南方醫科大學
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CELL & TISSUE ENGINEERING

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- What if lost limbs or organs could be regenerated?
- What if drug development and chemical testing were more efficient and less costly?
- Can deadly biological and/or chemical agents be rapidly identified?
- Are there ways to reduce our reliance on animal testing?

What's Tissue Engineering?

– **TE is an emerging multidisciplinary field involving biology, medicine, and engineering that is likely to revolutionize the ways we improve the health and quality of life for millions of people worldwide by restoring, maintaining, or enhancing tissue and organ function.** (**NIH**)

- Tissue engineering research includes:
  - biomaterials,
  - cells,
  - biomolecules,
  - engineering design aspects,
  - biomechanics,
  - informatics to support tissue engineering
  - stem cell research.

- A brief history of TE
  - First put forward in 1985
  - Pre-clinical research during 1990s
  - TEMP (Tissue Engineering Medical Product) in late 1990s

- A brief history of TE
  - The Multi-Agency Tissue Engineering Science (MATES) Interagency Working Group (IWG), 2000

The Multi-Agency Tissue Engineering Science (MATES) Interagency Working Group (IWG)

- Department of Agriculture (USDA)
- Department of Commerce
- National Institute of Standards and Technology (NIST)
- Department of Defense (DoD)
- Defense Advanced Research Projects Agency (DARPA)
- Centers for Medicare & Medicaid Services (CMS)
- Department of Health and Human Services (HHS)
- Food and Drug Administration (FDA)
- National Institutes of Health (NIH)
- Department of Energy (DOE)
- National Aeronautics and Space Administration (NASA)
- National Science Foundation (NSF)
- Naval Research Laboratory (NSF)
- Veterans Administration (VA)

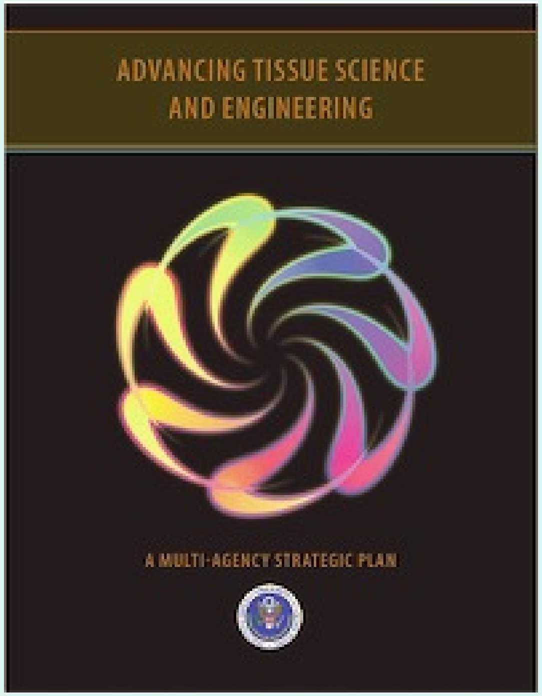
- **A brief history of TE**
  - **TERMIS (Tissue Engineering & Regenerative Medicine International Society,2005)**

termis®
Tissue Engineering International
& Regenerative Medicine Society

Advancing Tissue Science And Engineering

- A Multi-agency Strategic Plan (2007)

- From earliest diagnostic testing To the advanced stages of therapy.



Four overarching goals

- Understanding and controlling the cellular response;
- Formulating biomaterial scaffolds and the tissue matrix environment;
- Developing enabling tools;
- Promoting scale-up, translation and commercialization;

Understanding and Controlling The Cellular Response

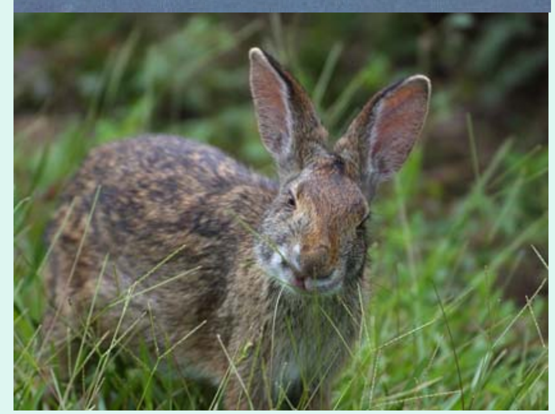
- **Tissue-Engineered Disease Models:**

- **3-D tissue models was established to study the growth of tumors in tissue beds and for use in drug screening.**

Understanding and Controlling The Cellular Response

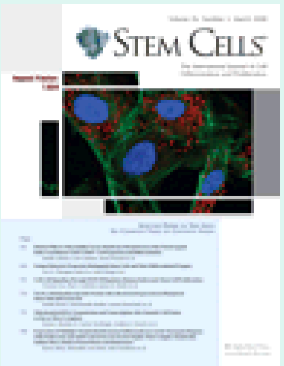
- Engineered Tissues Provide Alternatives to Animal Testing.

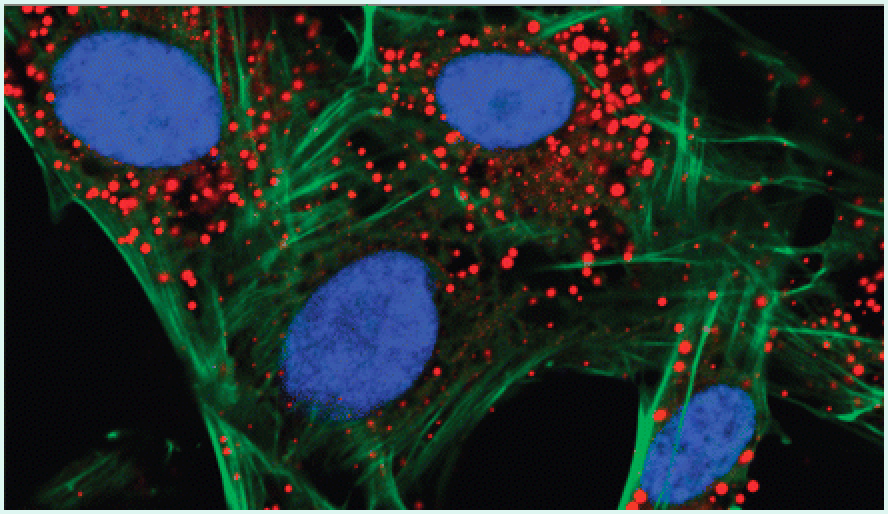
- Currently, engineered skin products are the most widely used.



Stem Cells for Tissue Science and Engineering

- Various tissues of the adult body have been used as a source of stem cells (e.g., fat, muscle, skin).
- To control cell phenotype and direct tissue formation is the ultimate goal.





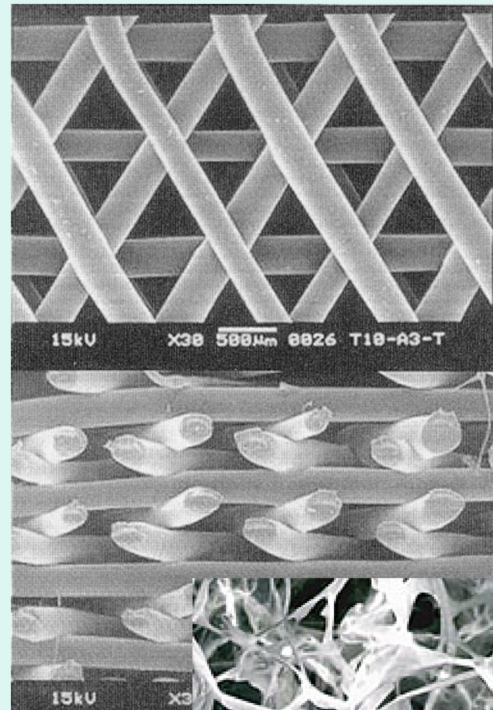
Formulating biomaterial scaffolds and the tissue matrix environment

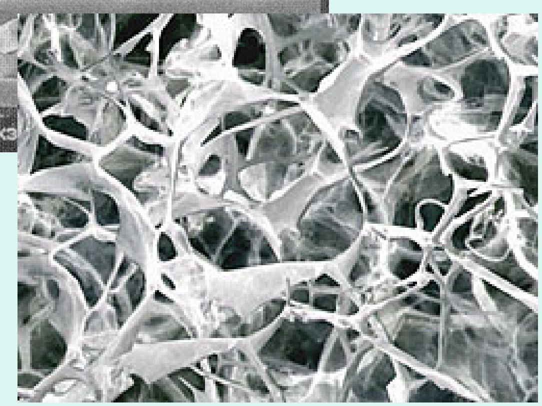
- Guide the growth, differentiation and organization of cells;

- Give support, strength and for to tissue and organs.

Formulating biomaterial scaffolds and the tissue matrix environment

- Hight molecular compound
  - Polylactic acid (PLA),
  - Polyglycolic acid (PGA),
  - Polycaprolactone (PCL)





Formulating biomaterial scaffolds and the tissue matrix environment

- Matrix:

  collagen, elastin, proteoglycans and wide variety of other proteins and signaling molecules.

Facing difficulties

- Understanding and quantifying the relationship between biomaterial scaffolding characteristics and physiological responses remain among the most pressing materials challenges.

Developing enabling tools

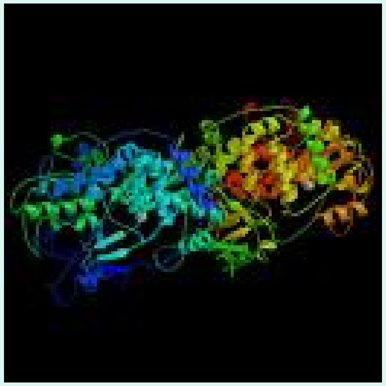
- The development of tissues is the result of molecular and supramolecular interactions that occur on a continuum of time and spatial scales in response to the many chemical and physical parameters within cells, between cells and within organisms.

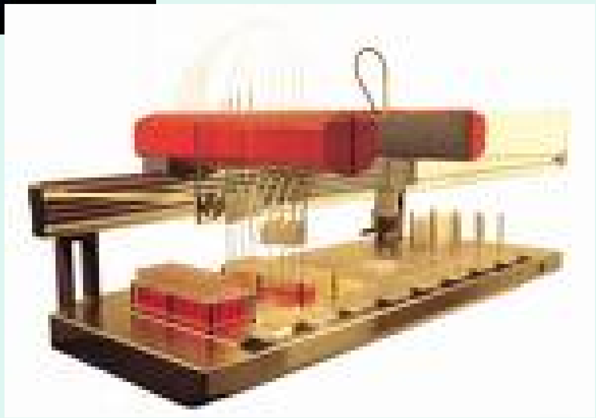
- Achieving sufficient insight into these complicated relationships needs knowledge and computational model.

Biomarkers, High-throughput/ Content Assays and Instrumentation

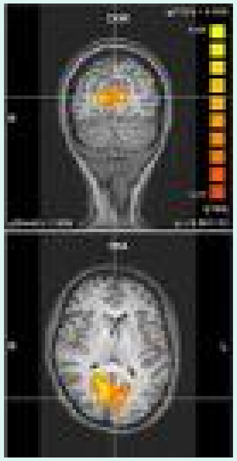
- Assessing the physiological state or condition of a cell or tissue

- Rapid screening of novel materials as candidates for scaffolding.

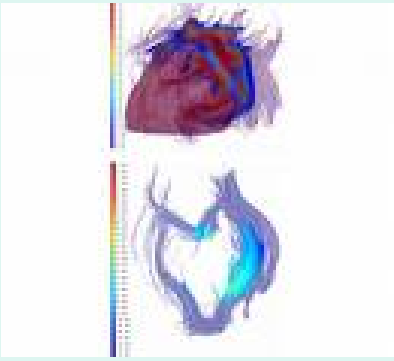


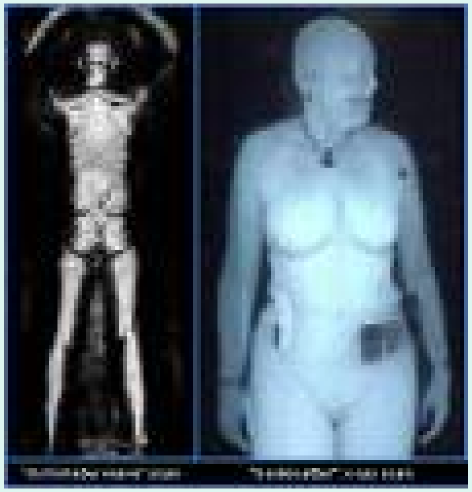


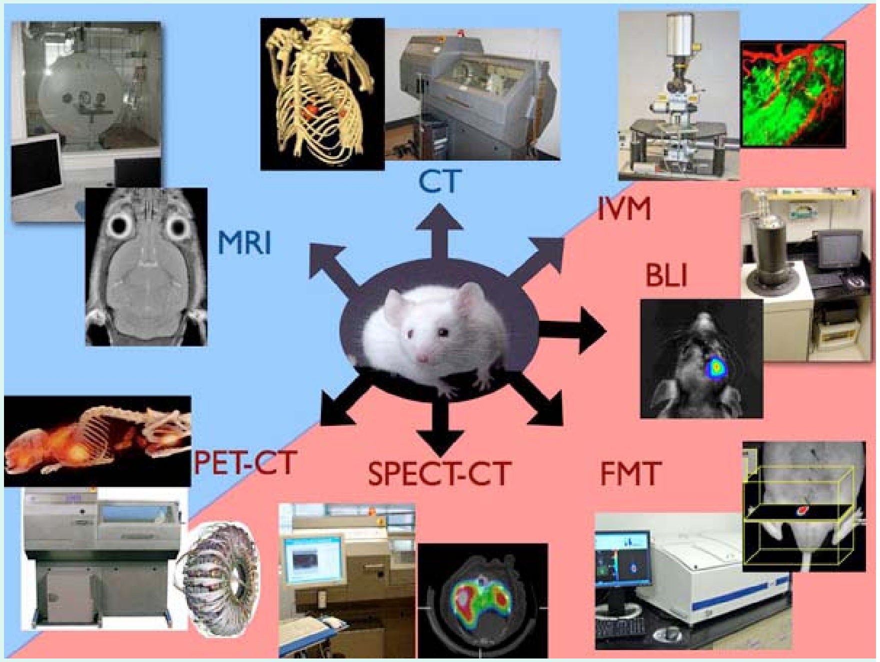
Imaging Technologies



- Imaging challenges include development, optimization, and integration of technologies at the many levels-from molecular to tissue to whole body.







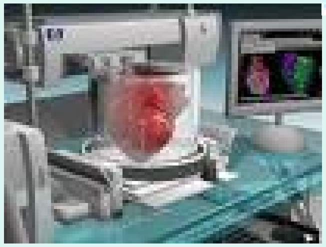
Computational Modeling and Bioinformatics

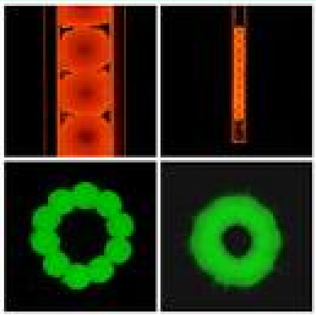
- Understanding the intracellular machinery, will require assimilating vast amounts of data into computational models;
- Such models will be critical for allowing prediction and subsequent testing of the large number of parameters that influence cells, tissues, and organs.

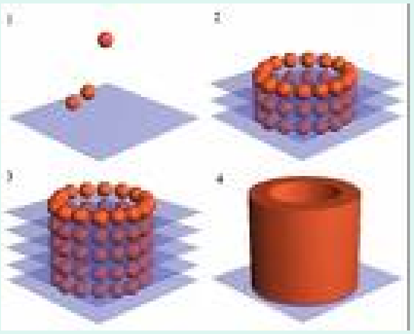
Fabrication Technologies

- Rapid prototyping (RP) technology was used in TE field;

- Majority of effort should on deposit cells in the layers during the fabrication process.



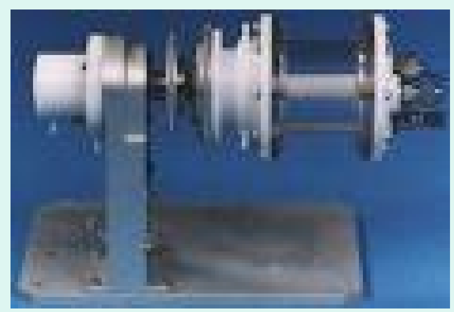




Bioreactors

- Producing 3D tissues in vitro requires;

- NEED: Design devices that can support self-assembly of multiple cell types into complex tissue structures.



Tissue Preservation and Storage methodologies

- It is very important for basic research, device development and clinical applications.

- Preservation techniques are far from perfect.

- Wood frogs

Promoting scale-up, translation and commercialization

- Much work to be done on the technical side in translating lab-scale fabrication techniques into large-scale production of high-quality products that meet GMP standards.
- TEMPs is “combination products” and need new standards and rules.

TEMPs Industrialization

Tremendous market potential

- **Organ replacement >65 ys, 1/5 (USA)**
- **8% medical spending，$350 Billion per year**
- **Operation $8 Million/year worldwide**
- **40-90 million days/year in hospital**
- **Bringing a new drug estimated $800 Million over 12 years**

Enterprise of TEMPs

- In 2002, 89 biotechnology organizations were involved in TE R&D worldwide.
- Theragnostices TEMP is anticipated to be $3.7 Billion by 2009.

TEMP Classification

- **Structure and function**
  - **Simple (Cartilage,tendon,bone,skin et al.)**
  - **Complex (Liver、Kidney et al)**
  - **Cell transplantation and capsule (Pancreas)**

- **Composition**
  - **Cells only(Epicel, Carticel)**
  - **Cell and biomaterial(Apligraf)**
  - **Biomaterial only(Alloderm ）**

Total spending

—— *Lysaght, Tis. Eng. 7,2001*

Enterprise of TEMPs

	Structural	Metabolic	Cellular
Examples	Skin,bone, heart valves	Bioartificial organs	Cell trans-plantation
Employee	1980(60%)	570(11%)	890(27%)
R&D spending	$3.63亿	$0.68亿	$1.74亿

—— Lysaght, Tis. Eng. 7,2001

Comparison of USA & European

	USA	European
Funding Sources	Industry	Government
Research focus	Application	Basic
Cellular sources	auto/allograft	autograft
Biomaterials	new material	modification
Bioreactor	On top	
Standards	On top	

WTEC, Jan, 2002


Thank you fro your attention!