talking about why large companies like Boston Scientific collaborate with UWEB. Those with the “know-how” are the leading experts most often found in academic institutions.

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Future Potential from front page

The New Industrial Post-Doctoral Program at UWEB

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Those with the Know-How
Wendy Naimark, a Principal Research Scientist at Boston Scientific, says industrial projects often depend on “thought people” with “know-how expertise.” She’s
Message from the Director of Industry Relations

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Should you desire to pursue some of our patented inventions, or if you need some new IP created for your use, the Sponsors enjoy global exclusive access to technological advances at UWEB. I am pleased to invite all our UWEB Sponsors to reflect on how far we’ve come in recent years and to work together toward our mutual goals. This publication, The Insider, is created solely for - and is not distributed beyond - the UWEB Sponsorship. I hope you find it informative and that you are inspired to work with us.

Andy Branca, Ph.D.
UWEB Director Industry Relations
July 22, 2003
Invention I

Coupled Chemistry
Hydrogels Crosslinked with Amino Acids

UWEB Director, Buddy Ratner and visiting scientist, Prabha Nair, Chitra Tirunal Institute for Medical Sciences and Technology (India), discovered a powerful but simple combination: Mix solutions of (poly) vinyl alcohol (PVA) with amino acids and the two gel rapidly.

The surprise is this couple’s natural chemistry. There is no covalent chemical cross-linking or catalysis necessary to form it. This hydrogel is non-toxic, and therefore, highly biocompatible. Implanted into mice, there was no evidence of inflammation or extensive foreign body encapsulation (Fig. 1). Even more, this perfect combo has no competition. This is the first hydrogel found to form non-covalently on the basis of inherent intrinsic chemistry. It is a chemistry that is basic but unique. The amino acid can form hydrogen bounds with the hydroxyl (OH) groups on the PVA polymer. More specifically, Ratner and Nair found a 6.7% (wt/wt) solution of PVA (MW 86,000-140,000) had an approximate viscosity of 130 cps at 37º C, as measured by a spindle with a shear rate of 10 rpm. Add the amino acid, and the gel thickened in proportion to the amount of glycine in the amino acid.

Although any naturally occurring or synthetic amino acid can be used, the best hydrogels formed with PVA solutions were found to be glycine, bicine (N,N-Bis(2-hydroxyethyl)glycine, glutamine, cysteine, arginine, lysine, histidine, and trans-4-hydroxyl proline, serine, or methionine. A mixture of certain amino acids like glycine and lysine with PVA and glycine and arginine were also highly successful. Furthermore, UWEB scientist, Maxi Boeckl has shown that simple diaminoo or dicarboxylic acid compounds can be used.

These two United States Pharmacopeia (USP) certified raw materials that polymerize rapidly could have a significant impact on medical applications. PVA-amino acid hydrogels can be used in surgical sealants and barriers mimicking or working with fibrin to heal tissue. They could also be used as ultrasound coupling gels, lubricants, hemostasis control materials, medical device coatings, and to prevent adhesion after surgery. In the operating room, doctors could easily use this hydrogel to control the release of drugs and other therapeutic agents.

**Figure 1**
Biocompatibility Testing (Intra Muscular)
The hard outer layer of a lobster or shrimp is a lot like human bone. It’s hard and needs to be tough because it stands up to pressure. So, University of Washington researcher, Miqin Zhang, looked to Chitosan—a polymer that is a derivative of the crustacean shells—as a potential biomaterial for bone tissue engineering. What she found was even more impressive.

Mix chitosan with alginate, then freeze-dry them to separate and the resulting scaffold is full of holes. Literally. Yet, nine times as strong as chitosan alone. The porous structure, Zhang found, is ideal for healing bone lesions.

Zhang cut Chitosan-Alginate scaffolds she’d created into a coin-like shape. Then she seeded bone-forming cells into holes she’d made in the center of each scaffold. After only one week, Scanning Electron Microscope (SEM) images showed cells attached to the surface and bone nodules rooted to it, too, with many differentiated and divided cells.

This technology could replace the current scaffolds being made from softer materials as well as the more solid ceramic materials currently on the market. The porous structure of Chitosan/Alginate hybrids is ideal for seeding and growing bone cells. This biomaterial depends on holes to heal wholly.

Invention Disclosure II
All W-hole-d-Up:
Chitosan/Alginate Hybrid Heals Bone Faster

Figure 1
SEM photomicrographs of the cross sections of a chitosan-alginate scaffold prepared using a freeze-drying technique. (A) Three-dimensional porous structure. (B) A detailed pore image. (C) A higher magnification image showing interconnectivity of the porous structure.

Figure 2
SEM images of osteoblasts cultured on chitosan-alginate scaffolds after one week of cell culture. (A) Osteoblast cells attached to the surface by discrete filopodia and exhibited microvilli on its dorsal. (B) A group cells with many divided cells. (C) Several bone nodules grown on the surface. (D) A single nodule with many differentiated and divided cells.
Miqin Zhang is a bone architect. That is, she is in the business of designing the material equivalent of bone. A professor of Materials Science & Engineering at the University of Washington, Zhang has developed a method of preparing porous hydroxyapatite scaffolds using a combination of gel-casting and polymer sponge methods. The result is a lot like bone.

Bone is naturally porous to allow bone tissue to regenerate. However, high-impact fractures are very difficult to heal completely and take a long time. Not to mention that the loss of entire bone segments can’t be replaced. Bone tissue engineers have attempted to make next-generation bone equivalents that were mechanically as strong as bone while still maintaining bone’s cancellous structure, without much luck. That is, up to now.

Zhang’s technique achieves both the mechanical properties of bone and its architecture. Polymeric sponges are infiltrated with a ceramic slurry containing monomers and initiators for rapid gelation via \textit{in situ} polymerization. The process produces an open, uniform and interconnected porous structure with a pore size of 200-400 µm, a compressive yield strength of ~5 MPa, and a compressive modulus of ~8 GPa. These figures are relative to the polymer sponges used. Alternating appropriately structured sponges, Zhang’s method can control porosity, pore size, and the geometry of the synthetic tissue. It’s just a matter of design.
Invention Disclosure

For the past six years, UWEB has disclosed a wide variety of inventions exclusively to UWEB Sponsors. If you have interest in discussing any of the titles in the list below, please contact Dr. Andy Branca, UWEB Director of Industry Relations.

Inventions:
• A Biodegradable, biocompatible polyurethane based on peptide segments
• A Biomaterials Treatment for Cancer
• A Method of Preventing Endothelial Cell Death in Angiogenic Biomaterials, Pending
• A New Technique for Fabrication of Macroporous Hydrogels
• A Novel Cationization Surface for SIMS Analysis of Polymers and other Macromolecules
• A Strategy to Enhance the Healing of Biomaterials, Pending
• A Tissue Engineered Heart Valve
• A tissue engineered small-diameter vascular graft, Pending
• A Tissue-engineered Heart Muscle Construct
• An SHA Self-assembled Monolayer Surface for Immobilizing Proteins and Biomolecules
• Angiogenic Biomaterials, Pending
• Biomaterial with Engineered Vascularization, Issued
• Cell Attachment Interface for Transcutaneous Devices
• Chitosan/Alginate hybrid scaffolds for bone tissue engineering
• Covalent Immobilization of Proteins and Peptides on Bioprosthetic Heart Valve Tissue
• Degradable Microvessells for Biomaterial Surfaces
• Fluorescent Porphyrins for Self Assembled Monolayers on Gold Surfaces
• Fluorocarbon Surfaces that Promote Cell Growth
• Hydrogels formed by Crosslinking with Amino Acids, Pending
• Immobilized Osteopontin for Healing of Implanted Biomaterials, Pending
• Improved Wound-Healing and Alteration of the Foreign Body Reaction Achieved by Local Inhibition of Expression of Thrombospondin 2 (TSP2), Pending
• Lubricious Coating by Plasma Polymerization
• Method to Enhance Cell Proliferation
• Mitigation of Bioprosthetic Heart Valve Calcification by Treatment with Sodium Cyanoborohydride at PH = 9.5
• New Cross-linkable Phospholipids for the Preparation of Supported Bilayers
• Novel Manufacturing Designs to Achieve Spatial and Temporal Control and Local Biologies Delivery
• Photoimmobilization of Osteopontin on Implant Surfaces
• Photosensitive Self-assembled Monolayers with Azide Head Groups: an Easy route for Modification of Surfaces, Pending
• Plasma polymerized temperature responsive polymer coatings with microheater control for protein and cell patterning
• Porous Biodegradable Scaffolds Based on Amino Acids for Tissue Engineering, Pending
• Preparation of porous hydroxyapatite scaffolds by combination of the gel-casting and polymer sponge methods, Pending
• Prevention of Ectopic Calcification of Bioprosthetic Valve Material by Using Reducing Agents (such as Glutathione and Vitamin C
• Purification of Thiol Molecule Using Gold
• Recognition Peptides Engineered into Streptavidin, Pending
• Reduced Foreign Body Giant Cell Formation in MCP-1 Mice, Pending
• Separation of Mixed Cell Populations
• Skinny Electrodes for Improved Healing
• Small Fiber Biomaterials, Pending
• Surface Immobilization of Alpha Tocopherol Succinate (Vitamin E) for Reducing Macrophage Mediated Inflammatory Response to Biomaterial Implants
• Synthesis of a Peptide Crosslinker
• Synthesis of Activated Carboxyl Nano Gold Particles
• Template Imprinted Materials by RFGD Plasma Deposition, Issued
• Therapeutic Delivery Using Biological Microtubes
• Type-1 Collagen Coating for the Natural Immobilization of Osteopontin
• Ultrasound Modulated Self-healing SAM-polymer Implants for Controlled Drug-delivery, Issued
• Use of b-sheet Motifs as Tensile Molecular Recognition Switches
• Use of Osteopontin to Inhibit Tissue and Implant Calcification, Issued
• Use of Phosphonoformic Acid (Tradename Foscarnet) to Treat Ectopic Calcification of Uremic Patients
Publications in Peer Reviewed Technical Journals


See Technical Journal Publications page 8


Publications in Peer Reviewed Conference Proceedings

“Natural Immobilization: The Use of Type 1 Collagen as a Natural Binding Agent of Osteopontin onto Poly(2-hydroxyethyl methacrylate) and its in vitro Effects,” Stephanie M. Martin, Jeffrey L. Schwartz, Cecilia M. Giachelli, Buddy D. Ratner. The 29th Annual Meeting of the Society for Biomaterials (abstract accepted), Reno, NV, April 30-May 3, 2003.

Affinity Coating to Bind Osteopontin to Poly(2 hydroxyethyl methacrylate),” Stephanie M. Martin, Jeffrey L. Schwartz, Cecilia M. Giachelli, Buddy D. Ratner. Polymer Preprints 2003, 44(1).


R Ohri, CM Giachelli “Mitigating Dystrophic Calcification of Bovine Pericardium by Osteopontin (Rescuing the Calcification Phenotype in Osteopontin-Null Mice),” Transactions of the Society for Biomaterials, 25, 199, 2002.


Publications in Trade Journals


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UWEB Director of Industry Relations

Shari Ireton and Elizabeth Sharpe
Managing Editors

From Trade Journal Publications page 10


Congratulations Alcon!

UWEB congratulates Alcon Laboratories of Fort Worth, TX on the recent FDA approval of its AcrySof® Natural Single-Piece Intraocular Lens. Alcon, a founding member of UWEB, specializes in products for vision correction, care and the treatment of diseases of the eye. The new IOL is the first foldable implanted lens that can filter out harmful UV and blue-light (on the market in the US.) It is designed to mimic the light-filtering properties of a healthy human lens. This design incorporates chromophores into the acrylate lens material that selectively filters out high-energy light. The product was introduced less than a year ago in Europe and is now available for lens replacement in the US.

UWEB is proud to work closely with its industry partners like Alcon that continue to improve medical devices, benefitting patients world-wide.

Good job, Alcon, and best wishes from your colleagues at UWEB.
Future Potential from front page

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