

BIOTECH *at* VIRGINIA

The Newsletter of the University of Virginia Biotechnology Training Program
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Making the Environment Attractive

By Meng Wang

AFTER Roseanne M. Ford received her Ph.D from the University of Pennsylvania in 1989, she came to University of Virginia to continue her work on bacterial chemotaxis, the ability of motile bacteria to direct their migration toward beneficial chemicals and away from detrimental ones. That same year, an oil spill, which occurred in Prince William Sound, Alaska, (noted as the largest disaster of this type in American history) attracted her attention and inspired her to apply bacterial chemotaxis to environmental bioremediation processes. “Chemotaxis interested me after I read Daniel Koshland’s book” said Dr. Ford, “in which he described bacterial chemotaxis as a good model to start understanding how humans respond to the environment.”

Using various computational simulation methods and microscopic approaches, Ford’s lab group has been investigating bacterial response to chemicals, especially pollutants that behaved as attractants, on different scales and in different environments. These



Roseanne M. Ford

cases range from single-cell three-dimensional swimming behaviors, to movement of bacterial population in microfluid system. Other technologies, like Magnetic Resonance Imaging (MRI) and genetic florescent bacteria, can also be applied to track the bacterial trips in different porous media.

The recent collaborative project between the United States Geological Survey (USGS) and Ford’s group broadened the

scope of investigation to natural systems. Field-scale chemotaxis experiments in Cape Cod, Massachusetts are revealing the role that chemotaxis plays in the environment. In recognition of these achievements Dr. Ford was recently distinguished with the title of Fellow of American Institute for Medical and Biological Engineering.

Besides being a professor in Chemical Engineering

see FORD, page 3

Inside:

Externship Highlights

Brian Schmidt
Alexander Baras
Emily Cushnie

Interview

Dave Patteson

Events

VaBio After Hours
Adventures Mountain
River Raft Trip

Externships Philips Research

By Brian Schmidt

GROETEN! I spent the summer in the Netherlands on an externship with Philips Research in Eindhoven characterizing microbubbles.

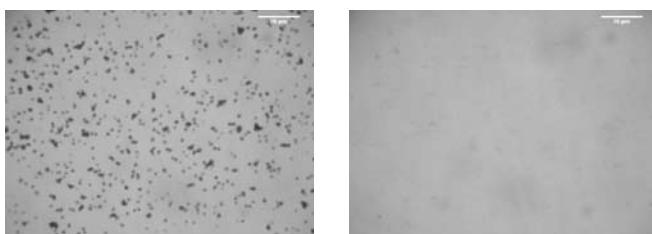
Investigators have designed a variety of agents that take advantage of the ability to interact with ultrasound to provide contrast for medical imaging and release therapeutics. One category is gas-filled microbubbles that have a stabilizing shell comprised of lipids, proteins, or polymers. Once injected, they strongly reflect ultrasound due to the mismatch in the acoustic properties of the encapsulated gas and surrounding blood, enabling the visualization of blood vessels, which normally yield poor contrast in an ultrasound image. Microbubbles can be used to enhance images of organ structure and measure blood perfusion. Several brands of microbubbles have already been approved by the FDA and are in clinical use.

Additionally, microbubbles can be targeted to specific biomarkers. Once injected, the microbubbles flow through the vasculature and accumulate at sites of disease. By targeting the microbubbles to adhere to specific vascular proteins, it will be possible to directly quantify the severity of a selected disease process. Because ultrasound can be used to destroy the microbubbles, they can serve as agents to deliver encapsulated therapeutic specifically at the diseased tissue.

There are significant challenges in developing actively targeted microbubbles capable of fulfilling the promises of the technology in the clinic. One of the limitations of most microbubble manufacturing methods is that they produce a broad distribution of bubble sizes. This is undesirable since large bubbles can become lodged in the capillary bed of the lungs and small bubbles cannot carry much therapeutic. An additional challenge is shielding the microbubbles from undesirable interactions with the body, such as immune recognition, while retaining sufficient capability to bind the target sites. The acoustic properties of the bubble must also be tuned for the desired application. For targeted delivery applications, the bubble must be robust enough to allow adhesion and prevent breakage and release at undesirable sites but structurally weak enough so the bubble will break at clinically permissible ultrasound intensities.

Philips has been developing polymer-shelled microbubbles that address many of these challenges. They have developed a manufacturing technology based on ink-jetting technique capable of creating bubbles that form a very narrow size distribution with a precisely-controlled mean diameter. Polymers that have been demonstrated to help shield objects from immune recognition and enable the conjugation of targeting ligands can be incorporated into the shell.

see PHILLIPS, page 7



Top: photo with my roommates and other Philips interns. Center: a visit to the windmills near Amsterdam on the river Zaan. Bottom left: targeted, polymer-shelled microbubbles manufactured using a filtration technique I learned at Philips have accumulated on a functionalized surface. The bottom right image was taken about .2 seconds later, after the application of ultrasound.

Novartis

By Alex Baras

WITH OUR CURRENT ABILITY to measure the transcript levels of nearly the entire human genome and specific genotypes from 100K or 500K single nucleotide polymorphisms (SNPs) in single assays comes the fundamental task of identifying which features of the human genome, are critically related to a particular biological phenomena being examined. With this data rich environment comes the necessity for analytic methodologies that are appropriate from both the statistical/algorithmic and biological standpoints.

I worked at the Novartis Institutes for Biomedical Research (NIBS) at Cambridge, Massachusetts. The specific project I was involved in was developing computational methods to analyze data from 100K and 500K single nucleotide polymorphism (SNP) DNA arrays. This technology allows one to interrogate 100K or 500K individual SNP genotypes from a sample in a single assay. At Novartis, they are particularly interested in identifying

SNP(s) that correlated with drug response in large studies that employ this technology. This type of pharmacogenetic approach will ultimately lead to personalized medicine in which patient response can be better predicted.

In univariate analyses attempting to correlate SNP genotypes to drug response requires rigorous statistical testing that is computationally intensive. Leveraging cluster computing methods and the C/C++ language I was able to reduce the computation time required for these analysis from a couple weeks to a matter of 15 minutes.

Outside of this specific project, I was able to interact with a variety of members from the global biomolecular discovery team at Novartis. This afforded me the opportunity to better appreciate the complexity and sheer volume of personnel and projects that a large-scale pharmaceutical employs in its research and development areas. ■

FORD, from page 1

Department, Dr. Ford also holds an administrative role as Associate Vice President for Research and Graduate Studies. Once she joined the Chemical Engineering department as a young faculty member, she began to devote herself to establishing relationships with students and other faculty. "Exciting research, compensation, [and] job placement opportunities are three most important stimuli for a school to attract students. I also try to make UVa [an] attractive place from those aspects," said Dr. Ford. She also mentored students from Chemical and Civil Engineering departments and from the Medical School, thus reflecting her appreciation for interdisciplinary communication.

Professor Ford considers the Biotechnology Training Program (BTP) a successful example from both academic and administrative perspectives. According to her, the interaction among students and faculty from different areas exposes students to various research projects, inspires their thinking on their current studies and also teaches them the language of new areas. Furthermore, externships provided by the program allow students the opportunity to experience an industry work setting and to experience society beyond academia. The coordination of this program is one that allows each student to feel a sense of a unified research community as opposed to one of isolation. ■

Tissue Genesis, Inc.

By Emily Cushnie

MY THREE MONTH INTERNSHIP was conducted at Tissue Genesis, Inc. (TGI); a privately owned tissue engineering company based in Honolulu, HI. TGI's primary goals involve the use of cell and tissue engineering research in conjunction with a proprietary platform technology to formulate commercial products for the field of regenerative medicine. Many of the TGI projects are investigated in collaboration with research labs at the University

of Arizona, the University of Hawaii, and the University of North Carolina at Chapel Hill.

The principal ongoing venture at TGI is the development of a single step, autologous, endothelialized vascular graft, which would be applicable to the cardiovascular artery bypass surgical market, as well as to the areas of end stage renal dialysis and peripheral bypass graft procedures. The basic

idea of the grafting process is that cells harvested from a patient's own body are cultured in a bioreactor and subsequently used to create a cell-lined vessel for surgical implantation in a matter of hours. Microvascular endothelial cells, stem

see GENESIS, page 7

... the grafting process ... allow(s) surgeons to process adipose tissue liposuctioned from the patient in order to derive therapeutic cells for immediate implantation.

Interview **Dave Patteson: Successful Biotech Business Executive**

By Gbemi Oredei

WHEN ASKED TO INTERVIEW DAVE PATESON, I admit I was a bit intimidated. For eight years, Dave Patteson served as President and CEO of Biotage, a globally renowned corporation. Recently, he has accepted a position as President and CEO of Advion Biosciences, a corporation that provides bioanalytical services and products. During my interview, it quickly became apparent that Dave Patteson is an engaging, polite, and extremely down-to-earth individual. Our interview was peppered with numerous interesting and captivating stories of major life events, which served to build Dave into a successful business leader.

Dave Patteson resides in Charlottesville, Virginia. Born in Richmond, Virginia, and raised in Chapel Hill, North Carolina, Dave worked on dairy farms as a young man, and the farmer's regimen seems to have been permanently ingrained in him to this day. Dave states, "I am the first one to work typically by 5:30–6am, but one of the first to leave by 5:30–6pm — so I have a work-life balance." It is apparent from his experience on farms that Dave was able to quickly learn the importance of time management.

During his undergraduate career, it was evident that Dave's work ethic would continue to develop and grow. When Dave was not working to pay for his schooling, he was involved in some activity or organization (Honor counsel Chief Justice, Fraternity leadership, etc.). The leadership roles he assumed in these groups prepared him for major business position he would assume later on in life.

Involvement in school organizations and work were not the only experiences responsible for developing Dave's leadership and business skills. Dave "was always in the presence of great mentors in both college and work..." Dave elaborated more on the idea of great mentors with a quite fascinating and inspirational story. During his sophomore year in college, Dave was privately insulted and deeply upset by some strong discouraging words of a Statistics professor, an event that very nearly made him consider ending his education. Dave countered the insults by enrolling in the professor's Statistics course and received the highest scores in the class in over seven years. The Stats professor and he went on to become fast friends. Dave also considers the "sponsorship and close relationships with potent individuals, including the founder of Genzyme...and additional exposure through being involved in several significant mergers and acquisitions" as major career milestones.

As a young man, Dave admitted, he never dreamed he would be in control of a global business entity. "I never had that as a dream per se. It was more of an *enlightenment*. I saw rather quickly in the busi-

ness environment there was a dearth of true *leaders* who understood the technical aspects of the business they ran. I put two and two together and realized if I was proficient technically or scientifically, and was a better manager/leader, and [if] I *out-worked* everyone around me (in a nice way), the rest would happen on its own. And it did."

Dave was asked to offer a few words of advice to those who may be interested in the idea of developing a business or heading their own companies/firms. He claimed that the keys for success are to: have confidence in oneself and have a willingness to work with others, "because building a strong business requires a blend of different ideas." Furthermore, he promotes the idea of surrounding oneself

"One should never confuse brilliance with experience, and I've been fortunate to have had a lot of exposure to a diverse set of conditions. And I have worked with others of equal or greater experience"

with "people who are mentally stronger." Dave also highlighted that it is important to establish a balance between intellect and experience when seeking to build and advance a company. "One should never confuse brilliance with experience, and I've been fortunate to have had a lot of exposure to a diverse set of conditions. And I have worked with others of equal or greater experience."

Moving On

Dave has left his position as President of Biotage, the leading provider of systems and consumables for medicinal chemistry, process development and genetic analysis, to become CEO of Advion Biosciences. When asked to compare his experiences at the two major corporations, Dave noted that, other than the product deck, there are a great number of similarities for their relative status of business life cycles.

Dave remarked on what he felt was the most important aspect of his work in his former position at Biotage, and now as CEO of Advion Biosciences. He noted that, at Biotage, his work centered on establish-

ing and maintaining a “dynamic organic growth scenario” coupled with a high company acquisition rate. He recalls that “We [Biotage] went from being an unknown name in the pharma/biopharma industry to being the largest supplier of synthesis, evaporation, workup and purification kit in the span of seven years...” What Dave considers to be the most important aspect of his work now as CEO of Advion Biosciences is, “1) Building a leadership team capable of getting the company to \$100M in revenues within the next few years. 2) Acquiring rational companies in our space to create a global provider with consistent earnings ... and 3) Leveraging the high organic growth and technical excellence in our existing Proteomics and BioMarker product line while never sacrificing Quality.”

His long term goals for Advion Biosciences include: forming and sustaining “a strong balance between our CRO BioAnalytical services business and the Biologics product business.” Furthermore, Dave seemed excited to employ, at Advion, the “Merger and Acquisition and Globalization experience” used at Biotage.

Dave Patteson and the BTP

As is expected, Dave Patteson has always supported budding scientists and biotech-based research. He has in the past and still does remain interested in continuing collaborations with colleges/

universities such as he has done with the University of Virginia. Furthermore, during the interview, Dave expressed an eagerness to continue providing internship/externship experiences for college students. Dave demonstrated an interest in continuing this relationship with BTP.

Dave stated that, “We [Advion Biosciences] hire interns year-round and are currently looking for any others to join. We have many new services which we will be offering ... all of which will require the best and brightest to come join us either for short or long duration work....”

It was quite exciting to have the opportunity to interview such an influential figure in the biotechnology industry. The wisdom and words of advice imparted by Dave Patteson is most helpful, not only to scientists, but to any one seeking to or merely interested in, developing themselves as entrepreneurs. There are many things to learn from successful businessmen such as Dave through studying their work ethic, becoming involved in mentor/mentee relationships, gaining experience, and outlining future goals and remaining true to those plans. One profound thought that was expressed by Dave, a thought that has shown itself to be valuable, is — when in a successful or advantageous position, do not forget to help others seeking to do the same, remembering that you were once in that position. ■



Events **UVa Biotech After Hours Event**

By Michelle Kofron

THE BIOTECH After Hours was held on March 16, 2006. This event was hosted by the University of Virginia's (UVa) Department of Biomedical Engineering and support was obtained from Diffusion Pharmaceuticals, LLC. Over 80 people were in attendance including members of The Virginia Piedmont Technology Council, VaBIO members, venture capitalists, UVa faculty, and students. The event was an opportunity for UVa graduate students and faculty to present their research to the local biotech community, as well as network, discuss biotech trends and research, product development and commercialization. Dr. Thomas Skalak, Chair of the Department of Biomedical Engineering, introduced the biomedical engineering program at UVa and announced the granting of the Wallace H. Coulter Foundation Translational Research Partnership Award to the department. The evening ended with Ankit Tejani leading tours of the biomedical engineering laboratories at UVa.

The Biotech After Hours is held on a regular basis and is an opportunity for Virginia businesses and the UVa academic system to come together and potentially develop collaborative efforts. One does not have to work in the life sciences or a biotech company to participate. Tanya Watson and Michelle Kofron represented the UVa Biotech Training Program (BTP) and answered several inquiries about the BTP externship program. ■



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New Trainees

By Gordon Laurie

CONGRATULATIONS AND WELCOME to Kristina Little and Dan Leslie on their acceptance into the BTP. Kristina is a student in Klaus Ley's lab and is a '06 graduate (BS) in Mathematics and Physics from the College of William and Mary. Dan received his BS in Chemistry from Colorado State University in '05, and is in the lab of James Landers. ■

Finals Weekend

SUNDAY, MAY 20 is quickly approaching. Don't miss out on Finals Weekend. Have questions about invitations, lodging, or parking, then visit <http://www.virginia.edu/majorevents/faqs.html> ■

Adventures Mountain River Raft Trip a Success

By Jace Fogle

ON SATURDAY, MAY 20, seven brave BTP trainees joined their fearless leader, Professor Laurie, for a guided whitewater rafting trip on the Lower New River in Hico, WV. The trip began at 7 a.m. when the group boarded rental cars behind Jordan Hall. Veteran BTP rental car drivers Jace Fogle and Rooshin Dalal safely navigated their colleagues through the picturesque West Virginia countryside, arriving at the Adventures Mountain River headquarters in just over three hours. There, the group was treated to a complimentary breakfast and organized themselves into different rafts: Jake Jordan, Tim Pabst, and Jace were in one boat and Meng Wang, Emily Cushnie, Rooshin, Michelle Kofron, and Professor Laurie were in another.

This trip was not for the faint of heart. Undeterred by air temperatures hovering around 70 degrees and water temperatures of 54 degrees, the group donned wetsuits, windbreakers, rubber booties, and crash helmets to brave the conditions. The ride consisted of an 11 mile stretch of river including Class 1 through 5 rapids. To pass over the rapids without flipping, rafters had to work as teams by paddling in unison according to directions from the guide. While nobody was lost in the rapids, certain trainees were helped over the side of the boat by their group member.

Participants were also treated to additional thrills. En route to the raft launching site, the rafters were driven by bus over

the New River Gorge Bridge, the highest vehicular bridge in the United States (876 feet). Toward the end of the trip, the rafts passed under this bridge in the water. Trainees also stopped for lunch on the side of the river and were given the opportunity to jump off an overhanging rock into the river. In addition, trainees were allowed to jump off their rafts and swim through one section of Class 3 rapids.

The group arrived back in Charlottesville about 9 p.m. that night. While tired, all group members agreed that the trip was a worthwhile team-building experience. ■

PHILLIPS, from page 2

I became interested in the project because of the advances in diagnosis and treatment this type of molecular imaging will bring to the clinic and because it is a great application of the more fundamental research I have been involved in at the University of Virginia. Understanding many of the biophysical and biochemical factors important for leukocyte adhesion simplified the task of designing an *in vitro* assay to quantify the adhesive potential of different microbubble constructs. The project also gave the opportunity to learn some of the fundamentals of ultrasound wave propagation while designing a flow system that would be minimally attenuating.

In addition to the research experience I gained in an industrial setting, the externship gave the opportunity to spend the summer in the Netherlands. One of the best things about staying on continental Europe is that there are so many places to visit that are just a short train or plane ride away. I visited 's-Hertogenbosch, Antwerp, Rotterdam, the Hague, Amsterdam, and Rome. I stayed in a Philips student house with interns from France, Switzerland, and Sweden, and I had the opportunity to make friends with many students from all over the world. ■

GENESIS, from page 3

cells, and other regenerative cells are obtained from a patient's own adipose tissue using a therapeutic cell technology, of which TGI is the executive licensee. The *in vitro* cell culture is performed using the Bio-Optimization System™ (BOS™), which is an automated perfusion bioreactor that was developed by TGI from requirements for NASA space shuttle missions. The BOS includes disposable biochambers and flowpath cartridges that are contained in a single unit that is about the size of a breadbox. It is designed to allow surgeons to process adipose tissue liposuctioned from the patient in order to derive therapeutic cells for immediate implantation. Cellular delivery may be accomplished via the aforementioned vascular graft or stent, as well as through self-dissolving wound dressing or direct injection to damaged tissue.

My contribution to the TGI research efforts this summer included, among other things, work on a wound study that investigated the use of adipose derived cells on a commercially available biodegradable wound dressing. I was able to participate fully in the experimental planning, preparation, execution and analysis of the project throughout the course of my three-month externship. In addition to gaining exposure to several procedures and techniques that I was previously unfamiliar with, my time in the TGI lab has exposed me to the sequential process of research and development at a small-scale biotech company. As I prepare to leave Hawaii, I feel lucky to have gained an invaluable image of the biotech world to which I can associate specific faces and experiences, a more robust idea of the commercial biotechnology field ... and a killer tan to boot! ■

The Faculty & Their Research

Gary Balian—(O&BMG) Biochemistry of connective tissue macromolecules.

Travis Blalock—(EE) CMOS digital and analog signal processor design.

Edward Botchwey—(BME) Development of new cell-material systems for bone tissue engineering.

David Brautigan—(M) protein Ser-Thr phosphatases and cell signaling circuits.

Giorgio Carta—(CE) Adsorption and ion exchange, chromatography, biocatalysis.

Zygmunt Derewenda—(MPBP) Protein structure and function: macromolecular crystallography; mechanisms of signaling by GTPases; protein-protein interactions.

Douglas DeSimone—(CB) Cell adhesion molecules in development.

Brian Duling—(MPBP&BME) Cell-cell communication in the vessel wall, including chemical, electrical, and mechanical processes that lead to coordination function of endothelial and smooth-muscle cells.

Victor Engelhard—(M) Structure and synthesis of antigens recognized by T lymphocytes; tumor immunology.

Erik Fernandez—(CE) Purification of biological molecules, protein structure, magnetic resonance imaging and spectroscopy.

Roseanne Ford—(CE) Environmental remediation, microbial transport in porous media.

Cassandra Fraser—(C) Polymeric metal complexes: synthesis, properties and uses.

Jay Fox—(M) Basement membrane structure and metalloproteinases.

H. Mario Geysen—(C) Combinatorial Chemistry.

Stephanie Guerlain—(SE) Information system development in the human genome era.

Bill Guilford—(BME) Vascular and molecular engineering.

Brian Helmke—(BME) Endothelial mechanotransduction, cellular biomechanics, nanotechnology tools for cellular bioengineering, cell-cell interactions in microcirculatory blood flow.

John Herr—(CB) Differentiation antigens expressed during mammalian spermatogenesis.

Rick Horwitz—(CB) Cell adhesion in development and pathology.

Donald Hunt—(C&P) Protein sequencing by mass spectrometry.

Isa Hussaini—(P&NS) Functional roles of low density lipoprotein receptor-related protein (LRP) and protein kinase C in astrocytic tumor invasive growth.

Donald Kirwan—(CE) Mass transfer and separation, crystallization, biochemical engineering.

James Landers—(C&P) Biological, bioanalytical and clinical chemistry.

Gordon Laurie*—(CB) Molecular control of epithelial differentiation.

Cato Laurencin—(O, BME, and CE) Biomaterials, tissue engineering, drug delivery and nanotechnology

Michael Lawrence—(BME) Biochemical, cellular, and mechanical factors regulating leukocyte adhesion.

Klaus Ley—(BME&MPBP) Molecular mechanisms of leukocyte adhesion and genetic engineering targeting atherosclerosis.

Timothy MacDonald—(C) Bioorganic and synthetic organic chemistry.

Christopher Moskaluk—(P) Genetic and genomic analysis of human cancers.

Pamela Norris—(MANE) Aero-gel technology.

Jason Papin—(BME) Computational systems biology, reconstruction and analysis of cellular signaling networks.

J. Thomas Parsons—(M) Protein kinases in cell adhesion.

William Pearson—(BMG) Protein evolution; transcription.

Ian Sarembok—(InMd) Role of inflammation in vascular injury and repair.

Thomas Skalak—(BME) Cardiovascular mechanics, microcirculation.

Ann Sutherland—(CB) Cell matrix interactions in mouse development.

Ronald Taylor—(BMG) Clearance of pathogens.

Martin Schwartz—(M) Integrin signaling and its relevance to mechanotransduction, cancer and vascular disease.

Judith White—(CB&M) Molecular mechanisms of viral and cellular adhesion/fusion proteins; molecular mechanisms of sperm-egg binding and fusion; ADAMS in fertilization and development.

Michael Wormington—(B) Post-transcriptional regulation of gene expression; Development of RNA-based therapeutics.

*Program Director

Biotech at Virginia

The Newsletter of the University of Virginia Biotechnology Training Program

Biotechnology Training Program
Application Deadline: April 24th

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Training Departments

| | |
|------|--|
| B | Biology |
| BME | Biomedical Engineering |
| BMBG | Biochemistry, Molecular Biology & Genetics |
| C | Chemistry |
| CE | Chemical Engineering |
| CB | Cell Biology |
| EE | Electrical Engineering |
| InMd | Internal Medicine |
| M | Microbiology, Immunology & Infectious Disease |
| MANE | Mechanical Aerospace & Nuclear Engineering |
| MMSB | Molecular Medicine & Systems Biology |
| MPBP | Molecular Physiology & Biological Physics |
| NS | Neuroscience |
| O | Orthopedics |
| P | Pathology |
| SE | Systems Engineering |