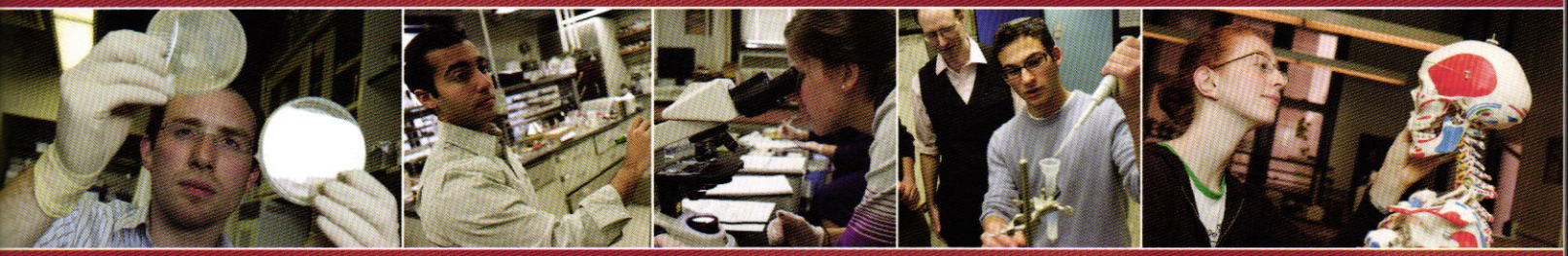

Undergraduate Research Abstracts

2010

Yeshiva University
Undergraduate Research Abstracts

Photos courtesy of Yeshiva University
Department of Communications and Public Relations
Photo Department

Layout: Lynn Sims

Dedication

In tribute to our friends and mentors,
Eli Steinberger z'l
(USRP Co-President 2006-07)
and
Donny Ladell z'l
(USRP Co-President 2005-06),
who we miss dearly.

Preface

It is our distinct pleasure to offer this issue of the *Undergraduate Research Abstracts* of Yeshiva College and Stern College for Women to the Yeshiva University Community. This magazine reports recent work in the natural and social sciences that our students are engaged in, both in and around our campus, and provides all of us with an opportunity to continue our learning.

It is, indeed, amazing to see how active our undergraduate students are outside the classroom. For so many of our students learning continues outside the classroom through scientific inquiry both on and off campus. This unique publication is a testament to our dedication and commitment to continue as a vibrant research community. It is a tremendous source of joy for faculty members to see the accomplishments of our students. We also hope that this will inspire many more students to actively participate in such explorations in the future. This publication also serves as a model for enabling the entire Yeshiva University Community to stay abreast of our endeavors.

We hope all of you will find this issue both informative and insightful. We thank all the contributors and we look forward to having many more abstracts in the upcoming years.

Raji Viswanathan, Ph.D.
Professor of Chemistry
Associate Dean for Academic Affairs
Yeshiva College

Introduction

Scientific research is thriving at Yeshiva University! Students are presenting at national and international conferences and winning prestigious prizes and scholarships. Thanks to our excellent science faculty and the enthusiastic leadership of our various clubs, a genuine scientific community has become a reality. We, the Undergraduate Student Research Presentations (USRP) club at Yeshiva College and the Student Undergraduate Research Group Experience (SURGE) at Stern College, are proud members of this community.

SURGE is a student run organization that works closely with faculty advisers to organize monthly presentations of student research and to help students prepare their presentations. We feature talks in pure and applied biology, chemistry, and physics, as well as clinical research. Our presentations help prepare students for graduate school in the sciences and serve as a gateway to advanced scientific research.

In addition to the student presentations that form our *raison d'etre*, USRP has presented lectures by Yeshiva's top mathematicians and scientists, briefs about recent Nobel Prize winning research, and a series of talks by internationally renowned neuroscientists. We maintain a website at YU Research.com to assist students in finding research positions and keeping abreast of the latest scientific discoveries.

In this spirit, we present the *Undergraduate Research Abstracts* to provide a small window into the research of Yeshiva University students. We hope you enjoy!

USRP 2009-10

Yossi Steinberger
Jerry Karp
Robert Rand
Arieh Greenbaum
Michael Kurin
Menachem Spira

Faculty Advisor
Dr. Neer Asherie
Department of Physics and Biology
Yeshiva College

SURGE 2009-10

Jenny Deluty
Hadassa Klerman
Tirtza Spiegel

Faculty Advisors
Dr. Margarita Vigodner
Department of Biology
Stern College for Women

Dr. Evan Minzter
Department of Chemistry and Biochemistry
Stern College for Women

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Biochemistry
Behavior of Two Oxidized Cholesterol Species in a Model Membrane System

by

Gordon, Sharon and Mintzer, E[1]
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Cholesterol is known to play an integral role in eukaryotic cell membrane function and structure. Oxidized cholesterol species (oxysterols) are formed either by enzyme catalysis or auto-oxidation and are known to be cytotoxic. The objective of this study was to investigate the interactions of two oxysterols, 7-ketocholesterol and 25-hydroxycholesterol, with brain-derived sphingomyelin in a model membrane system. A detergent solubility assay was utilized to qualitatively determine the extent of formation of detergent-resistant domains in multi-lamellar vesicles in which cholesterol was replaced by oxysterols. The vesicles were treated with the detergent Triton X-100 to observe the extent of membrane raft development through the analysis of spectrophotometric data. The preliminary results suggest that lipid raft formation is sensitive to the specific oxysterols used and their relative amounts. Based on these data, it is proposed that oxidized cholesterol species alter sterol-sphingomyelin interactions, affecting membrane raft formation.

Student Researcher
Sharon Gordon is a third year student majoring in Biology at Stern College for Women. She intends to pursue a career in medicine, with a focus in Women's Health. Sharon hopes to continue performing research in conjunction with her clinical career.
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Biochemistry
The Interactions of LPA with Model Membranes

by

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Lysophosphatidic acid (LPA) belongs to a group of phospholipids that serve as lipid mediators by interacting with G-protein coupled receptors (GPCR). The purpose of this investigation is to determine the details of the interaction between LPA and a model lipid membrane. It was hypothesized that, since LPA is abundant in vivo compared to the smaller number of GPCR, LPA interacts with the membrane directly. To probe these interactions, the technique of Isothermal Titration Calorimetry (ITC) was used. Two phase transitions — reconstitution and solubilization — were explored. The results suggest that LPA interacts with the model membrane with high affinity. Results also suggest that the phase of the phospholipid model membrane determines the specific nature of LPA-membrane binding. Using the ITC data, it is possible to suggest phase transitions from micelles to mixed micelles, as well as to re-aggregated micelles. The structural understanding of LPA as a regulatory molecule may have implications for the functional role of LPA in cellular activity.

Student Researcher
Julie Meir is a junior at Stern College for Women and is currently studying for her B.A. in Biochemistry. She is a co-vice president of the Chemistry Club, and helped it win the ACS community interaction grant. She enjoys classical music and horseback riding.
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Biochemistry
Hydroxyapatite Growth Inhibition by Osteopontin Hexapeptide Sequences

by

Silverman, L,[1] Saadia, M,[2] Ishal, J,[1] Tishbi, N,1 Leiderman, E,[1]
Kununov, I,[1] Recca, B,[1] Reitblat, C,[1] Viswanathan, R[1]
[1]*Yeshiva University, Department of Chemistry*
[2]*SUNY Downstate Medical Center*

The effects of three acidic hexapeptides on in vitro hydroxyapatite growth were characterized by pH-Stat kinetic studies, adsorption isotherms, and molecular modeling. The three peptides, pSDEpSDE, SDESDE, and DDDDDD are equal-length model compounds for the acidic sequences in osteopontin, a protein that inhibits mineral formation in both calcified and non-calcified tissues. Growth rates from 1.67 mM calcium and 1.00 mM phosphate solution were measured at pH 7.4 and 37°C in 150 mM NaCl. pSDEpSDE was a strong growth inhibitor when pre-adsorbed onto HA seeds from ≥ 0.67 mM solutions, concentrations where adsorption isoth67 mM solutions, concentrations where adsorption isotherms showed relatively complete surface coverage. The non-phosphorylated SDESDE control showed no growth inhibition. it adsorbed to almost the same extent as pSDEpSDE, it rapidly desorbed under the pH-Stat growth conditions while pSDEpSDE did not. DDDDDD exhibited weak inhibition as its concentration was increased and similar adsorption/desorption behavior to pSDEpSDE. Molecular modeling yielded binding energy trends based on simple adsorption of peptides on the [100] surface that were consistent with observed inhibition, but not for the [001] surface. The relatively unfavorable binding energies for peptides on the [001] surface suggest that their absorption will be primarily on the [100] face. The kinetic and adsorption data is consistent with phosphorylation of osteopontin acting to control mineral formation.

Student Researchers

Ben Recca is currently in his second year at Yeshiva College's Honors program. As a chemistry major and biology minor he has always appreciated and been intrigued by science. Although officially he is pre-med, he is unsure what exactly he wants to do after graduating. He enjoys hiking and camping, painting and planting. This summer he will be participating in a Georgia Tech research internship located in his birthplace and hometown, Atlanta Ga.
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Hailing all the way from Vilnius, Lithuania, Chanan Reitblat joined the Honors Program in 2008 and is currently a "real" sophomore. Apart from his underground career as a DJ, Chanan spends most of his time doing chemistry research in the Silverman Biomineralization Lab and organizing events as the President of the Yeshiva College Chemistry Club. Although he is a total chem-head, he also enjoys reading the classics, debating constitutional law, and playing Ultimate Frisbee.
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Biomathematical Modeling
Does the Method for Analyzing Melatonin for Circadian Phase Depend on the Conditions?

by

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The activity of the human circadian pacemaker, located in the SCN, is measured by its output rhythms, of which melatonin is the most accurate. Various methods of measuring the plasma melatonin rhythm exist, including curve-fitting, threshold-based and physiologically-based methods. We compared the variability of phase estimates derived from curve-fitting, threshold-based and physiological model methods using data from different conditions. Additionally, we determined the effects of missing data on the various methods by comparing variabilities of phase estimates for complete data sets to data sets with data removed in 2-hour segments for every 2-hour window. For complete data sets, there is no significant difference between analysis methods of melatonin onsets or between those of melatonin offsets, although the former are less variable than the latter. Gaps falling within two hours of the "DLMO-exact" method affected phase estimates; gaps at other times did not differentially affect analysis of the melatonin profile.

Student Researcher
Hadassa Klerman (SCW '11) is pursuing a biochemistry major. She plans to attend medical school and is also interested in the applications of mathematics and modeling to areas of scientific research ranging from circadian rhythms to effects of protein modification. When not in the chemistry lab, she plays multiple musical instruments and is a member of SCW's Chamber Music Ensemble.
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Biomedical Engineering
The Effect of Tβ4 on Actin Distribution

by

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[2]*Department of Biomedical Engineering, Wayne State University, Detroit, MI*

Thymosin Beta 4 is a naturally occurring protein which sequesters G-(or monomeric) actin. It has recently been shown to promote cell migration in many situations and particularly in the corneal epithelial cells we were studying. We set out to investigate the mechanism by which it does so, which is unclear. One hypothesis is that by sequestering G-actin, thymosin affects the F-(or polymeric) actin distribution within cells.(F-actin is known to affect both cell binding and cell movement.) We therefore studied the distribution of F-actin using fluorescent dye in both a control group and cells treated with various levels of thymosin.

Our results show that thymosin causes a reduction in F-actin levels generally and most noticeably around the nucleus. Our results did not vary with the amount of thymosin applied or the time it was left on. These results show a possible mechanism whereby thymosin causes cell migration by redistributing F-actin, leading to weaker cell binding.

Student Researcher
Joshua Blumenkopf is a first year (unofficial) Physics major. He hopes to become a theoretical physicist. In his spare time he likes listening to classical music and playing it on his clarinet.
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Biophysics
Spectral Modification to Genetically Encoded Single-chain RhoA Biosensor

by

Tsipora Huisman[1], Louis Hodgson[2]
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[2]*Gruss-Lipper Biophotonics Center, Department of Anatomy and Structural Biology, Albert Einstein College of Medicine, Bronx, NY 10461*

Rho family of p21 small GTPase is a class of regulator proteins that control numerous biochemical processes in a cell, including adhesion, contraction, and cell motility. Within this subfamily RhoA specifically mediates actin cytoskeleton dynamics, and myosin-mediated contraction. Recent findings indicate involvement of Rho GTPases during protrusion of the leading edge lamellipodium. However, it is not yet clear which pathways are being regulated at the leading edge and how such pathways intersect among different signaling cascades initiated by other family members of Rho GTPases including Rac1 and Cdc42.

A major issue in this area of study is that the signaling cascade involving RhoA, Rac1 and Cdc42 are interdependent and occur simultaneously at rapid rates, thereby precludes most conventional assay approaches. Therefore, to determine the kinetic relationship of the different Rho GTPases, it would be necessary to observe two or more different GTPase activities at the same time in a single living cell. Using the red-shifted fluorescent proteins (monomeric Cherry, monomeric tagRFP, monomeric Kusabira orange fluorescent protein) was necessary to shift the spectral requirement of RhoA to the red and far-red domain so as to make RhoA biosensor compatible with other sensors that require cyan and yellow colors to report their activities.

We used recombinant DNA technology to change the fluorescent proteins to red-shifted versions in the RhoA sensor. The intrachain linker lengths needed to be optimized to account for slight differences in molecular size and orientations of the new fluorescent proteins. We validated and characterized the new biosensors *in vitro* using spectrofluorometry in living HEK293T cell line. Based on our data we produced a significant improvement, up to 40% change in FRET ratio in biosensor response comparing all on versus all off conditions, using different linker lengths as well as different fluorescent protein pairs.

Student Researcher
Tsipora Huisman grew up in Amsterdam where she lived for 18 years. After her year in seminary, she decided to come to Stern as a Pre-Med student. Stern College has provided her with opportunities she never dreamed of having. Among these was doing research for a summer in the Albert Einstein School of Medicine. She really enjoyed it and is looking forward to having similar, but different, experiences in the future.
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Biophysics
The Crystallization of Proteins with Chiral Precipitants

by

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The phase behavior of protein solutions is not yet well understood. The inability to predict protein phase behavior inhibits progress in many biophysical problems such as the crystallization of proteins for structure determination. Our long-term goal is to make it possible to predict the phase behavior of protein solutions. We studied the phase behavior of thaumatin, a globular protein used as a model system in crystallization studies. It is known that the addition of L-tartrate ions leads to the rapid formation of protein crystals, but the available information about the solubility of these crystals is inconsistent. We have determined the solubility of thaumatin with L- and D-tartrate and are currently studying the effect of *meso*-tartrate and salt concentration. Our studies determined a heretofore-unknown influence of precipitant stereochemistry on protein solubility. L-tartrate forms bipyramidal crystals and displays a normal solubility; D-tartrate forms stubby and prismatic crystals and displays a retrograde solubility. Our results suggest that the chirality of additives may be another useful tool to alter the phase behavior of proteins.

Student Researcher
Arieh is a fourth year student majoring in chemistry with aspirations of becoming a physician by day, chemist by night, and theologian in between.
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Cancer Biology
U87 Cancer Cells Respond to Stable Stimuli Responsive Antioxidant Nanoprodrugs

by

Ilana Frankiel[1], Bong-Seop Lee[2], Talia Shear[3], Aruna Nalla[2], John Yu[2]
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[2]*Cedar Sinai Medical Center, Los Angeles, CA 90048*
[3]*Cornell University, Ithaca, NY 14850*

Nanoprodrugs are nanoparticles containing NSAIDs (non steroidal anti inflammatory drugs), created to release drugs upon stimulation in the body. NSAIDs have been proven experimentally to inhibit angiogenesis and stimulate apoptosis within malignant tumors, specifically COX-2 inhibiting NSAIDs have shown promising results by inhibiting prostaglandin production thereby preventing inflammation and tumor growth. However NSAID selectivity, delivery and efficacy remain barriers in creating anti-cancer treatments.

Based on the enhanced permeability and retention effect (EPR effect), solid tumors should be targeted through their vasculature. Through fenestrations in vascular endothelial cells at tumor sites, macromolecules can easily enter tumor tissues and accumulate there for long periods of time due to poor lymphatic drainage. Anticancer drugs enveloped in nano-sized carriers can be targeted towards tumor endothelial cells and will then accumulate due to the EPR effect. Although our nanoprodrugs range in size between 100 and 200 nanometers, they fell within the ideal parameters for drug carrier size, allowing them to flow freely through the bloodstream and escape renal filtration.

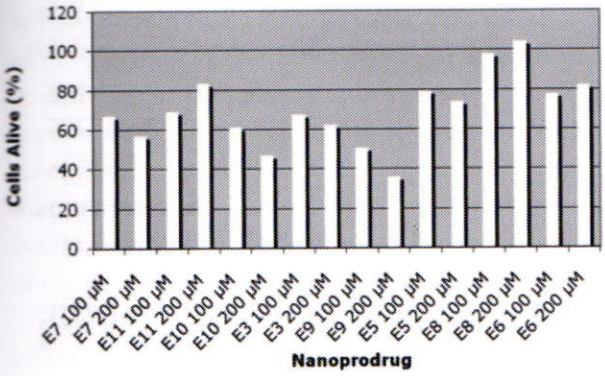
The nanoparticle size and hydrophobicity allows the nanosphere to enter the targeted cells through endocytosis and to enzymatically hydrolyze upon oxidation, releasing billions of drugs within the solid tumor. We created eight different nanoprodrugs, containing NSAID compounds (indomethacin, ibuprofen and naproxen) and structural compounds (ALA and TOCO), with varying sizes and components. In vitro U87 cancer cells cultures and HBVEC (human brain endothelial cells) cultures were prepared and treated with 100 μM and 200 μM nanoprodrugs. Cell counting showed the toxicity effects of the nanoprodrugs and allowed comparison between the healthy cells and the cancerous cells. Regarding the U87 cells, the results varied between the different nanoprodrugs, however E9 and E3 showed true toxicity, with less than 20% cells alive at cell counting. The HBVEC were minimally affected by the nanoprodrugs, with an average of 70% still alive at counting. Two of the very effective nanoprodrugs, E9 and E10 were further tested on the U87 and HBVEC cells in varying concentrations, between 10μM and 100 μM, in order to find the ideal concentration of toxicity to the tumor cells but not the healthy cells. 50 μM proves to be the ideal concentration, killing 84% of the U87 cells and only 20% of the HBVECs. In addition to comparing the different NSAID sets, the cell counting data allowed comparison between the different configurations of one NSAID set. More data must be collected, to prove the true toxicity of E3, E9 and E10, however the data collected shows its success.

E3	Ibu-TEG-ALA/TOCO
E9	Ibu_2TEG/TOCO
E5	NPX-TEG-ALA/TOCO
E7	NPX_2TEG/TOCO
E6	IND-TEG-ALA/TOCO
E8	IND_2TEG/TOCO
E10	FA-TEG-ALA/TOCO
E11	FA_2TEG/TOCO

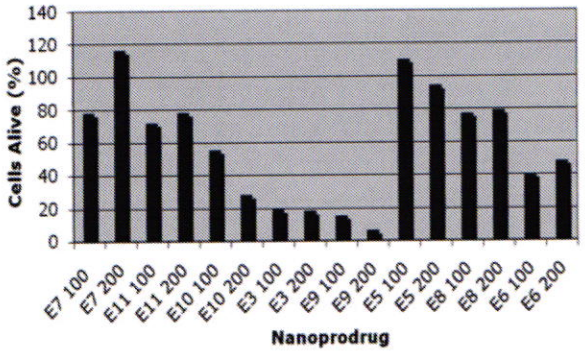
Figure 1: Nanoparticle label and chemical compound

Figure 2: Percentage of cells alive after treated by nanoprodrug

a) HBVEC



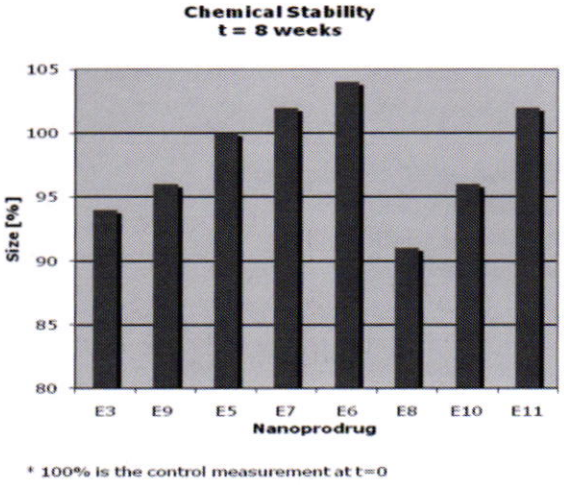
b)U87 cells



Additionally nanoprodrug concentrations were measured weekly using HPLC (High-performance liquid chromatography), allowing estimation of the chemical stability of the nanoprodrugs. All nanoprodrugs stayed fully intact over the 8 week period, with only normal insignificant changes. The stability of our nanoprodrug was further shown through weekly size measurement of the nanoprodrug. Although minute changes did occur in nanoparticle size, either larger through combination or smaller through degradation, no compound changed more than 10 nm in the 8 week period. The in-vitro study of our eight nanoprodrugs reveal their stability over time, toxicity against U87 cells and mild effect on human brain endothelial cells. In vivo testing in the future of our nanoprodrugs will be used to show their efficacy and response to body conditions.

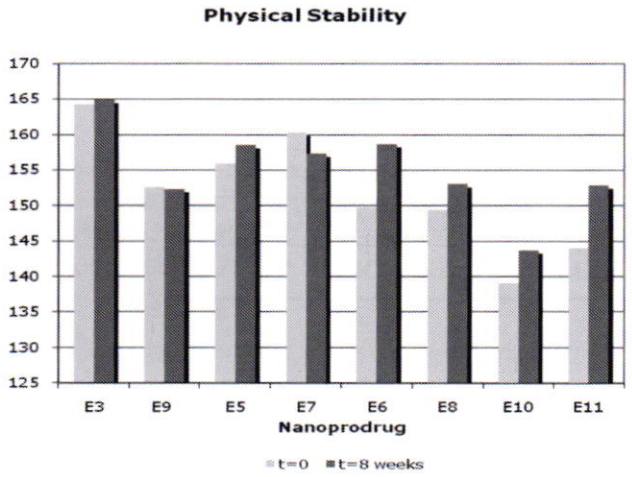
Figure 3:

a) chemical stability



* 100% is the control measurement at t=0

b) physical stability of nanoprodrug at t = 8



Student Researcher

Ilana Frankiel is currently a senior at Stern College, majoring in Biology and minoring in Business. She loves working with children and aspires to become a family care physician. Ilana is excited to spend her life working with people and is grateful to all those who have influenced her thus far.

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Cancer Biology
Olive Extract's Pro-oxidative and Pro-apoptotic Effects on Cancer Cells

by

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For years, it has been known that olives contain many health benefits. Olives are categorized as nutraceuticals, foods that improve health or protect against diseases. Olives contain polyphenols, molecules that have been proven to act as antioxidants and as anticarcinogens. Our laboratory has shown that certain polyphenols can also have pro-oxidative effects, especially on cancer cells.

Experiments were conducted using both normal fibroblast (HF-1) and human squamous carcinoma (HSC-2) cell lines derived from the human oral cavity. Neutral red (NR) assays indicative of cell viability have shown that HSC-2 cancer cells are more sensitive than HF-1 cells are to the cytotoxic effects of olive extract. To determine the specific cause of cell death we treated cells with olive extract, together with cobalt (II), pyruvate, or catalase, which decrease oxidative stress caused by reactive oxygen species in the cells. NR assays showed that these antioxidants protect cells from death by olive extract. Additional neutral red assays demonstrated that buthionine sulfoxamine, which prevents the replenishment of the cell's internal antioxidant, glutathione, enhances the sensitivity of the cancer cells to the cytotoxic effects of olive extract. These results bolster the theory that oxidative stress causes the death of cancer cells treated with olive extract.

The suggested mode of cell death is apoptosis, programmed cell death, which can often be a direct result of oxidative stress. Induction of apoptosis was indicated by fluorescent microscopy of HSC-2 cells treated with olive extract. These cells demonstrated characteristic signs of cell death, including hypercondensed nuclei and decreased cytoplasm. Gel electrophoretic experiments were also conducted in order to detect shearing of DNA, which is a hallmark of apoptosis; however, results have thus far been inconclusive. Experiments are currently being conducted to confirm olive extract-induced apoptosis, such as flow cytometry and Western blot analysis of enzymes involved in apoptosis, including PolyADP-Ribose Polymerase (PARP) and Caspase-3.

In summary, evidence provided by our lab demonstrates that olive extract has anticarcinogenic effects due to the induction of oxidative stress, which may lead to apoptosis.

Student Researcher
Ahuva Freilich is a biology major in her second year of Stern, interested in the field of medical genetics.
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Cancer Biology
Differential EGFR/ HER-2 Signal Transduction Pathway Protein Phosphorylation in Breast Cancer

by

Orli Haken[1], Stefani Thomas[2] , Zhongping Liao[2], Yunhu Wan[2], and Austin Yang[2]
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[2]*Molecular and Structural Biology Program, Greenebaum Cancer Center, University of Maryland School of Medicine, Baltimore, MD 21201*

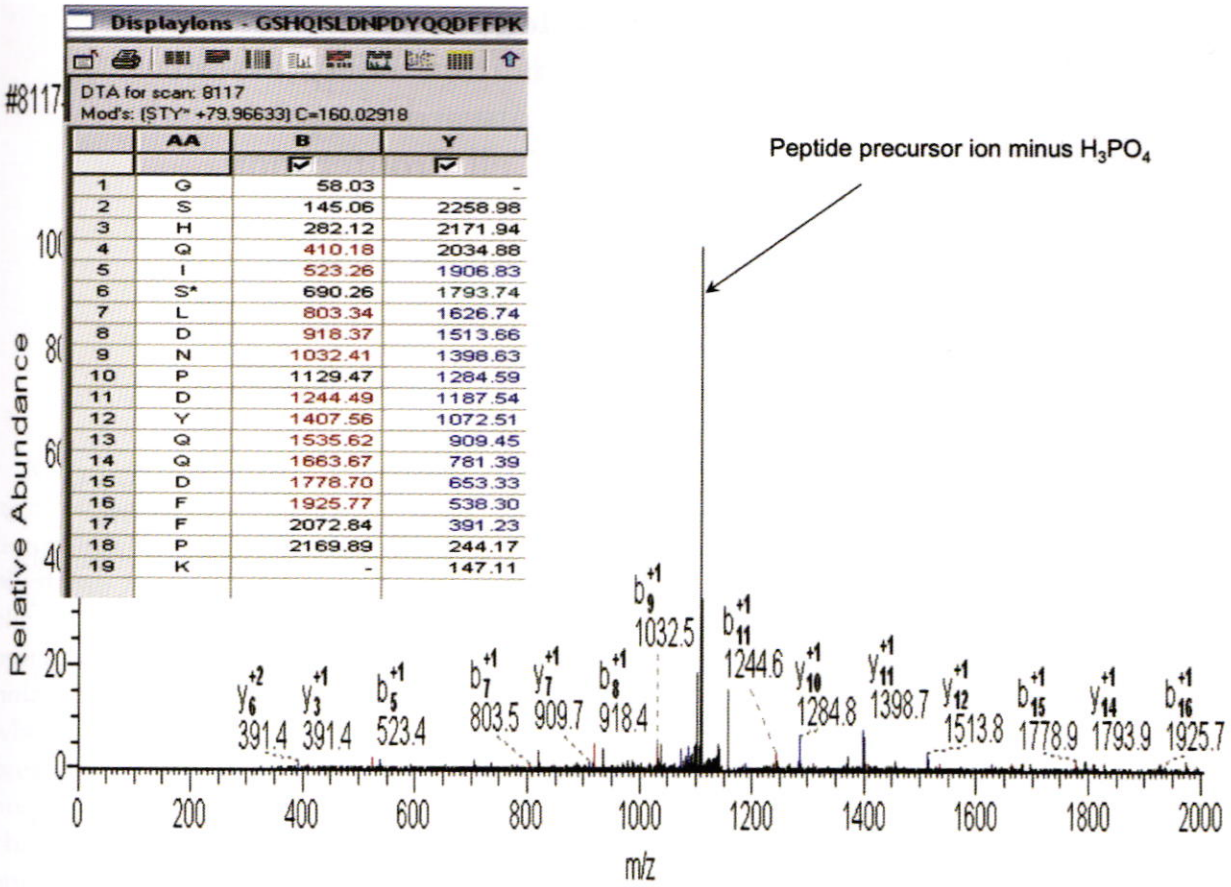
For years, it has been known that olives contain many health benefits. Olives are categorized as nutraceuticals, foods that improve health or protect against diseases. Olives contain polyphenols, molecules that have been proven to act as antioxidants and as anticarcinogens. Our laboratory has shown that certain polyphenols can also have pro-oxidative effects, especially on cancer cells.

Breast Cancer is the second most common lethal cancer in women. 30% of all cases are characterized by the overexpression of the Human Epidermal Growth Factor Receptor 2 (HER-2). Upon ligand binding, HER-2 forms a heterodimer with Epidermal Growth Factor Receptor (EGFR) on the cell surface, which then potentiates an intracellular signal transduction pathway that causes the phosphorylation of downstream proteins and the transcription of oncogenic genes. In order to more thoroughly understand the molecular mechanism of the EGFR/ HER-2 pathway, an analytical approach such as proteomics is needed in order to comprehensively analyze all the proteins in the signaling cascade. Proteomics is the large scale study of proteins, specifically their structures and functions.

The goal of this study was to perform a proteomic analysis of breast cancer cells to study global phosphorylation dynamics, and specifically the signal transduction pathway of EGFR/ HER-2. The experiment was conducted using SKBR3 cells, a Breast Cancer tumor cell line overexpressing endogenous HER-2. The workflow included lysis of the cells to produce soluble protein fractions, which were then reduced, alkylated, and digested with trypsin. The resulting peptide mixture was then desalted using C18 chromatography, enriched for phosphopeptides using Titanium Dioxide, and desalted again prior to Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) analysis. All peptide fractionation and enrichment steps prior to LC-MS/MS were performed using Stop and Go Extraction (Stage) Tips; an economical method for chromatographic separation without the use of an HPLC system. A human protein database search was run for protein identification.

The efficiency of our phosphopeptide enrichment method was ~78%. 801 phosphoproteins and 1004 phosphopeptides were identified from 500μg of protein from soluble cell lysate. Figure 1 is an MS/MS spectrum along with the ion coverage of a confidently identified phosphopeptide from the protein sample. This method had a broad dynamic range and allowed the identification of many different classes of phosphoproteins including signaling, receptor, cytoskeletal, and cell adhesion proteins, in addition to kinases and other enzymes.

Future studies include a temporal and quantitative phosphoproteomic analysis of the EGFR/ HER-2 signal transduction pathway in SKBR3 cells. The long term goal of this project is the elucidation of the EGFR/ HER-2 signal transduction pathway in Breast Cancer.



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2	S	145.06	2258.98
3	H	282.12	2171.94
4	Q	410.18	2034.88
5	I	523.26	1906.83
6	S*	690.26	1793.74
7	L	803.34	1626.74
8	D	918.37	1513.66
9	N	1032.41	1398.63
10	P	1129.47	1284.59
11	D	1244.49	1187.54
12	Y	1407.56	1072.51
13	Q	1535.62	909.45
14	Q	1663.67	781.39
15	D	1778.70	653.33
16	F	1925.77	538.30
17	F	2072.84	391.23
18	P	2169.89	244.17
19	K	-	147.11

Figure 1: Confidently identified Epidermal Growth Factor Receptor (EGFR) phosphopeptide.

Student Researcher

Orli Haken is currently a junior at Stern College majoring in Biochemistry. She plans to continue her education in the medical field, where she is interested in pursuing clinical research in Endocrinology. Orli loves to dance and ice skate and wishes to travel the world.

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Cancer Biology
Estrogenic Regulation of S6 Kinase 1 Expression Creates a Positive Feed-Forward Loop in Control of Breast Cancer Cell Proliferation

by

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The 40S ribosomal S6 kinase 1 (S6K1) acts downstream of the mammalian target of Rapamycin (mTOR), and is sensitive to inhibition by rapamycin. Chromosomal region 17q23 containing the *RPS6KB1* gene is frequently amplified in breast cancer cells, and S6K1 is over expressed in about 30% of cases. Overexpression of S6K1 correlates with increased rapamycin sensitivity. The role of S6K1 in disease development and progression is supported by the observation that S6K1 Over expression is associated with poor prognosis in breast cancer patients. However, the reason for high-level amplification of the *RPS6KB1* gene specifically in breast cancer, and not other cancer types is not well understood.

We have previously reported that S6K1 regulates growth of breast cancer cells by phosphorylating Estrogen Receptor α (ERα), and co-expression of S6K1 and ERα in breast cancer cells renders them sensitive to combination therapy with rapamycin and tamoxifen. In this study, we demonstrate that in response to estrogen activation, ERα activates expression of S6K1 by upregulating transcription of the *RPS6KB1* gene. Increased levels of S6K1 promote further phosphorylation and activation of ERα, creating a positive feed-forward loop. We hypothesize that this relationship promotes breast cancer cell growth, thus providing a selective advantage to S6K1- and ERα-overexpressing cells.

Student Researcher
Fannie Faige Seligman is currently a sophomore at Stern College for Women double-majoring in Philosophy and Biochemistry. She aspires to become a physician-scientist who spends her free time reading philosophy, gardening, and running home-made scientific experiments that will probably require a fire extinguisher present at all times.
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Cancer Biology
Development of an In Vivo Screen to Identify Novel Regulators of Tumor Growth and Metastasis

by

Tirtza Spiegel[1], Pamela Boimel[1], Cristian Cruz[2], Dr. Jeffrey Segall[2]
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Metastasis is the spread of neoplastic cells from a primary tumor site to secondary organs and involves angiogenesis, degradation of the basement membrane, invasion, intravasation, and extravasation. Ninety percent of deaths from tumors are due to metastasis, therefore study of metastasis pathophysiology is crucial. Previously 28 genes, identified to be correlated with patient survival across three clinical breast cancer microarray studies, were tested for their ability to regulate tumor growth and/or metastasis in SCID mice, using a lentiviral shRNA screen approach. From this screen we identified the homeobox 2 gene, which enhanced tumor growth both in the screen and for the individual cell line when downregulated. HOXB2 as well as other genes evaluated in the shRNA screen will be overexpressed to screen for regulators of metastasis and tumor growth with an open reading frame (ORF) pool. Quantitative Real-Time PCR (qRT-PCR) primers were designed to be used to determine the changes in the proportion of human breast cancer cells overexpressing up to 28 different genes after growth in the primary tumor and metastasis to the lungs. We have been analyzing the sensitivity as well as the specificity of the primers to detect their respective genes using qRT-PCR. Many of the primers had low specificity and seemed to prime against other ORFs, possibly due to contamination, primer dimers, and/or sequence overlap. We are currently evaluating *in vitro* growth of the HOXB2 knockdown cell line compared to the overexpression cell line and are comparing this to *in vivo* tumor growth curves. In preliminary studies HOXB2 gene had little effect on *in vitro* growth, although it seemed to increase primary tumor growth *in vivo*.

Acknowledgements

Thank you to the Roth Summer Research Fellowship Committee for funding and the Segall Lab for an enjoyable and educational experience.

Student Researcher

Tirtza Spiegel is a third year Biology major, with a focus on Cellular and Molecular Biology. She aspires to become a physician-scientist with a clinical interest in breast oncology, and to run a research program in cancer genetics and preventive oncology. Tirtza is a second year Resident Advisor in Stern College and does research in the Holz lab. Tirtza loves hiking and plans to climb Mount Kilimanjaro by the time she is thirty.

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Cancer Biology
Study of Biomarkers of Invasion and Cancer Stem Cells in Human Breast Cancer

by

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The major challenges faced by Breast cancer clinicians are metastasis and drug resistance, which cause a high rate of morbidity and mortality. Tumor cells can detach and give rise to micro metastasis, which usually go undetected until they grow. Some of these tumor cells remain dormant and the mechanism that causes the dormant cells to activate is still not understood.

We have seen that the microenvironment where the tumor cell resides has an effect on the tumor behavior and that the original genetic makeup is not the only effector. In vivo invasion assay and multiphoton microscopy based intravital imaging has shown that the primary tumor in rodents have a subpopulation of tumor cells that respond to chemoattractants present in the microenvironment produced by perivascular macrophages. These tumor cells are highly motile and do not proliferate, imitating cancer stem cells and are resistant to conventional chemo and radiotherapy. Cell surface biomarkers CD44 and CD24 have been used recently to identify breast cancer stem cells, and it has also been shown that these cancer stem cells can initiate a tumor and cause metastasis. We are quantifying biomarkers of invasion previously identified in our lab and the above mentioned cancer stem cell markers in fine needle aspirates (FNA) from human breast cancer patients. We will correlate this observation with tumor microenvironment of metastasis scores on these patients.

This research will give rise to an assay which will identify which of the cancers will metastasize. Clinicians can use this quick, painless, and inexpensive technology to test the potential metastatic nature. This technology can be applied to many different stem cells and invasion markers.

Student Researcher
Robert Stobezki is a senior majoring in Biology at Yeshiva University. For most of the past two years, he has been conducting research in Dr. Sumanta Goswami's laboratory at Yeshiva College. This experience has enriched his understanding of how scientific research is conducted and expanded his knowledge of advanced research techniques. Upon graduating from Yeshiva College and the Honors Program, he aspires to obtain a PhD in Biology in order to pursue a career in biomedical research.
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Cancer Biology
SUMO Proteins are Involved in Proliferation of Normal and Cancerous Spermatogenic Cells

by

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Spermatogenesis is a complex process of germ cell development occurring in the seminiferous tubules of the testis. For unknown reasons, the incidence of testicular cancer (the most common cancer tumor in American males between 15 and 34 years of age) has almost doubled since the 1930s and continues to increase, although effective treatments have led to a decline in mortality.

SUMO-small ubiquitin-like modifiers are a family of ubiquitin-related proteins implicated in a variety of cellular events including modulation of transcriptional activity, chromosome integrity and functions, DNA repair process, and nuclear-cytoplasmic transports. Importantly, SUMO has been implicated in the control of mitotic progression. Furthermore, literature has indicated that SUMO proteins play a role in the development and progression of cancer in different tissues. SUMO proteins have recently been localized to different types of testicular cells, however, the function of SUMO during spermatogenesis and its possible role in pathophysiology of testicular cancer remains unknown. This study aimed to investigate the possible role of SUMO in the proliferation of normal and cancerous spermatogenic cells.

Overexpression of SUMO2 gene in spermatogonia cell lines resulted in an increased proliferative activity of these cells as judged by using a proliferative marker PCNA. Experiments that employed tissue arrays with multiple cases of seminoma (a type of testicular cancer) and anti-SUMO antibodies, showed high level of SUMO expression in seminomas. Furthermore, different localization patterns were observed in different patients. A Western blot confirmed the high SUMO level observed in the seminoma samples. Finally, using the PCNA marker and the Western blot analysis the level of SUMO expression in seminomas was found to be positively correlated with the level of the proliferative activity of the tissues.

Together, our results suggest that SUMO may play a role in proliferation of normal and cancerous spermatogenic cells, and that SUMO may probably be used together with other markers to assess proliferation activity and, therefore, progression of seminoma. Further studies of different localization patterns observed in patients with seminoma may result in development of methods for more specialized treatment for testicular cancer patients in the future.

Student Researcher
Sahar Zaghi is a senior in Stern, majoring in Biology. She wishes to pursue a career in Reproductive Endocrinology. Alternatively, Sahar would love to be a photographer for *National Geographic* and hopes to beat Tirtza Spiegel by climbing Mt. Everest before she is 30. Also, contrary to popular belief, Sahar's first language is English.
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Cell Biology
Remodeling of the Actin Cytoskeleton in Cultured Endothelial Cells Exposed to Hyperoxia

by

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Premature infants are routinely treated with high levels of oxygen, in order to improve tissue oxygenation. It is well known, however, that hyperoxia ultimately causes lung damage and chronic respiratory insufficiency. Studies using cell cultures have demonstrated that hyperoxia causes visible changes in cell morphology.

One of the major factors in determining cell shape is the actin cytoskeleton. Actin can exist in a globular, monomeric form (G-actin), or polymerize into long filaments (referred to as filamentous F-actin). The actin filaments can further bundle together into long, sturdy stress fibers. The location and length of these fibers determine the morphology of the cell. We hypothesize that hyperoxia-induced reactive oxygen species (ROS) alters the actin cytoskeleton and shifts the equilibrium between polymerized filamentous actin and monomeric globular actin. The mechanism by which actin is reorganized by hyperoxia-induced ROS remains unknown.

Human umbilical vascular endothelial cells (HUVEC) were incubated overnight with an adenoviral vector coding for manganese superoxide dismutase (SOD). Control cells were transfected with LacZ coding adenoviral vectors. Dishes were placed in either room air (21% O_2), 3 days of hyperoxia (95% O_2/5% CO_2) or 5 days of hyperoxia. Using fluorescence microscopy, we found that the F-actin/G-actin ratio within stress fibers decreases during the course of hyperoxia and that SOD appears to restore the F-actin to G-actin ratio to normal. We also found that the cells become more stretched out and spindle shaped during hyperoxia, and that SOD appears to restore the morphology to normal.

Clinical Medicine

Use of A Collagen Microscaffold Dressing* to Reduce Postoperative Donor Site Pain: A Pilot Study

by

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Introduction

Back pain, a common cause of morbidity in adults, is an uncommon complaint in children. In adults, obesity and back pain are clearly related. The relationship between lumbar spine abnormalities and increased BMI in children is poorly established.

Methods

Investigator-initiated, IRB approved controlled prospective pilot to evaluate postoperative pain at split thickness donor sites of burn patients comparing treatment with collagen microscaffold wound dressing* plus hydrocolloid overlay, to hydrocolloid standard care alone, utilizing a single-blinded matched pairs randomized design. Subject is unaware as to which of two donor sites receives the investigational layer* under the standard of care. Main outcome measure: subject's self-assessment of each site using Numeric Pain Intensity Score (NPIS) at twice daily intervals through Postoperative Day (POD) 5. Eligibility: >18 years old; 2 separate donor sites; can provide informed consent; can complete NPIS; & <40% TBSA.

Results

3 subjects to date (target=10); mean age 60 yrs, (57-63 range); 2 male & 1 female. 2 of 3 subjects demonstrated reduction/elimination of pain (0-1) at the investigational* site immediately & consistently through POD5, whereas the standard of care alone ranged between mild-most severe pain (3-10) for half the assessments through POD5. One subject rated the investigational* site either equal to standard of care alone or slightly worse by 1-2 points.

Conclusions

Preliminary pilot data suggest that use of the collagen microscaffold* in conjunction with standard of care hydrocolloid ameliorates postoperative donor site pain.

*Product Notation

Puracol plus Ag Collagen Microscaffold Wound Dressing, Medline Industries, Mundelein, Illinois

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Clinical Research

Lumbar Disc Disease in Adolescents: MRI Abnormalities in Normal and Overweight Children

by

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Background

Back pain, a common cause of morbidity in adults, is an uncommon complaint in children. In adults, obesity and back pain are clearly related. The relationship between lumbar spine abnormalities and increased BMI in children is poorly established.

Objective

To assess the prevalence of lumbar spine MR abnormalities in adolescent children presenting with a traumatic back pain and to evaluate the relationship between Body Mass Index (BMI) and lumbar disc disease in these children.

Methods

602 consecutive lumbar spine MRI examinations performed in children, ages 12-20, for evaluation of back pain at a University Children's Hospital over a four-year period were retrospectively reviewed. Patients with scoliosis, tumor and trauma were excluded. Images were reviewed by a board-certified neuroradiologist, and the following criteria were assessed: presence of lumbar disc disease, presence of multi-level disease, nature of disc disease (one or more of: disc desiccation, disc space narrowing, disc protrusion, disc bulge), facet joint disease, spondylolysis and spondylolisthesis. When available from the electronic medical record, patient height and weight were used to compute age-corrected (BMI) and weight-for-age quartiles were calculated. Descriptive statistics and chi-square analysis were used to evaluate the significance of between-group differences.

Results

188 patients met inclusion criteria. Only 48% (91/188) of patients had a normal lumbar spine MRI. 52% (97/188) of patients had identifiable disease on lumbar spine MRI, of which 94% (91/97) showed lumbar disc disease. Six patients had non-disc related abnormalities, including 3 patients with isolated spondylolysis, two with isolated facet joint disease, and one with Scheurman's khyphosis.

Data were available to determine BMI in 108/188 patients. Among these patients, 49% (53/108) had BMI greater than the 75th percentile for age, and 51% (55/108) were below the 75th percentile. 41% of patients (44/108) were considered either clinically "obese" or "at risk for obesity", with BMI greater than 85% for age. Among patients with BMI greater than 85%, 64% (28/44) demonstrated MRI evidence of lumbar disc disease. Among patients with lower BMI, 44% (28/64) showed MR evidence of lumbar disc disease. There was a statistically significant higher incidence of lumbar disc disease between the incidence of lumbar disc disease between patients who were either obese or at risk for obesity when compared to those with lower BMI ($p=0.0338$).

Discussion

There is a high incidence of MR abnormalities of the lumbar spine in adolescent children presenting with back pain. There is a strong relationship between increased BMI in this population and the incidence of lumbar disc disease. This represents further evidence of end-organ damage associated childhood obesity.

Student Researcher
Jordana Schneider is a junior at Stern College for Women. She is double majoring in Biology and Psychology. She hopes to perform research on the therapeutic benefit of stem cells with the hopes of discovering a cure for many diseases.
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Clinical Research
Time to First Dose Oral Antipsychotics on Behavioral Medicine Units

by

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Huron Hospital is home to a 30-bed Behavioral Medicine Unit and a 10-bed Inpatient Detoxification Unit. Currently, the hospital utilizes the MyPractice/Epic System with a computerized physician order entry (CPOE) system to order, verify, and document medication administration. In addition, the two units are equipped with Pyxis MedStation, an automated dispensing cabinet (ADC), to facilitate medication administration. In the fall of 2009, Huron Hospital's Behavioral Medicine Unit is scheduled to receive Pyxis Profile, a software upgrade to the current ADC, aimed to reduce the time between prescription order entry and medication administration. This study was conducted as a retrospective chart review to evaluate the current delivery process of medication before the new software is installed. Data was collected retrospectively from the electronic Medication Administration Record (eMAR) and pharmacy dispensing history; this data included subject admission time, prescription order time, pharmacist verification time, and medication administration time. 100 charts were reviewed from subjects admitted to the two units between 3/21/09 and 6/4/09. The results were calculated to be the following:

Order Entry to Medication Administration	3 hrs. 54 min.
Order Entry to Pharmacist verification	5 min.
Pharmacist verification to Medication Delivery	45 min.
Delivery to Medication Administration	3 hrs. 4 min.

A similar study is recommended, after the installation of Pyxis Profile, to assess the impact of the software. This secondary study should be done 5 to 6 months after the implementation of the software, to allow for new data to be available. All inclusion criteria should be maintained.

Student Researcher
Helen Ayala Unger is a freshman at Stern College for Women planning to major in Biochemistry and minor in Mathematics. She aspires to be a researcher or physician-scientist, and is particularly interested in diabetes prevention and research. She enjoys reading, knitting, and making jewelry in her spare time.
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Endocrinology
Glucagon-Like Peptide-1 Receptor in Human Ovary

by

Kate Rosenblatt[1], Esther Feder[1], Rachel King[1], Sarah Ezaoui[1], Michael Goldman, M.D.[2], Takako Araki, M.D.[2], Miroslava Varadinova, M.D.[2], Pauline Suwandhi, M.D.[2], Yun Feng, M.D.[2], Amit Seth, M.D.[2] and Donna Seto-Young, Ph.D.[2]

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The glucagon-like peptide-1 (GLP-1) receptor is found in the gastrointestinal gut and also widely distributed in various tissues. Exenatide is an incretin hormone, which is an analog of the GLP-1 receptor. GLP-1 is secreted by the endocrine cells in the epithelium of the small intestine, in response to glucose, stimulating the release of insulin.

We attempted to determine if the GLP-1 receptor is present in human ovary cells. Seto-Young and colleagues established that the human ovarian tissue culture contained granulosa, theca, and stromal cells. These cells were cultured in the presence or absence of insulin, with or without 25 or 50 pM exenatide. Cells were lysed and RNA was extracted using RNAqueous PCR extraction kit (Ambion). RT-PCR was performed using GeneAmp EZ r*Tth* RNA PCR kit (Applied Biosystems). Samples were preincubated at 62°C for 40 min., and then incubated for 45 cycles of 15 sec. at 92°C and 40 sec. at 62°C. Primers for GLP-1 receptor were designed for a 240 base pair product. Forward primer used was 5'- GTG TTC CCC TGC TGT TTG TT-3'. Reverse primer used was 5'- CTT GGC AAG TCT GCA TTT GA-3'. cDNA was separated on 2.5% agarose gel and stained with ethidium bromide, then placed on a UV transilluminator. A single band was found at approximately 240 bp in the control sample. Cells stimulated with exenatide showed a band with increased intensity in a dose dependent fashion. Cells stimulated with insulin showed a band with increased intensity in a dose dependent fashion. However, the GLP-1 receptor mRNA expression is very low.

Steroid hormone concentrations in the tissue culture medium were measured using enzyme-linked immuno-sorbent assay (ELISA) (Alpco Diagnostics) or radioimmunoassay (RIA) (Diagnostic Systems Laboratories). Cells were cultured with appropriate steroid hormone substrates (30 µM pregnenolone, 15 µM DHEA, 3 µM testosterone or 3 µM androstenedione) in the presence or absence of insulin, with or without 25 or 50 pM exenatide. Exenatide stimulated progesterone by 18%. However, exenatide had no significant effect on testosterone or estrogen production.

The GLP-1 receptor is present in the human ovary, and is increased in dose dependent fashion by stimulation with exenatide, as well as stimulation with insulin. However, GLP-1 receptor expression is much lower than other steroidogenic enzymes such as steroidogen acute regulatory protein (StAR) or 3-β- hydroxysteroid dehydrogenase (3-β-HSD). GLP-1 receptors are stimulated by exenatide and insulin. Exenatide stimulated progesterone production by 18% and had no significant effect on testosterone and estrogen production. The role of GLP-1 receptor in human ovary requires further investigation.

Student Researchers

Esther Feder is a Junior at Stern College majoring in Biology. She has a clinical interest in adolescent medicine and aspires to become a physician. Esther loves sports and enjoys playing basketball and spending time with friends. *efeder1@yu.edu*

Kate Rosenblatt is currently a pre-med sophomore at Stern College for Women in New York City, and is majoring in Psychology. Although passionate about her medical aspirations, she also gets excited about reading classic literature and spending time with her family and friends.
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Rachel "Tzippi" King is a Biochemistry major and Music minor at Stern College. She enjoys singing and playing the harp in her free time. After graduation, Rachel hopes to attend medical school.
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Game Theory
Terminal Games with 3 Terminals Have Proper Nash Equilibria in Pure Positional Strategies

by

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We consider a graph G that consists of a set of vertices {V1, V2,...,Vn}, each with an associated player and set of outgoing edges. We call vertices *terminal* if they have no outgoing edges. The *play* is a collection of edges going out from each non-terminal vertex, and producing a unique path from the origin to either a terminal or a cycle (the *outcome*). The *payoff function* associates a certain value to each combination of player and outcome, that is, each player has his own ranking of preferred outcomes. We say that a game has achieved *Nash Equilibrium* if no player can switch the chosen edges out of his nodes to achieve an outcome preferable to the current one. We call this equilibrium *proper* if it does not terminate in a cycle.

In *On Nash-solvability in pure stationary strategies of finite games with perfect information which may have cycles*, Boros and Gurvich show that every connected game (that is, every game with some path from the origin to a terminal vertex) with 2 players or 2 terminal vertices has some proper Nash Equilibrium. We prove that any n player, 3-terminal game can be reduced to an n-1 player game by fixing the edges out of one player's vertices, in such a manner that the given player has no incentive to switch from the fixed edges. Using this conclusion, we prove that every game can be reduced to an equivalent 2-player game with the same Nash Equilibrium. We thereby inductively prove that every connected 3-terminal game has some proper Nash Equilibrium.

References

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Acknowledgements
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Student Researcher
Robert Rand is majoring in Mathematics and Computer Science at Yeshiva College. He intends to attend graduate school in one of the two disciplines and plans on solving the P = NP problem as soon as he hears back from a certain travelling salesman.
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Genetics
Population Genetic Consequences of Prairie Fragmentation

by

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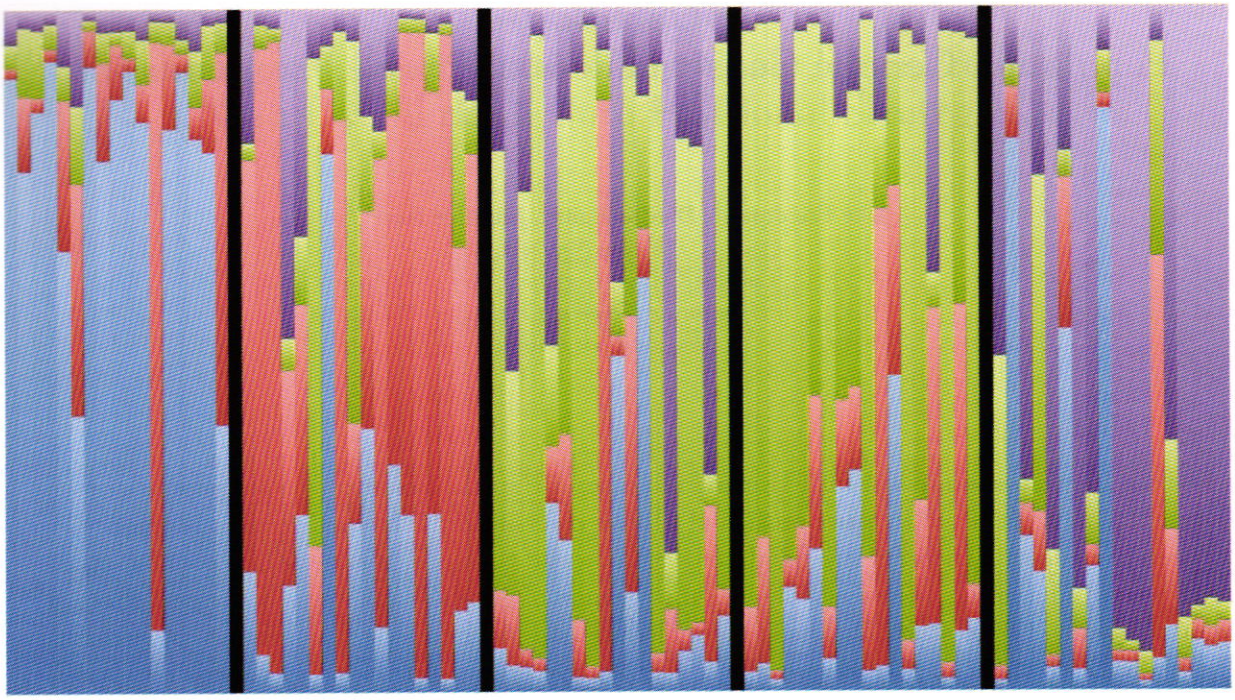
Habitat fragmentation reduces the size and increases the spatial isolation of plant populations. Fragmentation is predicted to cause erosion of genetic diversity and increased genetic divergence between populations. Theoretically, the diminished size and gene pool of fragmented populations disrupts genetic equilibrium in several ways: By the creation of genetic bottlenecks, increased effect of random genetic drift, elevated likelihood of inbreeding, and reduced gene flow between populations. These effects of fragmentation concern the conservationist because of their implications for species persistence. The resultant loss of heterozygosity and allelic richness can reduce population viability and limit a species' ability to respond to changing selection pressures.

Our investigation attempted to gauge the population genetic consequences of habitat fragmentation in prairie remnants in western Minnesota on a model prairie plant. Historically, the prairie was continuous across the sites, comprising one enormous population. The fragments we tested are the scattered remnants of the original population. The genetic effects of fragmentation are measured by three of its consequences: Inbreeding and fitness, population genetic diversity, and interpopulation genetic divergence.

As our study species, we selected the narrow-leafed purple coneflower, *Echinacea angustifolia* (Asteraceae). *E. angustifolia* is a model prairie species. It is long-lived, pollinated by native pollinators, and it prohibits self-fertilization and fertilization by close relatives. It is a common plant native to the tallgrass prairie and plains of North America.

Using SPAGEDI and STRUCTURE, statistical computer software for the assessment of population genetic parameters, we observed significant deviations from Hardy-Weinberg equilibrium in four of our nine study sites. This indicates that these populations have been subject to the effects of genetic drift. The eventual effects of genetic drift include an increasing expression of deleterious alleles and a loss of adaptive evolutionary potential. No significant loss of fitness or increase in inbreeding was observed, though this is likely because of *E. angustifolia's* long lifespan. To combat the effects of this genetic drift, efforts to restore gene-flow between subpopulations are now underway.



Study Site 1 Study Site 2 Control Study Site 3 Study Site 4

STRUCTURE uses a Bayesian algorithm to introduce population structure within a group of individuals. The software attempts to assign population groupings that, as far as possible, are not in genetic disequilibrium.[1] The results of the STRUCTURE simulation performed on our samples are illustrated above. Each column in the chart represents one individual. The likelihood of its assignment to each of the introduced genetic clusters is represented by its color.

Student Researcher
Jacob Friedman is a Philosophy major and Biology minor at Yeshiva College. He is especially interested in the intersection of Philosophy, Literature, and Theology, though he anticipates abandoning such pursuits as he makes his way toward medical school and a career in surgical medicine.
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Genetics
Investigating the Role of *Tbx1* in Chondrogenesis of the Periotic Mesenchyme

by

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Tbx1 is a transcription factor of the T-box family whose haploinsufficiency has been implicated in velo-cardio-facial syndrome/DiGeorge syndrome in human patients. *Tbx1* -/- mice exhibit severe defects in structures of the outer, middle, and inner ear. Since *Tbx1* is expressed in both the otic vesicle (OV) epithelium as well as the periotic mesenchyme (POM) surrounding the inner ear, we utilize a conditional mutant approach to dissect the roles of *Tbx1* in both of these domains. When *Tbx1* is ablated specifically in the POM using TCre to inactivate a floxed *Tbx1* allele (TCre KO), defects in structures derived from both the OV and POM are apparent; including a shortened cochlear duct and smaller cartilaginous otic capsule surrounding the cochlea. This suggests both signaling to the OV as well as defects in the POM cells themselves contribute to the phenotype. We hypothesize that loss of *Tbx1* in POM leads to premature chondrogenesis and thus prevents the cochlea from properly coiling. To test this hypothesis, we have successfully synthesized antisense riboprobes to assay for expression of chondrogenic markers (*Sox5, Sox6, Sox9, Col9a2, Col11a2, Mia1, and Pbx1*) via whole mount *in situ* hybridization. These probes will now be used to test for premature initiation of chondrogenesis in the POM of TCre KO embryos. This data will help us to better understand the molecular basis of hearing loss in both model organisms and human patients.

Acknowledgements

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Immunology
Endocannabinoid Protein Expression in Human Immunodeficiency Virus Encephalitis

by

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Cannabinoid receptors 1 and 2 (CB1 and CB2, respectively) are part of the endocannabinoid system along with intracellular enzymes (such as fatty acid amide hydrolase, FAAH) that degrade endocannabinoid ligands. Exogenous cannabinoids are potential therapeutics for treating neurological sequelae in HIV-infected patients because cannabinoids can suppress the immune system. Human immunodeficiency virus encephalitis (HIVE) is a pathological correlate to HIV-associated dementia, a condition that occurs in some HIV-infected individuals. Recently, Benito et. al. reported that CB2 receptors are upregulated in simian immunodeficiency virus encephalitis, a model for HIVE. We therefore sought to explore endocannabinoid protein expression in HIVE. We obtained paraffin-embedded human autopsy brain tissue sections from the National NeuroAIDS Tissue Consortium and divided them into four groups, HIV-seronegative (HIV-, n = 6, HIV-seropositive without brain pathology (HIV+, n = 12), HIV-seropositive with encephalitis (HIVE, n = 4) and HIV+ with co-infections/co-morbidities (HIV+/Coinfection, n = 5). Tissue sections were subjected to immunohistochemistry with several antibodies: anti-CB1, anti-CB2 and anti-FAAH. Immunolabeled sections were analyzed with microscopy and analysis of digital images was performed. Results indicate that CB1 and FAAH are present in neurons in all cases, while white matter CB1 staining in HIVE and HIV+/Coinfection cases was significantly above control levels. CB1 is upregulated in glia and perivascular macrophages based on morphology. Staining for CB2 illustrated immunoreactive perivascular macrophages, astrocytes and some microglia. Our results indicate that cannabinoid receptors are strongly expressed in HIVE brains and this may inform clinicians who are considering cannabinoids as adjunctive therapies for HIV-associated neurologic disorders.

Acknowledgements

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Student Researcher

Avital Bauman is a senior majoring in Biochemistry. She is President of the Student Medical Ethics Society and participates in the Women's Leadership Fellowship. Avital enjoys visiting art museums and traveling abroad, and she will be participating in Columbia University's cross-cultural bioethics trip (BioCEP) to Thailand this summer.
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Immunology
Constructing a Transgenic S2 Drosophila Cell Line Engineered to Express Potential T Cell Coinhibitor Protein

by

Chayim Goldberg
Research mentor: Xingxing Zang, MD, PhD,
Albert Einstein College of Medicine, Department of Microbiology and Immunology
Period of research: August 2008 - June 2009

Background

One of the more recent and most promising fields of research in immunology has been that of T-cell costimulation and coinhibition. In order for a naïve (non-activated) T cell to begin proliferating into differentiated effector cells that will actively recognize a specific antigen, two interactions must occur. First, the T cell receptor (TCR) must recognize an antigen being presented on the major histocompatibility complex (MHC) of an antigen-presenting cell (APC). Second, the CD28 receptor on the Tcell must be presented with a costimulatory protein from the B7 family. Without this signal, the T cell will enter a state of anergy (non-responsiveness to antigens) as the IL-2 gene, which is necessary for the T cell's clonal expansion, is regulated by signals derived from both the TCR and CD28 pathways. At the same time, T cell differentiation and clonal expansion is kept in check by coinhibitory signals and pathways, without which a massive overgrowth of T cells would result.[1] Receptors such as CTLA-4 and B7 family-member signals such as B7x and B7-H3 limit the production of IL-2, thus limiting effector-cell proliferation. As coinhibitory signals such as B7x, PD-L1, and B7-H3 have been found to be produced by APCs, tissues, and tumors, discovering their exact mechanism of action and ways to manipulate their expression holds much promise in the fields of cancer biology and autoimmunology.[2]

Goal and Methods

Under the tutelage of Dr. Xingxing Zang, my project was to produce monoclonal antibodies to target a protein titled "B7y" which is similar to B7x, a known coinhibitor. Antibodies to B7y would allow for the determining of the actual function of this protein as well as its source of production. In order to do produce these antibodies, a purified quantity of the B7y protein needed to be produced, which could be sent to a mAB facility. The strategy devised to produce this purified protein was to construct a plasmid consisting of a PMT expression vector (specifically designed for protein expression in S2 drosophila cells) with the B7y gene inserted into the multiple cloning site (MCS) and transfect this PMT-B7y construct into S2 immortal drosophila cells by means of Fugene 6 cationic transfection reagent. The transfected cell line was grown for one month and expression was then induced via replacement of growth-media with serum-free media and $CuSO_4$. The resulting protein was to be collected by means of affinity chromatography. The initial B7y gene insert was cloned by means of PCR and miniprep purification from transformed competent E coli cells.

1 K. Murphy, P. Travers, M. Walport: Janeways's Immunobiology 7th ed. (New York, Garland Science, 2008) p.346
2 Xingxing Zang and James P. Allison, Clin Cancer Res 2007;13(18) September 15, 2007

Results

While the construction and cloning of a PMT-B7y plasmid was confirmed to be successful by means of PCR screening and sequencing, the establishment of a stable transfected S2 cell line was not and no protein was present upon inducing expression and running the media through an affinity chromatography column. Further attempts beyond my time in the Zang lab have proven equally unsuccessful and investigations are currently being done to determine the reason for the inability of the S2 cells to express the B7y protein.

Student Researcher

Chayim Goldberg (YC 09, Biology and Jewish Studies) is currently an adjunct instructor, teaching a Principles of Biology Lab in YC and will begin his PhD studies at the Albert Einstein College of Medicine this coming August.

Medicine: Anaesthesiology
The Effects of Leaks in Masks During Preoxygenation

by

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Preoxygenation refers to filling the lungs with oxygen prior to inducing anesthesia and paralysis. The lungs act as an oxygen reservoir in case there is a significant amount of time between anesthetization and intubation. Ideal preoxygenation is achieved when the patient breathes 100% oxygen from a sealed mask for three to five minutes. This effectively replaces most of the nitrogen within the lungs with oxygen. Preoxygenation effectiveness is reduced if there is a leak between the mask and the face which allows the entrainment of air. If there is not a tight seal, such as in the case of a leak, optimal preoxygenation will not occur. The objective of this experiment was to quantify the effects of small leaks on the effectiveness of pre-oxygenation. Our aim was to use calculated lung oxygen concentrations caused by the leaks to estimate the duration of apnea that could be tolerated without risking consequences of hypoxia.

Subjects were instructed to breathe 100% oxygen for three minutes, delivered through masks with leaks. The leaks were simulated by placing different sized straws (coffee stirrer and normal straw, respectively) between the mask and the subject's face. End tidal oxygen volume was measured using a Respiract™ machine.

Our research showed that the leaks significantly reduced the fraction of inspired oxygen. With a coffee stirrer leak, the FiO_2 during inspiration was 85%, while with the straw, the FiO_2 during inspiration was 50%. The data proved that the subject was inspiring both outside air and delivered oxygen, and demonstrated the importance of having a tightly sealed mask during preoxygenation.

Student Researcher
Ari Cuperfain is currently in his first year at Yeshiva Colleg with plans to double major in Chemistry and Biology. In particular, he is interested in the chemical pathways of the heart. Ari is also a member of the Chemistry Club and philosophy, learning about science, and helping others.
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Medicine: Surgery

Transradial Puncture for Upper Extremity Hemodialysis Fistula Intervention: Early Experience

by

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Purpose

To report our experience using transradial access during interventional procedures for dysfunctional upper extremity hemodialysis fistulas.

Materials and Methods

15 interventions were performed utilizing the transradial approach in 12 nonconsecutive patients with dysfunctional or non-maturing fistulas (12 thrombosed, 5 female, age 44-91). 4 patients had radiocephalic fistulas, 4 brachiocephalic fistulas, and 4 brachial-basilic fistulas. Balloon angioplasty was done in 14, and stent placement in 5. In 5 procedures, rt-PA was administered for declotting; heparin was used in 3 procedures. Sheath sizes were 4F (n=8), 5F (n=6), 6F (n=5), 7F (n=3), 8F (n=1), 9F (n=1). Manual compression with a Tip Stop (Gambro; Lakewood, Colorado) bandage was used as the primary means for hemostasis in all cases.

Results

Transradial puncture using micropuncture (21G needle) technique was successful in 100% (15/15) procedures. Anatomic success (<30% residual stenosis) was 93.33% (14/15) and clinical success rate (resumption of successful hemodialysis) was 86.87% (13/15), including initial failures. In one intervention, the patient was found to have occlusion of the upper cephalic vein preventing declotting. In a second case, the patient's radiocephalic fistula failed following intervention due to acute thrombosis prior to hemodialysis. There was one complication due to a postangioplasty vein rupture, treated with a PTFE covered stent (Bard; Temple, Arizona). No radial puncture site complications or digital ischemia was observed.

Conclusion

Utilization of the radial artery is a safe and effective access for upper extremity fistula interventions. Use of Tip Stop bandage for hemostasis is inexpensive, and potentially preserves radial artery patency.

Student Researcher
Debra Zharnest is a junior at Stern College for Women majoring in English Literature. Debra takes great pleasure in writing and relishes the study of literature, particularly the satirical works of Shakespeare and Chaucer. She also has a deep rooted passion for Biology and medical research and currently serves as a clinical research assistant in the field of Radiation Oncology. Debra plans to pursue a career as a physician and hopes to one day combine her love of medicine and writing through medical journalism.
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Microbiology
Assessing the Radiotrophic Characteristic of Cryptococcus Neoformans

by

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Electromagnetic radiation is ubiquitous in our environment. When melanized, several genera within the fungal kingdom, including *Cryptococcus neoformans*, appear to be able to harness large doses of radiation and thrive in its presence. This radiotropism has been correlated with the presence of the pigment melanin within the fungal cell. Using an acapsular strain of *C. neoformans*, CAP67, we set out to further demonstrate that only melanized fungal cells are capable of responding positively to radiation. When grown in a minimal media containing L-Dopa, CAP67 is able to synthesize and incorporate melanin within its cell wall. Using melanized and non-melanized variants of CAP67, we performed Electron Paramagnetic Spin (EPR) spectroscopy of the samples illuminated with a white light source. We subsequently observed a significant increase in the strength of the EPR signal that was proportional to the time of illumination. These changes, which were significantly greater in the melanized samples spectra, demonstrate an alteration of electronic composition of the cell as a result of exposure to light. To further establish the radiotrophic tendencies of melanized CAP67, we also performed colorimetric assays of internal ATP levels. These assays were inhibited probably by a membrane-bound ecto-ATPase, and we suspect by inefficient lysis methods as well. Future assays will hopefully circumvent these issues and show a relationship between ATP levels and increasing radiation in CAP67. We also hope in the near future to do EPR spectroscopy on cell samples irradiated with ionizing radiation. Positive results would further support the hypothesis of melanin acting as a chlorophyll-like radiosynthetic pigment in fungal cells.

Student Researcher

Matthew Friedman graduated from Yeshiva College in January 2010 with a B.A. in Biology. He has a strong interest in biomedical research and bioethics, and hopes to channel these interests into a well-rounded career in clinical medicine. Matthew is also an avid runner and is training to run marathon-length distances in the near future.

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Molecular Biology
Novel Biosensor for Cdc42 – N-WASP Interaction, Based on Solvatochromic Dyes

by

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Cdc42, a member of Rho-family GTPase, regulates critical cellular functions including cell polarity maintenance and actin cytoskeleton rearrangement. Interaction of Cdc42 with one of its key downstream effectors, neuronal isoform of Wiskott Aldrich Syndrome Protein (N-WASP), has important implications with respect to cancer, where Cdc42-N-WASP binding plays a principal role in the establishment and function of invadopodia, invasive membrane extensions with matrix degrading activity vital for metastatic invasion of carcinoma cells. Studies utilizing fluorescent biosensors in live cancer cells have shown that N-WASP is active only at invadopodia, and does not impact normal cellular operations. Thus, inhibiting Cdc42-N-WASP interaction could be useful as a possible anti-metastatic therapy.

Based on previous research that detected endogenous Cdc42 activation in living cells by its binding to the Cdc42 binding domain (CBD) of hematopoietic WASP, we designed a new biosensor that uses the GTPase binding domain (GBD) of N-WASP. The derivatized GBD is attached to a solvent-sensitive dye that undergoes a great change in fluorescence emission intensity upon binding to activated, endogenous Cdc42. The new probe will be valuable in development of potential approaches for high-throughput screening of inhibitor libraries targeting Cdc42-N-WASP interaction, while minimizing spurious inhibition of hematopoietic WASP. Using recombinant DNA techniques, a novel biosensor for Cdc42-N-WASP interaction was produced and characterized in vitro.

Student Researcher
Fay Burekhovich is a fourth year Stern College student double majoring in Biology and Jewish Studies. She plans on becoming a physician, preferably in the field of neuroscience. In her free time, she enjoys working with special needs individuals and creating awareness about their conditions. One of her greatest wishes is to establish a special needs medical clinic.
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Molecular Biology
Elucidating the Toll Like Receptor Signaling Pathways of the Immune Response in Monocytes

by

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The innate immune response is initiated through diverse pathogen recognition receptors (PRRs) upon ligation with Pathogen Associated Molecular Patterns (PAMPs). Toll-like receptors (TLRs), a group of highly conserved and widely studied membrane receptors, recognize different components of microbes to generate a series of signals which lead to differential transcriptional activation and production of cytokines that will direct the immune response. The production of IL10, associated with a TH2 response, favors an overall anti-inflammatory response while production of IL12, IL 6 and Type I IFN often produce the TH1, inflammatory response.

The experiments conducted focused on TLR2 and TLR4 activation and perturbation of the mitogen-activated protein kinase (MAPKs) and IKK pathways shared by many PRRs. Three MAPKs, JNK, ERK, and p38, work in parallel to elicit a differential cellular response appropriate for the receptor pathway. While it is known that the these pathways contribute to differential IL12 and IL10 production in response to TLR2 and TLR4 activation, the mechanisms and criteria for the particular bias of cellular TH1 or TH2 response in not clear. Literature suggests that TLR4 may work more through the p38 pathway and less through the ERK pathway to produce more IL12 (TH1 inflammatory), while TLR2 signals through ERK to elicit more IL10 (TH2 anti inflammatory).

Thus, we hypothesized that inhibiting the ERK pathway in the TLR2 model would decrease its TH2 cytokines and bias it toward a TH1 response while inhibition of ERK, in the TLR4 model, would maintain its TH1 response bias. These receptor pathways are also known to produce maturation markers such as CD 80 and CD 86, which are necessary for T-cell interaction. Inhibiting many of the IKK and MAPK pathways should have an effect on the amount of maturation marker made and thus the effect the amount of interaction the DC will have with a T-cell.

This proposed mechanism toward biasing a TH1 or TH2 response was studied by RT- PCR analysis of up-regulation of cytokines after treatment with TLR2 or TLR4 agonist. Inhibition of MEK/ERK in U937 treated with LPS (TLR4 agonist) showed decreases in both genes for TH2 cytokines as well as increases in two of the three TH1 genes presented (Figure 2). This may be explained by supporting the TLR4 bias to TH1 theory. The cells treated with Pam3CSK4 (TLR2 agonist) show general decreases in their TH1 cytokines but general increases in their TH2 cytokines. If they were in fact ERK dependent, then inhibiting ERK should have shown an increase in TH1 and a decrease in TH2. Thus this data is partially inconclusive but nevertheless provides important insight into the inflammatory/anti inflammatory response.

With regard to CD 80 expression, the present data suggests that the IKK pathway is necessary for the production of CD80 and CD86 maturation markers. Inhibition of IKK leads to decreased expression of these markers and therefore decreased interactions with T-cells in the immune response.

Student Researcher
Jenny Deluty is a Senior at Stern College for Women, double majoring in Molecular Biology and Judaic Studies. In her free time, Jenny enjoys playing volleyball and has played for the YU Maccabees for 3 years. Jenny hopes to pursue her dream of becoming a doctor.
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Molecular Biology

Autophagy Involvement in Primary Cilia Growth in Mouse Fibroblasts

by

Jennifer Kraut[1], Birgit Satir[2], Peter Satir[2], Ana Maria Cuervo[2]
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Primary cilia are sensory organelles that display specific receptors and ion channels, which transmit signals from the extracellular environment via the cilium to the cell to control tissue homeostasis and function. These protrusions are formed in nearly all growth-arrested and differentiated cell types in vertebrates. Failure of an organism to form primary cilia may have devastating effects including certain human pathologies such as polycystic kidney disease and Bardet-Biedl syndrome.

Previous studies have shown that primary cilia formation is induced during starvation. Nutrient deprivation also activates the process of autophagy in cells. Autophagy is an intracellular process that results in the degradation of cytosolic components inside lysosomes in order to provide cells with nutrients during starvation. The fact that autophagy and primary cilia formation are occurring in the cell at the same time lead us to hypothesize that cellular components degraded through autophagy may be used as the building blocks for primary cilia formation.

To test this hypothesis, NIH3T3 cells, a type of mouse fibroblast, were grown in 10cm plates at 37°C until they reached confluence. They were then split into 12 well plates and some of the cells were grown in nutrient-rich media while others were grown in nutrient-deficient media for a period of 24 hrs. At the end of this time period, the cells were fixed with methanol and immunostained with antibodies against α-acetylated tubulin and *y*-tubulin in order to view their primary cilia and centrioles respectively under an immunofluorescence microscope. This same procedure was done for two additional NIH3T3 cell lines knocked-down for LAMP-2A or Atg7. Each of these cell lines is impaired for one type of autophagy, with the LAMP-2A (-) cells having a 95% reduction in chaperone-mediated autophagy (CMA) and the Atg7 (-) cells having an 80% reduction in macroautophagy.

It was expected that the mutant cells would not form primary cilia upon starvation if any of these types of autophagy is indeed required for their formation. However, we found that upon 24 hr. starvation both the control cells as well as the mutant cells are capable of forming primary cilia, allowing us to conclude that autophagy is not required for cilia formation. Interestingly, analysis of the length of the cilia in the control and the two mutant cell lines revealed that Atg7 (-) cells are capable of forming longer primary cilia (4-5μm) compared to control cells, whereas cilia in the LAMP-2A (-) cell line are shorter than in control cells. In addition, this last cell line displays long microtubule protrusions upon serum removal which do not appear in the control or in Atg7 (-) cells.

Based on these results, we conclude that primary cilia formation occurs independently of autophagy, however cilia elongation may require active CMA as cells with compromised CMA have shorter ciliary length. Future studies are needed to determine whether the cilia in each of the cell lines contain the same building blocks, such as PDGFR-α, which has shown to co-localize with the α-acetylated tubulin in the primary cilia in previous studies. Staining of primary cilia with those two antibodies in the cell lines deficient for macroautophagy or CMA will help us in identifying possible differences in cilia composition as result of changes in autophagy.

Student Researcher
Jennie Kraut is a senior at Stern College majoring in Biology and minoring in Women's Studies. In addition to being strongly involved with Yeshiva University's Medical Ethics Society as well as the Stern Biology club, her passion for scientific research has lead her to accept a Roth Scholars position this summer at Einstein. In her free time, Jennie enjoys running both competitively on the Stern Cross Country team as well as leisurely and hopes one day to run a full marathon.
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Molecular Biology
Gap Junction Remodeling and Post-translational Phosphorylation of Connexin43

by

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The gap junctions that connect cardiac cells to one another play a crucial role in the proper electrophysiology of the heart. Cardiac arrhythmias, including the ventricular tachyarrhythmia that leads to cardiac death, are thought to occur largely due to Gap Junction Remodeling (GJR) that occurs in response to various stimuli, such as high pressure and ischemia. Connexin 43 (Cx43) is the main cardiac gap junction protein so abnormal expression and function of this protein increases susceptibility to spontaneous tachyarrhythmias. The inhibition of Casein kinase-1 (CK1), which phosphorylates Cx43 at Serines 325, 328 and 330, results in the accumulation of Cx43 in the plasma membrane and thus a decrease in the amount of Cx43 at the gap junction locations.

The goal of this research was to establish that CK1-dependent phosphorylation of Serines 325, 328 and 330 of Cx43 is necessary for normal transporting of Cx43 to the gap junctions. The loss of this phosphorylation should play an important role in gap junction remodeling.

Two types of genetically engineered mice were prepared: Serines 325, 328 and 330 were substituted with negatively-charged glutamic acid to mimic permanent phosphorylation (S3E Knock-in mice) and were substituted with uncharged alanine to create an unphosphorylatable site (S3A Knock-in mice). The transgenic mice were compared at baseline and in response to muscle-weakening stimuli such as the Langendorff Ischemia Model and Transverse Aortic Constriction (TAC). Immunofluorescence was used to view changes in the amount of Cx43 in the transgenic mice as well as after stimuli by comparing the amount of Cx43 relative to the amount of n-Cadherin, a transmembrane protein. The S3A control exhibited less Cx43 than both the wild-type (WT) and S3E mice. After 30 minutes of Global Ischemia there was a decrease in the amount of Cx43 in all three samples relative to baseline, with the S3A mouse exhibiting the least amount of Cx43. After 2 weeks of TAC, S3A exhibited the least amount of Cx43. The WT sample, post 2-weeks of TAC, also presents evidence of the theory of lateralization, in which Cx43 that does not reach the gap junctions lies along the surface of the membrane.

Student Researcher
Danielle Lent is in her third year at Stern College for Women majoring in Biochemistry and minoring in English literature. She aspires to become a physician and is currently leaning towards pediatric cardiology. Additionally, she intends to read all the literary classics — defined as novels to which there are Sparknotes.
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Molecular Biology
Interactions Between Microtubules and Kinesin-13

by

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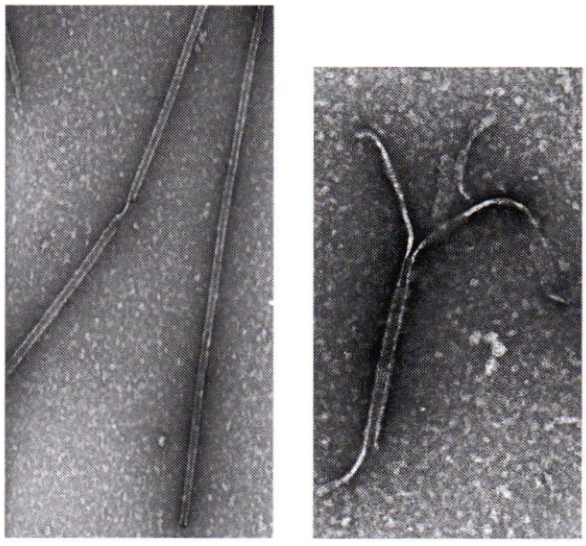
Kinesin, a superfamily of molecular "motors", uses ATP (adenosine triphosphate) to propel itself along microtubules. Kinesin-13's behave differently than other families, such as kinesin-1, and do not undergo unidirectional movement. Instead, they diffuse to the ends of the microtubules where they induce depolymerization. Microtubule depolymerization is an essential component of chromosomal segregation during mitosis. Kinesins are made up of three main components: a motor domain, neck, and coiled coil. The motor domain, which serves as the location for microtubule and ATP binding, is the minimal domain necessary for the depolymerization activity of kinesin-13's.

The mechanism by which kinesin-13's depolymerize microtubules is believed to involve the curving of tubulin protofilaments at the microtubule ends. We examined the interactions between kinesin-13 and microtubules in the ATP hydrolytic cycle using various nucleotide conditions. Previous research has shown that conditions of high affinity of kinesins for microtubules produce a regular protein-microtubule decoration pattern. Electron microscopy, from ongoing studies in this lab, revealed that in the presence of AMP-PNP (adenosine-5′-([β,γ]-imido)triphosphate), a non-hydrolyzable ATP analogue, some kinesin-13's form oligomeric rings and spirals around microtubules. We are currently exploring KLP59D, which does not to form rings during depolymerization. Surprisingly, we have found that this kinesin-13 removes tubulin from the interior microtubule lattice, a phenomenon not previously described for kinesin-13. In addition to initiating depolymerization at the ends, KLP59D cuts microtubules in the middle. These experiments are the first to demonstrate such findings, shedding light on the mechanism of kinesin-13 activity.



(a) (b)

Figure 1. D. melanogaster Kinesin13 KLP59D FL
(a) Severing of microtubules in the presence of ATP
(b) Depolymerization in ATP.

Student Researcher

Emily is a senior at Stern College for Women whose love of science has led her to major in Biochemistry. She is grateful to have been involved in various research projects during her time at Stern, the first of which was in the laboratory of Dr. Harvey Babich, Professor of Biology at SCW. She hopes to pursue a career in medicine with hopes of conducting research in the future as well.

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Molecular Biology
Identification and Quantification of Peptides in Hippocampal Tissue of PC7 Knockout Mice

by

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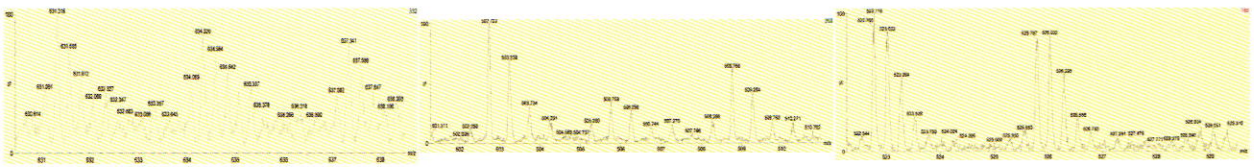
Pro-protein convertases (PCs), proteases that cleave peptide precursors to their intermediate forms, are implicated in multiple pathologies, including cancer, obesity, diabetes and neurodegenerative diseases. To investigate their individual functions, knockout (KO) mouse models have been developed for all nine PCs, with resulting phenotypes ranging widely from no observable effect to embryonic lethality. Only for the PC7 KO has no phenotype has been observed. To determine whether levels of peptides in hippocampal tissue underwent changes in PC7 KO mice, a peptidomics method was used to identify native forms of peptides and quantify their levels. Samples of hippocampal tissue from five wild-type mice and three PC7 KO mice were labeled with isotopic tags and then combined and analyzed with a mass spectrometer, and relative peak intensities were used to determine abundance of the peptide. Twenty-four peptides were identified; of those, ten were neuropeptides or other secretory pathway peptides, and the rest were from cytosolic proteins. Seven secretory pathway peptides as well as two other peptides showed a decrease in the KO mice, indicating that PC7 may, to some extent, play a role in peptide processing. Variable decreases in different forms of the same peptide imply that PC7 is involved at the level of post-translational modification. Further studies of peptide changes in PC7 KO animals are needed to replicate these results with additional animals and to examine other brain areas, with the goal of ultimately confirming the function of PC7 and potentially elucidating the mechanism of its processing capabilities.



(a) **(b)** **(c)**

Fig. 1 (a) No change in KO. The peaks are approximately the same height, indicating no down-regulation in the KO. Peptide was identified as a myelin basic protein fragment (Ac-ASQKRPSQRSKYLATASTMD) (b) Decrease in KO. The middle peak (KO) is substantially lower than those on either side. Peptide was identified as a proenkephalin fragment (YGGFMRF) (c) Variable controls. The control groups are not of uniform height, even considering that WT-1 was a pool of 3 mice and WT-2 a pool of 2 mice. Thus, levels of this peptide, a myelin basic protein fragment (Ac-ASQKRPSQRSKYLATA), vary from mouse to mouse.

Student Researcher
Chava Ruderman is a senior at Stern College for Women, majoring in Biology. She plans to become a physician with a focus on preventative medicine, particularly in the area of nutrition, and hopes to be an active participant in global health initiatives. Chava enjoys writing and playing piano, and would like to learn Spanish someday.
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Neurology
Headaches (HA) in Children and Adolescents (C/A) with Neurofibromatosis Type 1 (NF-I)

by

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Objectives

To provide additional data regarding HA in C/A with NF-1.To determine if NF-1 patients with abnormal MRI's have a higher frequency of HA then those patients with normal scans.

Background

NF-1 is an autosomal dominant disease associated with both CNS and systemic disorders that predispose to HA. These disorders include tumors, vascular abnormalities, hypertension secondary to renal artery stenosis, and pheochromocytoma. Although HA are thought to be more frequent in patients with NF-1, the data is limited and contradictory.

Methods

A literature review of HA in patients with NF-1. Review of 200 patients positively diagnosed with NF-1 in Cleveland Clinic between ages 6-18 years. Telephone interviews clarified data when necessary. MRI scans were reviewed. The HA frequency in those with normal scans were compared to those with abnormal scans.

Results

The literature suggests that 10-30% of patients with NF-1 have HA. These frequencies do not differ significantly from population controls.

Literature Review				
Study	# pts.	# HA	M/F	Mean Age
F Demario Jr.	132	62	25/56	16.5
A Creange	158	28	66/92	33
RAC Hughes	103	2	-	-
M Clementi	181	55	82/99	22
JM Friedman, PH Birch	1746	448	889/857	11.3

Of our 200 pts / avg age 12.9 years, M/F=114/86, 138 experienced No HA. 62 (31%) had HA (M/F=37/25). 31 (15.5%) were episodic migraine, 19 (9.5%) TTH, 8 (4%) Chronic Daily HA, 4 (2%) mixed HA.

Evaluation of MRI scans, 112 normal, 61 abnormal, and 27 insufficient data. There was an insignificant increased frequency of HA in patients with abnormal scans.

Conclusions

We concluded that the NF-1 population is no more subject to headaches than the general population. Headache is not a direct result of the systemic or intracranial effects of NF-I both in the overall NF-1 population and in those patients with specific MRI scan abnormalities. Despite our findings, if a patient presents with symptoms of increased intracranial pressure, hypertension, progressive neurological disease, and/or focal neurological abnormalities on neurological exam, further imaging and investigation is warranted.

Student Researcher

Daniel Elefant is a Junior at Yeshiva College majoring in biology. Currently, he conducts research under Dr. Sumanta Goswami. For fun, Daniel enjoys imbibing large quantities of assorted caffeinated beverages to see just how many days he can go without sleep. This past summer was spent working with Dr. A. David Rothner at Cleveland Clinic researching headaches. Eventually, Daniel plans to attend medical school, with specific interest in ophthalmology.

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Organic Chemistry
Design and Synthesis of Novel Boron Containing Alkene Derivatives to Study TGF-, Signaling Pathways

by

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It is well documented that biological pathways that govern embryonic development continue to be used in controlling adult physiology, and that deregulation of these pathways can lead to disease. Therefore, identification of small molecule modulators of gene networks active in early development can lead to a better understanding of component specificity for signaling pathways and ultimately the design of novel therapeutic and diagnostic agents for adult diseases. The TGF-beta signaling pathway deregulated in cancer and disease represents a prime candidate pathway for development of pharmacological modulators. We are interested in developing new compounds that interact with developmentally important receptor-mediated pathways such as the TGF-beta pathway, acting as antagonist or agonist.

From our previous chemical genetic screening on developing zebrafish embryos, we identified a lead molecule BT7 that modulates specifically a Smad-independent TGF-beta-regulated MAPK pathway, namely p-SAPK/JNK. In this project we focused to increase the potency and biological activity of our lead molecule BT7. Therefore, we synthesized functionally oriented boron containing alkene-derivatives of BT7 analogues.

To this end, we designed a protocol to synthesize these highly useful molecules. The desired products were synthesized with moderate to good yield by mixing the Wittig salts of various substituted benzyl phosphonium ylides, aldehydes, bases and DMF as solvent at room temperature. The products were purified using column chromatography techniques and then verified with NMR and HRMS analysis. This novel procedure not only streamlined the synthesis of the boron containing alkene derivatives efficiently, but also increased its yield and selectivity. We used this procedure to synthesize combretastatin analogues (antimitotic and TGF-beat signaling modulator). We are currently testing their relevance in the TGF-beta signaling pathways. In the future, an understanding of the mechanism behind this specificity could expedite development of new drug discovery, for example relevant to cardiovascular and cancer diseases.

Acknowledgements

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Student Researcher

Chaim is a senior in Yeshiva College majoring in Chemistry. He is also involved in many aspects of campus life-he is a Resident Adviser, cross country team member, chemistry tutor and Shabbat waiter. He would like to thank Yeshiva University for its tremendous support and incredible opportunities, both academic and extracurricular, that were offered to him throughout his college career.

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Physics
Functionalized Nanoparticles as New Tools for Bioanalysis

by

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Metallic nanoparticles can be used as basic materials for a wide variety of purposes including building blocks for nanoassemblies, substrates for enhanced spectroscopies such as fluorescence and Raman, and as labels for biomolecules. Nanoparticles have the potential to provide highly sensitive and informative data from a variety of biological systems when used with optical spectroscopy. Here we report how silver nanoparticles can be functionalized with specific biomolecular probes (aptamers) to indicate the molecular recognition of a target protein, thrombin, using Surface Enhanced Resonance Raman Scattering (SERRS). This study has found that the detection of larger analytes proves to be a difficult task since the enhancement of a SERRS signal depends on the stability of the nanoparticles and their ability to form dense aggregates. An enhanced signal is seen at nanomolar concentrations of thrombin, but this method still needs to be optimized to provide detection at lower concentrations with greater enhancement.

Student Researcher
Jacob Berger is a third year Physics major at Yeshiva University. For the past few years he has worked in Professor Asherie's laboratory at Yeshiva College researching protein crystallization and phase behaviour. This past summer, Jacob was awarded an American Chemical Society International Research Experience for Undergraduates (ACS IREU) scholarship to spend ten weeks in Glasgow, Scotland at the University of Strathclyde doing research at the University of Strathclyde in Glasgow, Scotland.
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Physics
Optimization of a Pickup Electrode for Operation in the Electrostatic Ion Beam Trap

by

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The Electrostatic Ion Beam Trap (EIBT), developed at the Weizmann Institute, has been shown to be useful as a high resolution mass spectrometer. Mass spectrometry in the EIBT relies on measuring the oscillation frequency of the ions with a pickup electrode located in the middle of the trap. The goal of this work has been to optimize the pickup electrode design and calibrate it for individual ion measurement by investigating the effect of various parameters on pickup electrode sensitivity. A signal wire connected to a pulsed power source was inserted into the pickup ring aperture to simulate moving ions. The induced charge on the pickup's surface from the current pulse was detected by a charge-sensitive pre-amplifier and along with the pulsed source signal was measured by an oscilloscope. Experimental results showed that orientation and design of the pickup system affected the pickup signal quality. A simple geometrical model was successful in explaining the effect of various parameters on the pickup sensitivity (See Fig. 1-3). The experimental results and geometrical model of the pickup demonstrated further progress towards achieving the optimum pickup design.

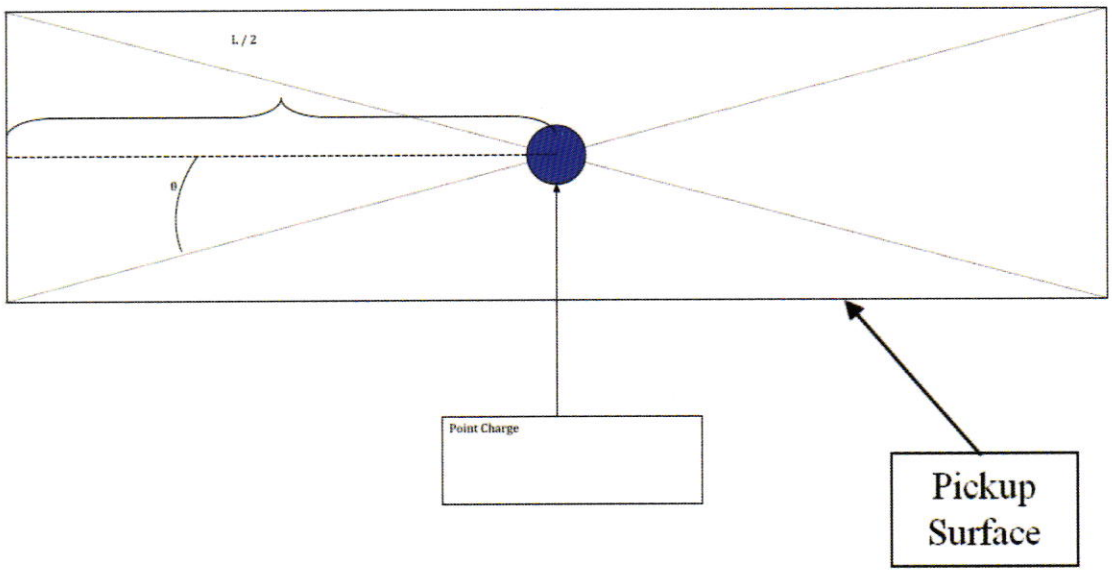

Figure 1: Geometrical model of pickup length, diameter, and total enclosure of a point charge.

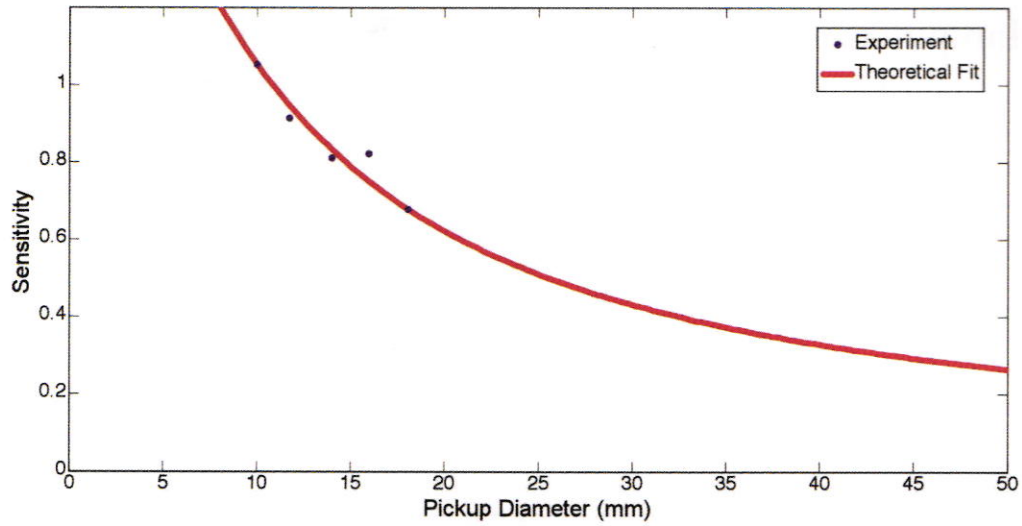

Figure 2: Geometrical model fit of pickup ring sensitivity as a function of pickup diameter for a 10mm length.

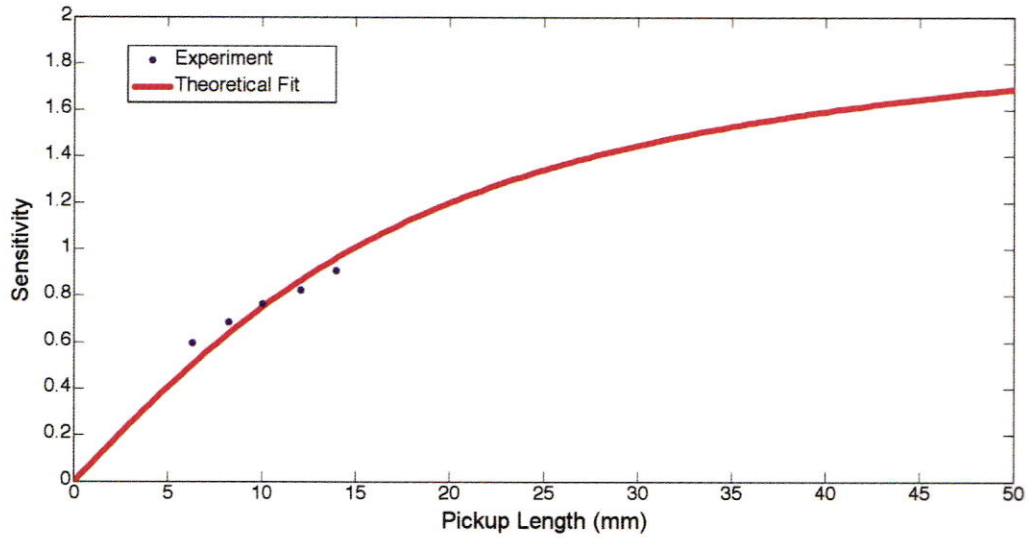

Figure 3: Geometrical model fit of pickup ring sensitivity as a function of pickup length for a 16mm diameter.

Student Researcher

Yitzchak Dachman, better known as Yitzy, is in his third year at Yeshiva College majoring in Pre-Engineering. He plans to study Mechanical Engineering through the 3-2 Combined Plan at Columbia University. Yitzy enjoys the outdoors and cool scientific experiments. He aspires to be a professional engineer, pioneering next-generation renewable energy systems.

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Physics

Manipulation of the Dynamics of Many-Body System Via Quantum Mechanical Control Methods

by

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We control the evolution of spin 1/2 chains with dynamical decoupling methods. Chains with on site disorder may be chaotic when nearest neighbor interactions are present. We apply a sequence of magnetic pi-pulses to eliminate the effects of the disorder. A system with both nearest neighbor and next nearest neighbor interactions is frustrated. The system is in the chaotic regime when the frustration is strong. A more complex sequence of pulses can be applied to specific sites in the chain to eliminate the contributions from the nearest neighbor term and allow the system to evolve as an integrable one. If the XY term in the system's Hamiltonian is stronger than the Ising interaction, the system is gapless. Otherwise, the system is in the gapped phase. By varying the time intervals between the pulses we apply to the chain, we can force the system to change its behavior from gapped to gapless and vice versa. The ability to manipulate the dynamic behavior of these quantum systems can be useful in attempts to obtain a particular transport behavior in quantum computing.

Student Researcher
Julie studied Mathematics and Physics at Stern College for Women and intends to graduate from the 3-2 Combined Engineering Program in 2011 with a B.A. from Stern and a B.S. in Electrical Engineering from Columbia. In addition to her studies, Julie enjoys discovering attractions in New York City and spending time with family and friends.
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Physics
Negentropy Generation and Fractality in Dry Friction of Polished Surfaces

by

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We consider the Robin Hood model of dry friction to study entropy transfer during sliding. For the polished surface (steady state) we study the probability distribution of slips and find an exponential behavior for all the physically relevant asperity interaction-distance thresholds. In addition, we characterize the time evolution of the sample by its spatial fractal dimension and by its entropy content. Starting from an unpolished surface, the entropy decreases during the Robin Hood process, until it reaches a plateau; thereafter the system fluctuates above the critical height. This validates the notion that friction increases information in the neighborhood of the contacting surface at the expense of losing information in remote regions. We explain the practical relevance of these results for engineering surface processing such as honing.

Student Researchers

Mordechai Kornbluth is in his second year at Yeshiva College, majoring in Physics and Pre-Engineering, and minoring in Mathematics and Semitic Languages. Although Semitics seems an unusual pursuit for a Physics student, he enjoyed studying Hebrew, Jewish Aramaic, and Syriac, and is therefore continuing with Arabic. Mordechai engages in rigorous Talmudic analysis on a regular basis, which both enhances and is enhanced by his knowledge of language. Professionally, however, Mordechai plans to pursue a doctorate and career in the hard sciences.
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Roman Sandler is a second year YU student majoring in Physics and Pre-Engineering. He plans on completing the YU/Columbia BA/BS Combined Engineering Program and majoring in Biomedical Engineering at Columbia. Roman plans to pursue a graduate degree in Neuroengineering and do research on Brain Machine Interfaces and Neuroprosthetics. Roman enjoys cooking and exploring the mountains and beaches of his native Southern California.
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Mordecai Segall is a junior studying Physics and Music in the Yeshiva College Honors Program. In 2007, he graduated as the valedictorian of his high school, Yeshiva University High School for Boys, and began studying in Israel at Yeshivat Har Etzion. Since his arrival at YU in 2008, he has been researching various physics projects with Dr. Zypman, including a quantum mechanics based analysis of the properties of nanowires. He intends to graduate in 2012 and pursue a higher level degree in Physics. Outside of school, he enjoys playing classical music on the clarinet.
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Physics
A Forward Analytic Model for the Control of Octopus Arm Movements

by

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The development of control schemes is critical for the design and implementation of robotic motion, as well as for understanding the neural mechanisms used to control an organism's appendages. The control scheme needed for a hyper-redundant manipulator, such as an octopus arm, is especially complicated due to the large number of degrees of freedom of the arm. To model an octopus arm in 2D, we divided the arm into a multi-segmented structure, with the muscles of each segment modeled as damped springs. The area of each segment was maintained constant throughout all simulations to mimic the arm of an octopus, which as a muscular hydrostat maintains a constant volume throughout its appendages. After the internal forces of each muscle in the arm were inputted, the geometry of each segment was calculated, with the added constraint that the shared muscles between segments must be of identical length. We found that when this method was implemented, each segment in the arm had its own unique stiffness, an issue that will be addressed in further research. The arm-drawing model was then enhanced by appending the model to a genetic algorithm, which calculated the fitness of each individual arm configuration to a given target point. This model may be further extended by alternating the target point between different locations to see whether modularity develops in the arm. In addition, the model can be broadened to a quasi-static model to study the motion that results from changes in force activations of different muscles.

Student Researcher
Aryeh Reinstein is a senior at Yeshiva College majoring in Physics and Computer Science. He is interested in pursuing a career in engineering and is particularly interested in the field of robotics. While he was hoping to combine his interest in robotics with his passion for squids, he was pleasantly surprised to investigate the octopus instead. He now wishes he could fit through a hole the size of a quarter the way a 600 pound octopus can.
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Physics
Effects of Surface Disorder on EXAFS Modeling of Metallic Clusters

by

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Small (1-5 nm) metal clusters may undergo significant surface relaxation under the influence of ligands, adsorbates and substrate-induced stress. As a result, the nearest neighbor distance between surface atoms can be reduced by up to 10% relative to those in the cluster core, enhancing the disorder in the interatomic distances. Accordingly, the pair distribution function extracted from EXAFS data under the standard assumption that the distribution function of nearest neighbor bonds is quasi-Gaussian yields systematic errors. Here we analyze the surface disorder effects with emphasis on their impact on the accuracy of the size and shape determination of nanocatalysts.

Student Researcher

Aaron Yevick is an honors student at Yeshiva University where he is studying Physics. His first research experience was in Brookhaven National Laboratory, where he conducted the research summarized above. He loves classical music, and when he is not working, he enjoys playing the violin and piano. He hopes to attend a graduate program in physics and become a physics professor.

Psychology

The Effects of Age on Object Memory and Spatial Abilities in Women

by

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The goal of the present study was to determine if aged women demonstrate cognitive decline on tests of object memory and spatial ability compared to young women. Thirty-two young undergraduate women (ages 19-24) were compared to fifteen aged independent living women (ages 71-90). An object array task was used to measure object memory and a mental rotation test was used to measure spatial ability. The object array task required participants to study black and white drawn objects and then to circle objects that they believed had moved positions or were novel to the array. The mental rotations test required participants to match objects that were rotated into different positions. Preliminary results suggest that aged women perform similar to young women on all object array conditions. However, aged women perform worse on the mental rotation test relative to young women. Therefore, our results thus far suggest that there is no age-related decline in object memory, but spatial ability appears to decline with age in women.

Student Researcher
Danielle Taylor is a senior at Stern College and is majoring in Psychology. Currently, she is Dr. Lauren Harburger's lab manager and is researching the effects of age and sex on memory.
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Psychology

Does Native Language Affect the Emergence of Novel Forms of Communication?

by

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In recent years, a number of researchers have begun to study the early stages of language emergence in the laboratory via methods that require people to invent novel forms of communication (Galantucci, 2009). It is unclear, however, to which extent these forms of communication are truly novel because participants in these studies are already competent users of a communication system: their native language. Does native language affect novel communication forms that emerge in the laboratory? To answer this question, we asked 24 pairs of participants to play a cooperative video game in which they had to invent signs for one of three different sets of images: *Object pictures*, *Maya glyphs*, and *Color patches*. These sets varied on how readily they could be linguistically labeled and on how much they afforded iconic representations. Object pictures had clear linguistic labels and afforded iconic representation, Maya glyphs afforded iconic representation but had no clear linguistic label and Color patches had clear linguistic labels, but did not afford iconic representation. Performance for pairs playing with Color patches was worse than for Maya glyphs and Object pictures. This result suggests an effect of iconic representation but not of native language. Methods that rely on novel forms of communication appear to be viable tools to study novel forms of communication.

Student Researcher
Reuven Turgel is a forthcoming Psychology graduate of Yeshiva University with a strong interest in clinically oriented psychology. This current study was conducted under the tutelage of Dr. Galantucci and the Yeshiva University Department of Psychology. Other research projects have included studying the psychosocial determinants of HIV transmission clustering at McGill University AIDS center. In addition to his research he has actively been involved with the special needs population in various capacities.
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Stem Cells
Neuronal Differentiation of H9 Human Embryonic Stem Cells

by

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Human embryonic stem cells (hESC) have immense potential in many different areas of health and medicine, such as disease models for drug therapy and models for human development. Pluripotent stem cells have the ability to differentiate into all cell types whereas neural stem cells (NSCs) are restricted to a neural fate, but maintain the capability to become any neural cell. We hypothesize that we can obtain neurons from hESC via a two-step process: differentiating hESC into NSCs and then into neurons. During this process, the NSC markers Sox2 and Nestin are expected to decrease while the neuronal marker TuJ1 increases. The two-step differentiation protocol uses neural proliferation media containing FGF was added for proliferation of the NSCs, followed by neuronal differentiation media with BDNF (brain derived neurotrophic factor), to promote neuronal differentiation as opposed to glial differentiation. Over four weeks, the NSC markers Sox2 and Nestin significantly decreased, while TuJ1 significantly increased. Further staining with MAP2 confirmed the presence of mature neurons, while GFAP, a marker for glia, showed a very small population of glial cells. Together, this information suggest that our protocol was successful in obtaining mostly neurons. Additional staining for neuronal subtype markers (VAChT, GAD65/67, VGAT, VGLUT) produced inconclusive results and experiments are ongoing to determine specific neuronal subtype differentiation. In conclusion, this protocol differentiates H9 hESC preferentially into neurons over glial cells.

Student Researcher
Barrie Cohen is a senior at Stern College for Women majoring in Biology. Barrie hopes to become a physician and work with children. Immediately following graduation, Barrie will be travelling to the Amazon Basin in Peru to provide care for the local children. In her spare time, Barrie enjoys reading and horseback riding.
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