Graduate Students

Michael Benchimol – Electrical Eng (ECE) – Mentors Esener PhD (NanoE) and Reid MD (Medicine)
Csilla Felsen - MSTP MD-PhD program – Mentors Bouvet MD (Surgery) and Tsien PhD (Pharmacology)
Alex Liberman – Mat Sci and Eng – Mentors Kummel PhD (Chemistry) and Blair MD (Surgery)
Casey Ta – Elect Eng (ECE) – Mentors Mattrey MD (Radiology) and Kummel PhD (Mat Sci)
Matthew Tyndall – NanoEngineering – Mentors Heller PhD (NanoE) and Carson MD (Cancer Center)

Postdoctoral Associates

Carlos Huang (Cancer Center) – Mentors Howell MD (Medicine) and Wang PhD (Cancer Center)
Roy Weinstain (Pharmacology) – Mentors Tsien PhD (Chemistry) and Mattrey MD (Radiology)
Michael Benchimol – Research Plan
Ultrasound-Triggered Exposure of Oncolytic Viruses

Treatment of cancer with oncolytic viruses has shown promising results in clinical trials, but is still limited by the body’s immune response. The objective of this project is to create a delivery mechanism to hide the virus and have the ability to selectively release it in the region of choice. To do so, I will employ a novel technology for the triggered release of payload in the form of an ultrasound (US)-destructible liposome.

Goal 1 – Fabricate and Characterize of Ultrasound-Sensitive Virus-Loaded Liposomes
• Investigate 2 fabrication methods, make a choice depending on encapsulation efficiency of virus & nanoparticles and preservation of virus infectivity
• Monitor ultrasound-triggered destruction using existing combined ultrasound-fluorescent microscope system
• Demonstrate release of GFP-expressing replication-deficient virus using Panc-1 and Hep3B cell lines

Goal 2 – Demonstrate Ultrasound-Triggered Virus Delivery in vitro
• Use replication-competent virus for eradication of cancer cell lines using HUVEC and HMEC cell lines as controls
• No-ultrasound controls on cancer cell lines should have inadequate viral dose to exceed threshold required for eradication

Goal 3 – Demonstrate Ultrasound-Triggered Virus Delivery in a Human Xenograft Tumor Model
• Study PK/PD properties of virus-loaded liposomes in BALB/c and CB-17 mice
• Test surface properties (PEG chain length, charge) to improve circulation time, biodistribution, and minimize cytotoxicity
• Measure antibody levels in serum with ELISA to demonstrate liposome’s ability to hide virus from immune system and determine proper dosing
• Assemble bath-type insonation setup for simultaneous in vivo ultrasound imaging and ultrasound-triggered virus delivery to mice

Clinical Mentor: Dr. Tony Reid (Medicine)
Basic Research Mentor: Prof. Sadik Esener (Elect. Eng. & NanoE)

Project Timeline

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<tr>
<th>Goal</th>
<th>Spr. '11</th>
<th>Sum. '11</th>
<th>Fal. '11</th>
<th>Win. '11</th>
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Before Ultrasound | After | Diffusion of Payload

Figure 1. Prelim. data showing demonstration of ultrasound-triggered liposome destruction.
Michael Benchimol – Education Plan

Basic Cell Biology and Biochemistry
   BENG 230A – Biochemistry
   BENG 230B – Cell & Molecular Biology

Basic Cell Biology and Biochemistry
   BGGN 235 – Biology & Biochemistry of Cancer Cells
   NANO 242 – Biochemistry & Molecular Biology

Technology Commercialization
   ENG 201 – Venture Mechanics

CT2 Training Grant Lecture Series

Skaggs Nanomedicine Lecture Series

Clinical Mentor: Dr. Tony Reid (Medicine)
Basic Research Mentor: Prof. Sadik Esener (Elect. Eng. & NanoE)
EXPERIENCE

Graduate Student Researcher, University of California, San Diego (2007-Present)

Ultrasound-Destructable Liposomes for Externally-Targeted Chemotherapy
- Fabricated liposomes containing perfluorocarbon microbubbles and nanoemulsions
- Captured high frame rate fluorescent movies of ultrasound-triggered liposome destruction
- Demonstrated efficient loading of chemotherapeutics and large biomolecules
- Showed low macrophage uptake and long circulation in a mouse

Ultrasound-Quenchable Fluorescent Particles for High-Sensitivity Deep Tissue Imaging
- Fabricated microbubbles surface-loaded with self-quenching fluorophore
- First demonstration of acoustically-quenchable particle using acousto-fluorescence setup

Phase-Shifting Fluorocarbon Nanoemulsions for Contrast-Enhanced Ultrasound Imaging
- Fabricated stable nanoscale emulsions of 8 different liquid fluorocarbons
- Demonstrated acoustic droplet vaporization with optical and ultrasound imaging

Design & Fabrication of Microfluidic Devices
- Manufactured devices capable of producing of monodisperse micron-scale liquid emulsions and gas bubbles
- Modeled liver sinusoid uptake with macrophages seeded in microchannels

Infrared Detection with coupled SPADs
- Built free-space optical link for single-photon detection of infrared light with single-photon avalanche photodiodes
- Demonstrated infrared detection at 250MHz

Active Perception Lab, Boston University (Summer 2005)
- Programmed FPGA for remote control of anthropomorphic robot and debugged using logic analyzer

EDUCATION

University of California, San Diego
Doctor of Philosophy, Electrical Engineering Spring 2012

University of California, San Diego
Master of Science, Photonics June 2008

Boston University, College of Engineering
Bachelor of Science, Electrical Engineering May 2006

TECHNICAL SKILLS

- Production of ultrasound-sensitive nanoemulsions, liposomes, and fluorescent contrast agents
- Experience in preparation of polymeric nanoparticles for drug delivery
- Operation of ultrasound transducers, hydrophone, clinical scanners
- Microfabrication – Complete knowledge of each step in the microfluidic device process cycle:
  - Idea → CAD → Photomask → Cleanroom mold fabrication → PDMS pouring & glass bonding
- Proficiency in optical measurement and alignment to within micron tolerances and experience with optical devices, components, and testing EQ

LANGUAGE SKILLS

Fluent in French

PUBLICATIONS

Journal

Conference
Csilla Felsen - CRIN Research Plan
Clinically Translatable Imaging Modalities for Cancer Detection and Treatment
Mentors: Roger Tsien (Pharmacology, BioChem) and Michael Bouvet (Surgery)

In medical and surgical decision-making, effectively distinguishing between cancerous and non-cancerous cells, or between benign and malignant tumors, is critical for optimizing patient outcomes. Activatable cell-penetrating peptides (ACPPs) enable objective visualization of large, invasive tumors. Previous studies focused on showing significant contrast in large, aggressive tumors, but determining the size and stage at which a variety of primary and metastatic tumors become detectable is more clinically relevant. My long-term goal is to improve cancer-imaging technology for early detection and intraoperative guidance of primary and metastatic disease. The next step in achieving this goal is to develop and test a model system for accurately assessing and comparing the most promising clinically translatable imaging technologies.

Goal 1 – Develop Optimize Probes for Rapid and Sensitive Detection of In Vivo Tumor Growth
• Design and build triple-modality reporter gene (bioluminescence, fluorescence, PET) with the best available luciferase, far-red or infrared fluorescent protein, and thymidine kinase
• Determine sensitivity and specificity of detection for each component

Goal 2 – Determine Detection Limits of Clinically Translatable Molecular Imaging Agents
• Evaluate how reliably (sensitive and specific) injectable agents can detect solid tumors of various sizes, grades, and stages and distinguish between indolent v. highly malignant, invasive tumors
• Develop and test injectable agents with optimal imaging potential, including: ACPPs conjugated to dendrimers with gadolinium chelates (or iron oxide nanoparticles) for T1 (or T2*)-weighted MRI, antibody fragments labeled with near-infrared fluorophores and \(^{18}\)F-fluorobates for PET imaging, and ACPPs conjugated to Cy5 for fluorescent imaging

Goal 3 – Characterize Intraoperative Use of Injectable Agents
• Determine what limits the efficacy of current technology for fluorescence-guided microsurgery
• Develop technology to address the limitations of FL-guided microsurgery

Figure 1 – General scheme for ACPPs. The polyanion (polyglutamate), attached via a cleavable linker to a polycation (polyarginine), blocks cellular uptake of the polycation. Proteases that cleave the linker release the polycation, allowing cellular uptake.
NanoEngineering and Physical Sciences track to complement current background in cell biology, biochemistry, and cancer biology

3 Classes in NanoEngineering and Physical Sciences
   MatSci 258 – Medical Device Materials
   CENG 207 – NanoMedicine
   BENG 280A/B – Principles of Biomedical Imaging

2 Classes in Epidemiology and Biostatistics
   Data Management and Informatics
   (Already completed: SOMC 218 – Epidemiology / Biostatistics)

Courses for all participants
   2 Lecture Series Each Year on Advanced Biology and Translational Medicine:
      CT2 – Principles of Cancer Treatment Development and Nanomedicine – Frontiers in Therapeutic and Diagnostic Delivery
   Technology commercialization: Eng 201 – Venture Mechanics
   Responsible Conduct of Research Training: BIOM 219 – Ethics in Scientific Research, as required by my graduate program

F31 proposal will be submitted by Fall 2011
### Education

<table>
<thead>
<tr>
<th>University</th>
<th>Degree</th>
<th>Started</th>
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<tbody>
<tr>
<td>University of California, San Diego</td>
<td>M.D./Ph.D., Biomedical Sciences</td>
<td>Sep 2008</td>
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<tr>
<td>California Institute of Technology</td>
<td>B.S. with Honor, Biology &amp; English</td>
<td>June 2008</td>
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### Research Experience

**Graduate Student Researcher** – August 2010 – Present  
Tsien Research Group – UCSD, La Jolla, CA  
Thesis research on developing and testing clinically translatable imaging technologies for detection and treatment of primary and metastatic tumors.

**Medical Student Researcher** – April 2009 – March 2010  
Varner Research Group – UCSD, La Jolla, CA  
Graduate student level cancer and cell biology research on integrin $\alpha_4\beta_1$ and PI3Kinase signaling.

**Undergraduate Student Researcher** – April 2007 – June 08  
Adolphs Research Group – Caltech, Pasadena, CA  
Social neuroscience research on subconscious processing of emotional faces.

**Undergraduate Student Researcher** – April – Sep 2005  
Fraser Research Group – Caltech, Pasadena, CA  
Developmental biology and imaging research on proteins and the mechanical dynamics of avian neural tube closure.

### Medical / Graduate Classes

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<tr>
<th>Medical / Graduate Classes</th>
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<tbody>
<tr>
<td>Basic Neurology</td>
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<td>Cell Biology / Biochem</td>
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<td>Epidemiology / Biostatistics</td>
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<td>Histology</td>
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<td>Human Disease</td>
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<td>Laboratory Medicine</td>
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<td>Principles of Pharmacology</td>
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<td>Social Behavioral Sciences</td>
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<td>Cancer Biology Journal Club</td>
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<td>Endocrinology, Repro, Metabolism</td>
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<td>Organ Physiology</td>
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<tr>
<td>Seminars in Biomedical Research</td>
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</table>

### Publication and Presentations

- **Felsen C**, Avraamides C, Garmy-Susini B, Varner JA  
  “Therapeutic effects of targeting integrin $\alpha_4\beta_1$ and its mechanism of action.” 2009 ASCB (poster), 2009 WSMRF (talk), 2010 *Journal of Investigative Medicine* Vol 58 (1)


- **Felsen C**, Lu C, Fraser SE (2005) “Neural Tube Closure and the Role of Dishevelled in Avian Embryos” Southern California Conference on Undergraduate Research, talk
Recurrence of ovarian cancer after a full course of chemotherapy remains 60-70%, and recurrence is treated with further courses of chemotherapy. Furthermore, chemoresistance in recurrent cases provides an additional hurdle in the treatment of many patients. The objective of this project is to develop a nanoparticle (NP), using a unique and novel lipid-polymer hybrid NP platform, which can contain two chemotherapy drugs, doxorubicin and paclitaxel, with sufficiently high drug loading that a few NPs can overcome a drug resistant cancer cell.

**Goal 1 – Optimize Nanoparticle Synthesis Process**

- Synthesize dual drug high dose (DDHD) NPs, dual drug low dose (DDL) NPs, single drug high dose (SDHD) NPs, and no dose (ND) NPs.
- Characterize NP properties such as size, surface charge, drug loading efficiency, etc.
- Characterize NPs in drug resistant ovarian and cervical cancer cell lines.

**Goal 2 – Further Evaluation of Nanoparticle Efficacy**

- Further analysis of DDHD, DDL, SDHD and ND NPs in an ex-vivo 3D matrigel model to model human ovarian cancer.
- Evaluate the therapeutic efficacy of the DDHD nanoparticles in vivo with xenograph tumor mice model.

Figure 1: DLS and SEM analysis of PLGA-lipid hybrid NPs.

Figure 2: The above images are the exact same sample; however, the image on the right has the green channel turned off in order to better visualize the extent of particle penetration and endocytosis. Above sample contained HeLa cells treated with Hoechst Nuclear Stain, CMFDA cytoplasmic stain, and 50μg/ml PLGA-Lipid-Folate NPs loaded with Nile Red.
Biochemistry and Cancer Biology track to complement current background in Engineering

**2 Classes in biological and biochemical foundations**
- BENG 230A Biochemistry
- BENG 230B Cell and Molecular Biology

**2 classes in cancer biology**
- BIMM 134 Biology of Cancer
- BCGN 234 Biology and Biochemistry of Cancer Cells

**Courses for all participants**
- 2 lectures Series Each Year on Advanced biology and translational medicine: Lecture series: CT2 – Principles of Cancer Treatment Development and Nanomedicine: Frontiers in Therapeutic and Diagnostic Delivery

**Technology commercialization:** Eng 201 – Venture Mechanics

**Responsible Conduct of Research Training:** By Advisor’s Recommendation

F31 proposal will be submitted by Fall 2011
Alexander Liberman - Curriculum Vitae
Moores Cancer Center 3855 Health Sciences Drive, La Jolla, Ca 92093
Office Number: 858-822-4266  email: aliberma@ucsd.edu

Education
University of California, San Diego Ph.D, Materials Science and Engineering  Started: Sep 2010
University of California, San Diego B.S., Bioengineering: Pre-medical  Graduated: June 2010

Work Experience

Graduate Researcher  - June 2010 - Present
Kummel Lab, UCSD
• Maintained Undergraduate Researcher projects/responsibilities.
• Optimizing gas filled Boron Doped Silica Nanoparticles for Contrast Ultrasound Imaging specifically for breast cancer tumors.

Undergraduate Researcher  - July 2008- September 2010
Kummel Lab, UCSD
• Developing and refining biodegradable drug delivery systems.
• Optimizing hydrophobic drug encapsulation within biodegradable PLGA nanoparticles.

Kummel Lab, UCSD
• Analyzed fluorescent tissue and touch prep slides for detecting breast cancer tumor cells as a part of a continuing study dealing with developing an inter-operative device for detecting positive margins in breast cancer tissue.
• Performed experimental procedures related to brightfield and fluorescent microscopy; as well as compiled, analyzed and documented procedures and results.

Graduate Classes
Solid State Diffusion and Reaction Kinetics
Nanomaterials and Properties

Abstracts:


Two types of liver lesions – focal nodular hyperplasia (FNH) and hepatocellular adenoma (HCA) – can be distinguished by their characteristic perfusion patterns in contrast enhanced ultrasound (CEUS), but it requires an expert radiologist for accurate diagnosis. The goal is to apply image processing to analyze CEUS videos and encode the perfusion information into a single color image, allowing easier and more accurate diagnosis.

**Goal 1 – Develop Application**
- Image Registration – correct motion within the imaging plane.
- Time Normalization – increase dynamic range of temporal data.
- Image Segmentation – detect contrast agent time of arrival.
- Color Coding – encode time of arrival with the color spectrum.
- Develop intuitive user to allow intuitive control of parameters.

**Goal 2 – Validation**
- Collect CEUS videos from multiple locations (hospitals, universities) to quickly compile a library for testing.
- Inexperienced radiologist and experienced radiologists will diagnose CEUS videos with and without the software.
- Test for accuracy, inter- and intra-observer reliability.
Biochemistry and Cancer Biology track to complement current background in engineering, physics and nanotechnology.

2 Classes in biological and biochemical foundations
- BENG 230A Biochemistry
- BENG 230B Cell and Molecular Biology

2 classes on cancer biology
- BIMM 134 Biology of Cancer
- BGGN 235 Biology and Biochemistry of Cancer Cells

Courses for all participants
- CT2 Lecture Series – Principles of Cancer Treatment Development
- Skaggs Lectures Series – Nanomedicine: Frontiers in Therapeutic and Diagnostic Delivery
- Technology commercialization: Eng 201 – Venture Mechanics
- Responsible Conduct of Research Training: BIOM 219 – Ethics in Scientific Research

F31 proposal will be submitted by Fall 2011
Casey Ta - Curriculum Vitae

Lab Address: Kummel Lab, Pacific Hall B100, 9500 Gilman Dr. 0358, La Jolla, CA 92093
Phone: 858-342-8214 E-mail: cnta@ucsd.edu

Education
University of California, San Diego Ph.D, Electrical Engineering Started: Sep 2007
University of California, San Diego B.S., Computer Engineering Graduated: June 2006

Job Experience
Graduate Student Researcher – 2008 – Present
Kummel Research Group, UCSD, La Jolla, CA
Developed an application to control a motorized fluorescent microscope to automatically scan a sparsely populated slide at low magnification and re-image the areas of highest cellular density at high magnification. Managed and educated a group of undergraduate students on fluorescent microscopy. Image processing to encode perfusion information from contrast enhanced ultrasound videos into a single parametric image.

Software Engineer – 2006 – 2009
Northrop Grumman Corporation, San Diego, CA
Designed and developed applications to plan and manage multiple tactical data link (TDL) communication systems as part of the Joint Interface Control Officers (JICO) Support Systems (JSS) project. Designed with Rational XDE, developed primarily with C++ and C#. Obtained Secret Security Clearance.

Kummel Research Group, UCSD, La Jolla, CA
Data acquisition and analysis of ChemFET surface trap states for analyte detection.

Cubic Transportation Systems, San Diego, CA
Development and testing automatic fare collection devices. Primarily C++ embedded programming.

Lab Assistant – 2004 – 2005
Jaffe Lab & Buckingham Lab, SIO, UCSD, La Jolla, CA
Created LabVIEW applications and circuit boards for remote and automated control of research equipment.

Graduate Classes
Solid State Electronics
Advanced Nanophotonics
BioElectronics
BioNanotechnology
Principles of Nanoscience
Nanoelectronics
Nanophotonics
Biochemistry
Cell and Molecular Biology

Publication and Presentations:
Technology has been developed that allows rapid detection of cancer and other disease related enzyme (MMP, Trypsin, Chymotrypsin) biomarkers directly from very small samples (5ul) of whole blood i.e., “no sample preparation”. Testing has been carried out on Diabetes patient blood samples and pancreatic cancer blood samples. The assay is ultrasensitive because enzyme biomarkers are catalysts that amplify the detection signal.

**Goal 1 – Develop POC/Home Monitoring Device**
- Fabricate Miniaturized silicon based devices
- Develop direct electronic (impedance) signal detection
- Imbed cell phone/wireless data transfer
- Develop Inexpensive/disposable cartridge
- Reduce sample to requires only 1-2 ul blood for finger stick sampling

**Goal 2 – New Cancer BioMarker Assays and Reagents**
- Develop New electronic ELISA type assays for known cancer related protein biomarkers (PSA, CA-125, AFP etc.) and for drug therapy monitoring
- Develop assays for new cancer related MMP 1,3,5,7,8,10 peptide reagents
- Incorporate new cancer related Kallikrein/Cathepsin peptide reagents

*Figure 1 – Shows basic scheme for using net charge changing peptide substrates (A) to detect cancer related proteases directly in whole blood samples (B)*
Biochemistry and Cancer Biology track to complement current background in engineering, physics and nanotechnology. My principle sources of biological and cancer knowledge have been from my protease research and graduate classes in BioNanotechnology, Nanomedicine, Nanosensors, and Advanced BioPhotonics.

2 Classes in biological and biochemical foundations
BENG 230A Biochemistry
BENG 230B Cell and Molecular Biology

2 classes on cancer biology to assist in development of enzyme assay for cancer markers
BIMM 134 Biology of Cancer
BIMM 150 Post-Genomics Biology
NANO 242 Biochemistry and Molecular Biology

Courses for all participants
2 lectures Series Each Year on Advanced biology and translational medicine: Lecture series: CT2 – Principles of Cancer Treatment Development and Nanomedicine: Frontiers in Therapeutic and Diagnostic Delivery
Technology commercialization: 1st choice = Eng 201 – Venture Mechanics. 2nd choice = Eng 202 – Enterprise Dynamics
Responsible Conduct of Research Training: BIOM 219 – Ethics in Scientific Research, as required by my graduate program

F31 proposal will be submitted by Fall 2011
Matthew T. Tyndall - Curriculum Vitae  
1414 Atkinson Hall | (858) 822-1276 | mtyndall@ucsd.edu

**Education**

- **University of California, San Diego**  
  Ph.D., Nanoengineering  
  Started: Sep 2009

- **University of California, Berkeley**  
  B.S., Engineering Physics  
  Graduated: May 2004

**Research Experience**

**Graduate Student Researcher** – June 2010 – Present

- Heller Research Group – UCSD, La Jolla, CA
  - Research on charge-changing substrates for protease detection with diabetic and cancerous blood samples.
  - Development of multiple Thrombin substrates. Research on dielectrohporetic separation of nano and micro particulates from complex media.


- Zettl Research Group - Berkeley, CA
  - Conducting graduate level research. Experiments with the creation of anodized aluminum oxide on silicon for the purpose of creating a nanotube array.

**Research Assistant** – October 2006 – November 2006

- CONCEPT Research Group - Berkeley, CA
  - Assisting in graduate level research. Experiments with pulsed laser deposition to create a lead ferrite oxide.


- BioPOEMS Research Group - Berkeley, CA
  - Assisting in graduate level research. Construction of a multi-physics computer simulation in FEMLAB (Matlab add-on) to model fluid flow in response to heat changes on the micron scale.

**Graduate Classes**

- Introduction to Nanoengineering
- Intermolecular & Surface Forces
- Structure & Analysis of Solids
- Nanoscale Synthesis & Characterization
- Nanoscale Physics & Modeling
- Nanomaterials and Properties
- Nanosystems Integration
- Nanomedicine
- BioNanotechnology
- Nanosensors
- Advanced BioPhotonics

**Current Work**

- Developing new single-sample devices and procedures for protease assay.
- Development of new substrates to monitor additional proteases.
- Elevator Pitch submitted to UCSD Entrepreneurial Challenge for a new way to aggregate and dynamically organize subjective information on the internet.
A peptide has been identified that dramatically increases the penetration of small molecules, antibodies and nanoparticles into tumors. This peptide will be used to improve the efficacy of intraperitoneal (IP) chemotherapy for ovarian cancer by increasing the penetration of drug-loaded nanoporous silicon nanoparticles (NP) into the tumor nodules that characteristically grow on the peritoneal surface. Further engineering of NP to direct them to the tumor nodules with ligands specific for ovarian cancer cells and to load them with drugs that interact synergistically can further increase the benefit of IP nanoparticle-based therapy.

**Goal 1 – Demonstrate that iRGD pretreatment will increase drug penetration into tumor nodules**
- Utilize a human ovarian tumor nodule model in nude mice and carboplatin-loaded nanoporous silicon NP
- Compare efficacy of IV vs. IP iRGD and determine kinetics of enhanced penetration for free and NP-bound carboplatin

**Goal 2 – Determine if multimerization of iRGD on the surface of NP or combinations of different ligands will enhance drug penetration**
- Determine whether multimerization of iRGD on the surface of NP, or the combination of iRGD plus a CD44 ligand capable of adhering the NP to the tumor nodule, will further increase its ability to enhance drug delivery
- Combine carboplatin with synergistically acting cytotoxins in NP to increase tumor cell kill

**Figure 1** – (a) Free IP drug penetrates tumor nodules poorly. (b) iRGD NP are more effective due to their ability to home to nodules and undergo iRGD-mediated deep penetration.
Nano Engineering and Physical sciences and Cancer Biology tracks to complement current background in engineering, physics and nanotechnology

2 classes in Nano Engineering and Physical Sciences foundations
   MATSCI 253: Nanomaterials and Properties
   NANO 247C: Bionanotechnology

1 class in Clinical Research Enhancement
   Biostatistics I

1 class in Cancer Biology to garner further knowledge about characterizing protein-ligand interactions
   BIMM 150 Post-Genomics Biology

Courses for all participants
   Two lectures series each year on advanced biology and translational medicine: CT² – Principles of Cancer Treatment Development and Nanomedicine: Frontiers in Therapeutic and Diagnostic Delivery

   Technology commercialization: 1st choice = ENG 202 – Enterprise Dynamics. 2nd choice = Eng 203 – Applied Innovation

   Responsible Conduct of Research Training: BIOM 219 – Ethics in Scientific Research

F32 proposal to be submitted by Fall 2011
Education
University of California, Irvine Ph.D., Biomedical Engineering, Graduated: June 2010
University of California, Irvine M.S., Biomedical Engineering, Graduated: June 2006
Boston University, Boston B.S., Biomedical Engineering, Graduated: May 2002

Job Experience
Postdoctoral Scholar – July 2010 – Present
Howell Group – Moores Cancer Center, UCSD, La Jolla, CA
Research on developing a high throughput screen for compounds targeting copper transporter receptor 2 (CTR-2).
Creating CTR2 KD cancer cell lines examine drug sensitivity, cell morphology, and transport mechanisms.

Graduate Student Researcher – Sept 2005 – June 2010
Putnam and Jeon Group (co-advised) – UCI, Irvine, CA
Engineered and designed microfluidic platforms to create microenvironments for cell co-culture studies. Research on cancer cell migration in 3D with various hydrogels and the effects of MMP2 and MT1-MMP knockdown.

Staff Research Associate – Dec 2002 – August 2005
Rozengurt Research Group - UCLA, Los Angeles, CA
Conducted transgenic animal studies using mice that were over expressing protein kinase D (PKD). Performed histological preparation and sectioning along immunohistochemistry. Managed own laboratory and was involved in overseeing and training new personnel.

Selected publications:
- Huang, CP et al., Engineering microscale cellular niches for three-dimensional multicellular co-cultures, Lab Chip, 2009, 9, 1740-1748

Graduate Classes
- Tissue Engineering
- Physiology
- Organ Transport Systems
- Applied Engineering Math I, II
- Biomedical Photonics
- Microfluidics
- Micro Implants
- Cell Biology Micro/Nanotechnology
Hydrogen peroxide ($\text{H}_2\text{O}_2$) has been associated with various human pathologies including cardiovascular and neurodegenerative diseases, inflammation and cancer, and also implicated in many cellular signaling pathways. In cancer, increased production of $\text{H}_2\text{O}_2$ has been strongly correlated with key processes such as initiation, transformation, progression and metastasis. Existing methods for monitoring $\text{H}_2\text{O}_2$ are either indirect or unsuitable for whole organisms’ studies because of lack of chemical specificity, unsuitable spectroscopic properties, low tissue penetration, unsuitability for intravenous applications, and/or unfavorable washing kinetics. As a result, our current understanding of this important molecule mostly relies on cell and tissue culture models. In order to study the direct connection between $\text{H}_2\text{O}_2$ and relevant normal or pathological processes, there is an urgent need to develop novel targeting mechanisms that enable its detection in live whole organisms.

Goal 1 - Construction and characterization of $\text{H}_2\text{O}_2$ activable cell-penetrating peptides (ACPPs).
- Chemical synthesis of $\text{H}_2\text{O}_2$-ACPP derivatives.
- *In vitro* characterization of specificity and reactivity.

Goal 2 - Detection of endogenous $\text{H}_2\text{O}_2$ in cell culture models.
- Detection of endogenous extracellular production of $\text{H}_2\text{O}_2$ in human cancer cell culture models.
- Detection of endogenous intracellular production of $\text{H}_2\text{O}_2$ in human cancer cell culture models.

Goal 3 - *In vivo* detection of endogenous $\text{H}_2\text{O}_2$ in cancer models in live mice with ACPPs-nanoparticle conjugates contrast agents.
- Synthesis of $\text{H}_2\text{O}_2$-ACPP-nanoparticle conjugates for magnetic resonance and ultrasound imaging.
- *In vivo* imaging of endogenous $\text{H}_2\text{O}_2$ in cancer models in live mice by magnetic resonance and ultrasound imaging.

Significance - Developing ACPPs for $\text{H}_2\text{O}_2$ detection will enable its imaging by a variety of modules including fluorescence, magnetic resonance, radioactive and ultrasound techniques. Importantly, the same detection mechanism could be further used for targeted delivery of therapeutic agents to the local site of oxidative-stress related diseases.

Figure 1 - Schematic diagram of $\text{H}_2\text{O}_2$-ACPP's mechanism of action. Following specific cleavage of the linker by $\text{H}_2\text{O}_2$, the polycationic cell-penetrating motif is free to dissociate from its inhibitory polyanionic fragment and penetrate into cells through the endocytic pathway or directly into the cytosol.
Classes from both the Cancer Biology and Nano Engineering tracks to complement current background in chemistry.

2 Classes in cancer biology
   BIMM 134 - Biology of Cancer
   BGGN 235 - Biology and Biochemistry of Cancer Cells

1 Class in Nano Engineering and Physical Sciences
   Nano 262 - Nanosensors

Courses for all participants
2 lectures Series Each Year on Advanced biology and translational medicine: Lecture series: CT2 – Principles of Cancer Treatment Development and Nanomedicine: Frontiers in Therapeutic and Diagnostic Delivery

Technology commercialization
ENG 201 - Venture Mechanics.

Responsible Conduct of Research Training
BIOM 219 - Ethics in Scientific Research

research proposals for post-doctoral fellowship will be submitted within 12 months to the following organizations: European Molecular Biology Organization (EMBO long-term fellowship) – Feb. 2011, Susan G. Komen for the Cure (Basic Research and/or Translational Research of breast cancer) – Sep. 2011, and American Association for Cancer Research (AACR Basic research and/or Translational Research post-doctoral fellowships) – Dec. 2011.
Roy Weinstain - Curriculum Vitae
Address: Tsien lab CMM west 310, 9500 Gilman drive, La-Jolla, CA 92093
Phone: 858-534-5268   Email: rweinstain@ucsd.edu

Education
University of California, San Diego  Post-doctoral fellow  Started: Nov. 2009
Tel-Aviv University, Israel  Ph.D., Organic Chemistry  Conferred: March 2010
Tel-Aviv University, Israel  B.Sc., Biology  Graduated: Sep. 2005
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Research Experience
  Doron Shabat research group, Tel-Aviv University, Israel

  Prof. Phil S. Baran research group, Department of Chemistry, The Scripps Research Institute, La Jolla, CA.
  Subject: Synthesis of heterocycled-based Self-Immolative Polymers.

• Undergraduate student researcher – Dec. 2004 – Sep. 2005
  Doron Shabat research group, Tel-Aviv University, Israel
  Subject: Antibody-catalyzed asymmetric reactions.

• Undergraduate student researcher – Apr. 2004 – Dec. 2004
  Talilla Volk Research group, Department of Molecular Genetics, Weizmann Institute of Science, Rehovot, Israel.
  Subject: Identification of novel HOW mRNA targets in the Drosophila mesoderm using microarray screen and consensus-RNA binding motif.

Publication and Presentations:


