RUTGERS

BIOTECHNOLOGY TRAINING PROGRAM
2019 HANDBOOK

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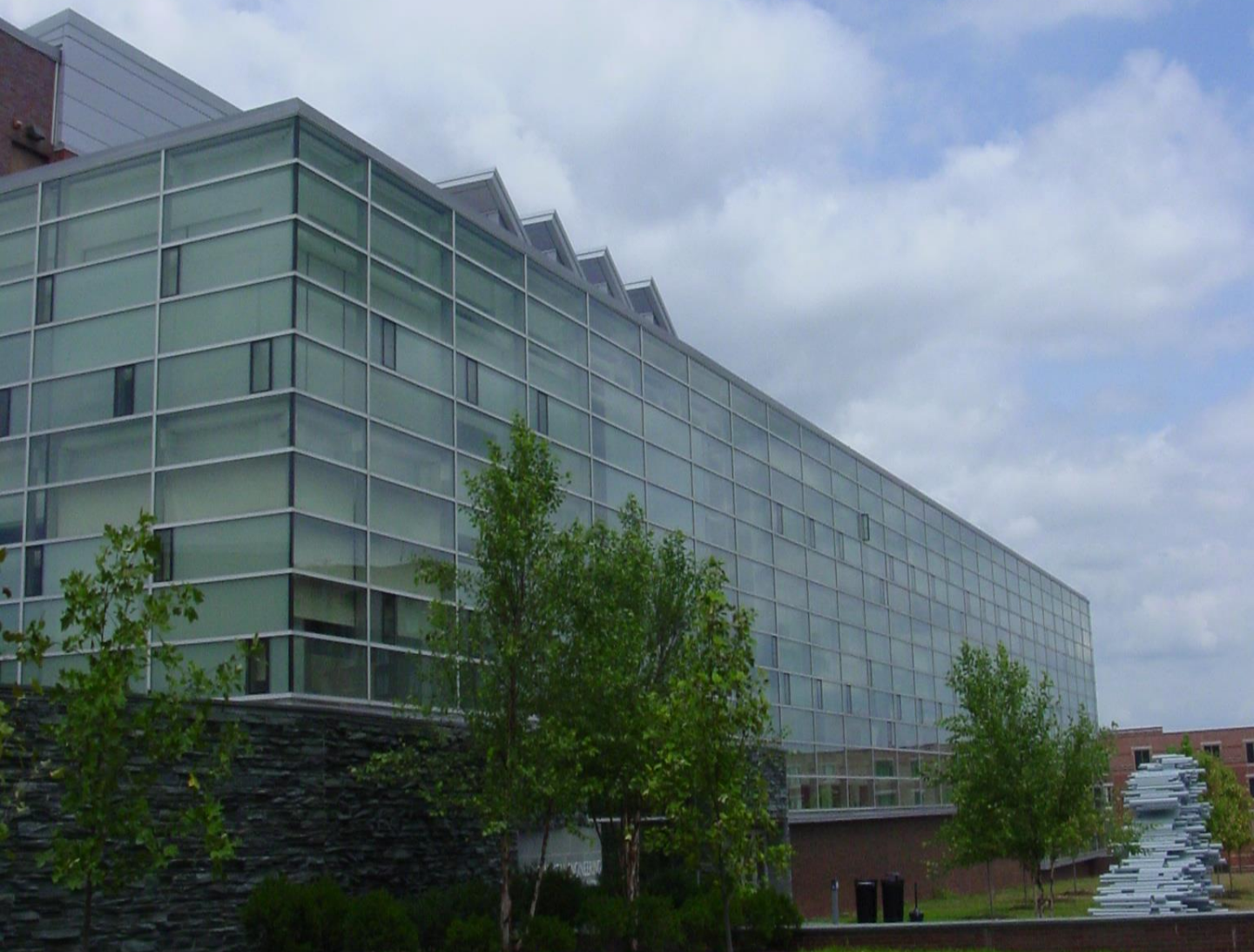

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BIOTECHNOLOGY TRAINING PROGRAM

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Humble Beginnings

Rutgers, the State University of New Jersey, was chartered in New Brunswick in 1766 as Queen's College, the eighth institution of higher learning to be founded in the thirteen colonies. Renamed Rutgers College in 1825, it became the land-grant college of New Jersey in 1864, attained university status in 1924 and was designated the state university of New Jersey in 1945. Most recently in 2013, 7 schools of the University of Medicine and Dentistry of New Jersey became part of Rutgers incresing the student population to more than 65,000 students and the overall budget to nearly $4 billion. Today, Rutgers is among the top 25 research universities in the nation, a member of the prestigious Association of American Universities, and the Big Ten conference.

In the 1980s, the state of New Jersey strengthened its commitment to science and technology with the passage of two major state bond issues benefiting higher education and the formation of the New Jersey Commission on Science and Technology. Rutgers was a major beneficiary of these initiatives, which resulted in unprecedented growth in faculty and facilities. As part of this growth, numerous distinguished scholars were added to the faculty and several new advanced technology research centers were formed. The new centers have consolidated the university's partnership with New Jersey's chemical, pharmaceutical and high-technology industries, thus offering expanded resources and research opportunities.

The Rutgers Biotechnology Training Program was established in 1989. Selected by the National Institutes of Health in 1990 to receive one of the first nine pre-doctoral training grants for biotechnology nationwide, the program offers individually designed educational, research, and internship opportunities to students pursuing doctoral degrees in a variety of related scientific disciplines. Growth and research synergies in medical biotechnology at Rutgers were further propelled by: 1) the establishment of the Center for Advanced Biotechnology and Medicine and the expansion of the Waksman Institute in the late 1980s, 2) the establishment of the Cancer Institute of New Jersey in the 1990s, and 3) the Rutgers "Renaissance in Bioengineering" supported by the Whitaker Foundation and several state and federal agencies from 2001-09.

Program Objective

The PhD Training Program in Biotechnology at Rutgers, The State University of New Jersey was established in 1989. It is one of the select group of such programs throughout the country funded by the National Institute of General Medical Sciences of the National Institutes of Health (NIH). The 2018-2019 year marks the 29th year of continuous NIH funding.

The aim of the program is to train a new breed of creative investigators who are able to translate basic science discoveries into technology developments for the needs of society, government, and industry. Students in the program; (1) become well-educated within a single biotechnology-related discipline (e.g. biochemistry, chemical engineering, molecular biology); (2) become fluent in the language, approaches and principles of the biological, chemical and physical sciences, in general; and (3) recognize the steps needed to take basic science discoveries and translate them into tools and technologies that benefit patient care, and mankind, in general.

The program is looking to produce skilled investigators and leaders for three different types of research careers: academia, large conventional industry, and the start-up environment.

Applying to Our Biotechnology Training Program

Before applying to the Biotechnology Training Program, a student must have gained admission to a life science, physical science, or quantitative science department at Rutgers University. Undergraduate training should include: biological science, general and organic chemistry, physics and calculus. A course in physical chemistry is also highly recommended. Selection to the training program is based on scholastic record as indicated by undergraduate and graduate grade point averages (GPA), Graduate Record Examination (GRE) scores, previous research experience, letters of recommendation, and other pertinent criteria such as an indication of leadership potential. A student must be a United States citizen or permanent resident to gain admission to the program. Entering students and those who are about to complete one year of graduate study are encouraged to apply. Students who are about to complete 2 years of graduate study may also apply, especially if they have taken some of the Biotech program required courses and participated in Biotech program activities during their first 2 years.

Rutgers University is an Equal Opportunity/Affirmative Action Institution. Minorities and Woman are especially encouraged to apply.

Additional information regarding the Biotechnology Training Program can be obtained by calling, or emailing Mary Ellen Presa, Biotechnology Training Program at: Rutgers University, Department of Biomedical Engineering, 599 Taylor Road, Room 231C, Piscataway, NJ 08854; (848) 445-6530 empresa@soe.rutgers.edu

Course Requirements

TABLE I

Subject	Credit Hours
Molecular and Cellular Biology	3
Biophysical Chemistry	3
Bioengineering or Computer Science	3
Ethical Scientific Conduct	1
Required Courses in Graduate Discipline	0-12
Bioengineering in the Biotechnology and Pharmaceutical Industries	3
Innovation and Entrepreneurship for Science and Technology	3
Topics in Advanced Biotechnology	10
Laboratory Rotations	2
Graduate Research	39-48
Total Credit Hours (Minimum)	**72**

Required Courses

Topics in Advanced Biotechnology I (16:125:603**):** After the Biotech Program fall orientation which takes place the last week in August, students and faculty meet biweekly during the fall semester for the Topics course. This forum introduces the new students to research opportunities

within the program and allows advanced students to sharpen their presentation skills by providing an experienced audience to critique their work. Students who do not have ongoing work to describe may present a recent paper from the literature which is chosen in consultation with the faculty/student group.

Topics in Advanced Biotechnology II (16:125:604**):** This course is one of the primary unifying threads of the Program. It occurs biweekly during each spring semester (3 hour sessions), and all students in the training program (those currently supported as well as those who were supported in the past) are required to attend. The course serves as a forum to: 1) highlight and unify ongoing biotechnology research on campus, 2) introduce emerging new areas of biotechnology to students and faculty, and 3) provide trainees with insight into the technological development of basic discoveries. Faculty guide students in the choice of literature articles that they will present. Critical analysis of data, its interpretation and implications are highlighted, and special attention is paid to applied research, technology-oriented issues, ethical considerations, and policy-oriented issues in the subject area. In this regard, invited investigators from industry play a key role. By having students enroll in the course during their entire graduate career (every spring semester), it is possible to involve advanced students in the selection of topics and seminar speakers (including the responsibility for organizing speakers) and to encourage their interaction with scientists from outside institutions.

Bioengineering in the Biotechnology and Pharmaceutical Industries (16:125:575)**:** The goal of this course is to offer students insight into the practical aspects of industrial bioprocessing. Industrial practitioners from various fields of expertise provide lectures and facilitate discussions highlighting problems and issues that engineers and scientists encounter. Topics vary from year to year but always include: drug discovery, drug metabolism, microbial fermentation and mammalian cell culture optimization and scale-up, monoclonal antibody, vaccine and gene therapy production, downstream purification, drug delivery, formulation, regenerative medicine, stem cell culture, tissue engineering, cellular therapies, regulatory considerations, manufacturing challenges, and clinical research. This course provides students with exposure to topics which are beyond the scope of a purely theoretically-structured course. After taking this course, students have a much better understanding of the challenges that engineers and scientists face in industrial bioprocessing.

Innovation and Entrepreneurship for Science and Technology (16:125:618:01)**:** This course introduces and outlines the fundamentals of "technology entrepreneurship" and introduces a framework for identification of high-potential, technology-intensive, commercial opportunities, gathering required resources (human and financial), and maturing the innovation to a commercializable product. The course places a specific focus on commercialization derived from scientific and technological research with special emphasis on biotechnology and the life science industry. The course is led by Susan Engelhardt and Martin Yarmush with guest lecturers from industry and academia. The course objective is to have students complete the class with: 1) an understanding of the major components of the life cycle from research to innovation to commercialization, 2) knowledge of the many ways that innovation manifests itself, in the context of start-up, corporate, social and public sector concerns, 3) practical methods to intelligently and objectively evaluate potential commercialization opportunities, and 4) a framework within which to consider the ethical issues that are intertwined with entrepreneurial activities. Through the collection of lectures and projects, students build upon the following critical skills for entrepreneurial success: 1) opportunity evaluation, 2) strategic thinking, 3)

motivation, oral and written communication, basics of start-up legal concepts, basics of startup finance and accounting. This course was developed in response to student demand.

An additional credit hour must be taken in the area of **"*Ethics in Science*"**.

Representative Courses

TABLE II

Field of Study	Courses
Molecular and Cellular Biology	Fundamentals of Molecular Genetics
	Advanced Cell Biology
	Biochemistry (Proteins)
	Biochemistry (Molecular Biology)
	Developmental Biology
	Immunology: Cellular and Molecular
	Cellular and Molecular Pharmacology
Biophysical Chemistry	Macromolecular Structure, Design and Eng
	Biophysical Chemistry I
	Biophysical Chemistry II
	Biointerfacial Characterization
	Nano and Microengineered Interfaces
	Enzymes and Proteins
	Protein Engineering and Design
Bioengineering of Quantitative Science	Biochemical Engineering
	Fundamental of Large Scale Fermentation
	Bioseparations
	Biopolymers
	Tissue Engineering I: Fundamentals II: Applications
	Stem Cell Biology and Bioengineering
	Quantitative Techniques for Biological Science
	Introduction to Molecular Modeling
Ethics	Ethical Scientific Conduct

In addition to these course requirements, each individual must fulfill the requirements set by their respective graduate program. Individuals receiving financial support from the program must maintain a 3.5 GPA; and show adequate progress toward their Ph.D. degree. A progress report is required from each student at the end of each semester. The biotechnology training program provides a stipend and tuition support for up to 2 years. During the remaining time, students are supported through research grants of their thesis advisors. Students who are supported by program funds must complete all the necessary forms prior to receiving financial support.

Typical Curriculum

TABLE III

FIRST YEAR	
Fall	3 courses
	1-2 Lab Rotations
	Ethical Scientific Conduct
	Bioengineering Seminar
Spring	3 courses
	Topics in Advanced Biotechnology
	Bioengineering in the Biotechnology and Pharmaceutical Industries
Summer	Industrial Internship
SECOND YEAR	
Fall	1-2 Courses
	Innovation and Entrepreneurship for Science and Technology
	Thesis Proposal Preparation
	Bioengineering Seminar
Spring	1-2 Courses
	Topics in Advanced Biotechnology
	Thesis Research
THIRD THROUGH FIFTH YEARS	
	Thesis Research
	Topics in Advanced Biotechnology
	Bioengineering Seminar
	Electives

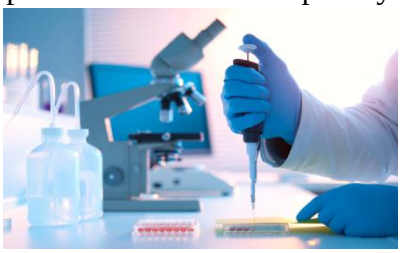
Laboratory Requirements

In addition to the extensive array of courses available at Rutgers, the program requires two types of laboratory based learning opportunities for students prior to initiation of their doctoral dissertation research.

Academic Laboratory Rotations

The goal of the academic laboratory rotation is to acquaint students with the techniques and

principles of biotechnology and to give the student this opportunity to work with different faculty members before choosing a dissertation advisor. This is especially important in an interdisciplinary program with a broad range of research opportunities. The trainees in the Biotechnology Program will be independent of departmental or research grant support and allowed maximum flexibility in their choice of research area. Direct experience can correct or affirm previous perceptions and give a preliminary assessment of how a student and potential mentor will interact with one another. Each student is expected to spend 6-7 weeks in the laboratories of 2-3 different members of the biotechnology faculty before selecting a dissertation advisor. Students are encouraged to take their rotations in different areas. Students will choose their rotations in consultation with the co-directors, as well as their particular graduate program director. At the end of each rotation the students submit a written summary of their work, and the faculty members give an appraisal of the work. The report is kept in the student's files as a record of their accomplishments. Students may opt out of this requirement if they have extensive prior laboratory experience.



Summer Industrial Internship Program

The purpose of this program is to provide an opportunity for the students to gain access to industrial facilities and become more aware of the "gestalt" and practice of industrial research and development. At a minimum, students spend eight weeks full time at an industrial site under the guidance of a particular industrial investigator. These experiences may, on occasion, lead to the involvement of an industrial mentor on the student's dissertation committee. Students who have prior extensive industrial experience may elect to opt out of this requirement; but many of these students still wish to do rotations in different fields. We are extremely fortunate to have a tremendous variety of experiences available. Two key individuals coordinate the program: Dr. Rene Schloss, a Senior Research Associate in Biotechnology, who works primarily with large companies, and Susan Engelhardt, Executive Director of the Center for Innovative Ventures of Emerging Technologies (who has access to both large and small companies). Among the Biotechnology Program's Industrial partners are: Amicus Therapeutics, Celgene Therapeutics, Colgate Palmolive, GE Healthcare, J&J Ethicon, Kessler Rehabilitation, Life Cell Corporation, Linguaflex, Merck & Co., Siemens, and Stryker Orthopaedics. Most of these major industrial sites are within daily commuting distance from the university and some recent examples of internships are listed below. The industrial rotation is usually completed during the first summer after the trainees' first academic year. Students may opt out of this requirement if they have extensive prior industrial experience.

Representative Industrial Internship Projects

TABLE IV

STUDENT	DEPT/ADVISOR	COMPANY
Jenna Newman	Biochemistry/ Mol Biology Andrew Zloza	Cellularity
Jeffrey Luo	Chemistry and Chem Biology Ki-Bum Lee	Merck
Liam Turk	Molecular Biology/ Biochem Davide Comoletti	Aleon Pharma
Victor Tan	Pharmacy Shengkan Jin	Celgene

Research Opportunities

Students can choose their PhD dissertation project from a wide variety of research topics. These topics fall into two core thrust areas as listed below.

Genomics, Proteomics and Structural Biology: The past few decades have seen great technical advances in molecular and cell biology that have led to the development of new therapeutics and diagnostics which will have a profound impact on medicine for years to come. With the Human Genome Project complete, a massive effort is being undertaken to build from the molecular level in a step-wise fashion all the way to complex behavior and function. This effort will require further discovery and analysis of biological systems together with integration of high throughput and genetic manipulation technologies in experimental biology, sophisticated data management and statistical analysis techniques from mathematics and computer science, and systems modeling and fabrication tools from engineering. Every major pharmaceutical company is currently invested heavily in "post-genome" technologies, and numerous biotechnology companies have been created in areas such as Genomics, Proteomics, and Systems Biology. Genomics-based products and technologies are estimated to exceed $50 billion by 2015. Faculty in this research area are involved in a multiplicity of endeavors and projects. These include: 1) new vector development, 2) identification and cloning of new transcription factors, 3) mRNA processing and microRNA biology, 4) translation, posttranslational modification, protein trafficking, and secretion, 5) macromolecular structure determination and protein engineering, 6) new tools for functional genomics, 7) systems biology, metabolic engineering, and gene network analysis, 8) environmental control of cell growth, protein production 9) engineering principles and scale-up of plant cell and animal cell culture, and 10) new tools for functional genomics.

Tissue Engineering, Regenerative Medicine, and Drug Delivery: Without question, one of the most fertile biotechnological areas for the development of new and innovative medical therapies for the next century lies in the realm of regenerative medicine and tissue engineering. Given the remarkable advances in fundamental understanding of the functions and behaviors of cells and tissues over the past few decades, we are poised in the beginning of the 21st century to translate this basic knowledge into vast improvements in the practice of medicine. By combining basic science, engineering problem-solving and clinical wisdom, age-old handicaps that used to devastate people's lives - blindness, deafness, paraplegia, organ dysfunction and failure, memory loss, and even death - may be circumvented by cell transplants, advanced drug delivery systems, intelligent prostheses, neural implants, artificial organs, and natural organs regrown after injury or disease. In addition to the latter, we foresee that cell and tissue-based integrated systems will, in the not-too-distant-future, become pharmaceutical industry standards for early and late stages of drug discovery and drug testing, in the same manner that combinatorial approaches have revolutionized early steps of drug synthesis and discovery. Finally, the NIH estimates that the current world market for replacement organ therapies is in excess of $350 billion, and the projected U.S. market for regenerative medicine is estimated at $100 billion. Faculty in this research area are: 1) investigating basic cellular and tissue phenomena, 2) developing new biomaterials, 3) investigating approaches for stem cell differentiation, and 4) developing methods and materials for the construction of functional tissue and organ substitutes, 5) developing devices that can support biological cells and tissues, 6) studying environmental control of cell growth, 7) investigating engineering principles and scale-up of stem cells, and 8) developing advanced methodology for drug delivery including targeted means and nanopharmaceuticals.

Faculty by Research Thrusts

GENOMICS, PROTEOMICS, AND STRUCTURAL BIOLOGY

Ioannis Androulakis
Eddy Arnold
Joseph Bertino
Martin Blaser
Linda Brzustowicz
Sam Bunting
Stephen Burley
Paul Copeland
Monica Driscoll
Michael Dunn
Richard Ebright
Marianthi Ierapetritou
Estella Jacinto
Peng Jiang
Victor Jin
Sagar Khare
Ki-Bum Lee
Peter Lobel
Kiran Madura
Joachim Messing
James Millonig
Guy Montelione
Vikas Nanda
Zhiping Pang
Ann Stock
William Welsh
Eileen White
Lawrence Williams
Martin Yarmush
Mikel Zaratiegui

TISSUE ENGINEERING AND DRUG DELIVERY

Francois Berthiaume
Li Cai
Bonnie Firestein
Joseph Freeman
Adam Gormley
Martin Grumet
Prabhas Moghe
Ronke Olabisi
Biju Parakkadan
Charles Roth
David Shreiber
Patrick Sinko
Jay Sy
Maribel Vazquez
Martin Yarmush
Jeff Zahn

Individual Development Plan (IDP)

NIH encourages use of IDPs for all trainees and requires that grant progress reports include a description of IDP

Goals of IDPs

The IDP helps individuals identify:

– Long-term career options they wish to pursue and the necessary tools to meet these
– Short-term needs for improving current performance.

The IDP process aims to:

– Assist in developing long-term goals;
– Assist in developing short-term goals that provide a clear sense of expectations;
– Assist in identifying milestones along the way to achieving specific objectives; and
– Provide a tool for communication between the trainee and faculty mentor.

Biotechnology Program IDP Requirement

- Each fall semester, trainees complete the IDP form and update their CVs (suggested format provided).

- If a trainee is required to prepare an IDP for another graduate program, the graduate program version may be submitted in place of the Biotechnology IDP.

- After completing the IDP and CV, trainees should meet with their advisors to discuss the IDP and to obtain signatures on the documentation form.

- The IDP form, the signed meeting documentation form, and an up-to-date CV should be submitted as pdf files by December 1 through the Assignments section of the Biotechnology Training Program site on Sakai.

- Students in their 1st year of graduate school should read the IDP, but are not required to complete it. An updated CV is required for all students.

BIOTECHNOLOGY TRAINING PROGRAM FACULTY

IOANNIS ANDROULAKIS

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Computational Systems Biology

Dr. Androulakis actively pursues research activities in the area of Systems Biology, loosely defined as an integrative modeling and experimental framework that approaches biological entities as "systems" in the physical and engineering sense. Of particular interest are issues related to "functional physiomics" in an attempt to establish functional links between cellular events, such as signaling, transcription and translation, and an expanding envelope of interactions which include the bidirectional links between cells, tissues, organs, environmental signals and physiological responses. The ultimate goal is to develop in silico methodologies that will enable translational research by elucidating putative mechanisms by which macroscopic responses, at the physiome level, can be functionally modulated through mechanistic interventions. Of particular importance are the opportunities of such an integrative approach applied to the inflammatory responses due to the critical role inflammation plays in a number of physiologically and clinically relevant situations. His work integrates a compendium of experimental systems, from cell cultures, to animal models, to human studies in order to address different questions at their appropriate level of detail.

EDWARD ARNOLD

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HIV. AIDS. drugs. vaccines. crystallography. structural biology

Many of the underlying biological and chemical processes of life are being detailed at the molecular level, providing unprecedented opportunities for the development of novel approaches to the treatment, cure and prevention of human disease. A broad base of advances in chemistry, biology, and medicine has led to an exciting era in which knowledge of the intricate structure of life's machinery can help to accelerate the development of new small molecule drugs and biomaterials such as engineered viral vaccines. Drs. Eddy Arnold and his colleagues are working to understand molecular mechanisms of drug resistance and apply structure-based drug design for the treatment of serious human diseases. In pursuit of these goals, the laboratory uses research tools from diverse fields, including X-ray crystallography, molecular biology, virology, protein biochemistry, and macromolecular engineering. Eddy's team of very experienced and gifted coworkers is the driving force behind the continuing progress.

FRANCOIS BERTHIAUME

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Metabolic and Tissue Engineering

My research area encompasses Metabolic and Tissue Engineering. In the former, we are developing a systems biology framework to characterize and treat the metabolic derangements of disease. Cellular metabolism occurs within a complex network of chemical reactions, is regulated at multiple levels (metabolites, proteins, genes and so on), and therefore therapies require a combination of approaches to simultaneously address multiple targets. To identify these targets, we gather large sets of metabolic data from disease models and combine them with mass balance analysis methods to generate a comprehensive map of the metabolic changes within the major metabolic pathways induced by disease. We also work with collaborators to link these observations to gene expression data to elucidate the underlying mechanisms responsible for the changes. This information provides a rational basis to develop multi-pronged therapies. We apply this framework in the context of two different applications: metabolic abnormalities associated with complex diseases, such as adult-onset diabetes, cancer, trauma, and so on, and metabolic reconditioning of organs that are rejected from the donor pool. In the area of Tissue Engineering, our focus is to develop methods that attract stem cells to a site of injury in order to promote faster wound healing and reduced scarring. It is known that adult stem cells, some of which coming from the bone marrow, naturally have the capacity to home into injured areas of the body where they grow and differentiate to form new tissue. Our goal is to elucidate this mechanism and to develop methods that enhance it using a combination of implantable polymeric scaffolds and stem cell attracting agents. We are specifically interested to use this strategy for improving the healing of skin wounds, in particular deep skin wounds that are susceptible to infection and scarring, as well as non-healing and chronic wounds, such as diabetic ulcers, venous ulcers, and bed sores.

JOSEPH BERTINO

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Cancer Pharmacology and Pre-clinical Therapeutics Program

Since coming to The Cancer Institute of New Jersey in 2002, I have collaborated with top experts in the field to help develop the latest generation of cancer treatments. I have had a special research interest in developing new drugs and understanding why drugs work or don't work, and I am currently exploring new treatments for one type of lymphoma, namely T- Cell lymphoma. By having the resources available that can only be found at a National Cancer Institute-designated Comprehensive Cancer Center, our team is able to translate these research findings and directly apply them to patient therapies.

MARTIN BLASER

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Human microbiome, early-life effects and mechanisms on disease development

My lab has been studying pathogenic bacteria and gastrointestinal biology since 1981 and the human microbiome since 2002. We conducted early 16S rRNA surveys of the esophagus, stomach, lung, and skin. Such studies helped establish the baseline present in health that then can be used to assess pathologic relationships. Nearly 20 years ago, we began to hypothesize that some of the diseases of modernization, including obesity, diabetes, malignancies, and immunologic disorders, were due to changes in the ancestral human microbiome. We have had especial emphasis on the role of the gastrointestinal tract microbiome in early life development, with consequences for how normal metabolism and immunity develop. Because of the widespread use of antibiotics, especially in young children, we have explored in animal models their role in perturbing the microbiome, and the downstream effects. More recently, we have been exploring microbiome changes that could be fueling the metabolic and inflammatory disease epidemics of obesity, IBD, asthma, allergies, type 1 diabetes, kidney stones, and particular cancers (including esophageal, gastric), respectively using mouse models to understand underlying mechanisms. We have used multi-"omic" approaches to address these questions. Specimens from mice of defined disease and control phenotypes permit linked analyses of tissue gene expression and gut metagenome with metabolic pathways to identify molecules that can be used for solutions to these problems.

LINDA BRZUSTOWICZ

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Medical and human genetics: the genetics of neuropsychiatric disorders

My research group applies the techniques of molecular and statistical genetics to approach clinically relevant problems in neuroscience, with the ultimate goal of understanding gene function in both the pathologic and normal states. We are currently studying schizophrenia, autism, and specific language impairment (SLI). Work directly conducted by my group includes development of phenotype definitions, subject recruitment and assessment (for autism and SLI), genotyping and statistical analysis for linkage and association studies, comparative genomic analysis, and gene expression studies. We have successfully identified functional variants in two susceptibility genes, NOS1AP which is involved in schizophrenia and EN2 which is involved in autism. Other areas of particular interest include the role of microRNAs in the control of gene expression in the human brain and enhancements to moderately high throughput genotyping technologies. Within Rutgers and UMDNJ, we work closely with Dr. Bonnie Firestein (Rutgers Department of Cell Biology and Neuroscience) and Drs. Jim Millonig and Manny DiCicco-Bloom (UMDNJ-RWJ Department of Neuroscience and Cell Biology) on understanding the molecular neurobiology of schizophrenia and autism susceptibility genes. Our primary collaborators outside of Rutgers/UMDNJ are Dr. Anne Bassett at the University of Toronto, who works on phenotype definition, subject recruitment and assessment for schizophrenia, Dr. Veronica Vieland at Ohio State University, who works on the development of advanced statistical genetics methods, and Dr. Christopher Bartlett, who works on the molecular genetics of specific language impairment.

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Cell survival and DNA repair in mammals

Healthy cell growth depends on the ability to properly repair DNA damage, but the outcomes of the DNA damage response can vary greatly. Some cells repair damage and continue growing normally, while other cells suffer apoptosis, senescence or become malignant cancer cells. The biological reasons for these differing responses are not always clear, but the consequences in terms of health (especially in aging and cancer) are profound. The goal of our research program is to show why different cells respond differently to stress, with the goal of reprogramming cells so that they repair damage in an advantageous way.

STEPHEN BURLEY

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Cell Death and Survival Signaling Program

Stephen Burley currently serves as Henry Rutgers Chair and University Professor, Founding Director of the Institute for Quantitative Biomedicine, and Director of the RCSB Protein Data Bank at Rutgers, The State University of New Jersey. He is also a Member of the Rutgers Cancer Institute of New Jersey, where he Co-Leads the Cancer Pharmacology Research Program. Burley is an expert in structural biology, proteomics, bioinformatics, structure/fragment based drug discovery, and clinical medicine/oncology.

LI CAI

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Regulation of Gene Expression in Stem Cells

Like a double-edged sword, stem cells have the potential to develop into many different cell types for regenerative medicine, but they are also the source of at least some, perhaps all, cancers. The normal and cancerous behavior of stem cells may be determined by their unique pattern of gene expression. The Cai lab focuses on the genetic mechanisms that regulate gene expression of stem cells in both normal development and tumorigenesis. We are using integrative computational and experimental approaches to identify, verify and characterize the genetic regulatory elements, e.g., the conserved non-coding DNA sequences and their interacting protein factors that involved in the regulation of stem cell gene expression. A thorough understanding of these mechanisms will provide the knowledge of stem cell development into various normal cell types as a repair system for the body, as well as a basis for the therapeutic treatments of cancers.

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Regulation of gene expression at the translational level, incorporation and utilization of selenocysteine

Our primary research question targets the protein synthetic machinery as one of the primary sites for the regulation of gene expression and an important sensor of the status of cellular metabolite concentrations including trace elements. The utilization of selenium exemplifies this relationship, and is required for the synthesis and function of an essential group of proteins that contain the amino acid selenocysteine (Sec). In fact, many selenoproteins are known to provide protection from cellular damage and transformation, thus making the synthesis and regulation of these proteins an essential area of research. Sec is incorporated into these proteins by a translational recoding event at specific Stop (UGA) codons that are found upstream of stable stem-loop structures known as Sec insertion sequence (SECIS) elements. While the UGA codon and the SECIS element are the only known cis-acting elements required for Sec incorporation, at least two trans-acting factors are also required: 1) the Sec-specific elongation factor (eEFSec) and 2) a SECIS binding protein (SBP2). One of the ultimate goals for our research is to be able to specifically regulate the expression of potentially beneficial selenoproteins in vivo. In order to achieve this goal, we must understand all of the factors that contribute not only to the basic Sec incorporation reaction but also to the regulation of this process. In addition to characterizing the structure and function of the known factors, much of our work is designed to test hypotheses regarding the identity and function of novel factors involved in the synthesis of selenoproteins utilizing both mammalian systems as well as yeast, a eukaryotic system that is devoid of the Sec incorporation machinery. The results derived from these experiments will not only significantly add to our current knowledge of Sec incorporation, but they will also provide insight into the basic mechanisms of protein synthesis during the elongation and termination phases.

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Developmental neurogenetics. molecular genetics of neuronal cell death. mechanosensory transduction in touch and feeling. molecular mechanisms of aging

One of the looming mysteries in signal transduction today is the question of how mechanical signals, such as pressure or force delivered to a cell, are interpreted to direct biological responses. A long-standing problem in the mechanotransduction field has been that genes encoding mechanically-gated channels eluded cloning efforts, resulting in a large gap in our understanding of their function. We have identified a new family of ion channels (the degenerin channels) that are hypothesized to normally function as the central mediators of touch transduction and proprioception (how the body maintains coordinated movement) in C. elegans. We are currently combining genetic, molecular and electrophysiological approaches to determine and compare the composition/regulation of mechanosensitive complexes in an effort to contribute to the understanding of the function of this newly discovered channel class.

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Tissue engineering of tendons and ligaments, resorbable biomaterials, wound healing

Orthopedic injuries are extremely common, especially to the knee. However, the avascular nature of the synovial areas makes it extremely difficult for injured soft tissues to regenerate. Failure to treat these injuries can lead to injury of other soft tissues, leading to cartilage degeneration and improper weight loading. These can cause a patient pain and discomfort, creating a need for tissue engineering of orthopedic tissues. Specifically, we focus on ligament, meniscus, and articular cartilage tissue engineering.

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Transcription, Transcription Inhibitors, Single-Molecule Biophysics

Transcription--the synthesis of an RNA copy of genetic information in DNA--is the first step in gene expression and is the step at which most regulation of gene expression occurs. Richard Ebright's laboratory seeks to understand structures, mechanisms, and regulation of bacterial transcription complexes and to identify, characterize, and develop small-molecule inhibitors of bacterial transcription for application as antituberculosis agents and broad-spectrum antibacterial agents.

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Dendrite patterning and synaptogenesis

Synaptic transmission requires spatial assembly of neurotransmitter receptors and associated signal transduction machinery at synaptic sites and the precise patterning of dendritic processes. Targeting of proteins to the synapse is a dynamic processing which there is a balance of assembly and disassembly of proteins at synaptic homeostasis. In fact, when learning occurs, recruitment of existing and newly synthesized proteins to the synapse is increased. In contrast, when disassembly of synaptic signaling molecules occurs faster than assembly, homeostasis is lost and disease states such as Alzheimer's Disease occur in which synaptic transmission is compromised. An important long-term goal our work is to understand how synaptic targeting of proteins is perturbed in pathophysiological states.

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The Musculoskeletal Tissue Regeneration

The Musculoskeletal Tissue Regeneration (MoTR) Laboratory primarily focuses on the repair and regeneration of tissue, mainly musculoskeletal tissue, through the use of tissue engineering techniques. We also investigate mechanisms of tissue damage and healing, cancer development, and molecular modeling of structural proteins.

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Bioinspired Nanomaterials

The Gormley Lab for bioinspired nanobiomaterials seeks to develop synthetic nanomaterials that mimic therapeutic proteins and growth factors used as therapeutics and in regenerative medicine. Using advanced synthetic and characterization techniques, ligands are being developed to directly interface with the cell's machinery of proteins in order to direct cell behavior. Other projects in nanomaterial self-assembly and nanoparticle-based diagnostics help build a research program that ranges from fundamental science to translatable medicine.

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Neural stem cells in development & neurological disorders

Transplantation of various types of stem cells have anti-inflammatory effects that control inflammation and promote recovery. Our lab studies human bone marrow mesenchymal stem cell (MSC) because they are anti-inflammatory and resist rejection even as allogenic transplants. MSC mitigate immune rejection of non-autologous transplants, which can be fatal, for example in Graft vs. Host Disease (GvHD), which often occurs after transplantation of hematopoietic stem cells to reconstitute blood cell production. Uncontrolled inflammation plays a major role in many disorders and injuries, such as spinal cord injury (SCI), and MSC restore a more normal balance between pro- and anti-inflammatory factors.

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Process Systems Engineering: Mathematical Modeling and Optimization of Complex Systems.

Our current work in metabolic engineering focuses on optimizing the function of liver cells in order to be utilized for bioartificial devices. Recent directions of this work include the integration of metabolic and regulatory networks as well as the analysis of the toxic effects of a variety of different substances including drugs, and environmental pollutants. Our work in this area is in collaboration with Professors Yarmush, Roth and Androulakis that bring expertise in the area of liver physiology, molecular bioengineering and bioinformatics.

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Growth control, cancer, immunology, protein synthesis and processing

My research aims to understand how cells make a decision between growth and survival depending on extracellular signals. Elucidating the mechanisms that allow cells to survive under adverse growth conditions is crucial for understanding how cancer and other growth-related diseases occur. My research employs mammalian cell and mouse models to understand how the mammalian target of rapamycin (mTOR) plays a central role in controlling cellular signals that switch from growth to survival by regulating protein synthesis and folding. My studies currently address mTOR signaling in normal and cancer cells. Another research emphasis is the role of mTOR in T cell development and immune responses. Our goal is to identify critical and specific signals in the mTOR pathway that can be targeted for development of cancer therapeutics and in particular, immunotherapy.

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Stem cells as a model of brain development and disease, stem cell regenerative medicine for neural repair

The goal of our research is to create human induced pluripotent stem cell (hiPSC) neural differentiation models for studying the cellular and molecular basis of human neural development and pathogenesis of neurodevelopmental disease, and to develop stem cell regenerative medicine to treat neurological disorders. We have been developing hiPSC-based in vitro 2-dimensional (2D) neural differentiation and 3D CNS organoid models and in vivo human chimeric mouse brain models to investigate how abnormal gene expression in neurodevelopmental disorders, such as Down syndrome, causes abnormal brain development, changes synaptic plasticity, and leads to cognitive deficits in these disorders. In addition, hiPSCs hold great promise for developing cell therapies to replace damaged brain cells and restore brain functions after CNS injury. We also study how to derive functionally competent neural cells from hiPSCs for neural repair. The basic and translational stem cell research we are pursuing critically bridges between the understanding of human neural development in heath and disease, and the development of stem cell medicine to treat neurological disorders.

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Development of experimental drugs that modify mitochondrial function for treatment of cancer, obesity, type 2 diabetes, non-alcoholic steatohepatitis (NASH)

Mitochondria are at the center of the most important medical challenges of our time: obesity, type 2 diabetes, NASH, cancer, and neurodegenerative diseases (see inserted figure). Mitochondria not only provide the majority of energy (ATP) for cellular activity but also are central in producing metabolic intermediates for macromolecule biosynthesis supporting cell proliferation. Moreover, the byproducts of mitochondrial oxidation, reactive oxygen species (ROS), are the main intrinsic causal factor of aging and aging related diseases including neurodegenerative diseases. My laboratory is interested in developing experimental therapeutics that modify mitochondrial activity and function for the treatment of obesity, type 2 diabetes, cancer, and neurodegenerative diseases.

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Design principles of molecular recognition

The Khare lab seeks to develop new enzymes and proteins using a combination of computational protein design and experimental characterization. Our goal is to develop a quantitative and predictive understanding of enzymatic structures and functions and use this understanding to inform various therapeutic and synthetic applications. Some areas of interest are biodegradation of pollutants, improving cancer chemotherapy, and designing catalytic protein drugs.

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Development of Novel Approaches to Probe Biomolecular Interactions of Cells In Vitro and In Vivo

The primary research interest of our group is to develop and integrate nanotechnology and chemical biology to modulate signaling pathways in cancer and stem cells. More specifically, our research focuses on identifying the various microenvironmental cues (e.g. soluble signals, cell-cell interactions, and insoluble/physical signals) affecting stem cell and cancer cell fate and thereafter utilizing these cues for the neuro-differentiation of stem cells and apoptosis of brain tumor cells. In addition, our group is also developing novel nanomaterials for applications such as cancer therapy, molecular imaging and bio-sensing.

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Lysosomal proteomics, diseases, and potential therapeutics

Our laboratory has pioneered proteomic methods for disease discovery that evolved from our basic research on lysosomal enzyme targeting. Lysosomes are membrane-bound, acidic organelles that are found in all eukaryotic cells. They contain a variety of different proteases, glycosidases, lipases, phosphatases, nucleases and other hydrolytic enzymes, most of which are delivered to the lysosome by the mannose 6-phosphate targeting system. In this pathway, lysosomal enzymes are recognized as different from other glycoproteins and are selectively phosphorylated on mannose residues. The mannose 6-phosphate serves as a recognition marker that allows the enzymes to bind mannose 6-phosphate receptors which ferry the lysosomal enzymes to the lysosome. In the lysosome, the enzymes function in concert to break down complex biological macromolecules into simple components. The importance of these enzymes is underscored by over forty different lysosomal storage disorders where loss of a single lysosomal enzyme leads to severe health problems including neurodegeneration, progressive mental retardation and early death.

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Ubiquitin-mediated protein degradation in DNA repair and signal transduction

The investigation of protein ubiquitination and degradation by the proteasome. We discovered that Rad23 is a shuttle-factor that can bind ubiquitinated proteins and deliver them to the proteasome, to initiate degradation. The domains in Rad23 that bind ubiquitinated proteins and the proteasome were identified. We are using molecular, biochemical and genetic methods (in both yeast and cell-culture based systems), to understand the mechanism of intracellular proteolysis and its significance in DNA repair, stress-response and human neurodegenerative diseases.

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Gene expression and evolution of seed proteins

An important aspect of gene expression is DNA modification and chromatin structure. Maize seems to be in particular suited for this purpose because the portion of the genome representing active genes is rather small. The maize genome has an even higher percentage of repeat elements than the human genome, 85% versus 50%. Therefore, detection of such epigenetic marks in maize had to be highly enriched for a fraction of the genome. Indeed, this specific histone acetylation correlated well with transcribed genes and could be verified with many known examples of genetic loci.

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Neurodevelopmental disorders, Autism Spectrum Disorder, neural tube defects, schizophrenia

My laboratory in collaboration with Bev Paigen's laboratory at The Jackson Laboratories positionally cloned the spontaneous mouse mutant called vacuolated lens (vl). A single allele of the vl mutation arose on the C3H/HeSnJ inbred background. Vl homozygotes display congenital cataracts and neural tube defects (NTDs). We determined that a mutation in the orphan G protein coupled receptor, Gpr161, results in the Gpr161vl phenotypes. Characterization of the Gpr161vl mutation indicates that C terminal tail of Gpr161 is truncated, leading to multiple effects on the protein including reduced receptor-mediated endocytosis.

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Cellular Bioengineering (Liver, Skin), Cell-Interactive Biomaterials, Micro/Nanosystems Bioengineering

The Moghe lab investigates cell-biomaterial interactions and nanotechnologies for biomedical and health science applications. A few research nuggets are summarized next. The Moghe lab recently showcased the ability of short wave infrared emitting nanoprobes to discern multi organ cancer metastases). The Moghe team has advanced a new class of polymer nanotherapeutics for treatment of cardiovascular disease. Additional innovations from the Moghe lab include the design of innovative shortwave infrared imaging probes for deeper tissue imaging of micrometastatic lesions, a new concept of high content imaging informatics of stem cell phenotypesand advance in the reprogramming and brain-transplantation of human induced neurons within 3D devices from induced pluripotent stem cells

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Cancer biology, influenza virus, structural biology, and structural bioinformatics

As Director of the NIH-funded Northeast Structural Genomics Consortium (NESG) of the NIGMS Protein Structure Initiative, Dr. Montelione leads an inter-institutional project in large-scale structural proteomics and bioinformatics. Goals of our work involve developing high-throughput technologies suitable for determining many new protein structures from the human genome project using bioinformatics, nuclear magnetic resonance spectroscopy (NMR) and X-ray crystallography. These structures provide important insights into the functions of novel gene products identified by genomic and/or bioinformatic analysis. The resulting knowledge of structure and biochemical function provides the basis for collaborations with academic laboratories and pharmaceutical companies to develop drugs useful in treating human diseases that are targeted to these newly discovered functions. The success of our approach relies on our abilities to identify, clone, express and analyze several hundred biologically interesting proteins per year; only a

fraction of the initial sequences chosen for cloning and analysis result in high-resolution 3D structures. However, this "funnel" process is yielding three-dimensional structures and new functions for some 200 proteins per year, and can thus have tremendous scientific impact. The NESG project has deposited more than 900 3D protein structures into the Protein Data Bank since its inception in the year 2000. Hypothesis-driven research areas enabled by this infrastructure and collaborations with other biologists include studies of protein complexes involved in influenza virus infection and innate immune response, networks of interacting proteins associated with human cancer biology, and ubiquitination pathways.

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Computational protein design, biomaterials, molecular evolution

Our group is interested in constructing new proteins for applications in biomedical research, nanotechnology and as tools for understanding how proteins fold and evolve. Significant progress has been made in the last decade using sophisticated computer programs to design proteins with novel folds and functions. We maintain and develop software for protein design, structure prediction and docking of protein-ligand complexes. Several design projects our group pursues include the computational design of an extracellular matrix, thermostabilization of peptide therapeutics with D-amino acids and prediction of allergenicity of food proteins.

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Tissue Engineering and Regenerative Medicine

The research in our lab involves tissue engineering and regenerative medicine to repair or build de novo tissues for treating defects due to injury, disease, aging, or spaceflight. Our approach is through the development of biosynthetic materials, which combine the best aspects of synthetic and biological materials to attain reproducible biomaterials that can drive or direct cell function. Current efforts focus on skin, orthopedic and retinal tissues.

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Mechanisms of synaptic regulation: From stem cell to the brain.

My laboratory studies the neural basis of the regulation of feeding, satiety, metabolism and obesity. Our studies may provide insights into the neural causes and consequences of childhood obesity. We also developed novel techniques for deriving neuronal cells from primary skin cells and pluripotent stem cells, providing novel opportunities to study the pathogenesis of neurological disorders, including pediatric developmental disorders and autism spectrum disorders.

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Cell Engineering

Our group develops new platform technologies for cell and gene therapy. To this end, we converge knowledge and techniques of cell/gene/tissue engineering, drug delivery, biomaterials, micro/macro-fluidic bioreactors, transport phenomena, chemical kinetics, computational biology, and bioprocess engineering. Our lab collaborates extensively with biology and clinical experts in hematology, oncology, rheumatology, surgery, and infectious disease to design and execute IND-enabling studies in support of human trials. Animal models of these disease areas are created in-house and pre-clinical studies of experimental therapeutics are performed using advanced principles of pharmacokinetics and pharmacodynamics. The research is conducted with a mindfulness of regulatory science and intellectual property for potential opportunities to translate the work with industrial partners or as a new venture.

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Gene-based therapeutics; bioinformatics and systems biology; hepatocyte differentiation; novel strategies for treatment of brain tumors

Our research involves the application of molecular and nanobioengineering approaches to cancer and to other biomedical problems. Much of our work centers on the development of technology for efficient gene silencing (using antisense or short interfering RNA). Current projects include: 1) novel lipid-polymer formulations for effective systemic and intracellular delivery of oligonucleotides; 2) silencing of osteogenic genes to prevent heterotopic ossification; 3) nanobioengineering of novel imaging agents toward image-guided tumor therapies; 4) understanding and targeting tumor stem cells; 5) surface and metabolic engineering of hepatocyte culture.

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CNS injury mechanics, tissue engineering, nerve and spinal cord regeneration, acupuncture, microfluidics

Research foci include the multi-scale analysis of CNS injury mechanics; biomaterial, tissue, and cellular engineering approaches for repair and restoration of neural functions; a biophysical analysis of traditional acupuncture; and the development of technology for electropration that is grounded in electrohydrodynamic theory.

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Pharmaceutics and Drug Delivery

The Sinko lab focuses on biopharmaceutics, pharmaceutical formulations and molecular-, nano- and micro-scale drug delivery with specific applications to the treatment or prevention of HIV/AIDS, breast and lung cancer, chemical terrorism countermeasures.

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Structure/function analysis of bacterial signal transduction pathways

Research in the Stock laboratory focuses on understanding the structure and function of signal transduction proteins and in particular, how covalent modifications regulate protein activities. All cells monitor their surrounding environments and elicit appropriate adaptive responses to changing conditions. Such stimulus-response coupling is essential for numerous and diverse processes such as growth and development, metabolic regulation and sensing. Signal transduction pathways, through which information is passed sequentially from one protein component to the next, provide the molecular mechanism for linking input signals to output responses. Despite great diversity in the types of stimuli and responses involved in different pathways, a limited number of fundamental molecular strategies are used for signal transduction. One such strategy is reversible covalent modification, which regulates the activities of proteins.

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Brain Disorders

Dr. Sy's research group is interested in developing new strategies for treating brain disorders. The lab focuses on three main thrusts: medical device prototyping, biomaterials development for improved compatibility and drug delivery, and understanding fundamental glial cell physiology. Designing and fabricating medical device prototypes allows new avenues to bypass anatomical barriers using minimally invasive strategies. This opens the doorway to deliver compounds and newly synthesized drug delivery vehicles to the brain. These tools allow us to target neurological disorders but also afford the opportunity to study brain physiology. In particular, the Sy lab is interested in examining how glial cells - the half of the brain that are non-neuronal - modulate biocompatibility of brain implants and pharmacokinetics of compounds and drug delivery vehicles.

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BioMEMS, Reg Med, Retinal Transplantation

The Research Laboratory develops microfluidic systems to evaluate the migration of progenitor cells and its implications in the health and development of the Nervous System. Research projects have utilized bio-nano-microtechnologies to examine the development and dissemination of neural tumors, collective behavior of glial and neuronal cells for regenerative medicine and synaptic interconnectivity of photoreceptor cells during retinogenesis and retinal transplantation.

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Computational chemistry, drug design, predictive toxicology, pattern recognition, bioinformatics, cheminformatics

Dr. Welsh's laboratory specializes in the development and application of computational tools for pharmaceutical drug discovery, predictive toxicology, and multi-dimensional pattern recognition. His laboratory's interests extend to the molecular design and modeling of synthetic polymers, protein-material interactions, and protein-ligand interactions. In recent years, his laboratory has participated in the discovery of potential drug candidates for the treatment cancer, severe and chronic pain, and infectious diseases.

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Molecular structure and reactivity

We study molecular structure and reactivity. Our goal is to bring new reactions into the arena of synthetic organic chemistry and to develop superior synthetic strategies. For each reaction a mechanistic framework is established. The transformation is then developed into a preparative method and applied to specific targets, such as to the synthesis of molecules that pose practical or academic problems of structural complexity.

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Apoptosis, Tumor growth control

Current research of the White Laboratory at Rutgers Cancer Institute of New Jersey has focused on translational research modulating the apoptosis pathway for cancer therapy and on the role of autophagy and cellular metabolism in cancer progression and treatment. The White group discovered that tumor cells activate the cellular self-cannibalization process of autophagy to survive the stress of tumor growth. This was the first demonstration that autophagy is a cancer survival mechanism for solid tumors and that inhibition of autophagy may be a novel approach to improve solid tumor therapy.

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Tissue Engineering, regenerative medicine, metabolic engineering, applied immunology

The research activities in Professor Yarmush's laboratory broadly address scientific and engineering aspects of various challenging areas in biotechnology and bioengineering. His lab is currently developing new nanoparticle technology to enhance wound healing and siRNA delivery; microfabricated tissue-on-a-chip-systems for drug and environmental toxin testing; pulsed electric field techniques to promote scarless wound healing and wound disinfection; liver organ re-engineering through recellularization of decellularized scaffolds and revitalization perfusion of marginal organs; supercooling preservation of cells, tissues, and organs; encapsulated mesenchymal stem cells for treatment of spinal cord injury, traumatic brain injury, and osteoarthritis; Autoantibody detection in cancer and other chronic diseases, tissue organoids for use in precision medicine, and development of an automated robotic venipuncture devices with point-of-care capabilities. Success in tackling these projects is enabled by the use of state-of-the-art techniques that include microfabrication and nanotechnology; physical biochemistry; genomics, proteomics and genetic engineering; cell biology and tissue engineering; advanced microscopic imaging; physiologic instrumentation; animal studies; and numerical simulation.

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Microfluidic devices for medical therapeutics and diagnostics

Dr. Zahn's research is focused on the development of microfabricated and microfluidic devices which can be used during clinical diagnosis, health management and treatment of disease, as well as supporting and monitoring microscale cell cultures. By employing basic microfabrication techniques we have developed a number of devices

which can assist in neuroengineering. His research combines modeling, device design, fabrication, and testing in an adaptive and iterative process for device optimization. Dr. Zahn`s current research projects include: multiphase microfluidics and electrohydrodynamics for DNA Purification, the use of transverse electrokinetics for DNA concentration, the development of blood separation and blood plasma biomarker analysis microdevices. a microfluidic high throughput cell electroporation platform, topographically patterned multielectrode arrays supporting neuron/myocyte cocultures, multiwell cell culture chambers to support mini-neurociruitry models, and neuroprobes to minimize tissue damage and gliosis. His research has been supported by the ADA, NSF, New Jersey Commission on Spinal Cord Research, the Wallace H. Coulter Foundation and NIH.

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Chromatin Dynamics, Heterochromatin, RNA interference, Transposons, Silencing, Replication, Genome Integrity, Fission Yeast genetics

The combination of DNA with the protein complement that regulates it is known as chromatin. Depending on the degree of compaction of chromatin we can distinguish two forms of organization, Euchromatin and Heterochromatin. While Euchromatin is open and accessible, Heterochromatin is a specialized form of chromatin with a highly compacted structure. It covers regions of the genome that are highly repetitive, and by ensuring a high degree of compaction it prevents transcription as well as recombination of the repeat elements. These are very important functions because most repetitive parts of the genome are derived from transposons, selfish genetic elements capable of moving within the genome and increasing their copy number. These potentially harmful parasitic sequences must be silenced to avoid their rampant spread and the mutation and genomic instability that it can cause. The other main types of sequences coated by heterochromatin are highly repetitive arrays of elements called satellite DNA. Over the course of evolution, heterochromatic satellite regions have gained new roles in the chromosome. For example, the pericentric satellite DNA is necessary for proper chromosome segregation through its participation in centromere formation. Since repetitive DNA constitutes a large proportion of eukaryotic genomes, heterochromatin plays a key role in their function and evolution, and loss of its regulation can lead to cancer and aging-related diseases.