



生物制造国际研讨会

INTERNATIONAL WORKSHOP ON BIO-MANUFACTURING

资助者 Sponsored by



美国国家科学基金会 National Science Foundation, USA (NSF)



中国国家自然科学基金委员会 National Natural Science Foundation of China (NSFC)



中国机械工程学会 Chinese Mechanical Engineering Society (CMES)



清华大学 Tsinghua University

组织者 Organizer

美国(USA): Myron SPECTOR (Harvard Medical School) 中国(China): 清华大学 颜永年 (Yongnian YAN, Tsinghua University) Wei SUN (Drexel University) 清华大学 林峰(Feng LIN, Tsinghua University)

时间: 6月29日~7月1日

Date: June 29th ~ July 1st

地点: 创新大厦A座会议室 (清华大学东门外)

Location: Meeting Room in Building A, Innovation Center(Plaza) (East Gate of Tsinghua University)

网站(Website): http://mem.drexel.edu/biomanufacturing/index.htm

者: 清华大学机械工程系生物制造工程中心

清华大学生命科学与医学研究院生物制造研究所

ed by: Center of Organism Manufacturing Engineering, Department of Mechanical Engineering, Tsinghua University Center of Bio-Manufacturing Engineering, Institute of Life Science & Medicine, Tsinghua University







生物制造国际研讨会

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STATE MANAGEMENT



CENTRAL PROPERTY.



AND REAL PROPERTY.



THE REAL PROPERTY.



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International Workshop for Biomanufacturing

June 29 – July 1, 2005, Tsinghua University, Beijing, China

29 June

Session 0: Open ceremony and general topic Chairman:Prof. Yongnian Yan

08:30 am - 09:00 am: Workshop-open: welcome ceremony and welcome addresses

- National Science Foundation, USA (Dr. Jian Cao)
- National Natural Science Foundation of China (Dr. Yuanzhong Lei)
- Chinese Mechanical Engineering Society (Dr. Peifan Ding)
- Vice chairman of Tsinghua University Council (Dr. Dongcheng Hu)

Session 1: General Chairman: Prof. Friedrich B. Prinz

9:00 am - 10:30 am:

- Dr. Christine Kelly (National Institute of Health, USA):
 Convergences of Life Sciences and Engineering Bioengineering Research
- Dr. George Hazelrigg (National Science Foundation, USA): Innovative Multi-Disciplinary Research in Manufacturing Machines and Processes
- Dr. Joseph Beaman (The University of Texas at Austin, USA):
 WTEC report and SLS fabrication for prosthesis

Break: 10:30 am - 10:40 am

Session 2: General Tissue Engineering

Chairman : Prof. Fuzhai Cui

10:40 am - 12:10 am:

- Dr. Myron Spector (Harvard Medical School, USA):
 Collagen-GAG Scaffolds for Tissue Engineering
- Dr. Changyong Wang (Beijing Institute of Basic Medical Sciences)

 Liquid type I collagen-based cardiac tissue engineering
- Dr. Mauli Agrawal (University of Texas at San Antonio, USA)
 Tissue Engineering Scaffolds: Materials and Architecture

Lunch: 12:10 pm - 1:30 pm

Session 3: General Tissue Engineering Chairman:Prof. Mauli Agrawal

2:00 pm - 3:30 pm:

- Dr. Xuetao Pei (Beijing Institute of Transfusion Medicine)

 Stem Cell Development and Liver generation
- Dr. Shenguo Wang (Chinese Academy of Sciences)

 Cell Scaffold and Its Challenge to Bio-manufacturing
- Dr. Scott Hollister (University of Michigan at Ann Arbor, USA)

 Designer Scaffolds for Tissue Reconstruction

Break: 3:30 pm - 4:00 pm

Discussions Session: 4:00 pm – 5:30 pm

Chairman: Prof. Myron Spector

Welcome Reception, Banquet at Tsinghua Unisplendure International Center 7:00 pm - 8:30 pm

Session 4: Cell Printing and Assembling Chairman: Dr. Christine Kelley

8:30 am - 10:30 am:

■ Dr. Yongnian Yan (Tsinghua university)

A practice on cell controlled assembly

■ Dr. Vladimir Mironov (Medical University of South Carolina, USA) *How to print organs?*

■ Dr. Thomas Boland (Clemson University, USA)

Drop-on-Demand Printing of Cells and Materials for Designer Hybrid ardiovascular Constructs

30

June

■ Dr. Douglas B. Chrisey (Wright State University, USA)

Issues for Tissue Engineering by Direct Write Technologies

Break: 10:30 am - 11:00 am

Session 5:Nano-Micro Biomanufacturing Chairman: Prof. Joseph J. Beaman

11:00 am - 12:00 pm:

■ Dr. Fritz Prinz (Stanford University, USA)

Manufacturing of nano-scale probes for observing oxidation reduction reactions in biological cells

■ Dr. Xiang Zhang (University of California, Berkeley, USA)

Micro and Nano-manufacturing: a merge of science and technology

Lunch: 12:00 pm - 1:30 pm

Session 6:Nano-Micro Biomanufacturing Chairman: Prof. Shenguo Wang 2:00 pm –3:00 pm:

■ Dr. Fuzai Cui (Tsinghua)

Self-assembling of nano-hydroxyapatite/collagen bone graft and its application

■ Dr. S.M. Zhang (Huazhong University of Science and Technology)

Fabrication and characterization of nano-hydroxyapatite / poly (D, L-lactide) composite porous scaffolds for bone and cartilage tissue engineering

Lab Tour at Tsinghua University: 3:30 pm - 6:00 pm

Biomanufacturing lab

Biomaterial lab

Bioengineering lab

Dinner: 6:30 pm to 7:45 pm

Evening: 8:00 pm to 9:30 pm: Tsinghua-MIT Video Conference on Biomanufacturing

Prof. Linda Griffith and Prof. Yanni Yannas from MIT will attend and present.

Session 7: Computer Aided Tissue Engineering Chairman: Prof. Xiang Zhang

July

8:30 am -10:30 am:

■ Dr. Selcuk Guceri (Drexel University, USA)

PCL Composite Scaffolds for Bone Tissue Engineering

■ Dr. Paulo Bartolo (Polytechnic Institute of Leiria, Portugal):

Biomanufacturing of hard and soft tissues"

■ Dr. Michael Liebschner (Rice University, USA)

Tailoring Tissue Replacement Scaffold Properties Through a Combinatory Approach of Computer-Aided Tissue Engineering and Rapid Prototyping

■ Dr. S.H. Masood (Swinburne University of Technology):

Tissue Engineering of Tri Leaflet Heart Valves

Break: 10:30 am - 11:00 am

Session 8: Computer Aided Tissue Engineering Chairman: Prof. Guceri

11:**00** am - 12:**00**pm:

■ Dr. Chengtao Wang (Shanghai Jiaotong University)

Prosthesis engineering and bio-manufacturing

■ Dr. Dichen Li (Xi'an Jiaotong University)

Free fabrication of bone scaffolds with microchannels based on stereolithography

■ Dr. Andrea Caruso (Therics Co., USA)

Commercial Application of TheriForm™ in Orthopedics

Lunch: 12:00 pm - 1:30 pm

Session 9: Computer Aided Tissue Engineering Chairman: Prof. Bartolo

2:00 pm - 3:40 pm:

■ Dr. Jian Liu (Fourth Military University)

Application of bioactive artificial bone based on RP technique to repair segmental bone defect in big animals

■ Dr. Feng Lin (Tsinghua Univesity)

Fabrication of branchy vessel tissue scaffold with layered wall

Dr. Xiaohong Wang (Tsinghua University)

The challenges for liver manufacturing

Dr. Zhuo Xiong (Tsinghua University)

Fabrication of porous scaffolds for tissue engineering via low-temperature deposition

■ Dr. Wei Sun (Drexel University)

Computer Aided Tissue Engineering

Break: 3:20 pm - 3:50 pm

Closing Banquet at Teng-Ge-Li Ta-La Restaurant: 5:45 pm to 9:00 pm



清华大学机械工程系 清华大学生命科学与医学研究院 清华大学国家 CIMS 工程中心

型光识更过那中心 全物制造研究所 识更过形分中心

CRLF—Center of Laser Rapid Forming, Dept. of Mechanical Eng. Tsinghua University

CBM—Center of Bio-Manufacturing, Institute of Life Science and Medical, Tsinghua University

NATIONAL CIMS Engineering Research Center, Rapid Prototyping Division

额张卢林王吴熊袁全成称人清峰红东卓达义华教教副副副博高工程级投授授授授授授授授授授授授授授授授授授授授授授授授授授授授授授



Prof. Yongnian Yan

Prof. Renji Zhang

Prof. Qingping Lu

Dr. Feng Lin

Dr. Xiaohong Wang

Dr. Rendong Wu

Dr. Zhuo Xiong

Engineer Da Yuan

Engineer Da Tuair

Engineer Yongyi Quan

Technician Lihua Chen

Team of our research and teaching group

研究方向:

- 1. 生物体制造
- 2. 材料微输运
- 3. 快速制造
- 4. 预应力重型装备的 CAD/CAM 和数字模拟

RESEARCH DIVISIONS:

- 1.Organism-Manufacturing(OM)
- 2. Materials Droplets Transportation Technique
- 3. Rapid-Manufacturing(RM)
- 4.CAD/CAM and Simulation of Heavy Equipment of Pre-stress

Division I

生物体制造

Organism-Manufacturing(OM)

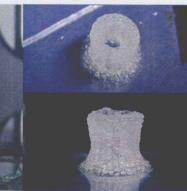
Cell Controlled 3D Assembling 细胞受控三维组装



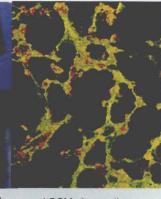
New Type Cell 3D Assembler 新型细胞三维组装机



细胞受控组装过程



Controlled assembling process 3D Analogy Tissue Precursor (ATP) 含有活细胞的三维 ATP



LSCM observation 抗原抗体染色



Cellular structure 蜂窝结构 (三级)



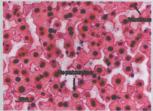
Reticular structure 网状结构 (二级)

A hierarchical model of one kind of ATP

三级分级结构



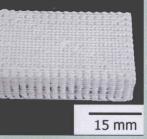
Location structure 单元结构(一级)



Histologic image 组织切片HE染色

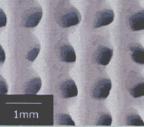
组织工程支架材料.工艺.设备

Materials. Technologies. Equipments for Tissue Scaffold



组织工程血管支架

Vascular Scaffold



耳软骨支架 Auricle scaffold



隐形牙矫治器 Invisible appliance



三维分级血管支架 Multilayered branchy vascular scaffold



断面图 Section view



耳廓软骨支架



鼠背活皮肤耳廓 Artificial auricle scaffold Implanted under the skin of a rat



Aligner model

矫治器 Aligner





治疗 Therapy

料 微 运 技 材 输 **Division II**

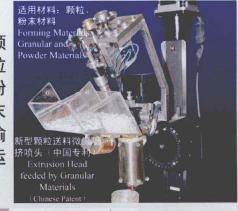
Material Droplets Transporting Technique



微 流 喷 挤



颗 粒 粉 末 输 运



激光导引直写 Laser Guided Direct Writing (LGDW)





高压电场材料 微输送 Material Feeding Under High Voltage Electric Field

Division III

制 速 RM — Rapid Manufacturing

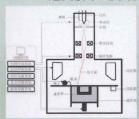
电子束直接金属成形

电子束选区熔化技术

Electron Beam Selective Melting-EBSM



EBSM-I 设备外形图 (EMSM-I Forming Machine)



EBSM-I 设备原理图 (Schematic Diagram of EBSM-I) (the Part from Arcam)



等离子束间接金属成形

等离子喷涂与电弧喷涂

Plasma Spraying and Electric Arc Spraying-PS&EAS



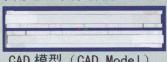
等离子喷涂设备外形图 (PS Forming Machine)



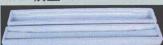
- 不锈钢喷涂层厚 10mm Stainless Steel Spraying the thickness: 10mm
- 2 锌过渡层 Zn Transition Laver
- 3. 铋锡合金 Bi-Sn Allov

不锈钢快速模具截面图 (Stainless Steel Rapid Model)

采用电弧喷涂制模工艺制造汽车后横梁地板件快速模具



CAD 模型 (CAD Model)



硅胶模 (Silica gel Model)



金属模具 (Metel Model)





冲压件 (the Pressing Part)

Division IV 预应力重型装备的CAD/CAM和数字模拟 CAD/CAM And Simulation Of Heavy Equipments Of Pre-Stress

研究内容

重型机械设计中的预应力原理

Theory of pre-stress in heavy equipments desgin

重型承载机架和工作缸的预应力设计

Pre-stress design in heavy frame and cylinder 预应力重型装备的液压传动

Hydrostatic transmission in pre-stress heavy equiment

预应力钢丝缠绕结构

Pre-stress Wire Wound structure

模锻和挤压模具的数字模拟

Numerical simulation of die forging and extrusion die 塑性变形工艺数字模拟

Numerical simulation of plastic deformation process 预应力重型装备的计算机控制

Computer control in pre-stress heavy Equipment

重型装备的超高压密封系统

Seal system with very high pressure of heavy equipment



4万吨板料成型压机 已投产 sheet metal forming press Tonnage:40000 tons



1万吨板料成形压机 已制造30余台 sheet metal forming press Tonnage:10000 tons Made:30

(1985)



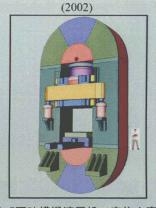
7800吨陶瓷砖压机 已制造200余台 Ceramic tile hydruaulic press Tonnage:5000 tons Made:200



5000吨陶瓷砖压机 已制造50余台 Ceramic tile hydruaulic press Tonnage:5000 tons Made: 50

(2003)

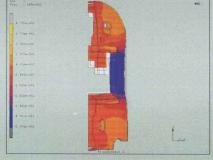
1000吨多向模锻压机 已投产 Multi-ram forging press



3. 5万吨模锻液压机(实施方案) Die forging hydruaulic press

Tonnage: 35000 tons
(2005)

Tonnage:1000tons (1982)



7800吨陶瓷砖液压机承载机器有限元分析 Finite Element Analysis of Hydraulic Press Frame

(2003)

Stress-Max Principal

93.7

47.9
2.10
-43.7
-89.5
-135
-181
-227
-273

Domage
0.165
0.144
0.124
0.103
0.0625
0.0618
0.0412
0.0208
0.000

钢管挤压过程有限元模拟 Finite Element Simulation of Steel Pipe Extrusion (2005)

生物制造工程: 定义

Bio-Manufacturing Engineering: Definition

生物制造的广义定义:

Bio-Manufacturing (General BM)

广义 生物制造 ■模仿生物体的结构和行为的科学——生物的学习和仿效 the Science of Simulating of the Structure and Behavior of Organism:Emulation of Life-form

利用生物过程进行制造的科学——生物质的制造

the Science of Manufacturing Based on Bio-Process: Organic-Mass Manufacturing

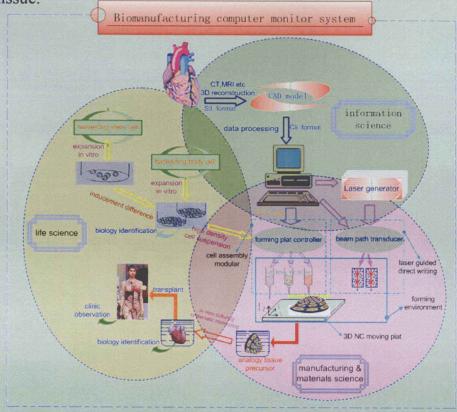
修复和制造生物体的科学——生物体的制造(狭义生物制造)
The Science of Rehabilitating and Manufacturing of Organism :OM(Special BM)

生物制造的狭义定义——生物体的制造:

OM-Organism Manufacturing (Special BM)

运用现代制造科学和生命科学相结合的原理和方法,通过对多种细胞或细胞团簇的直接或间接受控组装,形成具有新陈代谢功能的生物体——类组织前体,经培养和训练,完成用以修复或替代人体的病损组织的替代物

The organism--3D Analogy Tissue Precursor, which has the function of metabolism is made of various cells or cell clusters with the technologies of direct or indirect controlled assembly. This technology is based on the principle and means combined modern manufacturing science and life science. After cultured and trained, the tissue and organ is formed and can repair or replace the humans' defunct tissue



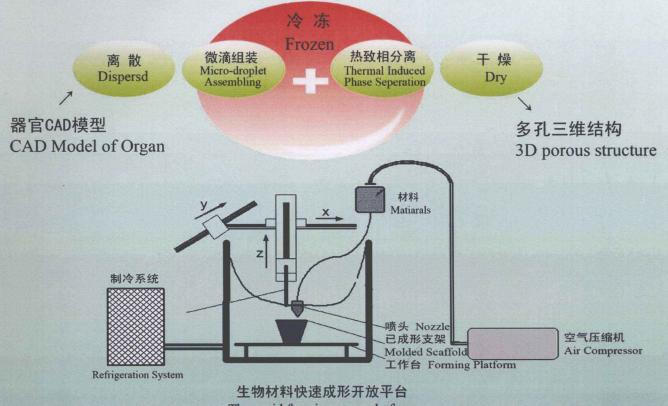
生物体制造学科集成图 The Discipline Intergration of OM (Special BM)

2005. 6. 15制

生物体制造工程关键工艺

Key Processes of Organism-Manufacturing Eng.

(1) 低温沉积制造工艺 Low Temperature Deposition Manufacturing-LTDM



The rapid forming open platform

(2) 细胞受控组装制造工艺



细胞组装机 Cells Assembler **Extruding Container**

Forming Platform

Platform

Research Programs and Funding **Opportunities at the National Institute** of Biomedical Imaging and Bioengineering



Christine A. Kelley, Ph.D. **Director, Division of Discovery** Science and Technology

ational Workshop for Biomanufacturing June 29-July 1, 2005 Tsinghua University Beijing, China

Outline of Presentation

- · Quick tour of the NIBIB
- · Snapshot of NIBIB funded research
- · Research funding and training opportunities



Quick tour of the NIBIB



The NIBIB is the Newest Institute at the National Institutes of Health

Brief History:

· December, 2000

After many years of lobbying by the imaging and bioengineering communities, the NIBIB was signed into law by President Clinton.

April, 2002

First grants to support research were awarded

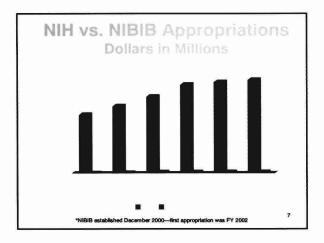
September, 2002

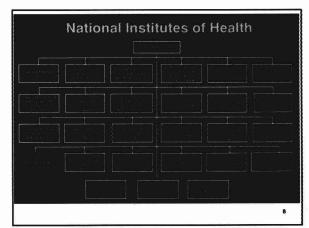
Roderick Pettigrew, Ph.D., M.D. joined the NIBIB as the first Institute Director

· Personnel: Currently about 50 staff members



- FY 2005 NIBIB Conference \$298.2 Million
- · FY 2006 President's Budget **Request for NIBIB** \$299.8 Million





NIBIB Mission

Improve human health by leading the development and accelerating the application of biomedical technologies. The institute is committed to integrating the physical and engineering sciences with the life sciences to advance basic research and medical care.

NIRIR Vision

To profoundly change health care by pushing the frontiers of technology to make the possible a reality.

A big challenge for the NIBIB is promoting multidisciplinary research



- Clinicians, biologists
 and engineers speak in
 different languages
- 2. Clinicians and biologists may not know what is technically possible; engineers may not know the biomedical problems.
- 3. Continued, ongoing collaboration essential

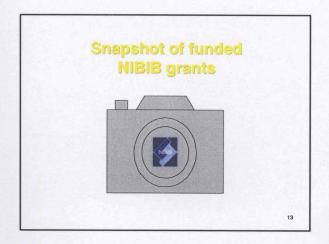
NIBIB Research Programs in Biomedical Imaging

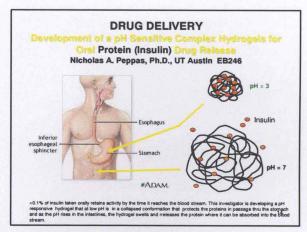
- Imaging device development
- ·Image computation, display, perception, and screening
- ·Contrast agent and molecular probe development
- ·Image-guided therapies and interventions
- •Development of low-cost medical imaging devices
- ·Multi-modality imaging
- ·Methods for non-invasive cell and molecular imaging

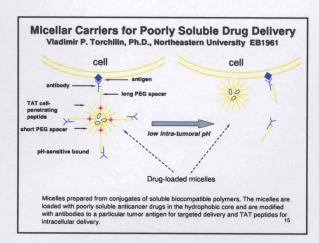
Scope of Scientific Programs
Division of Discovery Science and Technology

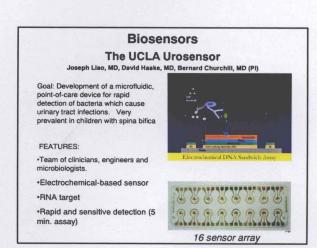
- Advanced Biomaterials
- Bioinformatics
- Biomechanics and rehabilitation engineering
- Drug and gene delivery systems and devices
- Image processing, displays, and perception
- Mathematical models and computational algorithms
- Medical devices & implant science
- Platform technologies (lab-on-a-chip)
- Remote diagnosis and therapy (telehealth)
- Sensors
- Surgical tools and techniques
- Tissue engineering

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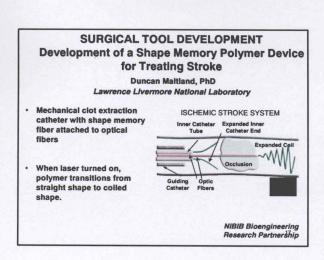




Image-Guided Intervention in Neocortical Epilepsy

Dr. James Duncan, Yale University, R01 EB000473

- Dr. Duncan heads a BRP (Yale, Albert Einstein College of Medicine, the University of Minnesota, and BrainLAB,) a mulitdisciplinary team specializing in image-guided surgery.
- MRI of a patients brain. Overlay shows where the brain is active while performing a language task as quantified by fMRI and EEG.
- The integration of this data into a common space is used to identify the epileptogenic tissue and surrounding regions to plan and guide neurosurgery



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Rehabilitation Engineering

Deep Brain Stimulation for Parkinson's Disease Dr. Hunter Peckham, Case Western Reserve University



A thin wire is implanted deep into the brain in an area involved in motor control. The wire comes out of the skull, under the skin to the pectoral area where it connects to a pacemaker-like device.

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Telehealth Development of Multi Sensor Fusion Algorithms for Remote Circulatory Monitoring

H. Harry Asada Massachusetts Institute of Technology Andrew Reisner Massachusetts General Hospital





Wearable

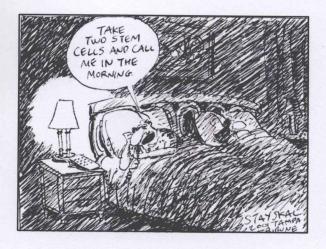
The MIT Ring

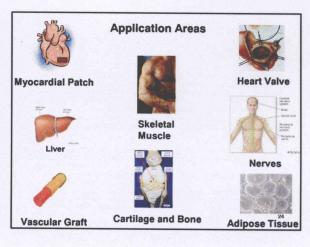
Developing a multi-modality wearable ring sensor system, through the development of novel multi-sensor fusion algorithms, to enable long-term, remote circulatory monitoring. The signals are transmitted locally to a PDA then over the internet to the physicians office.

Tissue Engineering and Regenerative Medicine

- Engineering of tissue in vitro for subsequent implantation in vivo, to repair, replace, maintain or enhance organ function.
- Regeneration of tissue in vivo for the purpose of repairing, replacing, maintaining, or enhancing organ function.







Tissue Engineering Program Current Portfolio

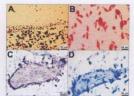
Scientific Subcategory	# of Active Grants	Total Costs (million \$)
Biomolecules and Cells	10	3.4
Scaffold Development / Tissue-engineered therapies	24	6.6
Enabling Technologies	10	2.8
Total	44	\$12.8 M

Functional Tissue Engineering of Articular Condyle for Replacement

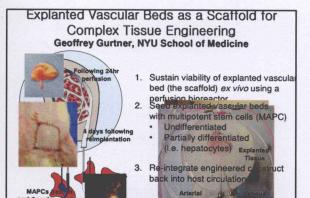
Jeremy Mao, R01 EB2332, University of Illinois at Chicago

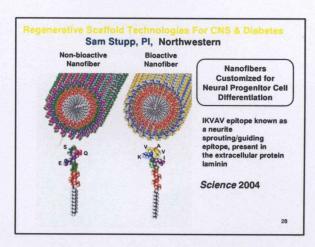


Tissue-engineered humanshaped mandibular condyle from rat mesenchymal stem cells



Histology following 8 wks of *In vivo* implantation showing both chondrogenesis and osteogenesis from 26 mesenchymal stem cells.





Use of Micropatterning Techniques to Control Stem Cell Differentiation Chris Chen, Johns Hopkins University Soft Uthography Cell regulatory scheme Ingineering cell achaeve Human mesenchymal stem cells differentiated into osteoblasts (blue) and adipocytes (red). Use of micropatterning techniques to control mesenchymal stem cell shape. Cell shape induces molecular signals controlling differentiation. Stem cells forced into spherical shapes become fat cells, those allowed to stretch and flatten become bone cells. The research offers a means to control stem cell differentiation with the long-term goal of regenerating or repairing damaged tissue

Potential Future Directions Tissue Engineering

 Development of enabling technologies for tissue engineering with an emphasis on: 1) real-time, non-destructive tools to assess function; 2) computer-aided tissue engineering, and; 3) bioreactor and tissue preservation technologies.

Background: Tools and technologies currently available are limited.

Direction: Lead the development of enabling technologies that are crucial in aiding and translating tissue engineering applications to improve human health

Development of engineered 3D human tissue model systems for basic and clinical research as well as drug discovery and development.

Background: Inaccuracies and high costs of animal studies to predict human response, safety and efficacy.

Direction: Promote the development of engineered 3D human tissue model systems that closely mimic the complex environment and interaction of humans organ systems.

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Bigggagtor Schematic 27