Letter from the Editor

Dear TERMIS Members,

From August 31 to September 3, 2009 we will gather in Seoul, Korea for our 2nd TERMIS World Congress that will be held at the Lotte Hotel World, in conjunction with the 2009 Seoul Stem Cell Symposium. The abstract deadline is tomorrow. Please submit your abstract at www.termis.org/wc2009.

I like to encourage you to attend this conference not only because this conference will reflect worldwide advances in regenerative medicine and tissue engineering from a clinical and basic research point of view, but as the noble laureate.

Albert Szent-Györgyi von Nagyrapolt (1893-1986) said,

“Research is to see what everybody else has seen and to think what nobody else has thought.”

I look forward seeing you in Seoul!

Sincerely,
Dietmar W. Hutmacher

Edited and Compiled by:

Dietmar W. Hutmacher, PhD, MBA
Queensland University of Technology

Sarah Wilburn
TERMIS Administrator
Welcome to New TERMIS Officers & Council Members

At the end of 2008, the TERMIS membership participated in the election to vote for new members of the TERMIS Governing Board and the three regional Councils. We would like to welcome all the newly elected officers and council members.

Newly Elected Governing Board Members

TERMIS-AP Continental Chair-Elect
Yilin Cao

TERMIS-NA Continental Chair-Elect
Robert Guldberg

Members-At-Large: Emerging Countries
Marta Fontanilla

Member-At-Large: Europe
Rui Reis

Member-At-Large: North America
David Kaplan

Newly Elected Council Members

Asian-Pacific Council
Ahnond Buynyaratvej
James Goh
Dietmar Hutmacher
Ruszynam Idrus
Gilson Khang
Wei Liu
Chandra Sharma
Hsing-Wen Sung
Yasuhiko Tabata
Masayuki Yamato
Xingdong Zhang

European Council
Antonio Campos
Alicia El Haj
Erhan Pişkin
Heinz Redl

North American Council
Brenda Mann
Buddy Ratner
Shelly Sakiyama-Elbert
Bill Tawil
William Wagner
**2009 TERMIS 2nd WORLD CONGRESS**
In Conjunction With: the 2009 Seoul Stem Cell Symposium

*August 31 – September 3, 2009*
*Lotte Hotel World*
*Seoul, Korea*
*www.termis.org/wc2009*

**Science and Technology for Patients!**

**DEADLINE FAST APPROACHING!** Submit your abstract by Tuesday, March 31, 2009.


This world congress will have more than 35 Symposia Sessions in the scientific program (running in length from 1 ½ hours to 2 hours), each organized around a specific theme or topic. Also, the congress will have 15 ~ 20 General Sessions in the scientific program. Individual talks in each session range from 15 to 30 minutes in length (30 minutes for keynote speakers).

Abstracts must be submitted before Tuesday, March 31, 2009 through the online abstract submission website ([http://www.termis2009wc.org](http://www.termis2009wc.org)). Notification of acceptance of abstracts will be prior to April 30, 2009.

**Deadline for the Submission of Abstracts:** Tuesday, March 31, 2009

For further information, contact to the Scientific Program Chairmen.

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Secretary  
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E-mail : termis2009wc@cescon.co.kr
Plenary Lecturers (Confirmed)

- **Anthony Atala, M.D.**  
  Professor, Chair, Department of Urology; Director, Institute for Regenerative Medicine  
  Wake Forest University, USA  
  : “Regenerative medicine: Current concepts and changing trends”

- **Jeffrey A. Hubbell, Ph.D.**  
  Professor/Director, Regenerative Medicine and Pharmacobiology Laboratory,  
  EPFL, Switzerland  
  : “Engineering matrices and morphogens to manipulate cellular behavior in vitro and in vivo”

- **Teruo Okano, Ph.D.**  
  Professor/Director, Institute of Advanced Biomedical Engineering and Science,  
  Tokyo Women’s Medical University, Japan  
  : “Clinical application of cell sheet tissue engineering and future perspectives”

- **Xing Dong Zhang, Ph.D.**  
  Professor, Engineering Research Centre in Biomaterials  
  Sichuan University, China  
  : Title (TBA)

- **Sung Wan Kim, Ph.D.**  
  Professor, Department of Pharmaceutics & Pharmaceutical Chemistry,  
  University of Utah, USA  
  : “Designed polymers for therapeutic gene delivery”

- **Shin-Yong Moon, M.D.**  
  Professor, Department of Obstetrics & Gynecology, Seoul National University  
  Hospital, Republic of Korea  
  : Title (TBA)
Keynote Lecturers (Confirmed) (Alphabetical order)

1. Toshihiro AKAIKE (Tokyo Institute of Technology, Japan)
2. Stephen BADYLAK (University of Pittsburgh, USA)
3. Frank BAIJEENS (Eindhoven University of Technology, Netherlands)
4. Yilin CAO (Shanghai Jiao Tong University, China)
5. Chong-Su CHO (Seoul National University, Republic of Korea)
6. Andre CHOO (Bioprocessing Technology Institute, Singapore)
7. Karen L. CHRISTMAN (University of California, USA)
8. Fu-Zhai CUI (Tsinghua University, China)
9. Alex FAULKNER (King’s College London, UK)
10. W.F.J. FEITZ (Radboud University, Netherlands)
11. Joseph A. FRANK (National Institutes of Biomedical Imaging and Bioengineering, USA)
12. Axel HAVERICH (Hannover Medical School, Germany)
13. Patricia HEBDA (University of Pittsburgh, USA)
14. Dietmar W. HUTMACHER (Queensland University of Technology, Australia)
15. Suong-Hyu HYON (Kyoto University, Japan)
16. Kazunori KATAOKA (University of Tokyo, Japan)
17. Keung Nyun KIM (Yonsei University, Republic of Korea)
18. Andreas LENDLEIN (Berlin-Brandenburg Center of Regenerative Therapies, Germany)
19. Song LI (University of California, USA)
20. Yong LI (University of Pittsburgh, USA)
21. Wei LIU (Shanghai Jiao Tong University, China)
22. Peter MA (University of Michigan, USA)
23. Paolo MACCHIARINI (University of Barcelona, Spain)
24. Sakis MANTALARIS (Imperial College London, UK)
25. Tony MIKOS (Rice University, USA)
26. Shin-Ichi NISHIKAWA (RIKEN, Japan)

- Ronald D.G. McKay Ph.D.
  Senior Investigator, Laboratory of Molecular Biology, National Institute of Neurological Disorders and Stroke, National Institutes of Health, USA

  : “Stem cell signaling in health and disease”

- Dong-Wook Kim, Ph.D.
  Director, Stem Cell Research Center, Korea
  Professor, Yonsei University College of Medicine, Seoul, Korea

  : Title (TBA)
27. David NEWBLE (The Automation Partnership, UK)
28. Tae Gwan PARK (KAIST, Republic of Korea)
29. Roderic PETTIGREW (NIH, USA)
30. Stefano PLUCHINO (IRCCS San Raffaele, Italy)
31. Mahendra RAO (Johns Hopkins University, USA)
32. Rui L. REIS (University of Minho, Portugal)
33. Alessandro SANNINO (University of Lecce, Italy)
34. Chandra Prakash SHARMA (Sree Chitra Tirunal Institute for Medical Sciences & Technology, India)
35. Songtao SHI (Center for Craniofacial Molecular Biology, USC School of Dentistry, USA)
36. Michael SITTINGER (Berlin-Brandenburg Center of Regenerative Therapies, Germany)
37. Stephen STROM (University of Pittsburgh, USA)
38. Toshio SUDA (Keio University, Japan)
39. Wei SUN (Drexel University, USA)
40. Hsing-Wen SUNG (National Tsing Hua University, Taiwan)
41. Doris TAYLOR (University of Minnesota, USA)
42. Ming-Song TSAI (Cathay General Hospital, Taiwan)
43. Minoru UEDA (Nagoya University, Japan)
44. Andrew WEBSTER (University of York, UK)
45. Pamela YELICK (Tufts University, USA)
46. James YOO (Wake Forest University, USA)
# 2009 TERMIS World Congress Session List

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Developments in tissue engineering and regenerative medicine are expected to have a large impact on our society. Among others, they have great potential for treating the diseases and injuries that other therapeutic technologies cannot. However, such expectations can only be realized if the technologies fit into the healthcare system of modern societies. There are challenges in establishing this fit, and advancement in science may not be able to resolve these alone.

Tissue engineering and regenerative medicine have attracted the attention of social scientists, and they have some valuable insights to offer. This symposium provides you with an opportunity to interact with social scientists working in the area of tissue engineering and regenerative medicine. The aim is to explore ethical, political, economic, regulatory and demographic issues that together influence technological development in this burgeoning field.

From social science, we invite two distinguished speakers: Prof. Andrew Webster (Univ of York, UK) and Dr. Alex Faulkner (KCL, UK). Prof. Webster will investigate the issues of standardization and automation, and Dr. Faulkner will focus on the issues of regulation and market authorization. All of these issues have practical relevance to the future of tissue engineering and regenerative medicine.

To create a constructive dialogue between science and social science on these issues, we invite discussants who share their interests in these issues. Each discussant will have 10 – 15mins to present their thoughts. In their presentation, discussants are expected to engage with discussion with these two speakers, and evaluate the relevance of their arguments in their local context. We also welcome papers on these issues from science point of view.

If you are interested in participating this session, please submit your abstract through the Congress website (http://www.termis2009wc.org) using the specified format. As a discussant, please briefly describe your position on these issues and whether you think it is for social science and science to engage, within the 250 word limit. If you have any queries, please contact the session organizer.

We look forward to hearing from you.

Session Organizer:
(koichi.mikami@sbs.ox.ac.uk)
**Laboratory Features**

**Lab Feature 1. Hajime Ohgushi**  
**Lab Feature 2. Buddy Ratner**

**Lab Feature 1. Tissue Engineering Research Group, RICE, AIST**

Hajime Ohgushi (MD, PhD),  
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http://unit.aist.go.jp/rice/index.html

1. Outline of laboratory  
Since Tissue Engineering Research Center (TERC) was established on April 1, 2001, (The TERC was renamed as RICE: Research Institute for Cell Engineering on April 2004), we have managed the cell processing center for clinical application on tissue engineering. We conducted various technological developments with corporate partners to overcome problems in clinical application for tissue engineering. To promote early clinical application for tissue engineering, we established the medical system for bone/cartilage regeneration technology using bone marrow derived mesenchymal stem cells (MSCs) that can be readily accepted in the society. We also are focusing on treatment of vascular/heart disease, liver disease and metabolic disease. Therefore, our laboratory is becoming one of the premier tissue engineering centers in Japan.

2. Research activities  
Researches in our laboratory focus on regenerative medicine by stem cell transplantation and tissue engineering technology. We have attempted to regenerate various tissues including bone, cartilage, heart and liver. Moreover, considering commercialization of regenerative medicine, we have also attempted to establish the evaluation method as standards for safety and efficacy of the tissue engineering.

(1) Human cell processing center  
Unlike conventional treatment, regenerative medicine involves the process of growing (proliferation) and processing (differentiation) cells by engineering techniques for cultivation. To prevent bacterial contamination, cultivation must be conducted in strictly controlled, bacteria-free environment, as cell processing center (CPC) that specialized in growing human cells (Figure 1). CPC is supplied with air from which fine particles are removed by HEPA filter and cell culture is conducted in sterile cabinets of the CPC. In CPC, operator is absolutely necessary for growing and processing cells, but human operators may serve as a source of contamination. To minimize entry and exit of operator into CPC, we developed an automatic cell observation device. As shown in Figure 2, using this device, image of any culture dish in any position designated by the user can be observed from remote control via LAN. The cells can be observed without entering CPC, and sterile environment remains intact. We were able to develop technology that contributes to improvement of quality control and reduction
of worker load. Ideally, cell culture that involves no human hands is desirable, and we are now working on automatic cultivation device.

Fig. 1 Flow diagram from culture to transplantation of patient cells

(2) Technology for selecting target cell
Cell growth process is the first process in any regenerative medicine. However, since the harvested cells contain various types of cells, separation of target cell from the mix of cell is necessary. In our experience of MSCs culture, we observed that the growth rate decreases when the nucleus of MSCs became thin and the cells flattened in shape. Therefore, we decided to estimate the proliferative ability by measuring this phenomenon quantitatively. And we found the correlation between the thickness of MSCs measured by atomic force microscope and the cell proliferation activity. The atomic force microscopy is extremely expensive, difficult to operate and takes time to make measurement. Therefore, we developed the proliferation activity measurement device by measuring the thickness of area of MSCs nucleus and the shape of cell (plane) using light microscope image (Figure 3). The device we developed has excellent cost performance, and it is expected that it will be used in various places in the future.

Fig. 2 Automatic cell observation device

Fig.3 Cell thickness measurement device

(3) Verification of cell differentiation
In the development of regenerative medical technology, we have worked on the technologies for bone regeneration. Bone regeneration involves the method for regenerative tissue engineered bone in which MSCs are differentiated into osteoblasts with bone formation ability by cell cultivation, and the bone matrix is formed on biomaterial by these osteoblast. Various types of biomaterial are used to create tissue-engineered bone. Here we describe clinical application of tissue-engineered bone for total joint replacements.
Many osteoarthritic and rheumatoid arthritic patients underwent total joint replacements. These prosthetic devices have problems including aseptic loosening of the implant. To prevent loosening we developed regenerative cultured bone on joint prostheses. Fresh bone marrow would be collected from the patient and the MSCs isolated, expanded in number in culture and subsequently cultured on the surface of the prostheses under osteogenic conditions.

Thus, the surface of prostheses would be covered with bone derived from patient’s own cells. We call the bone on the prostheses as “regenerative cultured bone”. About 6 years have passed since the first case was treated with the cultured bone, and there have Benn more than 50 cases in total. Although the observation time is short, there had been no side effects such as inflammation or infection or loosening at the implant site, which is adverse event for artificial joint.

(4) Standard for regenerative medicine
As mentioned above, we are in the process of establishing the evaluation method of biomaterials used in bone regeneration medicine. Therefore, we are considering international standardization of the evaluation method. In International Organization for Standardization (ISO), we submitted the proposal “In vivo bone formation in porous material using mesenchymal stem cells – Standardization of to evaluate bone forming ability of biomaterials” to commence activities toward regenerative medical technology standardization originating from Japan. Figure shows the bone formation in the material conducted according to the proposal.

(5) iPS cells for regenerative medicine
Various kinds of cells are used in regenerative medicine. In 2007, Prof. Yamanaka developed induced pluripotent stem (iPS) cells, instead of ES cells which have ethical issue. We established iPS cell from a wisdom tooth bud cells which are usually discarded in dental clinic (Figure 5). However, both ES and iPS cells cause tumor called teratoma and their safeties have not been established for clinical practice. Further studies are therefore needed to determine whether iPS cells will be beneficial for regenerative medicine.
Research Institute for Cell Engineering (RICE),
National Institute of Advanced Industrial Science and Technology
Acknowledgements
We thank Professor Y. Takakura at the department of Orthopaedics, Nara Medical University. For development of automatic cell observation device, we thank Mr. M. Harada of Biomedical Business Division and Mr. H. Yamamoto of Human Ecology Research Center, in joint development with Sanyo Electric Co., Ltd. For cell thickness measurement device, we thank Mr. H. Fukuda of Medical New Business Project, as this is joint research with Olympus Corporation. Original figures (Fig 1 -4) are from the Journal (Synthesiology Vol1, No3 155-160, 2009); courtesy of AIST.
Lab Feature 2. Tissue Engineering at the University of Washington

Buddy D. Ratner and Christopher Barnes
University of Washington Engineered Biomaterials (UWEB21)
Seattle, WA 98195 USA

Overview

The first biomaterials research program arrived at the University of Washington (UW) in 1970 when Professor Allan Hoffman transitioned from M.I.T. to Seattle. Buddy Ratner arrived at the UW in 1972. His laboratory started up in 1974. Now, the University of Washington has more than 20 faculty members strongly associated with biomaterials and tissue engineering.

A number of large, federally-funded research efforts have provided a solid foundation of equipment and ideas for the Ratner laboratory and for the University of Washington. These programs include NESAC/BIO, UWEB, SUWA and BEAT. They will each be elaborated on in this section.

In 1983, the National ESCA and Surface Analysis Center for Biomedical Problems (NESAC/BIO) received its first funding from the NIH. This center provides surface analysis instrumentation and expertise to the biomedical research community. Twenty-five years later and with $5M+ in state-of-the-art surface analysis instrumentation, NESAC/BIO under the leadership of Professor David Castner continues to bring access to modern surface analysis methods to biologists, physicians and engineers worldwide.

University of Washington Engineered Biomaterials (UWEB), a National Science Foundation Engineering Research Center (ERC) was funded from 1996-2008. The focus of this collaborative center was to create biomaterials that could heal and integrate with the body with the end goal -- improved functionality of medical devices. UWEB brought together 30 professors, 150 students and 30+ companies with the intent of borrowing ideas from modern biology, implementing them into biomaterials and exploring their in vivo performance in pre-clinical settings. We came to realize that UWEB ideas of a vascularized, afibrotic reconstruction of the surgical site have much resemblance to central ideas in tissue engineering. Hence UWEB added a significant tissue engineering component to its research portfolio. The UWEB ERC was funded by the NSF for 11 years. Now it is evolving into UWEB 21, a restructured partnership with the biomedical device industry to enhance healing, improve device performance and apply tissue engineering concepts for tissue and organ replacement and repair.

Our strong base in reconstructive wound healing led to the year 2000-funded NIH Bioengineering Research Partnership (BRP)
BEAT (BioEngineered Autologous Tissue or, possibly, allogeneic tissue), focused on tissue engineering heart muscle and the Singapore-University of Washington Alliance (SUWA), focused on the esophagus. In addition, many other tissue engineering projects were launched at the University of Washington around that time, often based on ideas developed in UWEB.

The strong UWEB platform also led to a collaboration with Nanyang Technological University (NTU) of Singapore, funded by A*Star. This 2002-2007 collaboration, the Singapore-University of Washington Alliance (SUWA) had a major program in esophageal tissue engineering.

This article overviews many of the tissue engineering programs on our Seattle campus as of 2008. It is organized around our platform technologies (our technological tools), specific tissue engineering projects and technology commercialization.

A portion of our University of Washington tissue engineering group is pictured in a recent photo (Figure 1). Much of the tissue engineering research takes place in the Foege Building (the Bioengineering building, opened in 2006 on the 800+ acre UW campus, see Figure 2), the School of Medicine South Lake Union campus, and other sites such as Children’s Hospital of Seattle.

Figure 1: UWEB tissue engineering group from left to right: (Bottom Row) Marisa Sylvester, Buddy Ratner, Cecillia Giachelli, Anna Galperin; (Top Row) Erasmo Lopez, Lauran Madden, Eric Sussman, Michael Linnes, Ari Karchin, Christopher Barnes, Colleen Irvin, Shai Garty, Floyd Karp, Felix Simonovsky, Jason Tung.
I. Platform Technologies for Tissue Engineering

Technologies are in place at the University of Washington to characterize, create, and implement engineered tissue constructs. Overviews of some of these technologies are presented in this section.

Surface Analysis and ToF-SIMS with Special Application to Decellularized Extracellular Matrices

The creation of new biomaterials for medical devices, controlled release systems and scaffolds has been a strong, consistent theme at the University of Washington for almost 40 years. In a symbiotic relationship, UWEB and the NESAC/BIO center have worked together to precisely characterize the critical outer molecular surface of new biomaterials. NESAC/BIO employs a number of state-of-the art surface analysis instruments including electron spectroscopy for chemical analysis (ESCA), time of flight secondary ion mass spectrometry (ToF-SIMS) and atomic force microscopy (AFM). We have used these analytical tools to ensure freedom from contaminants, monitor bio-immobilization reactions and examine surfaces for cell adhesion.

In a collaboration with the laboratory of Professor Stephen Badylak at the University of Pittsburgh McGowan Center for Regenerative Medicine, decellularized extracellular matrix (ECM) scaffolds have been analyzed with ToF SIMS in order to assess the molecular composition of the outermost 1-2 nm of decellularized ECMs from both porcine and rat origin. With this technique, the goal is to chemically characterize the surface functionality of these materials to gain molecular insights potentially unseen with traditional immunohistochemistry. Can we relate regenerative capacity in different tissues to surface chemistry? Multivariate statistical methods to analyze the SIMS data will help us answer this question. The majority of this work has been performed by Christopher Barnes, a Chemical Engineering Ph.D. student in Buddy Ratner’s lab in collaboration with NESAC/BIO and Bryan Brown in Professor Badylak’s lab.

Human Embryonic Stem Cells

In a collaboration funded by the National Institutes of Health, The Bioengineered Autologous Tissue (BEAT) project is working towards engineering heart tissue replacements for patients with myocardial infarction. Significant effort has been expended on the study of human embryonic stem cells (hESC) as a cell source for potential therapies. hESCs can be differentiated into proliferating cardiomyocytes in vitro through timed addition of growth factors. The BEAT program funds a “stem cell core” that provides these difficult-to- handle cells to investigators.

Biomaterials are used to further understand and harness stem cell potential by creating defined microenvironments that control cell fate at the device interface. In the scaffolds section of this article, this application for biomaterials and stem cells will be described.

Although the presentation of ECM-derived proteins and growth factors has been the focus of many tissue engineering studies, few studies to date have reported the presentation of cell-surface ligands for control of cellular differentiation. The Notch signaling pathway is one cell-cell signaling pathway active in numerous cell fate decisions. In collaboration with Drs. Cecilia Giachelli and Charles Murry, Notch-signaling biomaterials have been developed and are currently being investigated for their ability to control human embryonic stem cell and cardiomyocyte cell fate. The cells are applied by either straight injection or in conjunction with biomaterials as a seeded tissue engineered heart muscle (discussed below) to clinically relevant models of myocardial infarction. Work for this project is being performed by Bioengineering students Jason Tung and Lauran Madden.

Inflammation, Angiogenesis, and Wound Healing

Wnt Signaling for Tissue Engineering
Activation of the canonical Wnt signaling pathway is found during both development and adulthood. Its downstream effects are diverse and include cell growth, migration, differentiation, and cancer propagation. Understanding the role of Wnt signaling during the foreign body reaction (FBR) and subsequently modifying scaffolds to modulate this pathway upon implantation could lead to improved therapeutic outcomes in vivo. In collaboration with Dr. Randall Moon’s laboratory at the University of Washington and the Howard Hughes Medical Institute, a study is currently underway to elucidate the temporal and cell-specific activation patterns of Wnt signaling upon the implantation of synthetic scaffolds into host organisms. Future studies will focus on the effects of either activation or inhibition of the Wnt pathway on the foreign body reaction. These results may be used to create methods for modulating Wnt signaling for tissue engineering. Such modulation of Wnt signaling may be achieved by the incorporation of Wnt activators or inhibitors (e.g., proteins and small molecule drugs) into the scaffold or growth media. Bioengineering Ph.D. student Eric Sussman is spearheading this project.

**Macrophage Phenotype and Tissue Engineering**

The macrophage is the cell that orchestrates the foreign body reaction (FBR). It plays a pivotal role in determining the biological outcome observed with implanted devices including influencing the extent of inflammation, angiogenesis and the formation of the foreign body capsule. Macrophages responding to wound healing environments (e.g., tissue damage or a biomaterial implant site) may acquire various activation states, which are characterized by different markers and behaviors, often referred to as macrophage polarity. A commonly-cited classification system for macrophage polarity uses the M1 and M2 activation states. M1 cells are considered pro-inflammatory because their behaviors include the release of pro-inflammatory cytokines and other inflammatory products such as reactive oxygen species. M2 macrophages are considered anti-inflammatory because they release anti-inflammatory and pro-fibrotic cytokines. Studies are being done to characterize macrophage polarity in the FBR and to better understand how modulating polarity by such means as scaffold physical morphology or by treatment with drugs can be used to achieve more desirable outcomes in vivo. Work on this project is being performed by Eric Sussman, a Ph.D. student in the Buddy Ratner lab, in collaboration with the laboratory of Dr. Randall T. Moon.

**Scaffolding Fabrication**

**Biodegradable Polymer Synthesis**

Biodegradable 2-hydroxyethyl meth-acrylate (poly(HEMA)) and N-isopropyl-acrylamide (poly(NIPAM)) based polymers with defined molecular weight are being synthesized by atom transfer radical polymerization (ATRP) using a bifunctional polycaprolactone (PCL) based initiator. ATRP offers precise control over molecular weight and macromolecular structure of the polymers during synthesis. By using a bifunctional macroinitiator, polymers twice as long as the desired degradation product size, but with improved mechanical properties can be synthesized. Additionally, PCL and poly(lactic acid) based crosslinkers can be used to create degradable polymeric hydrogels. By controlling the type and molecular weight of initiators and/or crosslinkers, linear polymers and hydrogels with tunable biodegradation rates can be synthesized.

In addition to the above synthesis strategy, novel biodegradable polyurethane segmented block copolymers are being developed as scaffolding materials. These polymers can be produced either as linear chain macromolecules or crosslinked into a three-dimensional structure. The multi-step bulk synthesis
has been developed to create linear polymers with peptide-like segments incorporated into the backbone. These new polymers, upon degradation in biological environments, release only low molecular weight molecules that are readily cleared in vivo. The polymer synthesis effort has been led by Sarah Atzet, a recent Ph.D. graduate from our program, Dr. Anna Galparin and Dr. Felix Simonovsky.

**Vascularized, Non-Fibrotic Healing and Sphere-Templated Polymers**

Strategies to produce vascularized, non-fibrotic healing of biomaterials in this lab have focused on both tailoring of scaffold geometry and modification of surface and bulk compositions to control biomaterial healing. Such healing is critical for tissue engineered constructs as well as medical devices. The sphere-templating technique (Figure 3) allows for the creation of biomaterial scaffolds with tightly controlled, uniform pore sizes. This has allowed for the evaluation of the effects of scaffold pore size on healing in a subcutaneous implant model in mice. By comparing several different pore sizes, an optimal pore size, approximately 35 micron diameter, has been found to enhance angiogenesis. In these scaffolds, increased angiogenesis and little fibrous encapsulation is observed. To further promote scaffold integration and reduce fibrosis around biomaterials, the transforming growth factor beta (TGF-b) signaling pathway has been targeted. The lab is currently evaluating a surface coating that presents bio-attractants for TGF-b to inactivate it thus increasing angiogenesis and reducing fibrous encapsulation. These strategies are being explored by students Lauran Maddan, Eric Sussman and Marisa Sylvester.

**Fibrin Templated Porous Scaffolds**

Dr. Ceci Giachelli and Bioengineering student Michael Linnes are working to create fibrin based scaffolds.

![Image](image_url)
hydrogels have been researched as a promising tissue engineering scaffolding material for over a decade. Past failures of these materials have been due to their inherent mechanical weakness and limited ability to be infiltrated with cells from the host. Implementing the sphere templating technique developed in the Ratner lab enabled the creation of a mechanically sound material while preserving the native fibrillar nature of polymerized fibrin\(^1\). In vitro, cells proliferate within the scaffold and in vivo, host cells infiltrate into the open porous network. Various processing parameters have been adjusted to slow degradation of the material without the use of protease inhibitors, which are traditionally used to prevent fibrin degradation past 4 weeks both in vitro and in vivo. The use of fibrin should help to enhance blood vessel formation within the scaffold due to its pro-angiogenic degradation. In a collaboration with Prof. Suzie Pun’s laboratory, these sphere templated fibrin scaffolds have also shown promise in non-viral gene delivery\(^2\).

II. Tissues and Organs

The platform technologies section provided an overview of the various approaches this lab is taking towards the creation and characterization of functional and implantable tissue equivalents. Numerous projects are currently underway to create constructs for specific tissues. These tissues are listed below.

**Heart Muscle Tissue Engineering (An NHLBI Bioengineering Research Partnership)**

Three major obstacles for repair of damaged heart tissue are loss of vascularized, functional tissue, scarring and the inability of cardiomyocytes to proliferate. Delivery of human embryonic stem cell-derived cardiomyocytes to the injured area has potential to improve heart function, but cells alone cannot decrease fibrosis and probably do not engraft. Implantable scaffolds seeded with functional hESC derived cardiomyocytes have been developed to simultaneously address the major issues of heart tissue damage. For this, our biodegradable version of poly(HEMA) is templated to form a 3D architecture that mimics native myocardium - aligned channels seeded with cardiomyocytes interspersed by a porous network with high diffusive capacity similar to vasculature. In vivo, the spherical pore structure surrounding the parallel channels encourages infiltration of host vessels. The cell-biomaterial interface is optimized for cardiomyocyte survival and growth by altering bulk polymer composition or by surface modification, e.g. protein immobilization. Heart tissue constructs are matured in vitro for functionality and ischemic resistance in preparation for implantation. Also, electrical properties of the heart muscle are being addressed. Work on this project is being performed by PhD student Lauran Madden in collaboration with the laboratories of Drs. Charles Murry and Mike Laflamme.

![Figure 5: Corneal Implantation surgeries in a rabbit model: (A) corneal implant built as a one piece material with porous skirt, and semi-rigid optic core, (B) surgical implantation of collagen-hydrogel scaffold, (C) Micrographs of repopulated micro-porous scaffolds. See ‘Oph-thalmologic’ section.](image)
Corneal blindness, affecting 12 million people, is the second leading cause of treatable blindness worldwide. While corneal transplantation using high-quality human donor corneas has been successful in selected developed countries, the majority of the people with corneal blindness today remain untreated because of the lack of donor cornea. Currently available artificial corneas for human use include the Boston-keratoprosthesis (K-pro) and the AlphaCor. Both corneal substitutes have limited use clinically because of the poor integration with host tissue, leading to high risk for catastrophic infection and extrusion.

To meet this need, polymeric materials with sphere-templated porous structures that can integrate with the host leading to reconstruction of the scleral structure have been developed. These artificial corneas (made as a single piece) consist of a transparent polymer optic-core interconnected with a suturable, porous polymer periphery.

Different materials were investigated using a rabbit model where porous disks were implanted on the cornea and followed for up to three months post-implantation (See Figure 5). Work for this project is being performed by Dr. Shai Garty in collaboration with the laboratory of Dr. Tueng Shen.

Orthopedic Applications

Sphere templated fibrin scaffolding has been modified by researchers in the Giachelli lab to act as a template for bone growth through calcium phosphate deposition and direct incorporation of nanocrystalline hydroxyapatite. The resulting materials have been shown to promote bone formation in a mouse calvarial defect model and upregulate alkaline phosphatase activity in vitro. Work on this project is being performed by Thanaphum Osathanon in Dr. Ceci Giachelli’s lab in collaboration with Michael Linnes, Dr. Martha Somerman and Dr. Buddy Ratner.

Mesenchymal Stem Cells

Under appropriate culture conditions, mesenchymal stem cells (MSCs) isolated from adult bone marrow may develop into bone, cartilage, or fat among other cell types. With funding from the Coulter Foundation, in collaboration with Dr. Paul Manner of the UW Department of Orthopedics and Sports Medicine, we use MSCs seeded onto a double-sided scaffold with defined, sphere-templated pore structures for regenerating hyaline articular cartilage. The design of the scaffold device is intended to allow biological regeneration of diseased or damaged cartilage surfaces in hips and knees.

The scaffold is made of poly(HEMA) and uses the sphere templating technology created in the Ratner lab. One side of the scaffold is designed to sustain and promote chondrocyte growth while the other side of the scaffold is optimized for bone attachment and formation. In a rabbit model, MSCs were seeded onto one side of the scaffold and cultured to differentiate into chondrocytes. The device can then be implanted into the rabbit knee. In parallel to the rabbit studies, in vitro tests are done using human mesenchymal stem cells seeded onto the scaffolds. Substances to enhance bone anchoring to the scaffold, such as hydroxyapatite, collagen I, or BMP2 can be incorporated into the material and this will be part of future studies. Work for this project is being performed by Colleen Irvin and Christopher Barnes in collaboration with Dr. Paul Manner.
**Bladder Tissue Engineering**

The aim of this project is to improve manufacturability and functionality of tissue engineered urinary bladder devices using autologous urothelial and smooth muscle cells (SMCs). A bioreactor design has been created that will provide biochemical and mechanical stimulation to bladder SMCs seeded in novel biodegradable porous scaffolds. The scaffold is constructed as a one-piece spherical sac with internal sphere-templated porosity favoring cellular integration and vascularization. Autologous urothelial cells will be seeded on the internal surface of the construct to form the urothelial lining.

Extensive mechanical property characterization of the scaffolds and the tissue generated will be performed. Further characterization will include histology, immunohistochemical assays for differentiation, apoptosis assessment, proliferation measurement, and growth factor measurements. We aim to produce functional urinary bladders with reduced variability in physiological parameters such as capacity, leak point pressure, and compliance. The initial clinical application envisioned is treatment of neurogenic bladder disease. Work on this project is being performed by Erasmo Lopez in collaboration with Dr. Claire Yang from UW-Medical School, and Dr. James Bassuk from Children’s Hospital Research Institute in Seattle, WA.

**Esophageal Tissue Engineering**

In a collaboration with the Nanyang Technological University (NTU) in Singapore and funding provided by A*STAR of Singapore, a project for engineering esophageal tissue was begun in 2002. Drs. Buddy Ratner and Cecilia Giachelli were the two principal investigators at University of Washington and worked closely with Dr. Sandy Chian at NTU to develop various scaffolding designs. Two examples were the esophageal acellular matrix (EAM)\(^5\) and the electrospun micro-fibrous polymeric scaffolds. In addition, a novel study was performed which showed the ability to control esophageal epithelial cell differentiation on a biomaterial surface via the chemical attachment of a Notch-ligand\(^5\). The Notch pathway is important in cell-cell signaling in early embryonic development.

**Ligament**

For this project, the hypothesis is that a mechanically stimulated, multi-phasic, fibroblast seeded scaffold will lead to the development of heterogeneous collagen organization as seen in the transition region between soft tissue and bone. The first phase of the project was to utilize melt electrospinning to manufacture a biodegradable multi-phasic scaffold with a continuous gradient between tension and compression regions. This step required the design of a thermally stable, biocompatible polymer, and a novel collector allowing for user-defined alignment of an electrospun scaffold. The second phase of the project will be to mechanically stimulate electrospun, multi-phasic scaffolds seeded with ACL fibroblasts. This step will be used to test the hypothesis that a combination of scaffold architecture and mechanical stimulation regime will result in tunable collagen I : collagen II expression. It is expected that distinct, region-specific mechanical cues will be transmitted to resident cells resulting in heterogeneous collagen expression. Work for this project is being performed by Ari Karchin in Dr. Joan Sanders’ lab in collaboration with Dr. Buddy Ratner’s lab.
Vaginal Wall Reconstruction and Reinforcement

Pelvic organ prolapse (POP) is a prevalent condition described as a bulging of the vagina by the pelvic organs into or even through the vaginal canal. Two hundred thousand surgeries for POP are performed in the US annually. Use of synthetics such as Dacron meshes for strengthening the vaginal wall often leads to complications such as erosion and pain. We are exploring the possibility of rebuilding strong, muscular vaginal wall using silicone elastomer sphere-templated porous structures in a rabbit model. This collaboration is led by Dr. Michael Fialkow.

III. Technology Commercialization and Tissue Engineering

UWEB had an important goal – to take technology from bench to commercialization. Such translation brings the benefits of taxpayer-funded research back to the taxpayer in improved medical therapies. Dr. Andy Branca, the UWEB Industry Coordinator, spearheaded efforts to bring UWEB technologies to commercialization. More recently, Dr. Branca has been managing the Department of Bioengineering Coulter Program to continue this translation effort. In 2008, at least three tissue-engineering companies are up and running to commercialize new technologies stemming from the UW. These companies include:

Healionics, Inc., Redmond, WA, which has licensed the sphere templating technology from the University of Washington. Their first product, a glaucoma drainage device for dogs that heals into the sclera, will be on the market in early 2009.

Ratner Biomedical Inc., Bellevue, WA, is bringing tissue engineering ideas to nerve regeneration.

This company is also licensing technology from Johns Hopkins University.

BEAT BioTherapeutics, Inc., Bellevue, WA will develop the BEAT concepts of heart muscle regeneration.

IV. References
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Phase I - Update on...

May 27-29, 2009 • Saint-Raphael (France).

Objectives
Regenerative medicine aims to restore the functional activities of tissues and organs by using the concept of cellular and tissue engineering. This concept includes all the technologies that use living cells and / or materials (synthetic or natural) in order to improve, regenerate or replace the impaired function of tissues or organs. This concept largely exceeds the traditional concepts of biocompatibility and requires a strong interdisciplinary work between physic, chemistry, cell biology, material science, and clinic. The objective of this workshop is to provide a broad public basis of cell and tissue engineering reporting on the latest scientific and technological advances in the fields of materials and their interfaces with the cells and tissues. The audience consists of basic researchers, clinicians and engineers that will exchange their views on the advanced techniques of molecular and physicochemical characterization of the interfaces cells / tissues / materials in an attempt to identify the advantages and the limits of the current therapeutic solutions based on tissue engineering concepts.

Audience
Academic and industrial researchers, clinicians, engineers and technicians, doctoral and post-doctoral students, working in laboratories, hospitals or center of investigations and regulation agency. The lectures will be given in English.

Maximum number of participants: 60

Program
Recent progress in the field of materials and cells for tissue engineering will be presented. In particular, biodegradability, nanostruktration and biofonctionalization of materials will be discussed. The methods of physicochemical and molecular charaterization of materials and their interfaces with cells and tissues will be investigated in detail. Methods of cell cultures in static and dynamic conditions and relevant methods for cell imaging will be also widely discussed. Finally, examples of applications in the field of skin, bone, cartilage and vessels engineering will be presented and analyzed through a round table dedicated to the transfer of technology from the bench to the bedside.
With the participation of: Mario Barbosa (Porto, Portugal), Ivan Martin (Basel, Switzerland), Nicolas L’Heureux (Novato, USA), Clemens Van Blitterswijk ( Enschede, The Netherlands), Josep A. Planell (Barcelona, Spain), Pierre Weiss (Nantes, France), Didier Mainard (Nancy, France), Odile Damour (Lyon, France), Patrice Laquerrière (Reims, France), Philippe Lavalle (Strasbourg, France), Karine Anselme (Mulhouse, France), Michel Vert (Montpellier, France), Luc Sensebe (Tours, France), Laurent Laganier (Lyon, France).

TERMIS-EU Directory

We encourage those members within the European Chapter to please register to the TERMIS-EU Directory. The Directory was created to link the EU members at one location and enables EU members to search for members within your own area of research. To register today, please visit https://www.termis.org/directory.php.
2010 Chapter Meetings

**TERMIS-EU: Galway, Ireland**
Conference Dates: 13-17 June, 2010
Meeting Chair: Prof. Abhay Pandit
Conference Venue: Galway Radisson SAS Hotel

**TERMIS-AP: Sydney, Australia**
Conference Dates: September 2010
Meeting Chair: A/Prof. Geoffrey McKellar

**TERMIS-NA Orlando 2010**
Conference Dates: December 5-8, 2010
Conference Location: the Hilton located at the Downtown Disney Resort
Conference Chair: Anthony Atala, MD
Scientific Chair: James Yoo, MD, PhD
Hosted by: Wake Forest Institute for Regenerative Medicine

2011 Chapter Meetings

**TERMIS-EU 2011: Granada, Spain**
Conference Dates: 7-10 June 2011
Conference Location: Granada Exhibition and Conference Centre
Conference Chair: Antonio Campos Muñoz, MD, PhD
To request further information, please send an email to acampos@ugr.es.

**TERMIS-NA 2011: Houston, Texas**
Conference Dates: Fall 2011
Conference Chairs: Antonios Mikos, PhD and Jennifer West, PhD
Hosted by: Rice University

**TERMIS-AP 2011: Singapore**
More Information Coming Soon

2012 3rd TERMIS World Congress

In Vienna, Austria

September 5-8, 2012

Hofburg Congress Center

"Tissue Engineering and Regenerative Medicine"
Conference Chair: Heinz Redl, PhD
Program Chair: Martijn van Griensven

Ludwig Boltzmann Institute for Trauma Care in the AUVA Research Center and
the Austrian Cluster for Tissue Regeneration
Expertissues – NoE
TERMIS

To request further information, please send an email to Office@lbitrauma.org.
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**Tissue Engineering, 2009 Subscription Rates**

*Tissue Engineering*, Official Journal of the Tissue Engineering and Regenerative Medicine International Society, has been receiving increasing numbers of excellent reviews and methods papers. *Tissue Engineering* (Part A) has traditionally focused on hypothesis-driven scientific reports. The Reviews and Methods journals will enable the flagship *Tissue Engineering* to bring these valuable papers to the readership on a much larger scale.


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*Tissue Engineering, Part A*

Co-editor: Antonios G. Mikos, and Peter C. Johnson

The flagship journal provides a fundamental understanding of structure-function relationships in normal and pathologic tissues with the ultimate goal of developing biological substitutes. The Journal brings together scientific and medical experts in the fields of biomedical engineering, biomaterials science, molecular and cell biology, genetic engineering, and surgery to present and discuss advances in this emerging field.

*Tissue Engineering, Part B, Reviews*

Co-editors: John P. Fisher, Antonios G. Mikos, and Peter C. Johnson

This new journal meets the urgent need for high-quality review papers due to the rapid expansion of the field. The Journal presents critical discussions, analyses, and concise summaries of research in different aspects of the field to assess where we are now and future directions.
**Tissue Engineering, Part C, Methods**
Co-editors: John A. Jansen, Antonios G. Mikos, and Peter C. Johnson

This new journal presents procedures and protocols that will be adopted by the tissue engineering community as the research is translated into clinical applications. Authoritative papers will bring consistency to the research methods employed and help the field grow and mature.

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Upcoming Meetings Endorsed By TERMIS

April 2009

- **8th Annual Meeting of the Midwest Tissue Engineering Consortium**
  Conference Dates: April 3-4, 2009
  Hosted by: University of Pittsburgh
  Deadline for submission of abstracts: January 31, 2009

- **35th Annual Northeast Bioengineering Conference**
  Conference Dates: April 3-5, 2009
  Hosted by: Harvard-MIT Division of Health Science and Technology

May 2009

- **Preservations of Cells, Tissues and Gametes Short Course**
  Short Course Dates: May 18-20, 2009
  Hosted by: The Center for Translational Medicine and
  the Department of Mechanical Engineering at the University of Minnesota
  PDF

- **Cell-Based Therapies & Tissue Engineering CTTE 2009 Short Course**
  Short Course Dates: May 18-21, 2009
  The Skeletal Research Center and the Department of Biology at
  Case Western Reserve University, Cleveland, Ohio
• **12th Ceramics, Cells and Tissues Conference: Surface- Reactive Biomaterials as Scaffolds and Coatings**
  Conference Dates: May 19-22, 2009
  Conference Location: Faenza, Italy

• **ICRS 2009**
  Conference Dates: May 23-26, 2009
  Conference Location: Hotel Intercontinental, Biscayne Bay Miami, FL

• **Workshop-INSERM Summer School « Tissue engineering: study of the interfaces materials/cells/tissues »**
  Phase I: May 27-29, 2009 in Saint-Raphael (France)

  Organizing committee:
  Joëlle Amédée, email: joelle.amedee@inserm.fr
  Didier Letourneur, email: didier.letourneur@inserm.fr
  Jérome Guicheux, email: jerome.guicheux@nantes.inserm.fr

**June 2009**

• **10th Advanced Summer Course in Cell-Materials Interactions-Self Assembly: from nature to clinics**
  Conference Dates: 22-26 June 2009
  Conference Location: Porto, Portugal

• **ICMAT 2009 - Symposium A: Advanced Biomaterials and Regenerative Medicine**
  In conjunction with the 2nd Asian Biomaterials Congress
  Conference Dates: 26 June - 3 July 2009 in Singapore

**July 2009**

• **International Conference on Bioprinting and Biofabrication in Bordeaux (3B’09)**
  Conference Dates: July 6-8, 2009
  Conference Location: Bordeaux (France)

• **2nd Annual Business Education Course, The Business of Regenerative Medicine: From Stem Cells to the Market Place**
  Course Dates: July 13-16, 2009
  Course Location: Cleveland, Ohio
August 2009

- [Rice University’s Annual Short Course Advances in Tissue Engineering](#)
  
  Short Course Director: Dr. Antonios G. Mikos, Professor of Bioengineering and Chemical & Biomolecular Engineering at Rice University
  
  Short Course Dates: August 12-15, 2009
  
  Short Course Location: Rice University Campus

September 2009

- [FSB2009](#)
  
  Conference Dates: September 7-11, 2009
  
  Conference Location: Lausanne, Switzerland
  
  Conference Venue: Beaulieu Convention Centre, Lausanne

- [2009 World Stem Cell Summit](#)
  
  Conference Dates: September 21-23, 2009
  
  Conference Location: Baltimore Convention Center, Baltimore, MD

October 2009

- [bone-tec 2009 – International Bone-Tissue-Engineering Congress](#)
  
  Congress Dates: 8 – 11 October, 2009
  
  Congress Location: Hannover, Germany
  
  Deadline for symposia proposal: 31 March, 2009
  
  Deadline for abstract submission: 31 May, 2009

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