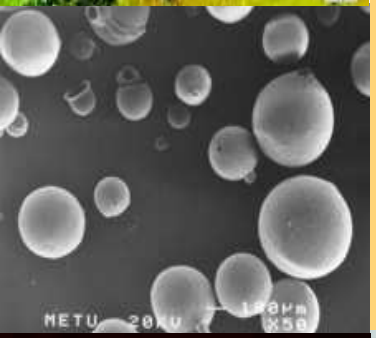
METU Center of Excellence in Biomaterials and Tissue Engineering

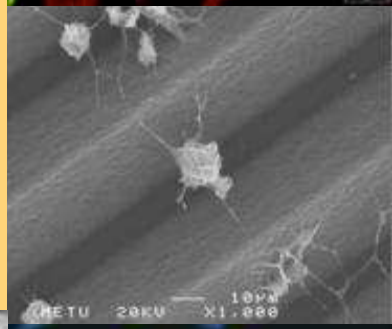
Middle East Technical University, Ankara 06800 Turkey

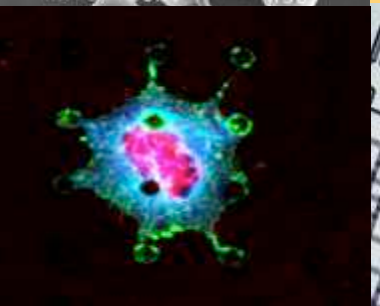
Prof Dr Vasıf Hasırcı

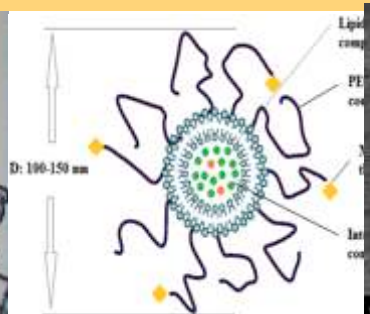
www.biomaten.metu.edu.tr

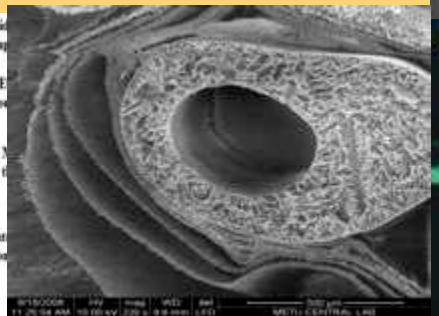


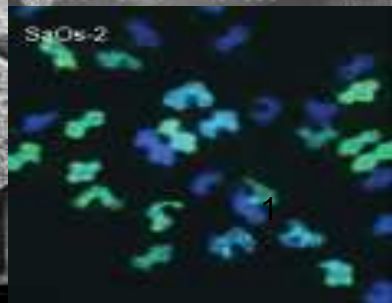




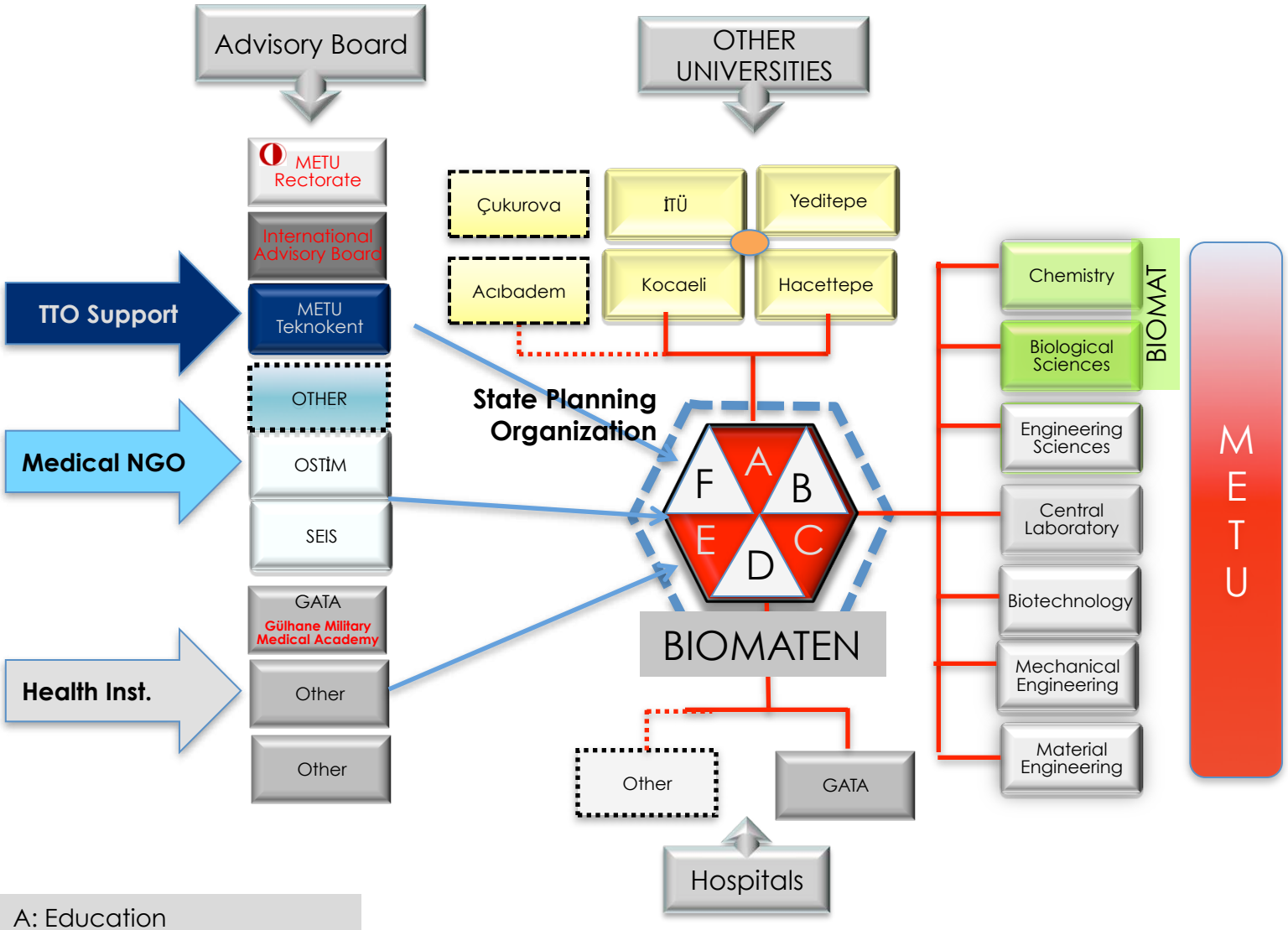






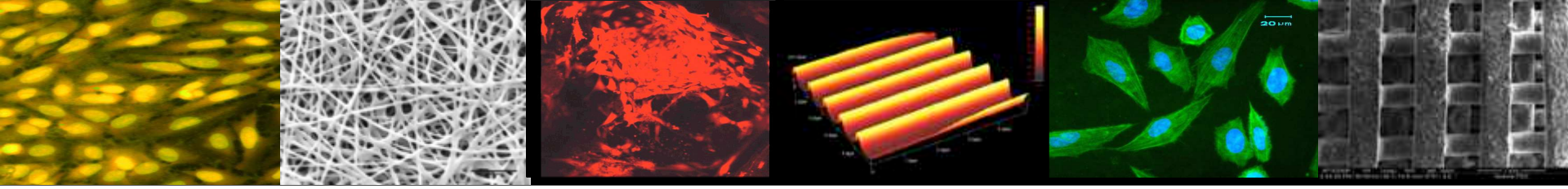


BIOMATEN Organization



A: Education
B: Research
C: Reference Point
D: Prototype Product
E: Characterization
F: Certification

BIOMATEN: Center of Excellence in Biomaterials and Tissue Engineering



BIOMATEN MEMBERS

METU

Prof. Dr. Vasif Hasirci	Biological Sciences
Prof. Dr. Nesrin Hasirci	Chemisty Dept.
Assoc. Prof. Dr. Caner Durucan	Metal.& Materials Eng
Assoc. Prof. Dr. Aysen Tezcaner	Engineering Sciences
Assoc. Prof. Dr. Dilek Keskin	Engineering Sciences
Assoc. Prof. Dr. Can Ozen	Biotechnology Dep.
Assoc. Prof. Dr. Senih Gurses	Engineering Sciences
Asst. Prof. Dr. Ergin Tonuk	Mechanical Engineering

Scientific Project Specialists

Assoc. Prof. Dr. E. Turker Baran	BIOMATEN
Dr. Arda Buyuksungur	BIOMATEN
Dr. Menekse Ermis Sen	BIOMATEN
Selcen Alagöz	BIOMATEN

Staff

Zeynel Akın	BIOMATEN
Ramazan Kavak	BIOMATEN

Other Institutions

Prof. Dr. Hayati Bilgic	GATA
Prof. Dr. Kezban Ulubayram	Hacettepe University
Prof. Dr. Erdal Karaoz	Kocaeli University
Prof. Dr. Gamze Torun Kose	Yeditepe University
Assoc. Prof. Dr. Fatma Nese Kok	ITU
Assoc. Prof. Dr. Ayse Aksoy	Hacettepe University
Asst. Prof. Dr. Halime Kenar	Kocaeli University
Asst. Prof. Dr. Deniz Yucel	Acıbadem University
Asst. Prof. Dr. Pınar Yılgor	Cukurova University

Local Advisory Committee

Metin Demir	SEIS
Orhan Aydın	OSTİM
Mustafa İ. Kiziltas	METU Technopark
Biomaterials and Tissue Eng. Soc.	BTES

International Advisory Committee

Prof. Dr. Mehmet Toner	Harvard- SBI (USA)
Prof. Dr. Pankaj Vadgama	U. London IRC (ING)
Prof. Dr. David Kaplan	Tufts U. (USA)
Prof. Dr. Rui L. Reis	U. Minho (POR)
Prof. Dr. Banu Onaral	Drexel U. (USA)
Prof. Dr. Utkan Demirci	Stanford (USA)
Prof. Dr. Ali Khademhosseini	Harvard-MIT (USA)

FUNDING SOURCES

NATIONAL

TÜBİTAK

METU

DPT

SAN-TEZ

EU FP6 and FP7

EXPERTISSUES

BioPolySurf

cornea

SkinTreat

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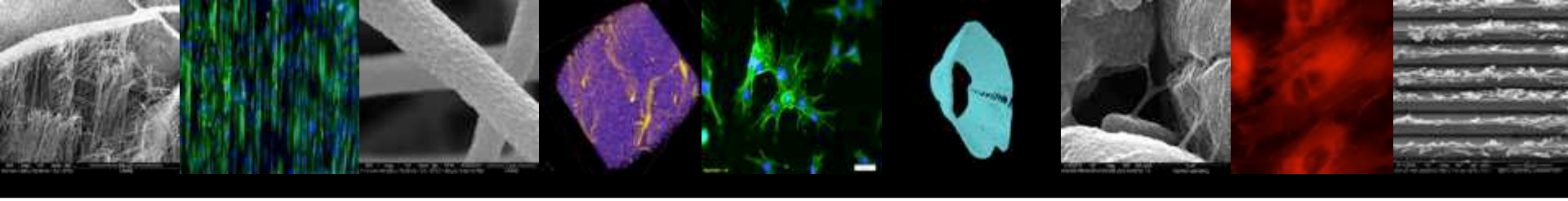
CENTER OF EXCELLENCE IN BIOMATERIALS AND TISSUE ENGINEERING

METU BIOMATERIALS AND TISSUE ENGINEERING RESEARCH CENTER

BIOMATEN



OBJECTIVES OF BIOMATEN

Biomaterials and Tissue Engineering is an exciting branch of science developing with the contributions of researchers from basic sciences, engineering and medical fields. Especially in the last ten years, research on this subject has shown an increase in our country as well as in the world. To put high-level research results into practice, medical sector, non-governmental organizations (trade unions, societies), hospitals, universities and relevant state agencies are required to work together. BIOMATEN was established to meet this requirement to bring together all the stake holders and unite them around common goals. BIOMATEN activities include theoretical and practical training, research and organization of scientific meetings, consulting and guidance for various academic, governmental and industrial institutions.

CONTRIBUTION OF BIOMATEN MEMBERS TO EDUCATION

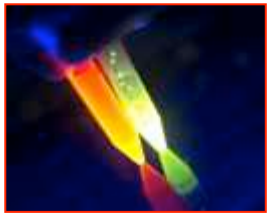
BIOMATEN members teach undergraduate and graduate level courses about Biomaterials, Tissue Engineering, Stem Cells, Nanotechnology and Biotechnology in addition to their basic education areas Chemistry, Biology, Mechanics, Materials and Medicine, and organize workshops and conferences. In addition, they provide information and counselling for private and public enterprises.

RESEARCH FACILITIES AND EQUIPMENTS

- ✓Material Characterization
- ✓Mechanical Testing
- ✓Surface Characterization

- ✓Cell Culture and Biocompatibility Testing
- ✓Contact Angle Measurement
- ✓Particle Size Analysis
- ✓Plasma Treatment
- ✓Micro-CT

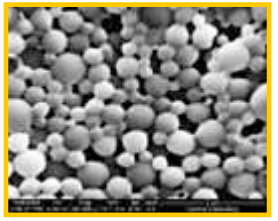
- ✓Scaffold Production for Tissue Engineering
- ✓Atomic Force Microscopy
- ✓Confocal Laser Scanning Microscopy
- ✓Rapid Prototyping
- ✓Scanning Electron Microscopy (SEM)

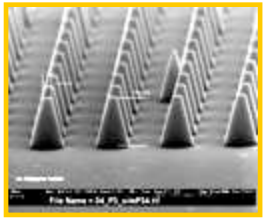


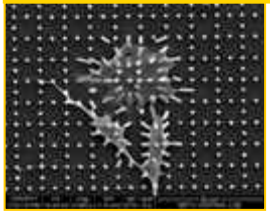
AB 2014

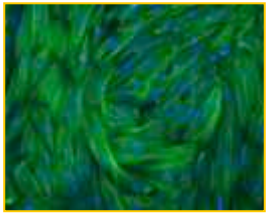
RESEARCH TOPICS

- ✓Orthopedic Implants
- ✓Bone Cements
- ✓Nanobiomaterials
- ✓Tissue Engineering (Bone, Cartilage, Meniscus, Cornea, Nerve, Muscle, Vascular Grafts)
- ✓Biosensors
- ✓Drug Release Systems
- ✓Liposomes, Micro and Nanoparticles
- ✓Motion and Gait Analysis
- ✓Hard and Soft Tissue Testing
- ✓Bioglass Surfaces and Coatings
- ✓Peptide Drug Discovery and Design









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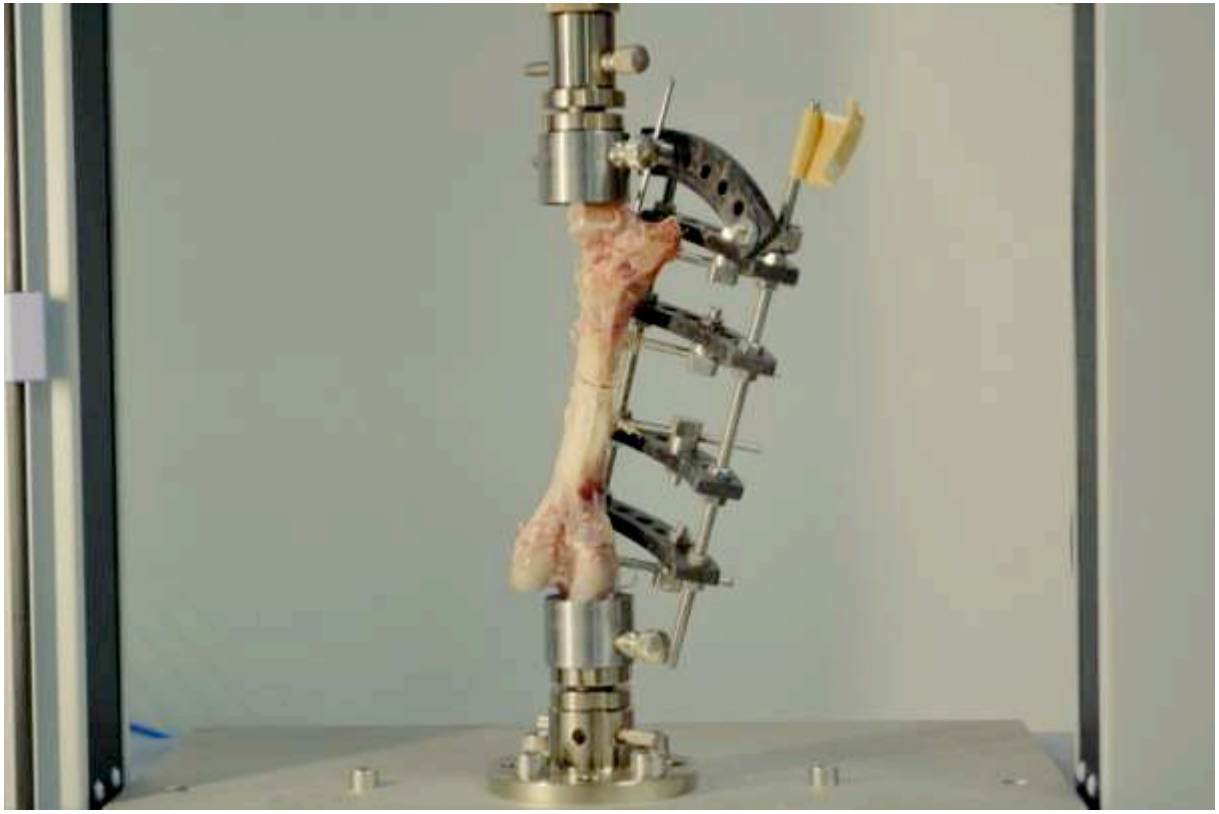
Mechanical Testing on Biological and Biomedical Materials and Products



Simple tension, compression, three and four point bending experiments in dry or wet environment. Elongation and width change measurements by non-contact video extensometer, strain measurement and experimental stress analysis up to 32 points by electric resistance strain gauges. Determination of coefficient of friction between two materials, design and production of custom fixtures for material testing for your specimens.

E. Tonuk Group

METU-Kiss Computerized Gait and Motion Analysis System

Planning and evaluation of treatment, alignment, adjustment and evaluation of prosthetic and orthotic devices can be done by the in-house gait and motion analysis system of METU.

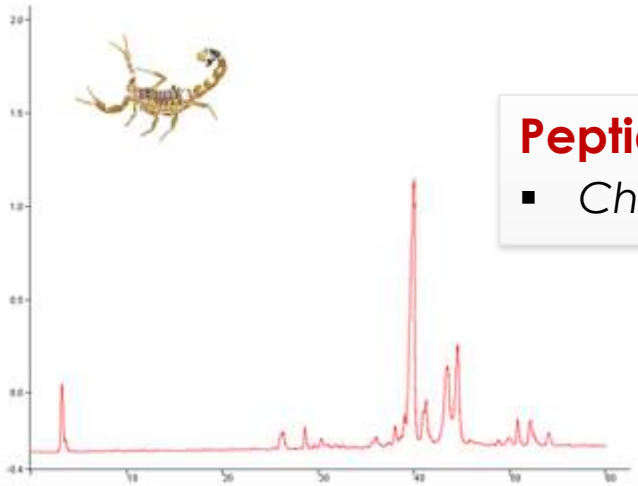
C. Ozen Group

BIOMATEN

Peptide Drug Discovery and Design

Peptides are mini-proteins with remarkable range of biological activities

METU SYBORG is a BIOMATEN research group focused on discovery and design of peptide drugs



Peptidomics

- *Characterization of animal venom peptides*

Bioactivity Screening

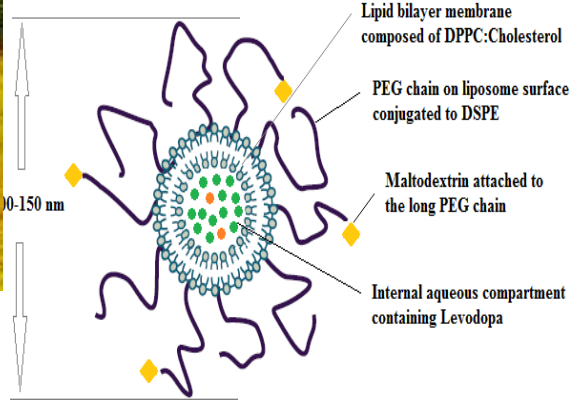
- *Ion channel assays; lead discovery for cancer, pain, autoimmune diseases, and other disorders*

Structure-based Drug Design

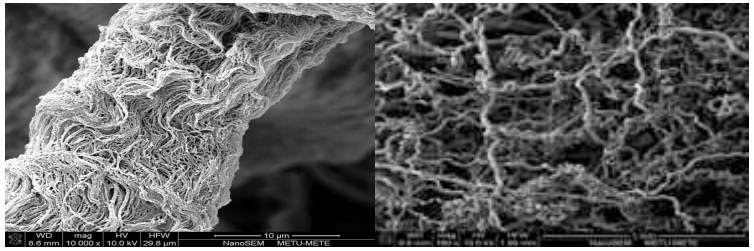
- *Structural and thermodynamic characterization of peptide-protein complexes*
- *Rational drug design based on peptide scaffolds*

Cell loaded microspheres
for cartilage repair

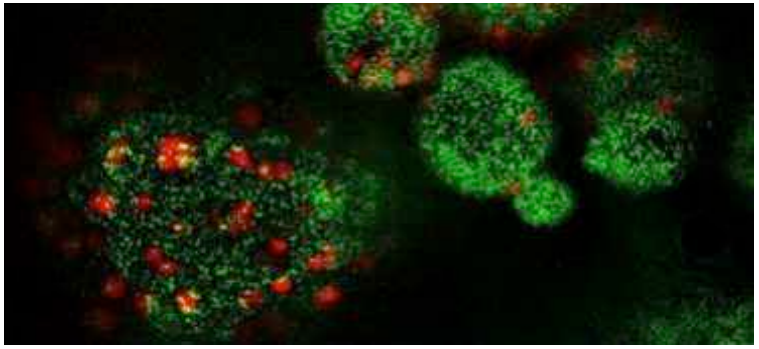
BIOMATEN



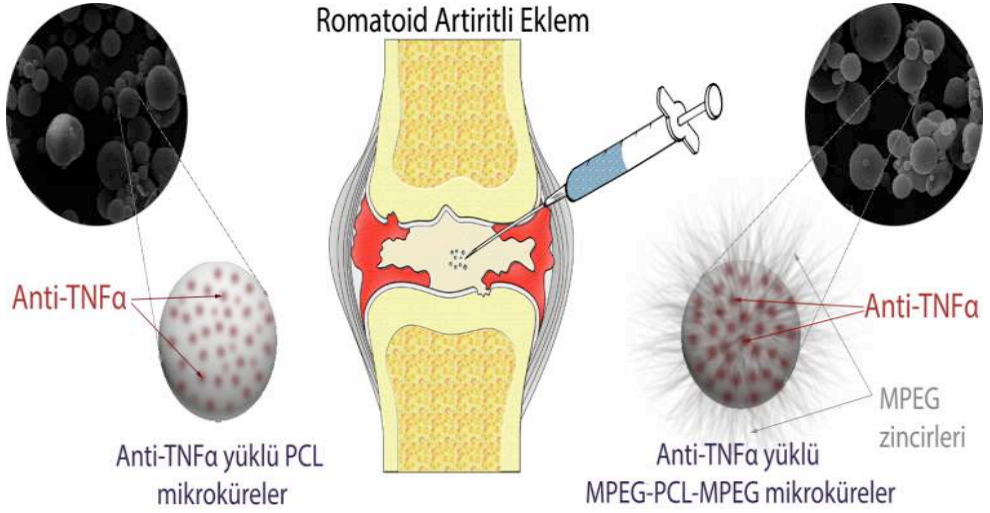
Liposomal anticancer agent
delivery system



Electrospun fibers for
Bone Tissue Engineering



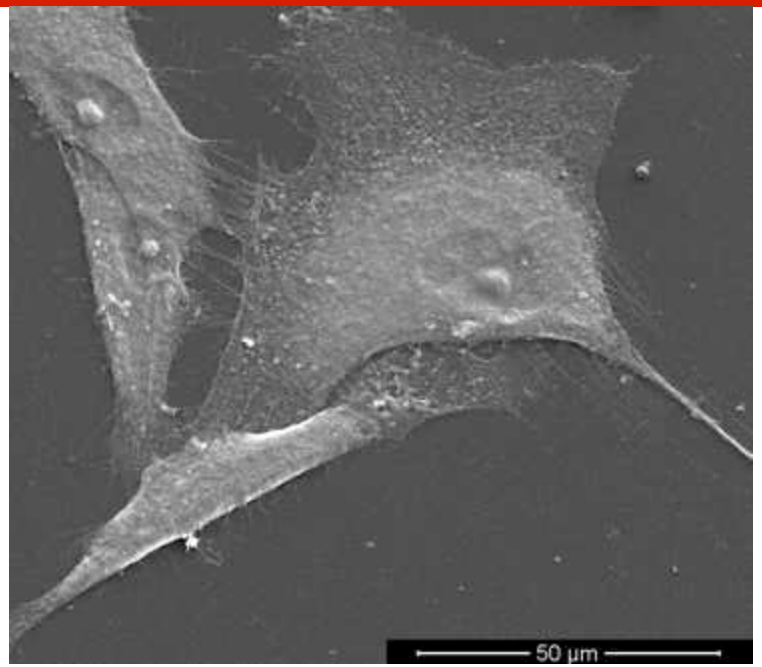
Bone cells on hydroxyapatite
microspheres



Drug loaded microspheres for rheumatoid arthritis treatment
(Patent application made)

A. Tezcaner and D. Keskin Group

In Vitro
Modified Surfaces and Cell Distortion

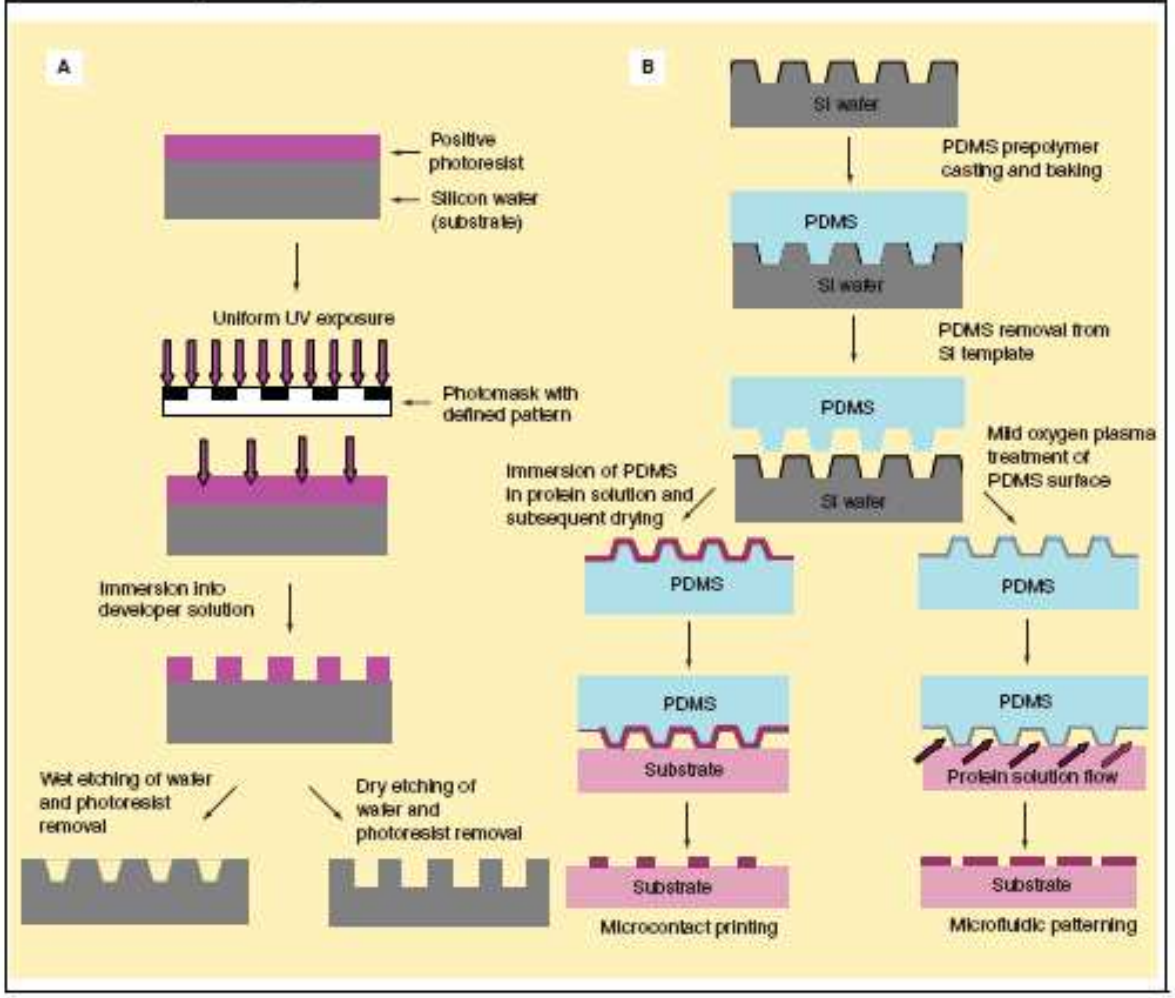


Nano and Micromodified Surfaces

REVIEW – Hasirci & Kenar

Photolithography

Figure 1. Representative schemes for the production process of (A) micropatterned silicon template by photolithography and subsequent etching and (B) micropatterned substrates using microcontact printing and microfluidic patterning.

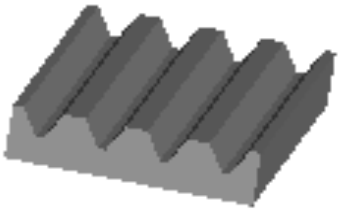


Hasirci, V. Pepe-Mooney, B.J. **2012**, Nanomedicine, DOI 10.2217/NNM.12.7

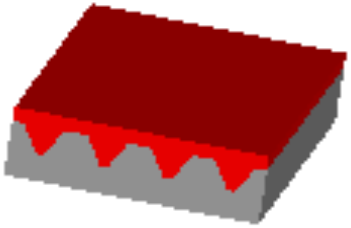
V. Hasirci and H. Kenar, Nanomedicine 2006, 1(1), 73-89

Preparation of Micro and Nanopatterned, Surface Modified Film

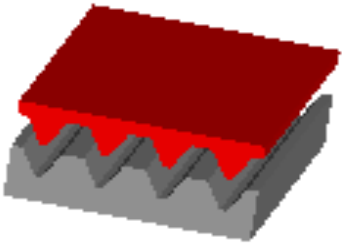
Micro/nano patterned Si Wafer



Solvent casting of Polymer Film



Peeling the film off the Si Wafer



Bioactive cue adsorption or covalent immobilization and cell seeding on the micropatterned films

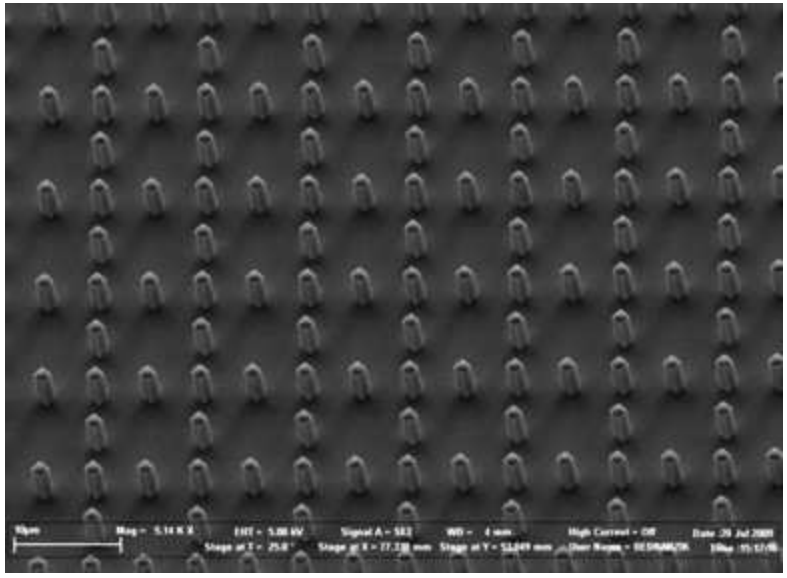
Nanopillars

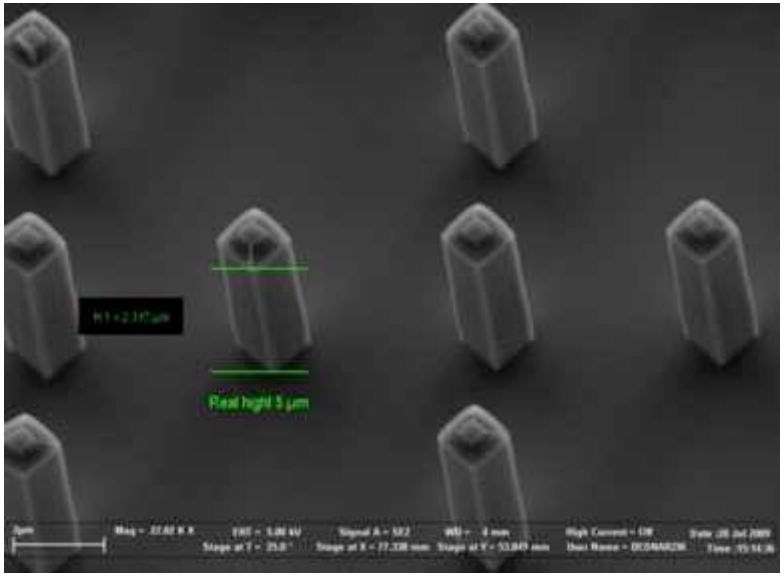
BIOMATEN

Used Template: Mold6

Rod height : 5 µm

First replica: PDMS

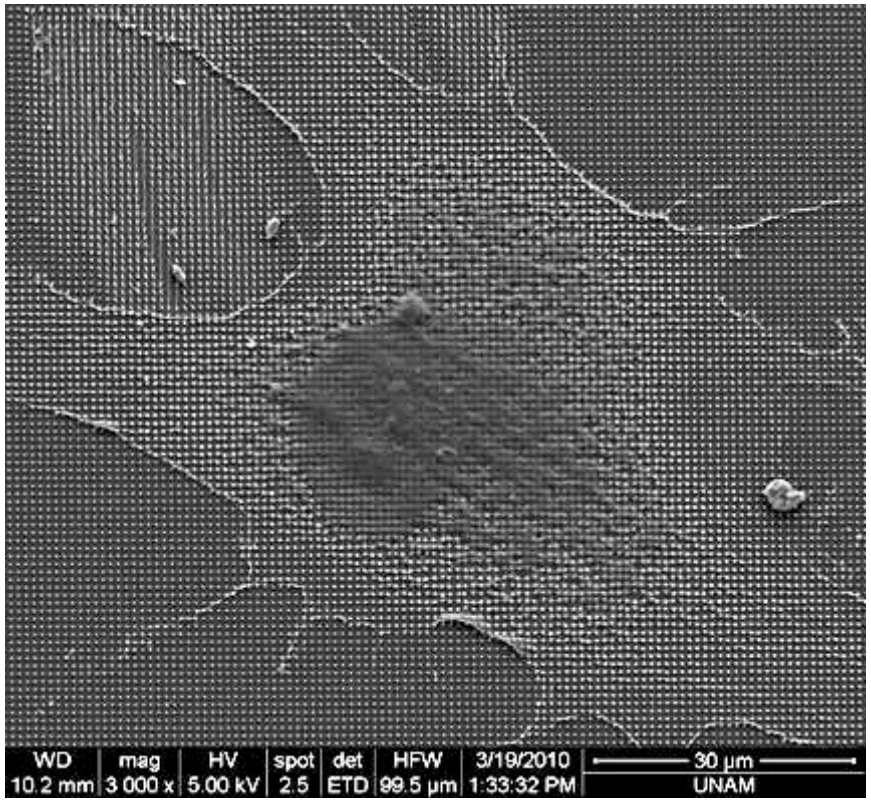


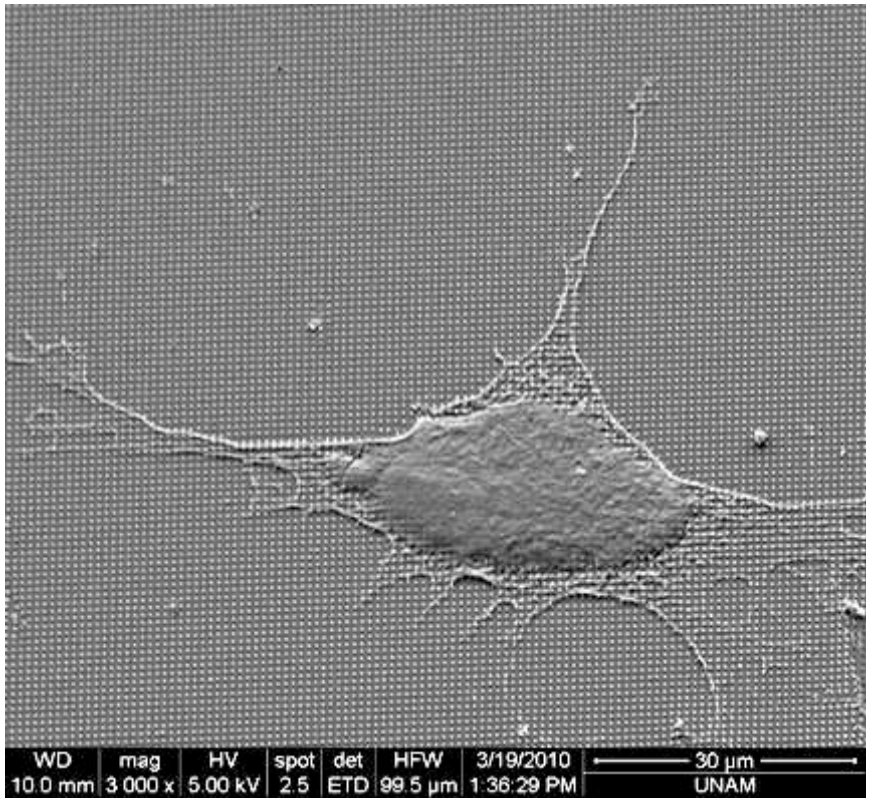


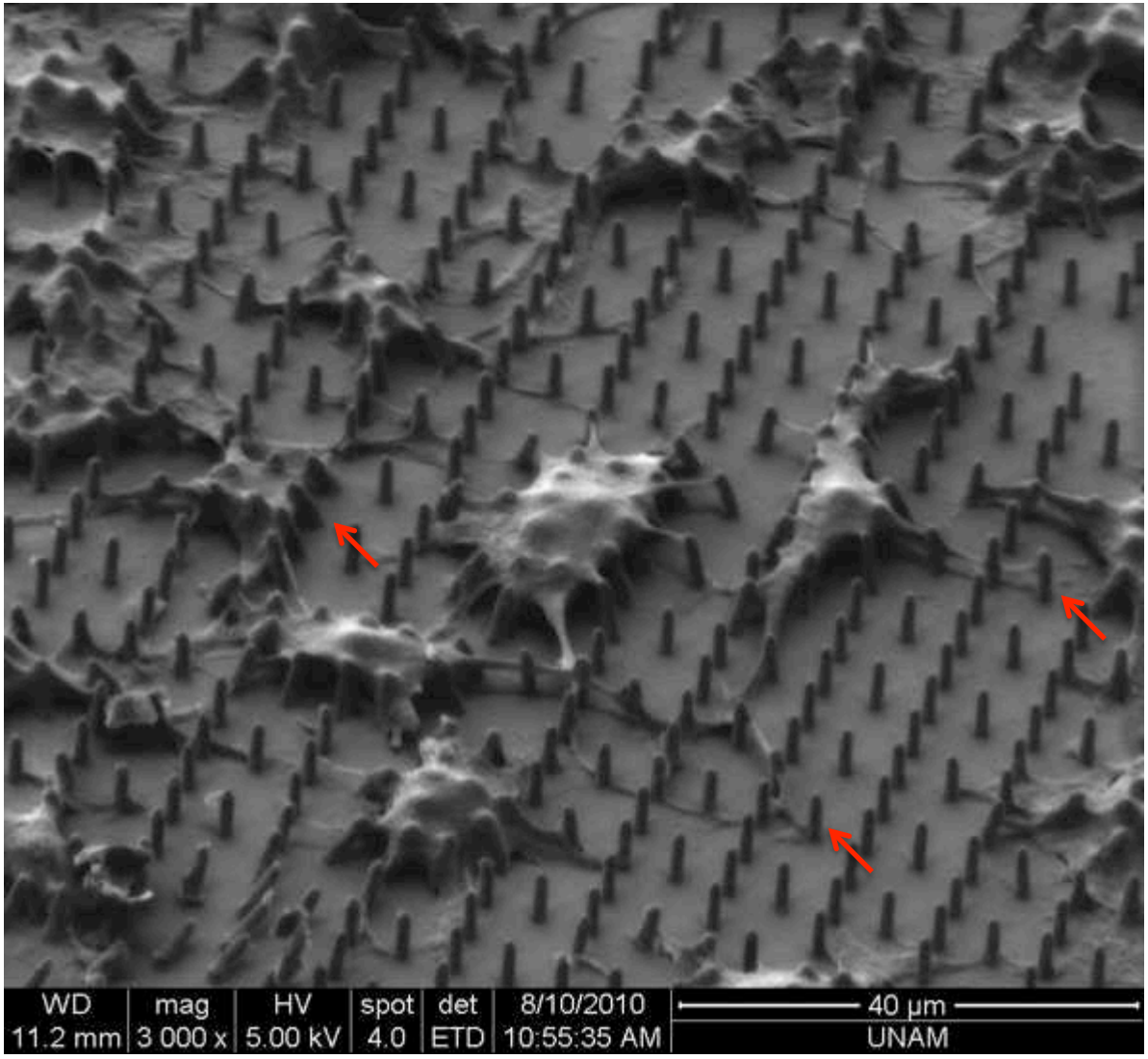
SEM micrograph of original master copy of Mold6

Padeste, C., Özçelik, H., Ziegler, J., Schleunitz, A., Bednarzik, M., Yücel, D., Hasırcı, V. **2011,** Microelectronic Engineering, 88, 8, 1836-1839

Saos-2 on nanopillars







Due to force applied by the L929 cells drastic bendings in the structure of pillars were observed. Cytoskeletal response of L929 cells is more significant when compared with Saos-2 cells.

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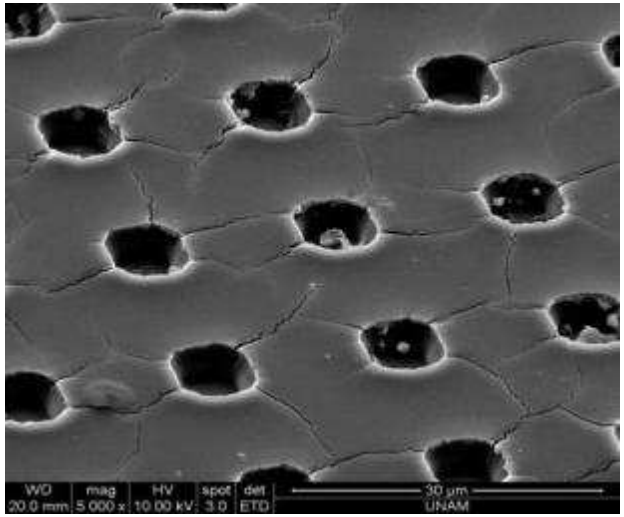
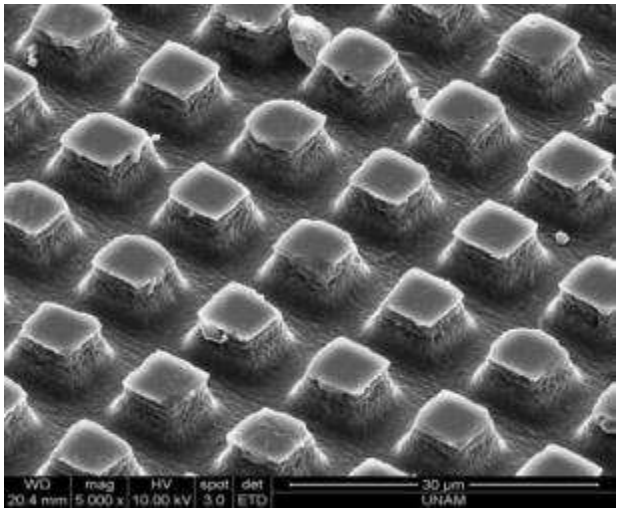
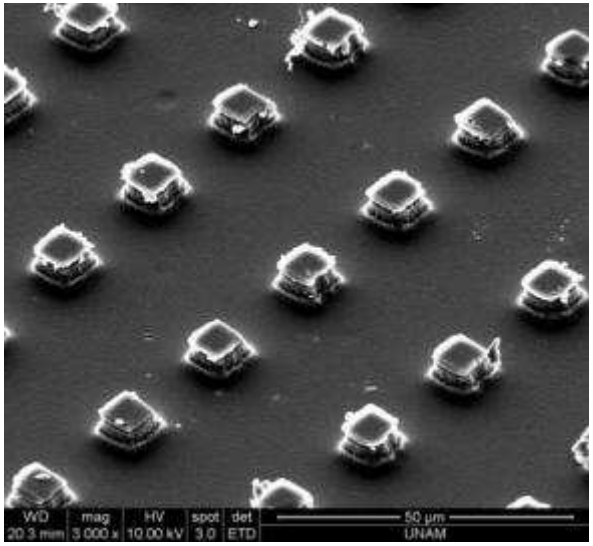
Micro Modified Surfaces



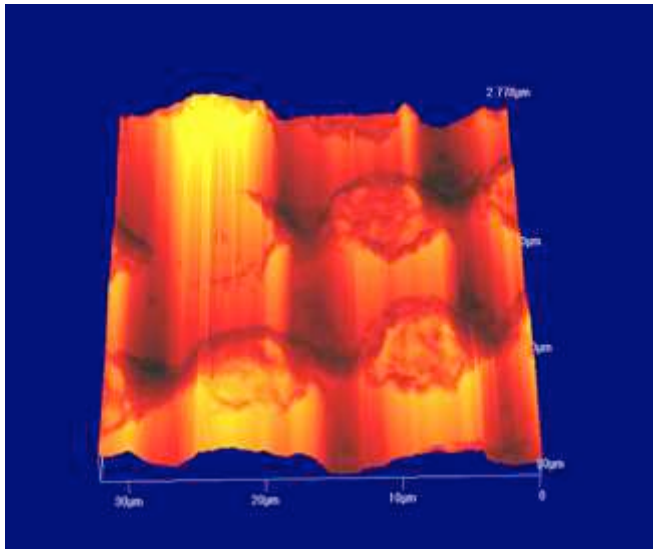
C1 patterned PLLA film



C2 patterned PLLA film



D1 patterned PLLA film



AFM

and Cell Distortion

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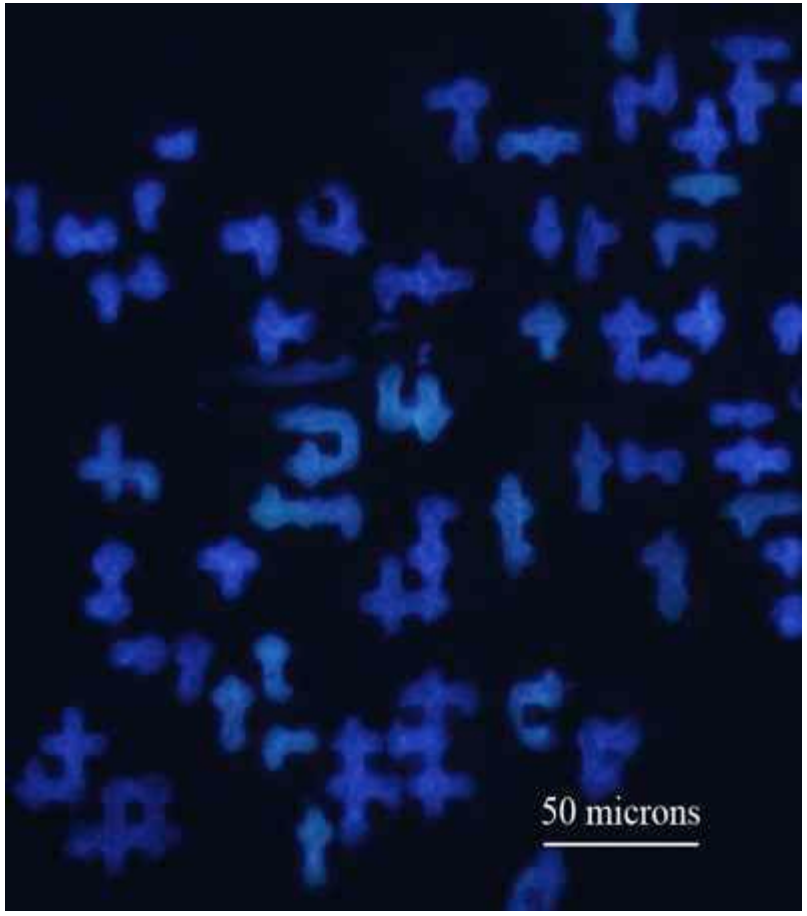
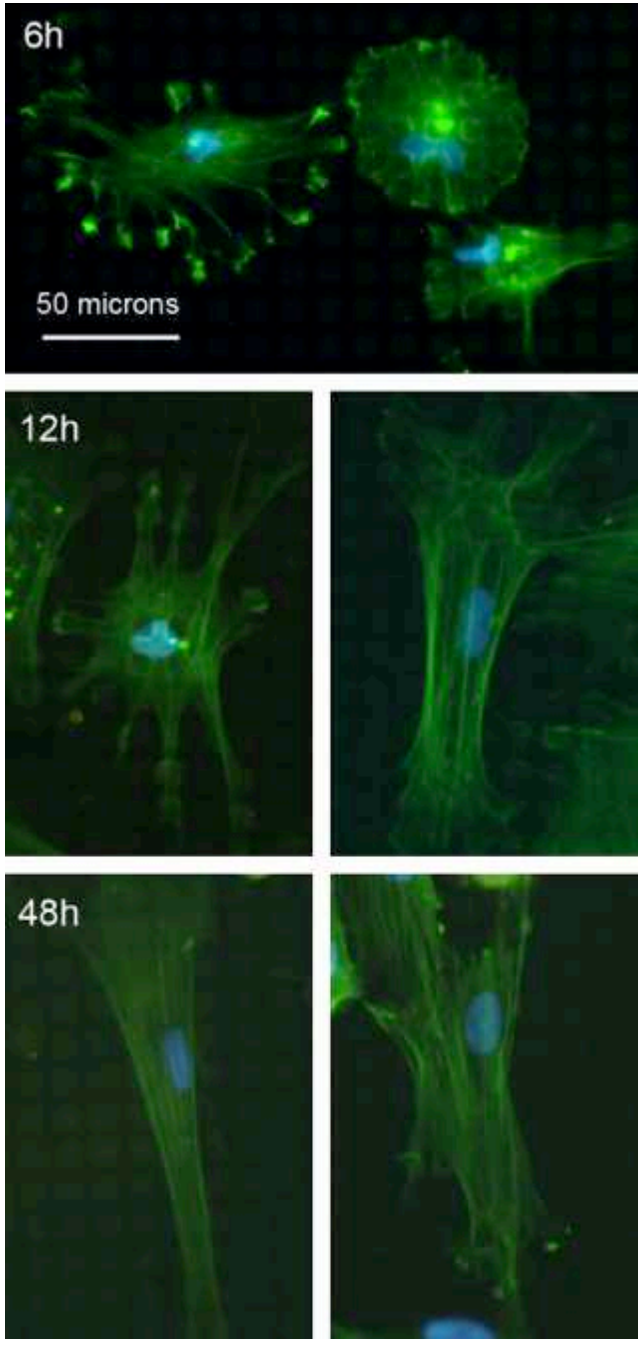


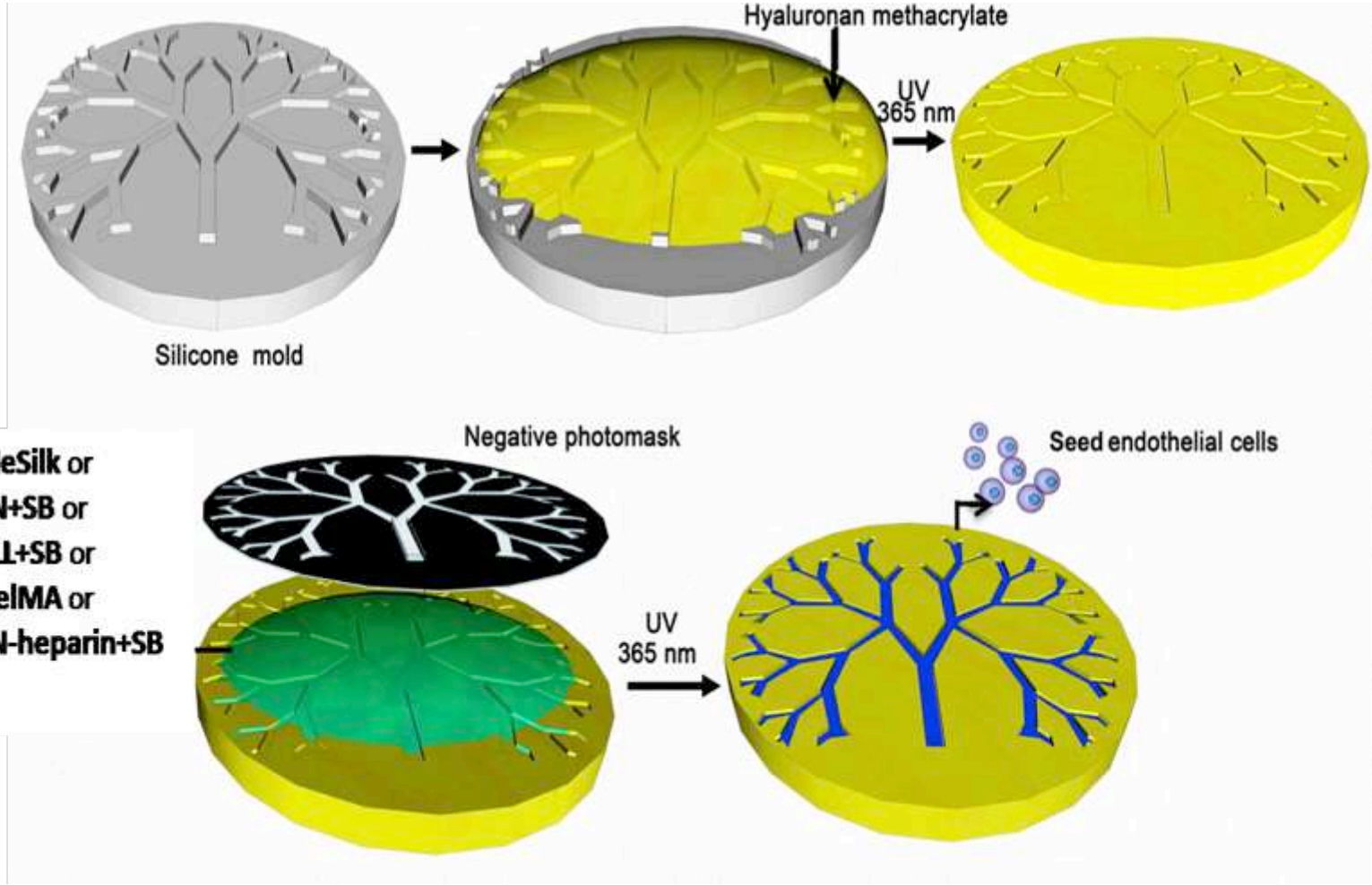


Ozcelik H., Padeste C., Hasirci V. (**2014**) Colloids and Surfaces B: Biointerfaces. DOI:10.1016/j.colsurfb.2014.03.019.

P.M. Davidson, H.Özçelik, V.Hasirci, G.Reiter , K.Anselme,**(2009)** Advanced Materials 21, 1–5, 2009

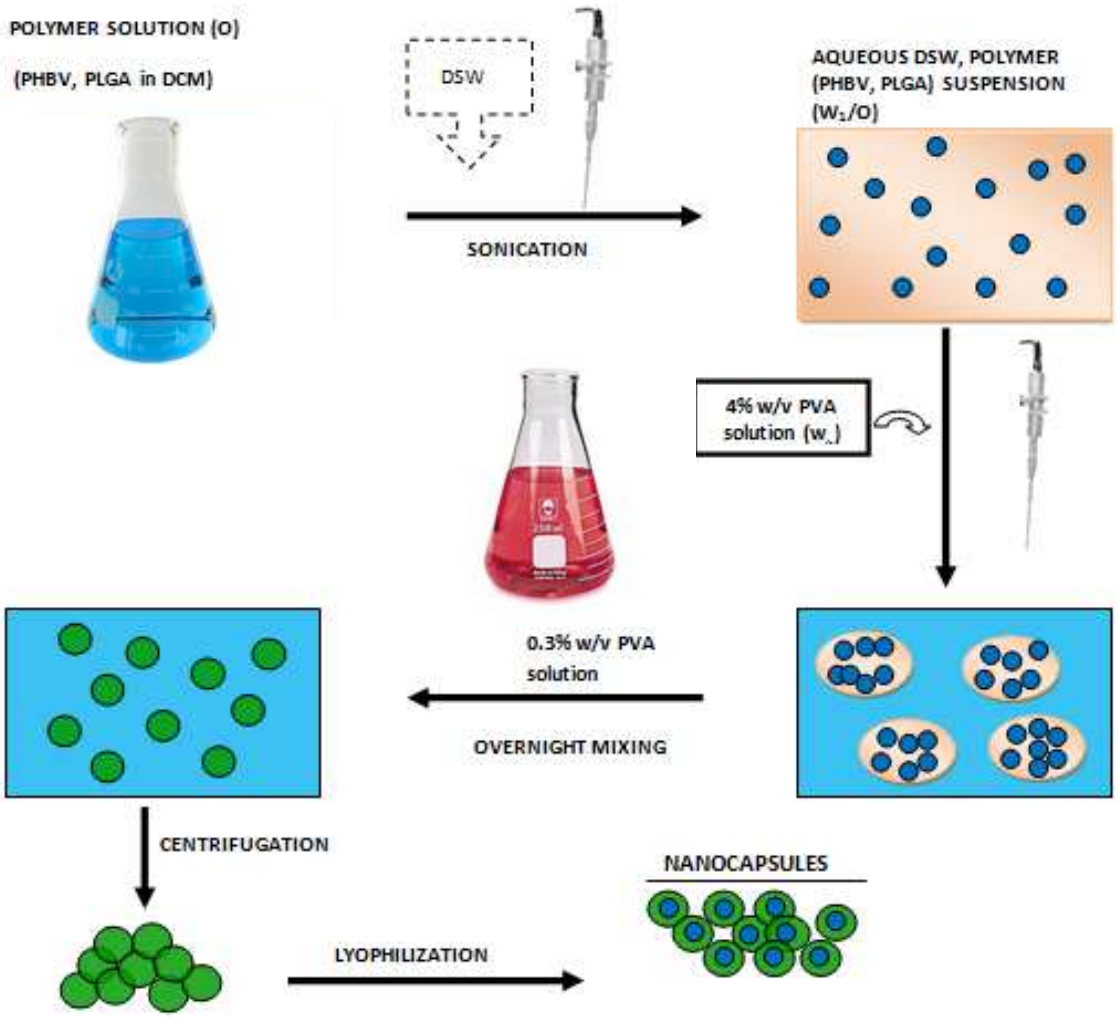
Photolithography for Vasculature

BIOMATEN

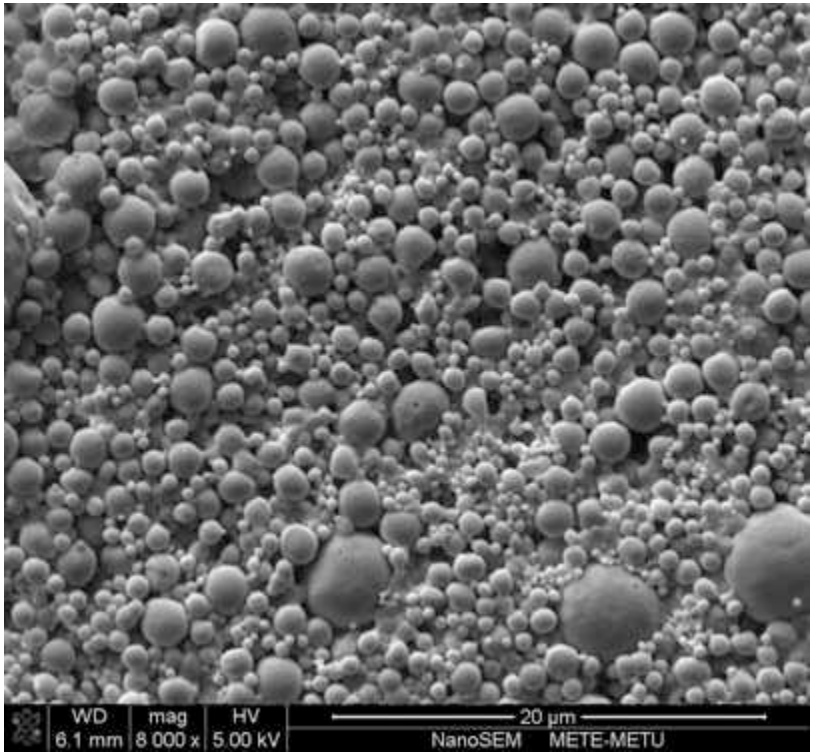


Preparation of Polymeric Nanocapsules

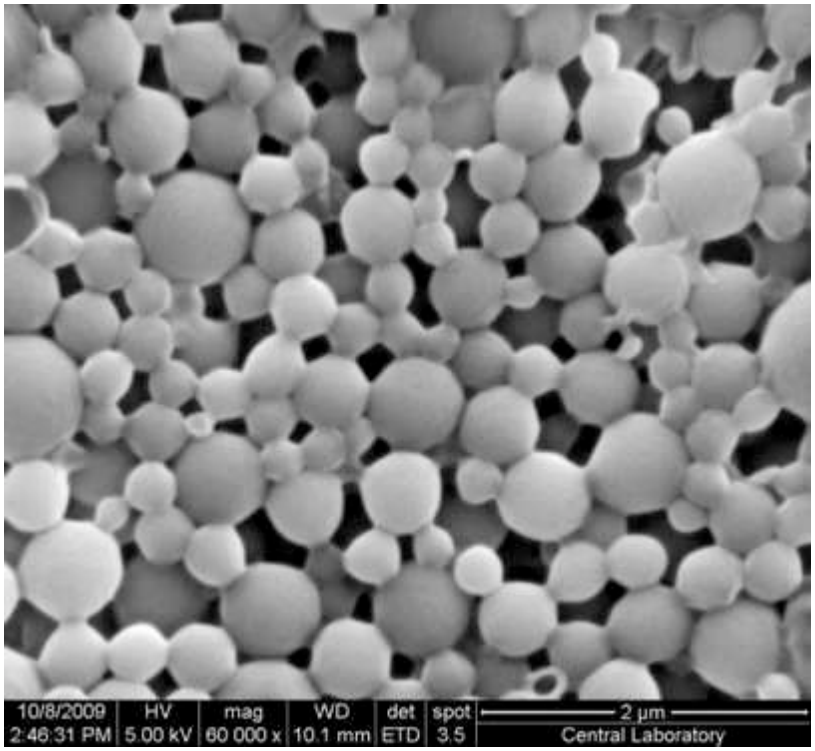
Spray dryer



PHBV / PLGA



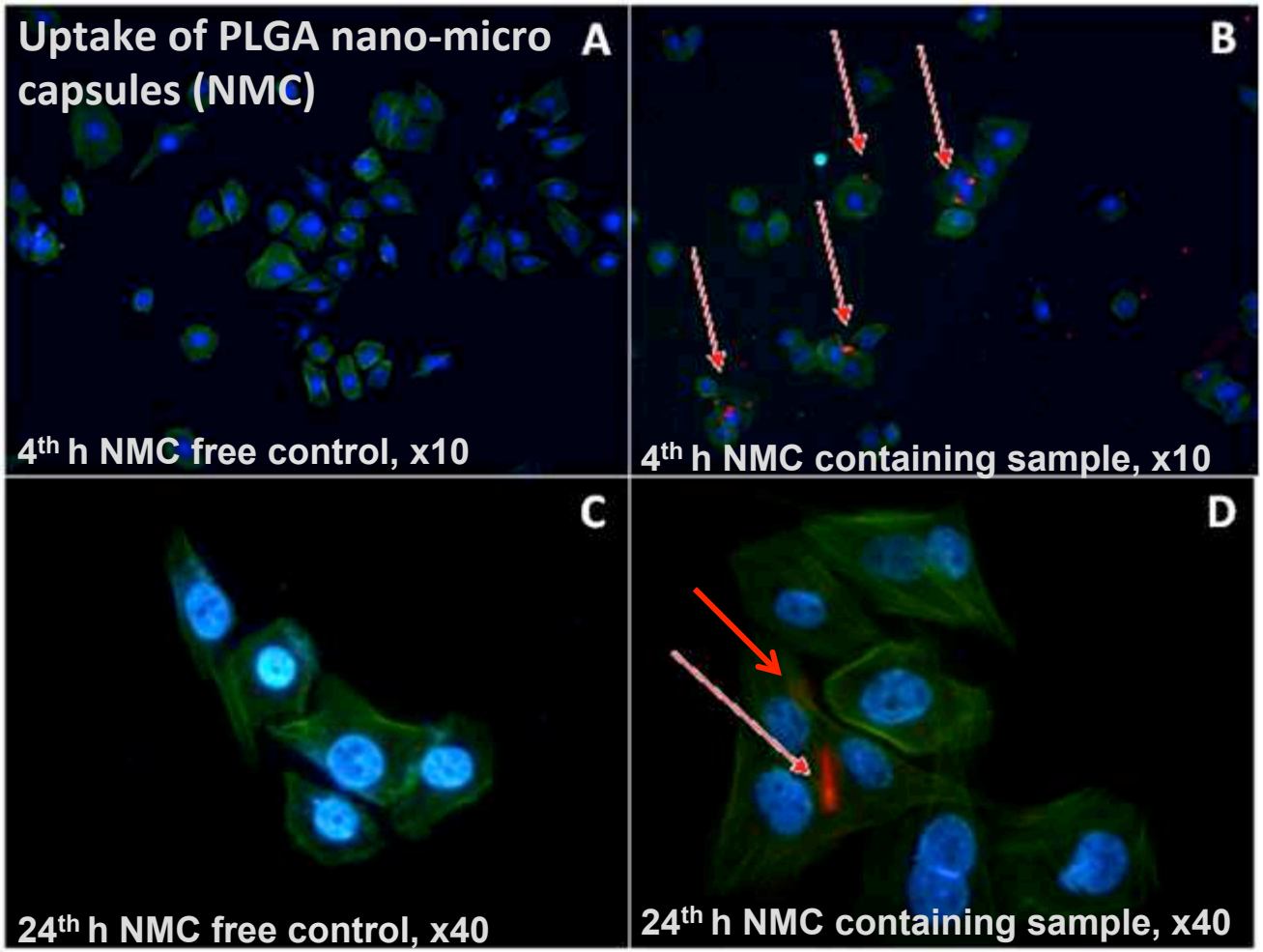
PHBV5 NPs; Unloaded NS
Average Diameter: 650 nm



PLGA NPs; RP loaded NS (450 nm)

Eke G., Kuzmina A., Goreva A., Shishatskaya E., Hasirci N., Hasirci V. (**2014**) Journal of Nanomaterials Science: Materials in Medicine. DOI:10.1007/s10856-014-5169-5.

Uptake of PLGA Nano-Microcapsules By Saos-2



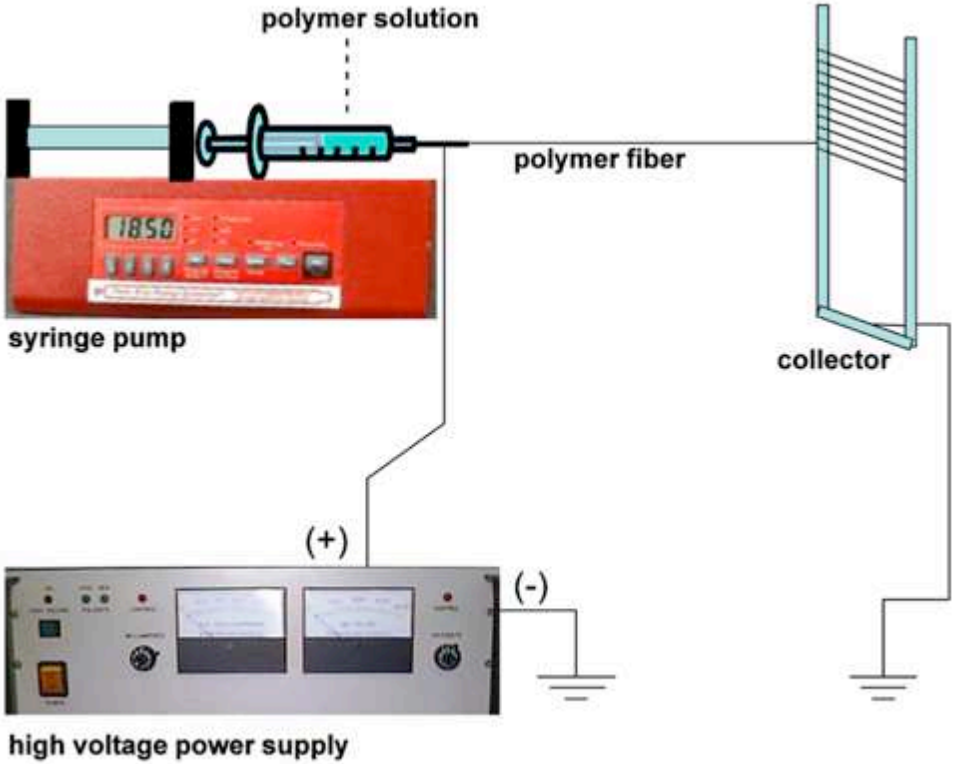
up by Saos-2 cells.

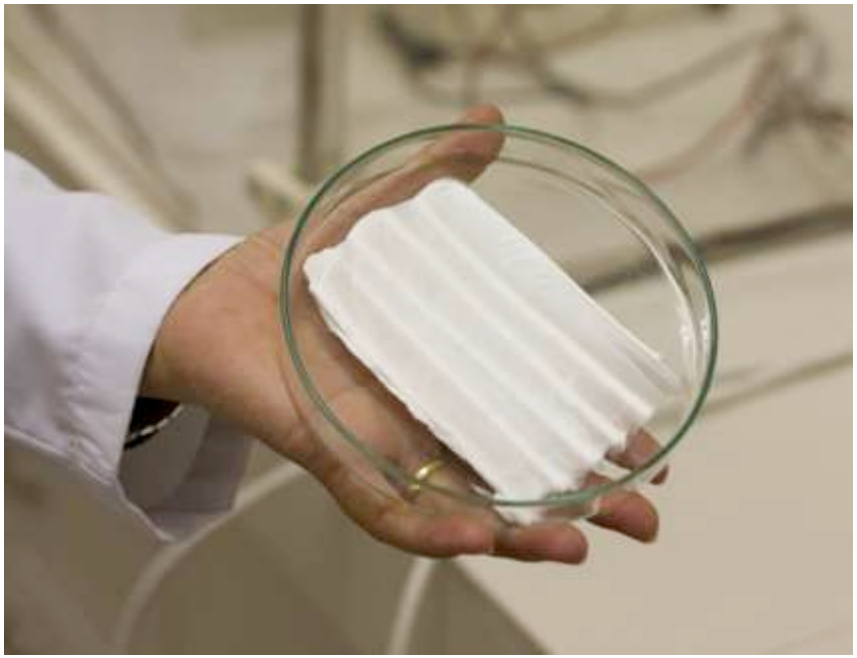
A. Küçükturhan MSc Thesis-FP7 Skin Treat Project

BIOMATEN

Cardiac Patches, Vascular Grafts, Nerve Guides

Electrospinning System

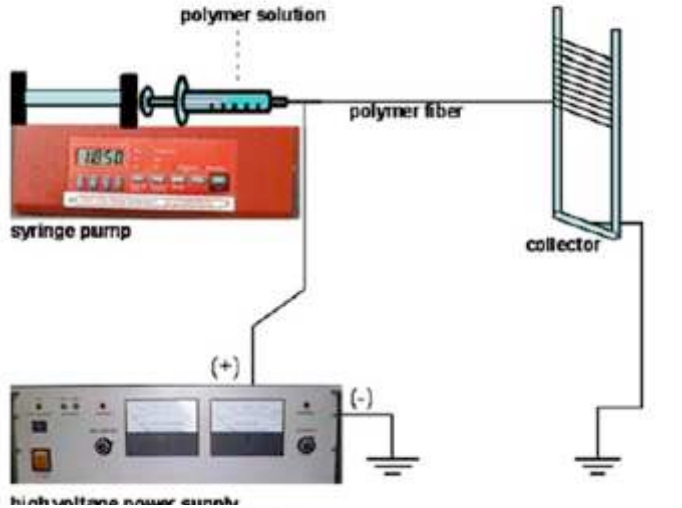


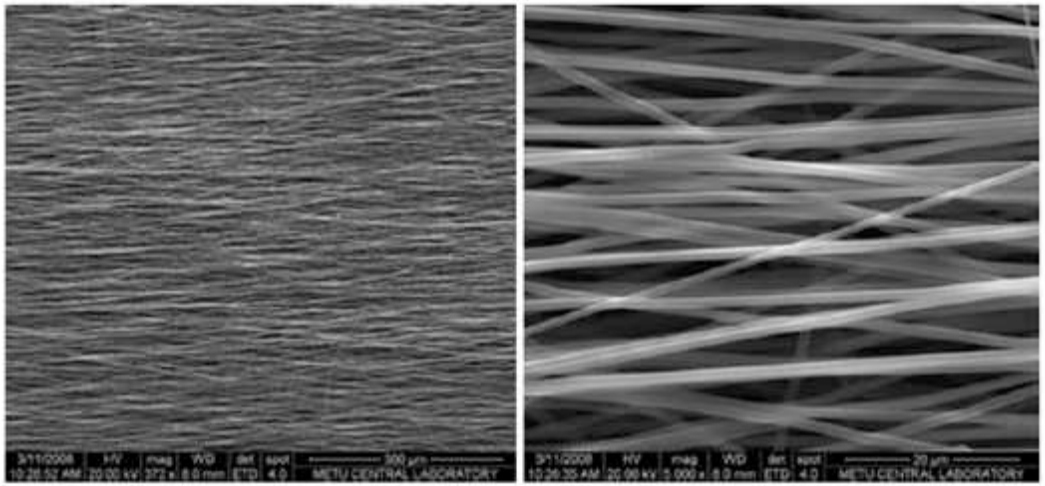


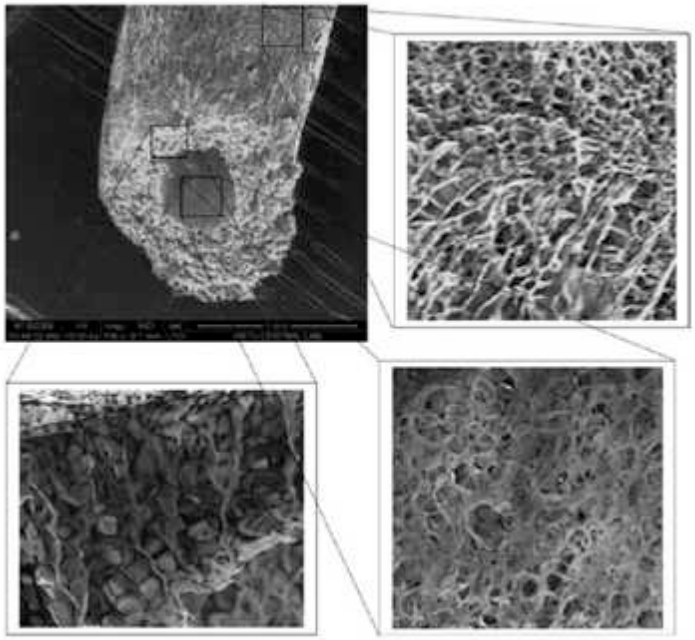
D. Yucel, GT.Kose, V. Hasirci, (**2010)** Polyester Based Nerve Guidance Conduit Design, Biomaterials 31 1596–1603,

Electrospinning for Cardiac Patch

J Mater Sci: Mater Med







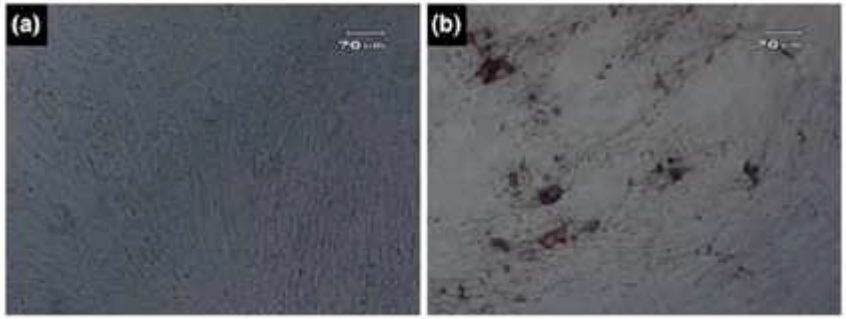
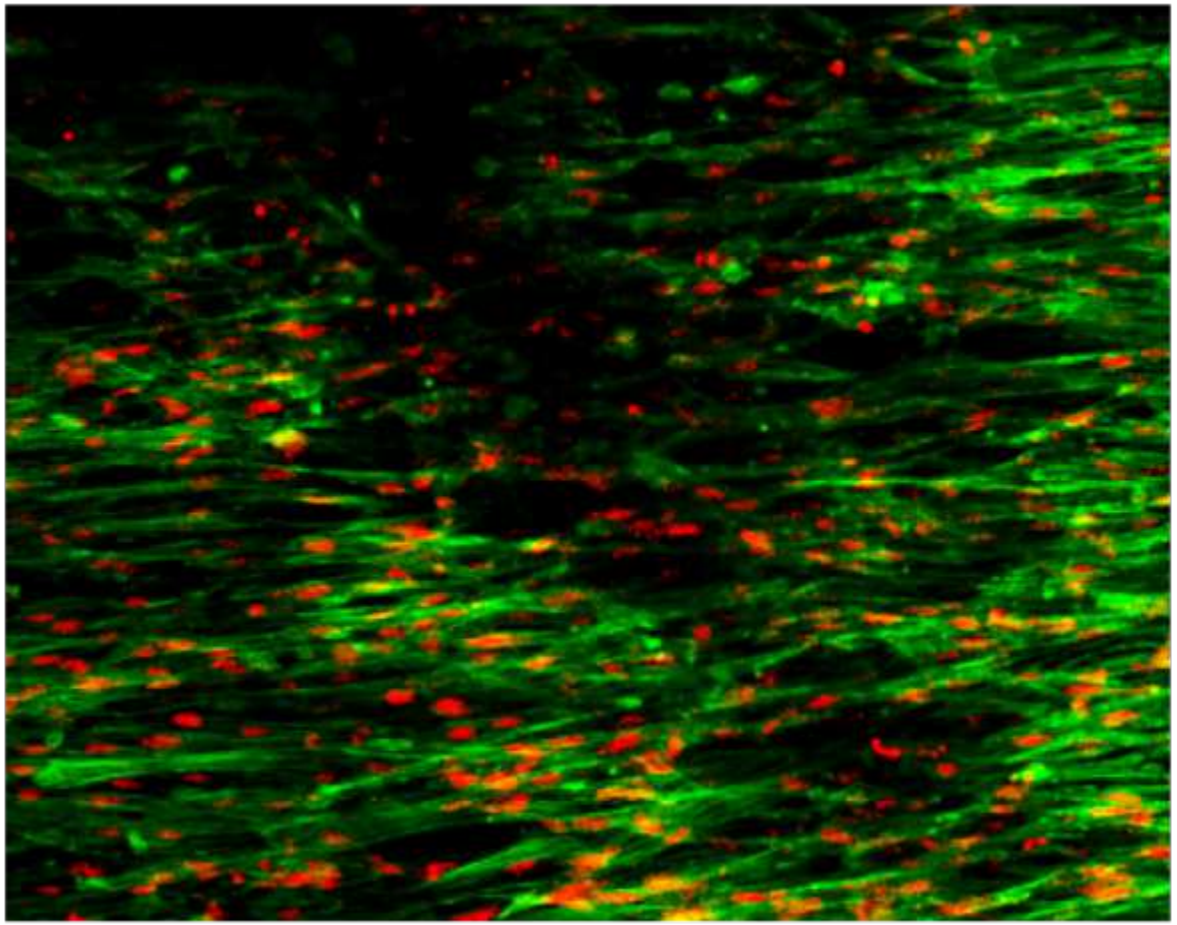


Fig. 5 Light micrographs of WJ MSCs. **a** undifferentiated, **b** differentiated into bone cells. von Kossa staining. (×100)

Design of a 3D aligned myocardial tissue construct from biodegradable polyesters

H. Kenar · G. T. Kose · V. Hasirci

WJSCs Grown On Aligned Fibrous PHBV-P(L-D,L)LA:PGS Mats (14 Days)



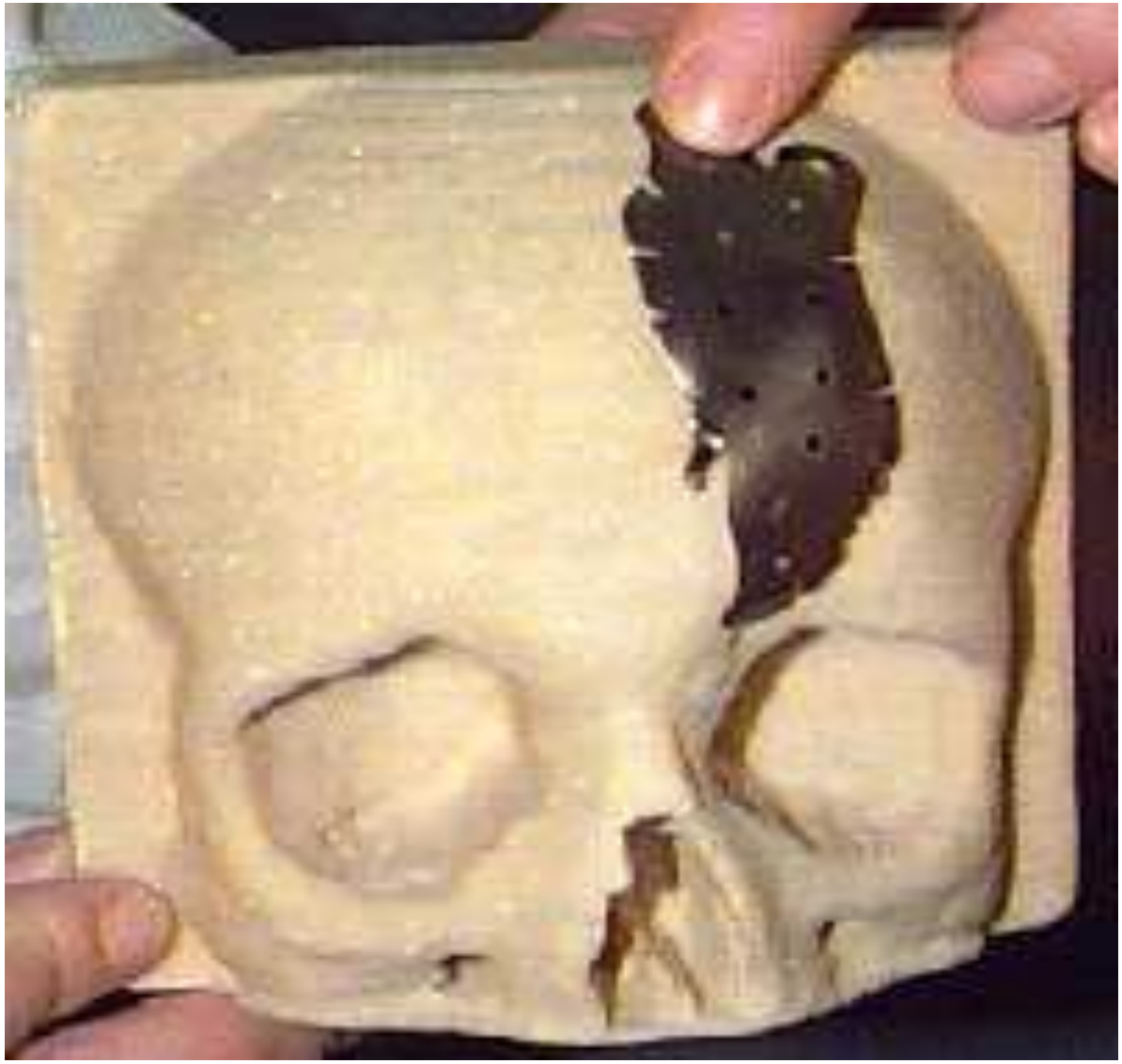
Green: filamentous actin stained with FITC-Phalloidin,
Red: cell nuclei stained with PI.

Kenar, H., Kose, G.T., Toner, M., Kaplan, D.L. Hasirci, V. (**2011**) Biomaterials, 32, 23, 5320-5329

BIOMATEN

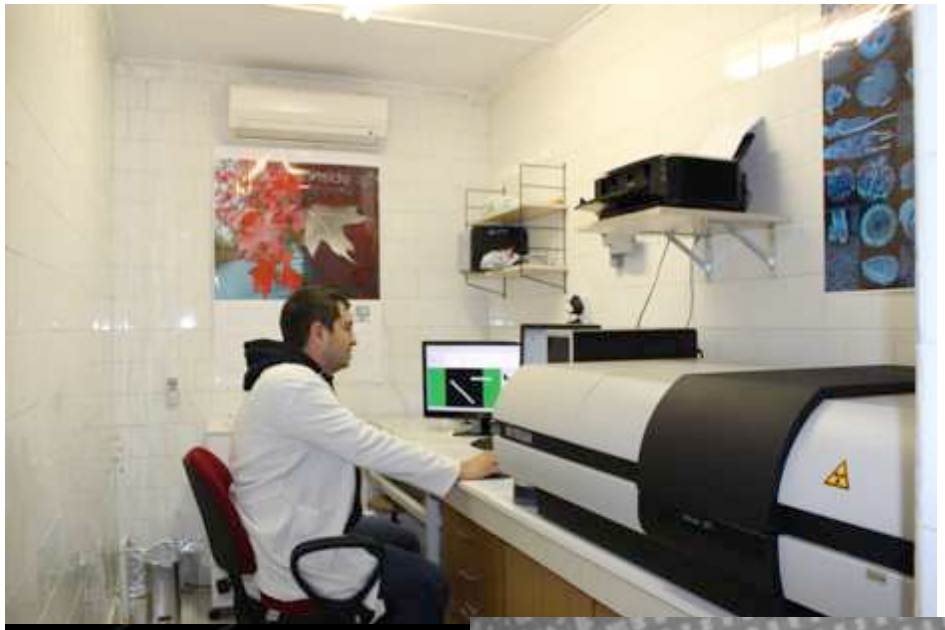
Additive Manufacturing for Patient Specific Bone Implant Preparation via Tissue Engineering

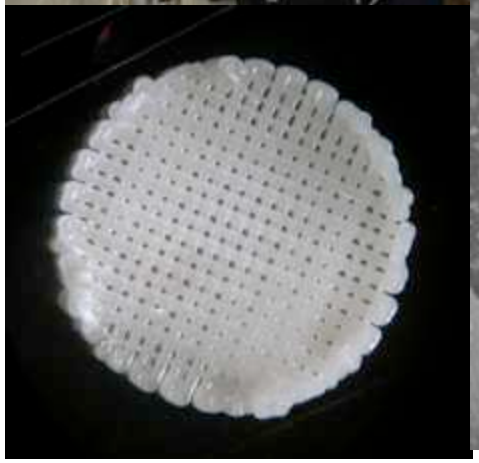
Patient Specific Implants

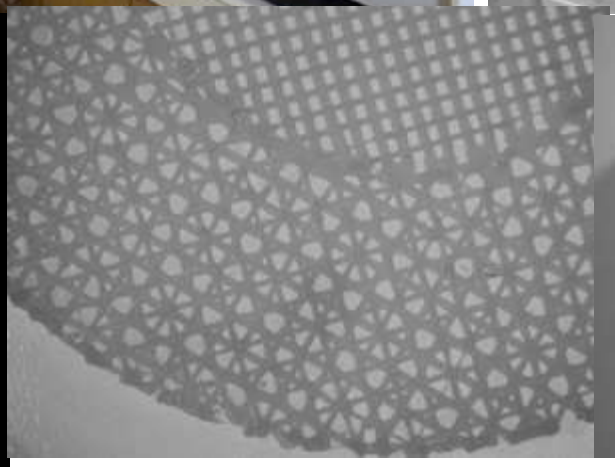


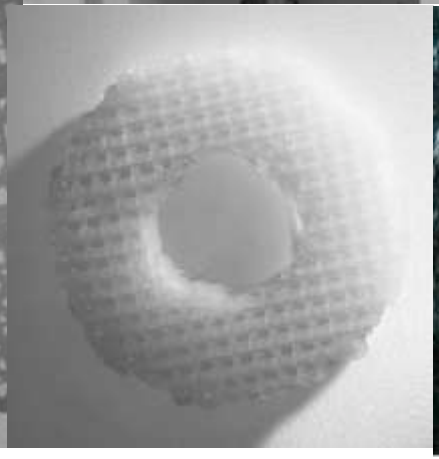
Patient Specific Implants

BIOMATEN





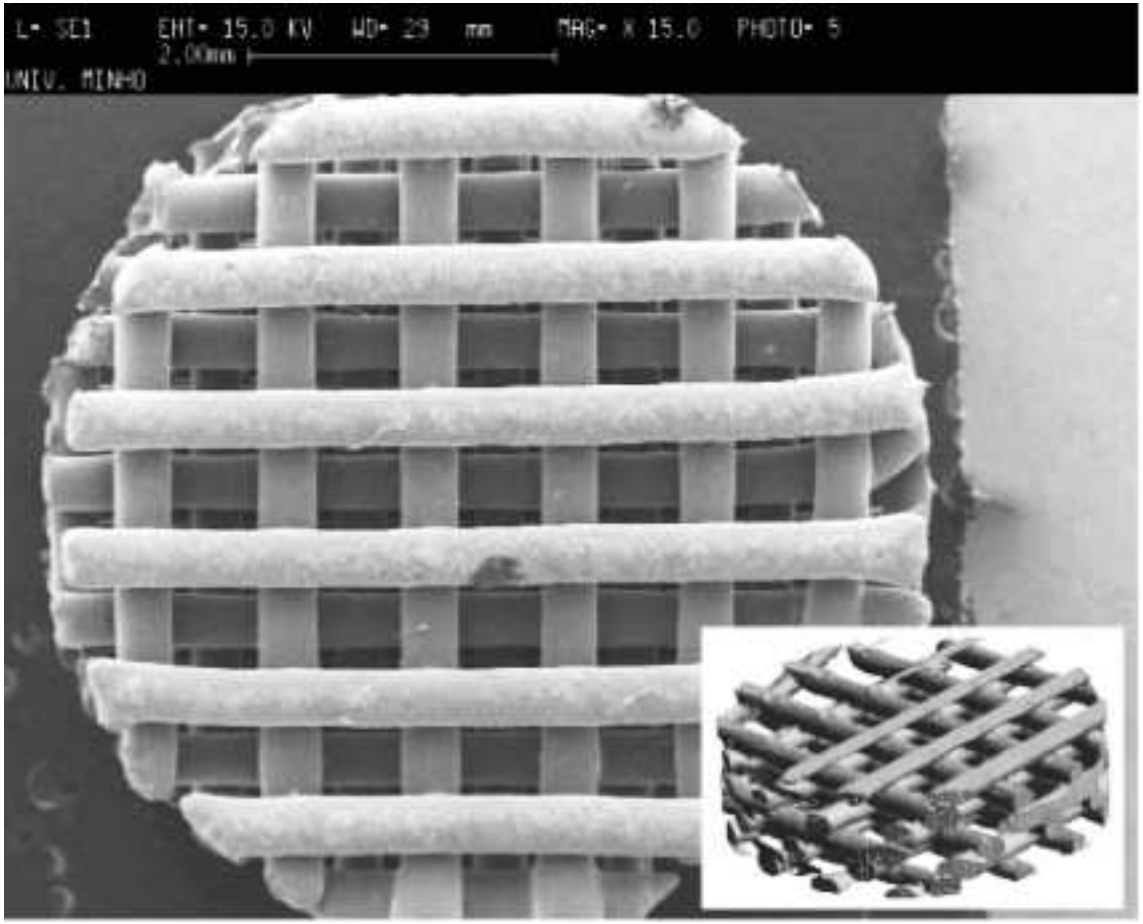


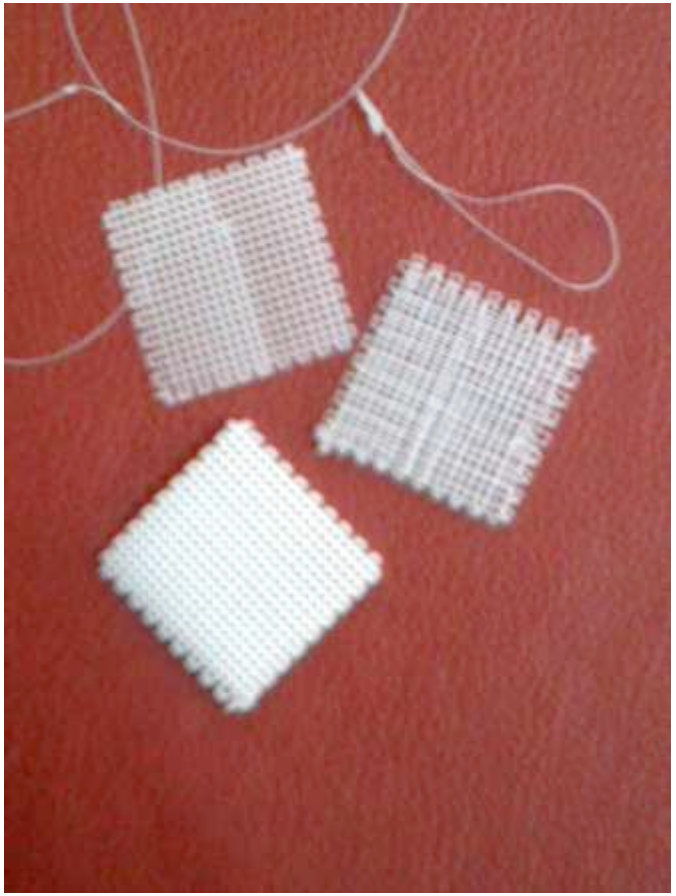


Patient Specific Implants

BIOMATEN

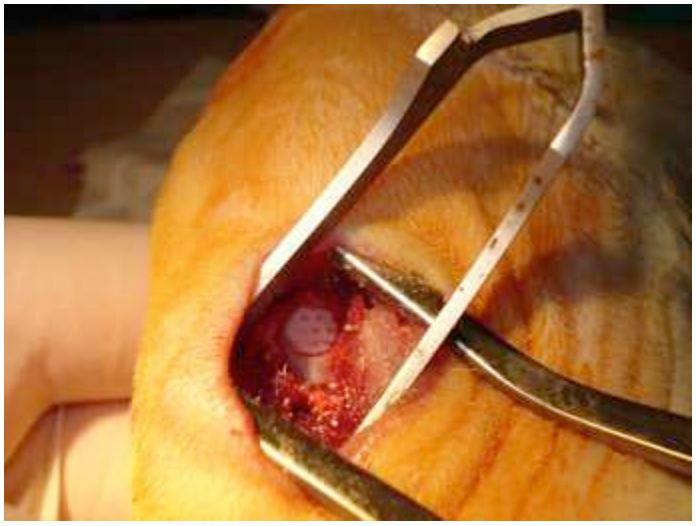
Rapid Prototyped Microfibrous Scaffolds

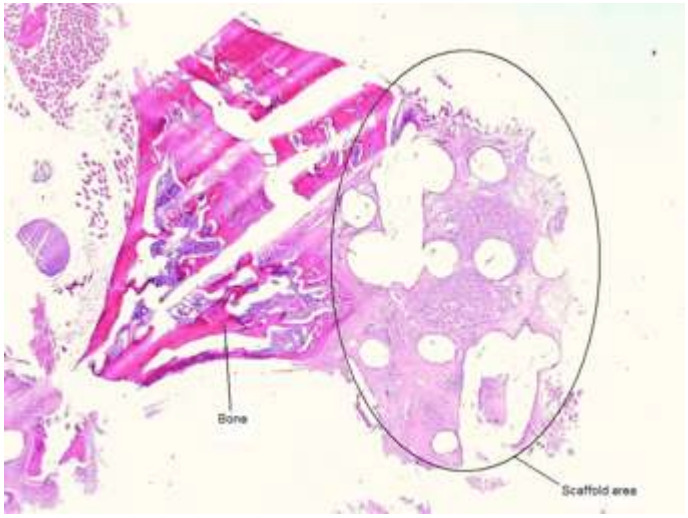


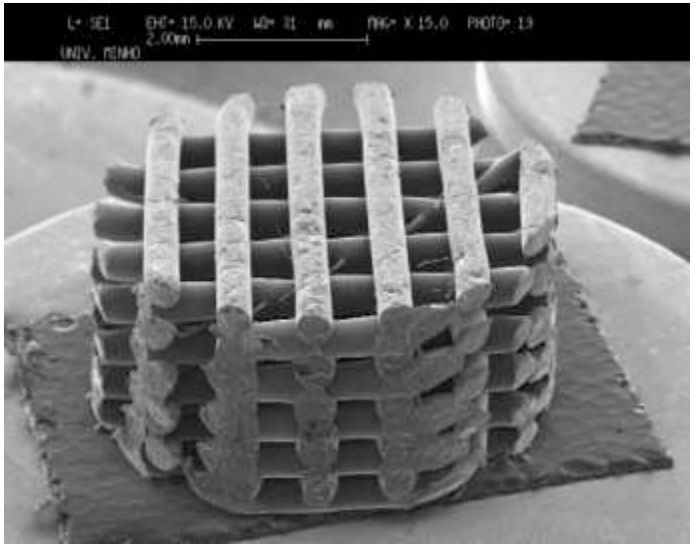


P. Yilgor, R. A. Sousa, R. L. Reis, N. Hasirci, V. Hasirci, Macromol. Symp. 2008, 269, 92–99

Implanted Scaffold (in Vivo)



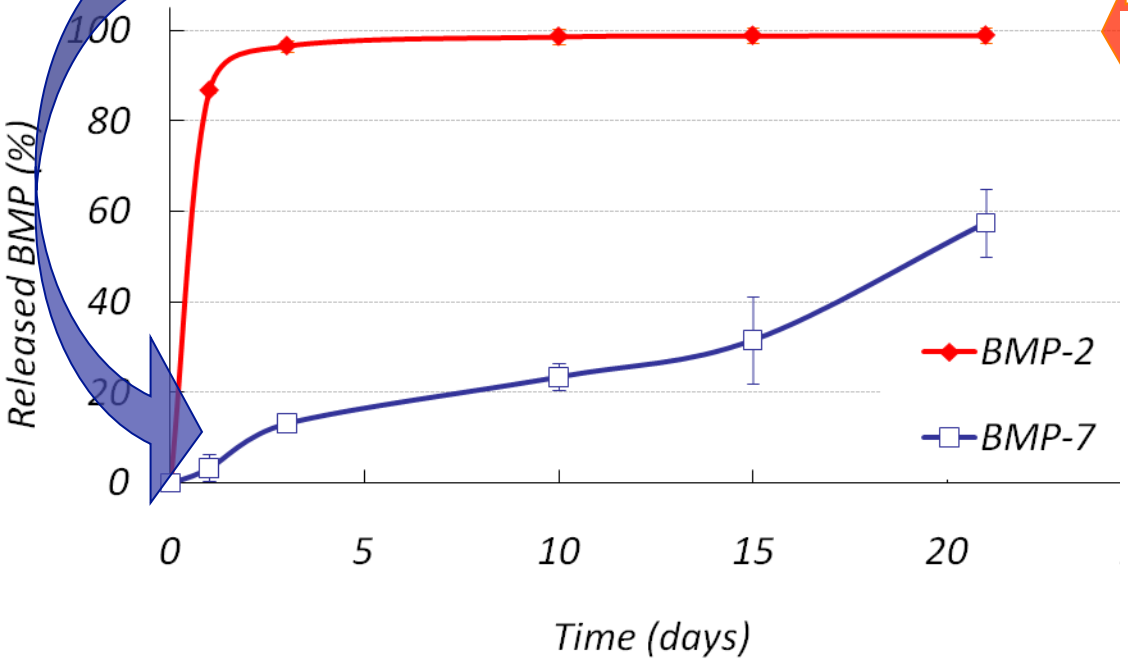


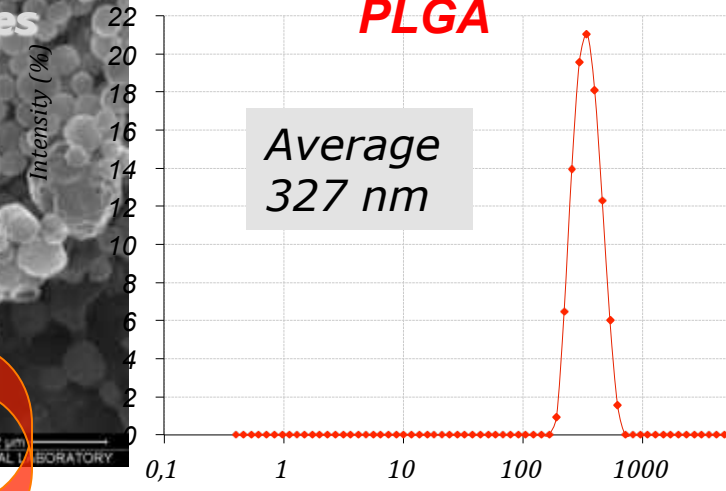


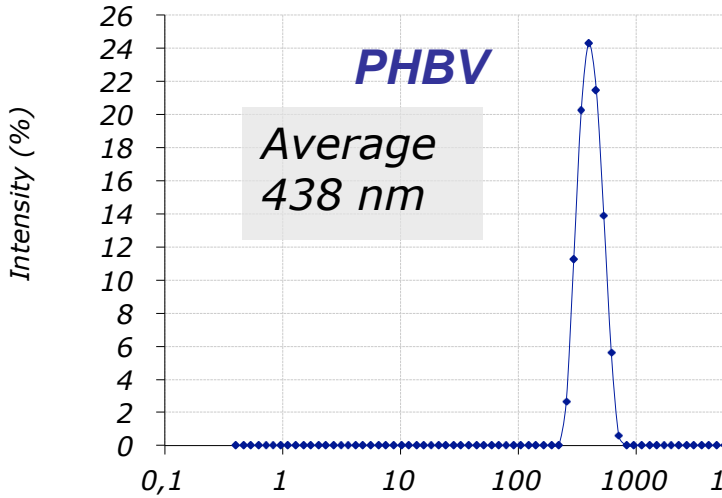
PY Huri, G Huri, U Yasar, Y Ucar, N Dikmen, N Hasirci, V Hasirci, Biomedical Materials,(doi 10.1088/1748-6041/8/4/045009)

P.Yilgor, G.Yilmaz, M.B.Onal, I.Solmaz, S.Gundogdu, S.Keskil, R.A.Sousa, R.L.Reis, N.Hasirci, V.Hasirci, J Tissue Eng Regen Med, (doi: 10.1002/term.1456)

BMP Release







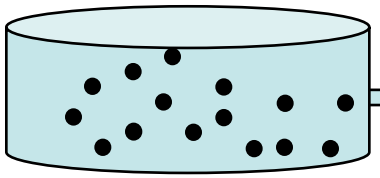
Yilgor et al., Biomaterials, 2009

Products/Potential Products

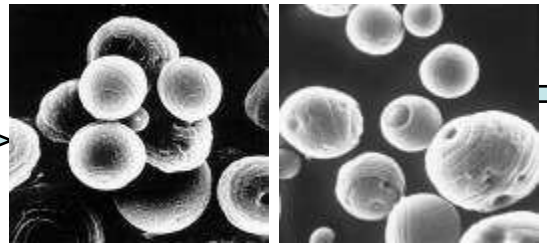
BIOMATEN

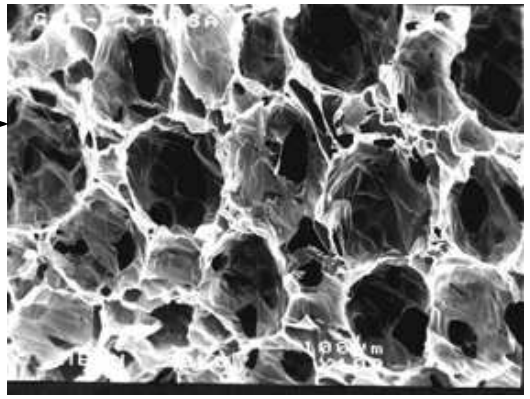
2010

Wound Dressings:
Approach to GF Releasing Sponges



Micro and nanoparticles carrying bioactive agents

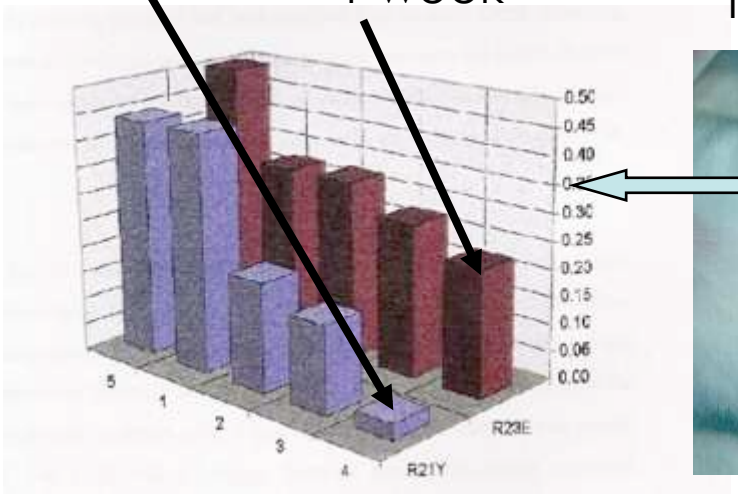




In vivo w/ rabbits

10 days

1 week



4 OCAK 2011

BIOMATEN

Notified Body No. 1023
INSTITUTE FOR TESTING AND CERTIFICATION, Inc.
Zlin, Czech Republic – www.itczlin.cz

EC CERTIFICATE

No. 11 0001 QS/NB

issued in compliance with the Council Directive 93/42/EEC as amended, which is implemented by the Czech Government Order No. 336/2004 (Collection of Laws) certifies that the products – medical devices of Class III,

NEODERM® Absorbable Wound and Tissue Dressing
GNMD Code: 34615

manufactured by company

ARS ARTHRO BIOTEKNOLOJI A. Ş.
Cyberpark B Block 702A Bilkent, Ankara 90-06800, TURKEY

are manufactured under conditions fulfilling the quality system requirements of Annex II, Section 3.2. of the Directive 93/42/EEC, as amended.

The Notified Body No. 1023 has performed an audit of the above products quality system covering the design, manufacture and final inspection of the certified products. The quality system has been assessed, approved and is subject to continuous surveillance according to Annex II, Sections 3.3. and 5., of the Directive 93/42/EEC. The detailed description of the system parts, requirements and measures applied by the manufacturer are presented in the Final Report No. 803600978/2011, which is enclosed to this Certificate.

This Certificate is issued under the following conditions:

1. *It applies only to the quality system maintained in the manufacture of the above referenced models of the medical devices and it does not substitute the design or type-examination procedures.*
2. *The Certificate remains valid until the manufacturing conditions or the quality system are changed but until the **3rd January 2016** at the latest.*
3. *The Certificate validity is conditioned by positive results of surveillance audits.*
4. *After receiving of the complementary EC Design-Examination Certificate related to the above referenced models, and fulfilling of the relevant EU legislation, the manufacturer shall affix to each medical device, of the above referenced models, the CE marking followed by the number of the Notified Body according to this example:*

CE 1023

Issued in Zlin, on 4th January 2011

RNDr. Radomír Čevelík
Representative of the Notified Body No. 1023

Notified Body No. 1023
INSTITUTE FOR TESTING AND CERTIFICATION, Inc.
Zlin, Czech Republic – www.itczlin.cz

EC Design-Examination Certificate

No. 11 0002 CN/NB

issued in compliance with Council Directive 93/42/EEC as amended, which is implemented by the Czech Government Order No. 336/2004 (Collection of Laws), certifies that the products – medical devices of Class III,

NEODERM® Absorbable Wound and Tissue Dressing
GNMD Code: 34615

manufactured by company

ARS ARTHRO BIOTEKNOLOJI A. Ş.
Cyberpark B Block 702A Bilkent, Ankara 90-06800, TURKEY

fulfil the essential requirements specified in the Annex I of the Directive 93/42/EEC relating to it, taking into account the product's intended use.

The Notified Body No. 1023 has executed the EC design-examination of the above-mentioned product according to the Annex II, paragraph 4, of the Directive 93/42/EEC. The detailed product descriptions, documents, assessment procedures and evaluation of the examination are presented in the Final Report No. 803600978/2011, which is enclosed to this Certificate.

This Certificate is issued under the following conditions:

1. *It applies only to the design of the above referenced models of the medical devices.*
2. *It does not imply that the Notified Body has performed any surveillance or control of their manufacture.*
3. *The manufacturer is obligated to assure that all medical devices of the respective models conform to the type whose design has been approved by this Certificate.*
4. *The Certificate remains valid until the approved design is changed but until the **3rd January 2016** at the latest.*
5. *After receiving of the complementary EC Certificate, confirming the manufacturer's quality system approval by the Notified Body No. 1023, and fulfilling the relevant EU legislation, the manufacturer shall affix to each medical device, of the above referenced models, the CE-marking followed by the number of the Notified Body according to this example:*

CE 1023

Issued in Zlin, on 4th January 2011

RNDr. Radomír Čevelík
Representative of the Notified Body No. 1023

Examined Patent Certificate

Approved in 2006

T.C.
TÜRK PATENT ENSTİTÜSÜ

İNCELEMELİ PATENT

No: TR 1998 00053 B

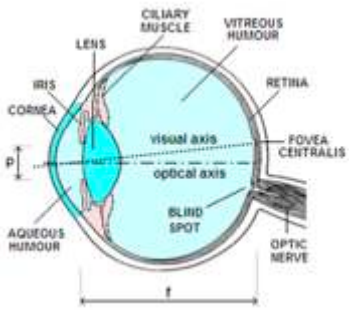
Bu patent, 551 sayılı Patent Haklarının Korunması Hakkında Kanun Hükmünde Kararname uyarınca ***14/01/1998*** *tarihinden itibaren* ***20 yıl*** *süre ile yenilik ve tekniğin bilinen durumunun aşılması konusunda yapılan inceleme sonucunda* ***incelemeli*** *olarak verilmiştir.*

Doç. Dr. Yusuf BALCI
Enstitü Başkanı

TÜRK PATENT ENSTİTÜSÜ

H. Bilgic, M. Demiriz, M. Ozler, Tayfun Ide, N. Dogan, S. Gumus, A. Kiziltay,T. Endogan, V. Hasirci, N. Hasirci, J. Biomater. Tissue Eng., 3, 2, 205-211, **2013**

Cornea Engineering

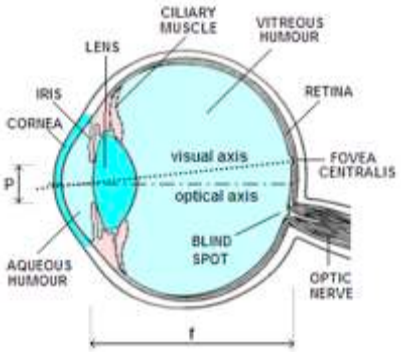


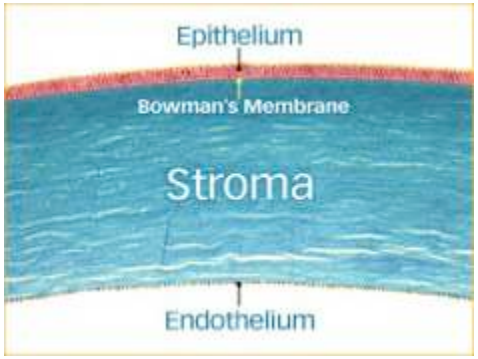
Reconstruction of a Functional Human Cornea

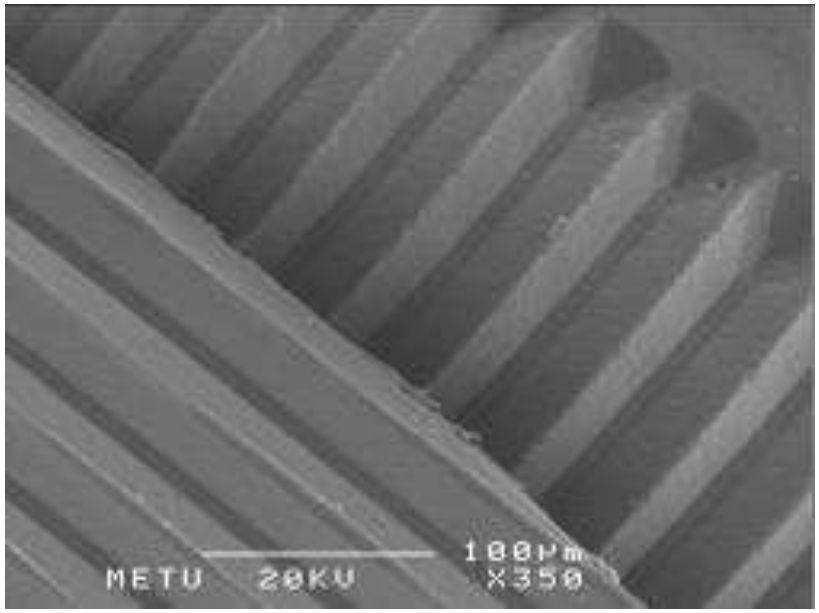
Kilic, C., Girotti, A., Rodriguez-Cabello, J., C., Hasirci, V. (**2014**)
Biomaterial Science, 2, 318-329

(FP6 Project Cornea Engineering)

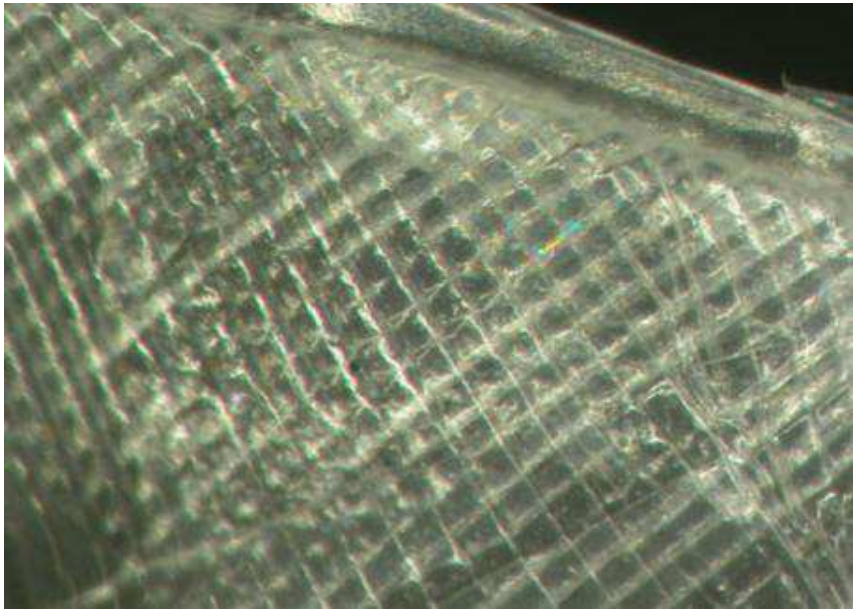
Collagen Film Stacks for Artificial Cornea







Collagen film stacks central part (Mag. x6)



Collagen film stacks, edge (Mag. x15)

Patent

Stacked, PatternBiomaterials and/or Tissue Engineering Scaffolds

Turkish Patent Office Patent

P-07-012

1/1

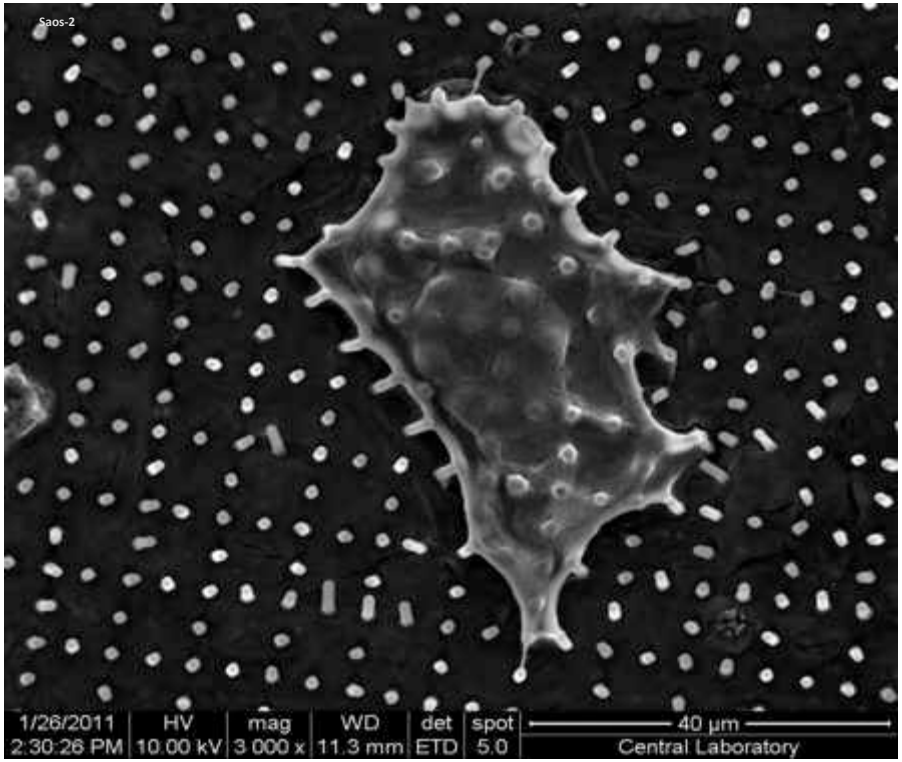
PCT POWER OF ATTORNEY

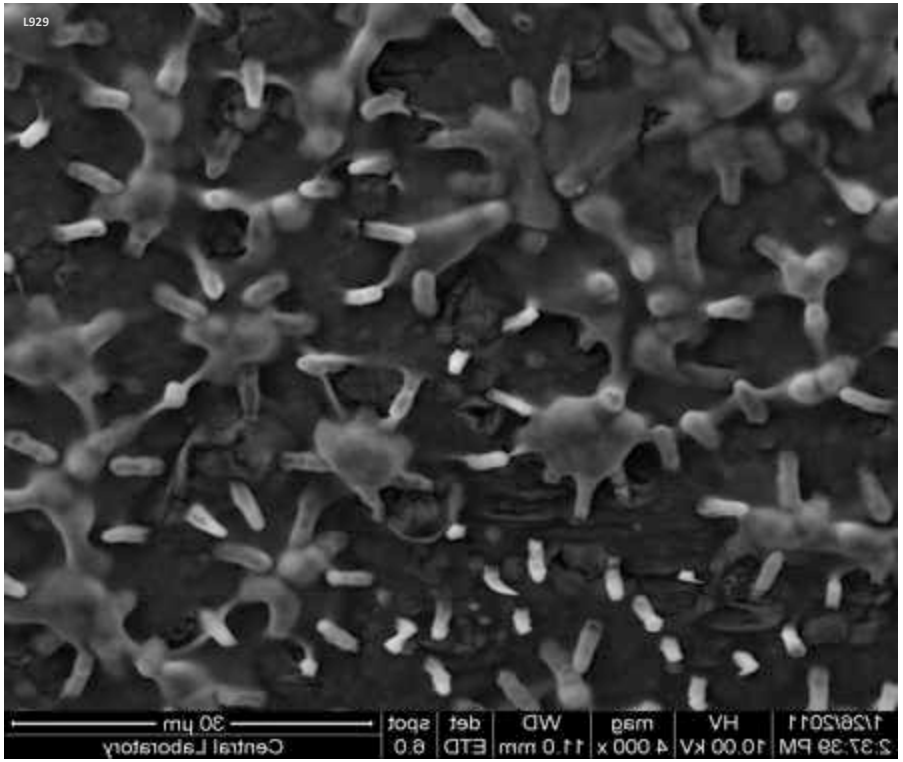
0-1	PCT Power of Attorney (for an international application filed under the Patent Cooperation Treaty) (PCT Rule 90.4)	
0-1-1	Prepared Using	PCT-SAFE [EASY mode] Version 3.51.015.190 MT/FOP 20061001/0.20.5.7
1	The undersigned applicant(s)	HASIRCI, Vasif
1-1-1	hereby appoints (appoint) the following person	YALCINER, Ugur Gursad Tunus Caddesi No: 85 / 8 Kavaklidere 06680 ANKARA Turkey
1-2	as	agent
1-3	to represent the undersigned before	all the competent International Authorities
1-4	in connection with the international application identified below:	
1-4-1	Title of invention	STACKED, PATTERNED BIOMATERIALS AND/OR TISUUE ENGINEERING SCAFFOLDS
1-4-2	Applicant's or agent's file reference	P-07-012
1-4-3	International application number (if already available)	
1-4-4	filed with the following Office as receiving Office	Turkish Patent Institute (RO/TR)
1-5	and to make or receive payments on behalf of the undersigned	
2-1	Signature of applicant, agent or common representative	
2-1-1	Name (LAST, First)	HASIRCI, Vasif
2-1-2	Name of signatory	
2-1-3	Capacity	
3	Date	15 March 2007 (15.03.2007)

Eurasia Patent

Better or Non-Stick Surfaces

Saos-2 and L929 Cells on "Softer" PLLA-PLGA Micropatterned Films





- Both types of the cells spread over softer PLLA-PLGA pillars
- An interesting observation is the sagging of the cytoplasm (hammock type) and the nuclei of Saos-2 cells between the pillars

Patent

A GRID CONTAINING SYSTEMATICALLY DISTRIBUTED MICRO-NANOPILLAR COATED FIELDS TO CONTROL CELL ADHESION

Field of Invention

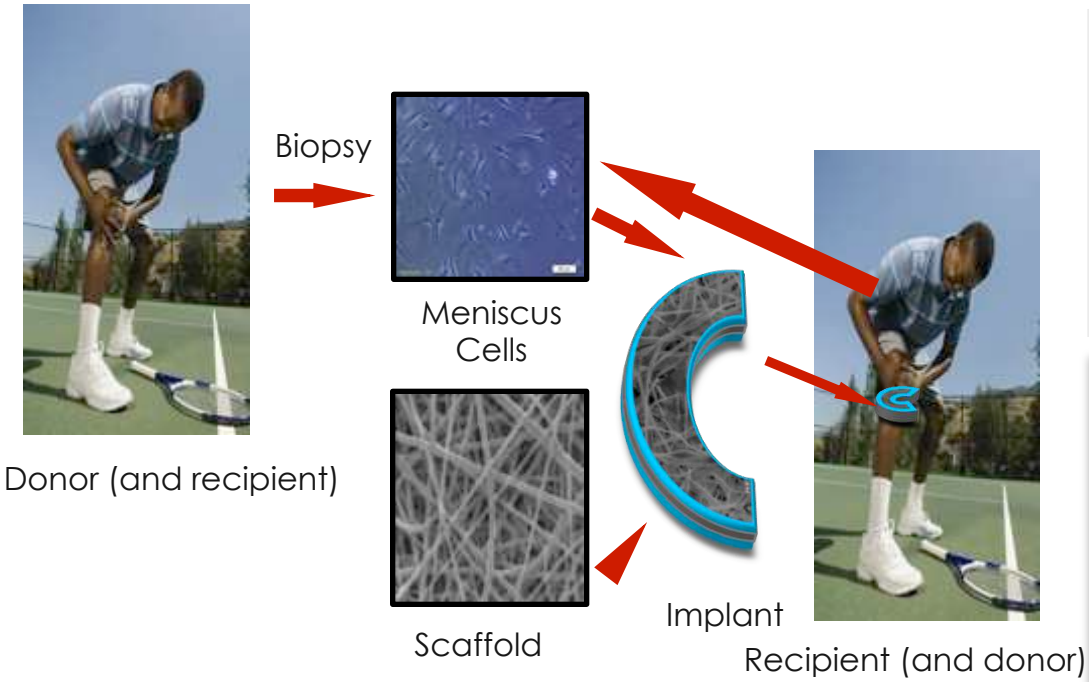
The present invention relates to micro-nanopatterned surfaces with precisely controlled physical cues in the form of rods or pillars in a grid with distances systematically varied to form fields with different cell adhesive and cell alignment properties. The test surfaces are polymeric films produced by solvent casting on a template carrying the inverse of the patterns on the polymer. Surface coating with macromolecules and substratum stiffness are two additional parameters which can be modified in different uses. The present invention achieves control over cell adhesion through surface nano/microtopography, with and without any chemical modification, and will provide many advantages in the design of sensing microdevices and improvement of biomedical implant surfaces.

Prof. Dr. Vasıf Hasırcı, Hayriye Özçelik, Dr. Celestino Padeste

Application to Turkish patent Office: 2012

Tissue Engineering for Meniscus Substitute

An interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function or a whole organ (Langer & Vacanti, 1993)



Limitations of the current methods:

- Long regeneration time
- Shrinkage of implants
- Low mechanical properties

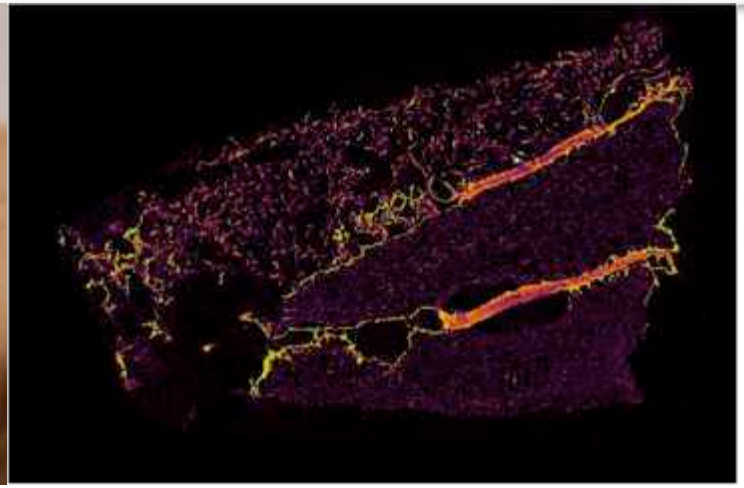
What this study brings:

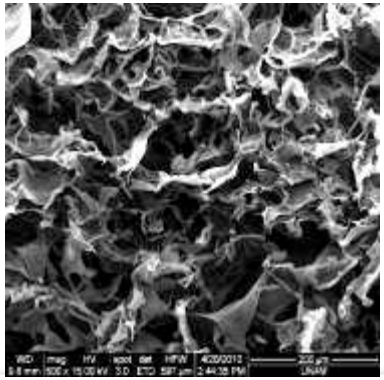
- Cell-seeded
- Collagen-based
- Biodegradable
- Biocompatible

implant aiming at solving these problems

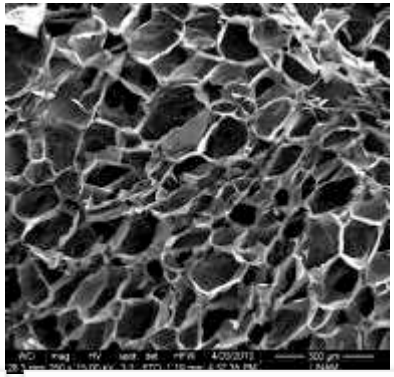
onges w/o Cells For Meniscus TE

Scanning electron micrographs of uncrosslinked Coll-CS-HA and Coll I foams





COLL-CS-HA foam



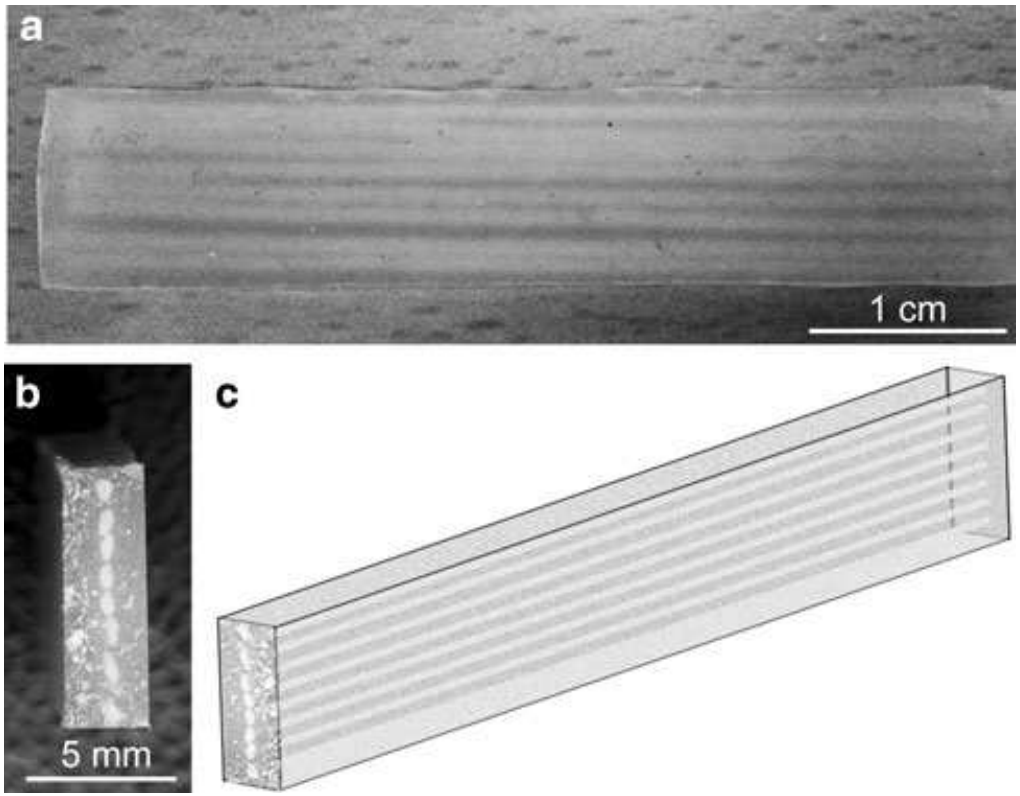
-20°C Coll I foam

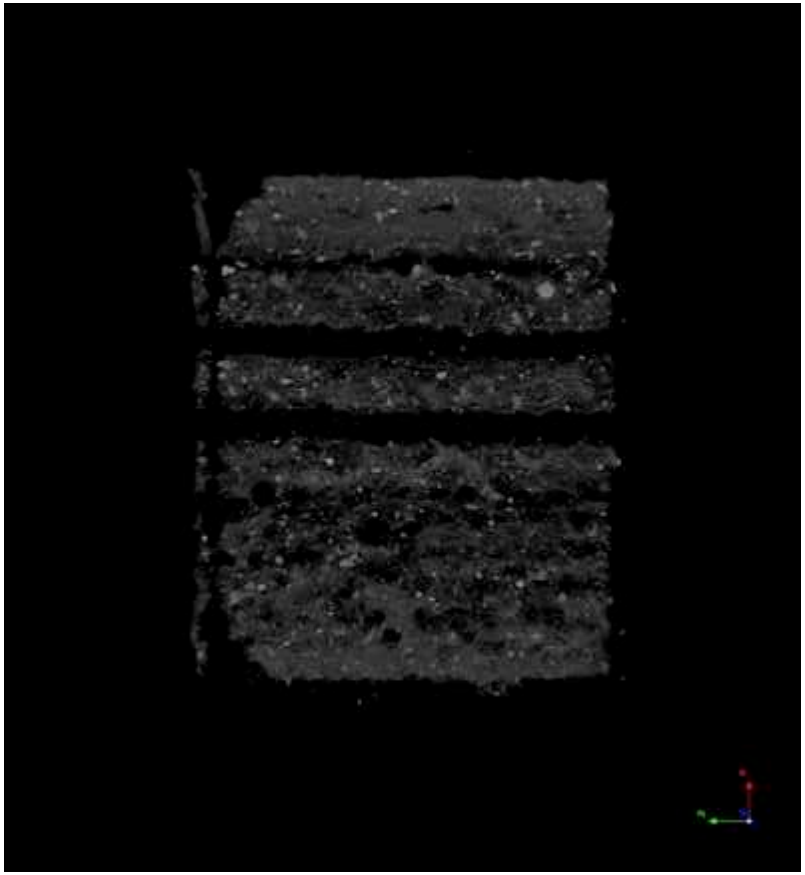
Bahcecioglu, G., Buyuksungur, A., Kiziltay, A., Hasirci, N., Hasirci, V. **(2014)**. Journal of Bioactive and Compatible Polymers, 29(3), 235-253.

Halili A. N., Hasirci N., Hasirci V. **(2014)**. Journal of Material Science: Materials in Medicine, 25, 1195-1209.

A Ndreu Halili, N Hasirci, V Hasirci (**2013**), J. Biomater. Tissue Eng. 3, 2, 173-184,

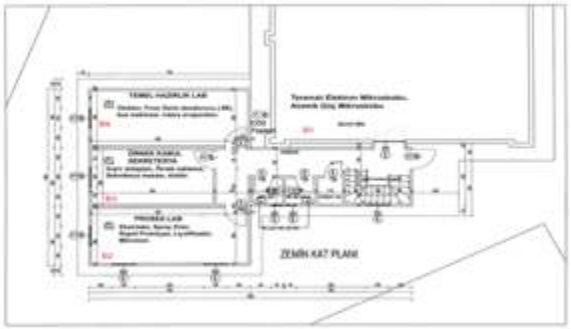
Biodegradable Bone Plate

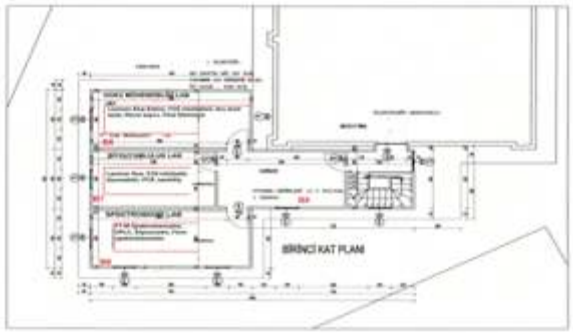




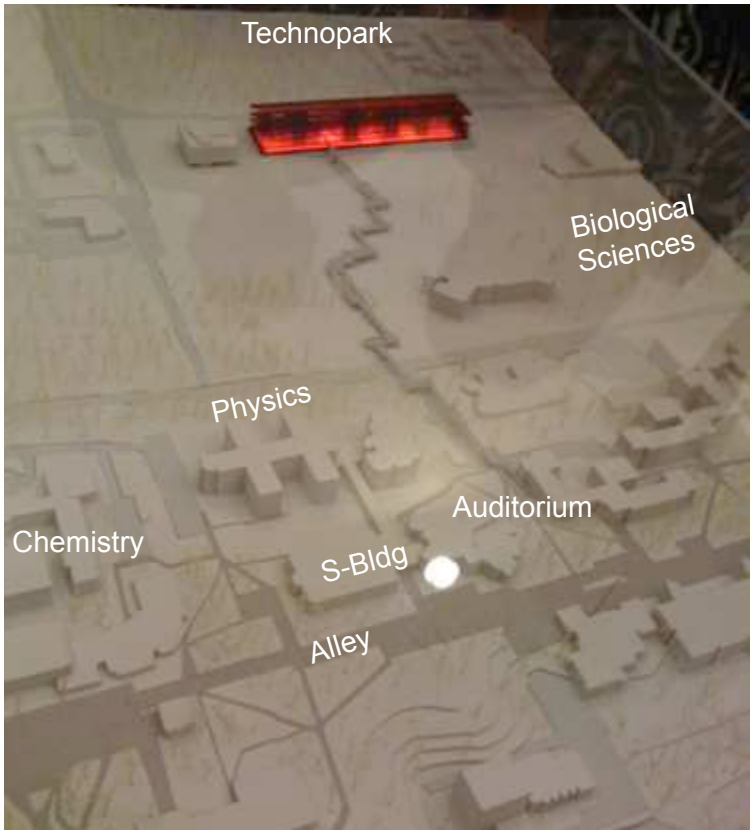
E Aydin, J A Planell, VHasirci, (2011) J Mater Sci: Mater Med 22:2413

The Temporary Building





Now



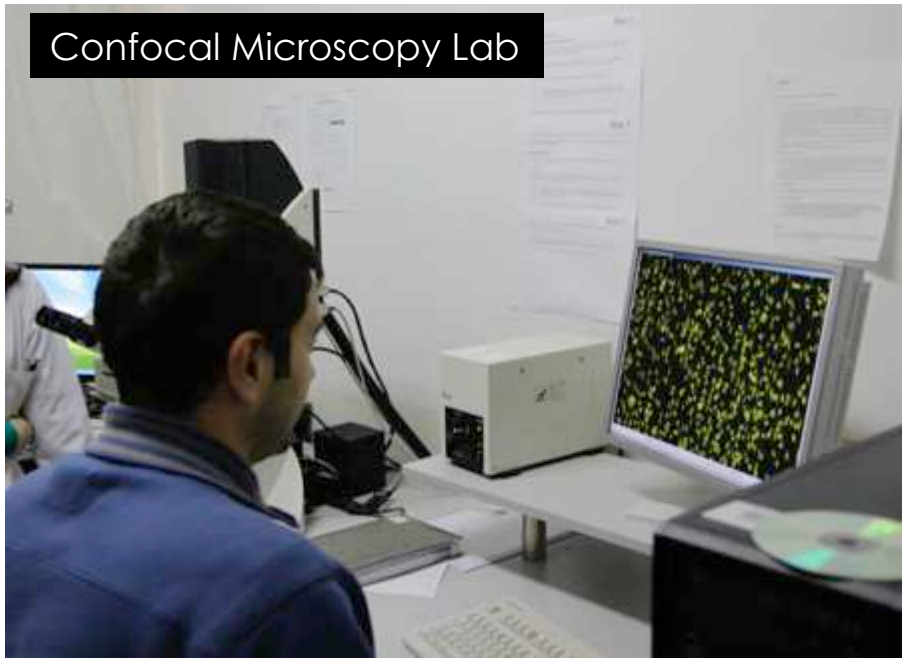
Facilities

Molecular Biology Lab

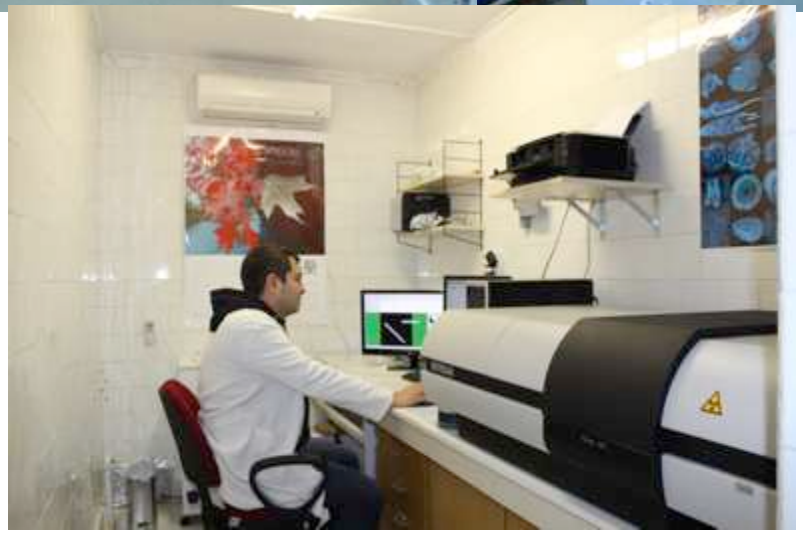
Cytotoxicity Lab

Microscopy Lab

Confocal Microscopy Lab



In Vitro and microCT



And we need (and luckily get) financial support

Thank you