Undergraduate Research Abstracts

A publication of Yeshiva College and Stern College for Women

2012-2013 Volume 6.

Yeshiva University

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Yeshiva University

Undergraduate Research Abstracts Journal
A Publication of Yeshiva College and Stern College for Women
Volume 6 : 2012-2013

Dedication

In tribute to our friends and mentors,

Eli Steinberger z'l
(USRP Co-President 2006-07)
&
Donny Ladell z'l
(USRP Co-President 2005-06)

Who founded many student research initiatives, including this journal, at Yeshiva College. May we continue to honor their memories through the exhibition of Yeshiva's ongoing undergraduate exploration of science.

Foreword

The journal you are about to read presents a synopsis of the research carried out by the undergraduate students of Yeshiva University during the past academic year (2012-2013). This issue of the Undergraduate Research Abstracts Journal, like those of previous years, reflects the enthusiasm at Yeshiva College and Stern College for Women for doing research and sharing the process of discovery with others.

Our students work in an impressive array of fields. Physics, chemistry, biology, mathematics, computer science and psychology are all represented here. Some of the research was carried out on campus with YU faculty members; some was done at other universities or national labs. In many cases the findings will be presented by the students themselves at international conferences and then published in leading journals.

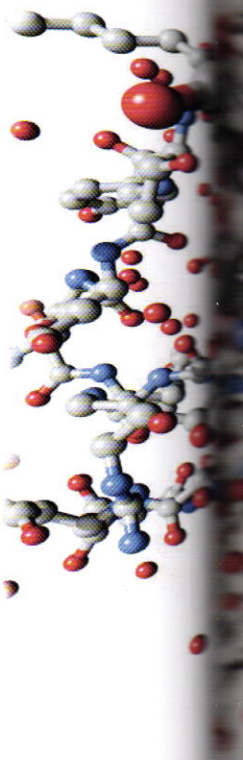
What unites all of the work presented here—from summer research projects to multi-year endeavors—is the students' curiosity about the world. It is a privilege to be the faculty advisor of this journal and be inspired by this curiosity. I hope you will be inspired too.

Neer Asherie

Associate Professor of Physics and Biology
Yeshiva University

Introduction

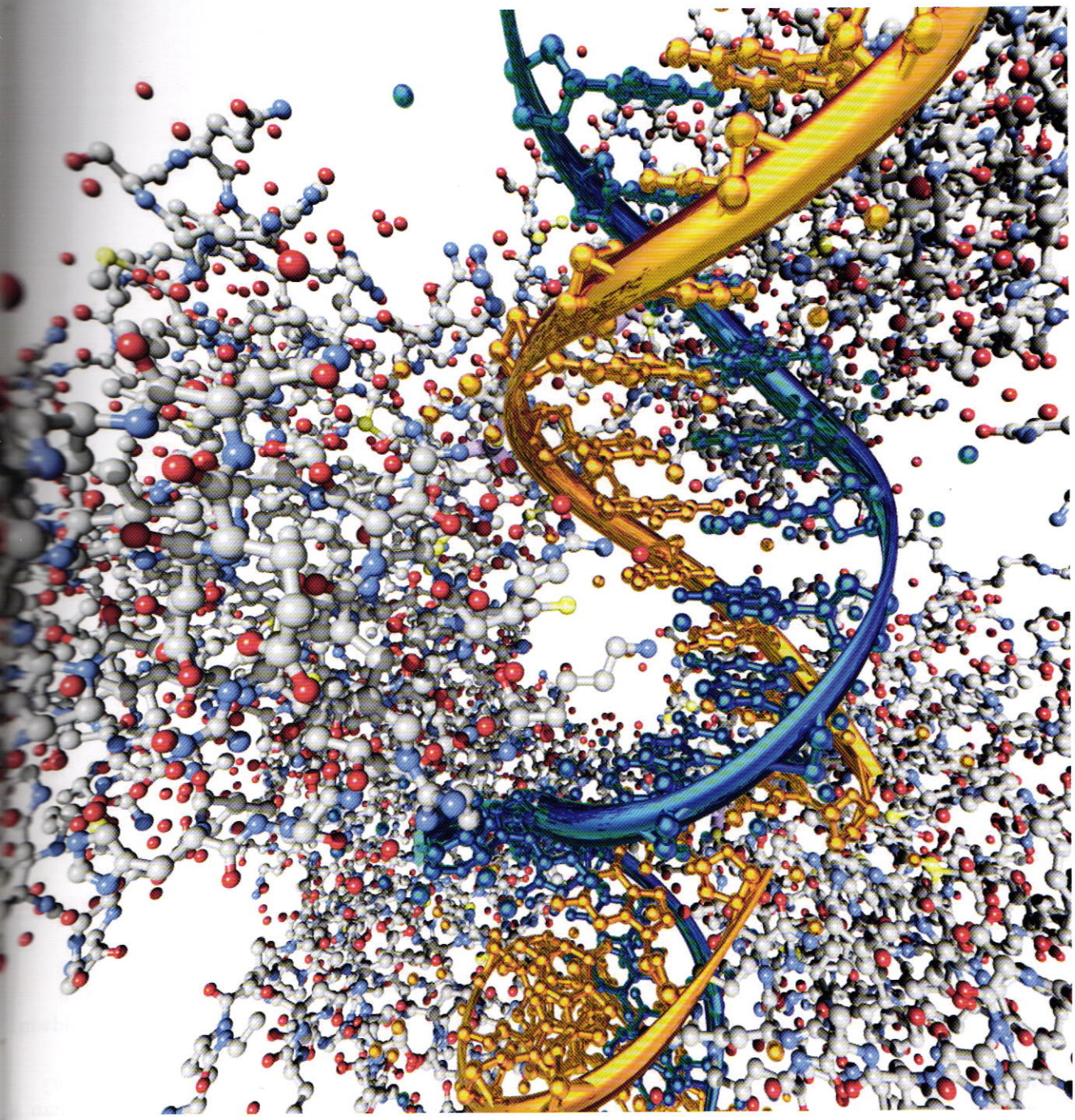
For many students in both colleges of Yeshiva University- Yeshiva College and Stern College for Women- the sciences are not merely academic disciplines, but rather, a part of everyday life. Our school is home to numerous clubs in the areas of Biology, Chemistry, Physics, Engineering, Psychology, Mathematics, Computer Science, and Neuroscience, each of which provides students with vibrant events featuring talks on cutting edge developments in the scientific world and seminars given by experts in various scientific disciplines.



Additionally, many students at Yeshiva University dedicate their time during the academic year to take advantage of opportunities to work in the research laboratories of the esteemed and passionate faculty members of Yeshiva College and Stern College for Women. On top of this, several students also spend their summers participating in highly competitive research programs such as the Roth Institute Scholars Program in Biomedical Research at Albert Einstein College of Medicine, the YU Research Internship Program at Bar-Ilan University, and numerous other prestigious national and international programs. These experiences not only enhance the scientific knowledge of our students, but also expose them to the role that scientific research has in advancing an institution.

The Undergraduate Research Abstracts Journal is a compilation featuring the fruits of the work, dedication, and passion of dozens of Yeshiva University research students. We would like to thank each of the authors featured in this publication. We would also like to thank the science faculty members of YU for their dedication to their research students. Lastly, we would like to extend a special thanks to the Office of the Provost of Yeshiva University for providing the financial backing for this project. Without their support and commitment, this Journal would not have been possible.

The Editors



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Cancer Biology

Autooxidation of Gallic Acid, a Nutraceutical in Pomegranate and Tea, Induces Oxidative Stress in Oral Carcinoma HSC-2 Cells

by

Bersson, Ayelet R.; Esan, Hannah; Lahasky, Tova; Loshinsky, Aliza Y.; Miller, Sarina H.; Nathan, Amy L.; Schuck, A.G.; Weisburg, J.H.; and Babich, H.

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Nearly half of cancers diagnosed in the United States are caused by unnecessary life choices including smoking, drinking, and unhealthy eating. The lack of consumption of fresh vegetables and fruits is a major factor contributing to an elevated risk of cancer development. This potential chemopreventive effect is related to the high levels of numerous non-nutritive phytochemicals, termed nutraceuticals, in fruits and vegetables. This study evaluated the anticancer potential of gallic acid, a polyphenol common in many foods (e.g., pomegranate) and plant-derived beverages (e.g., green and black teas).

Human oral carcinoma HSC-2 cells were more sensitive than normal gingival HF-1 fibroblasts to a 24-hr exposure to gallic acid (GA), as assessed by the neutral red cytotoxicity assay. Midpoint cytotoxicity (NR_{50}) values were approximately 75 μM GA for the HSC-2 cells, and approximately 140 μM GA for the normal fibroblasts. As shown with the FOX assay, gallic acid was a strong generator of hydrogen peroxide (H_2O_2), suggesting that its mode of cytotoxicity may be through the induction of oxidative stress. Reduced glutathione (GSH) is the cell's main protector against damage by oxidative stress. The cytotoxicity of GA to HSC-2 cells was potentiated by a co- or pre-exposure of GA with the GSH depleters, D,L-buthionine-[S,R]-sulfoximine (BSO), 1-chloro-2,4-dinitrobenzene (CDNB), and bis(2-chloroethyl)-N-nitrosourea (BCNU), each inhibiting a different enzyme in the recycling of glutathione (Fig. 1).

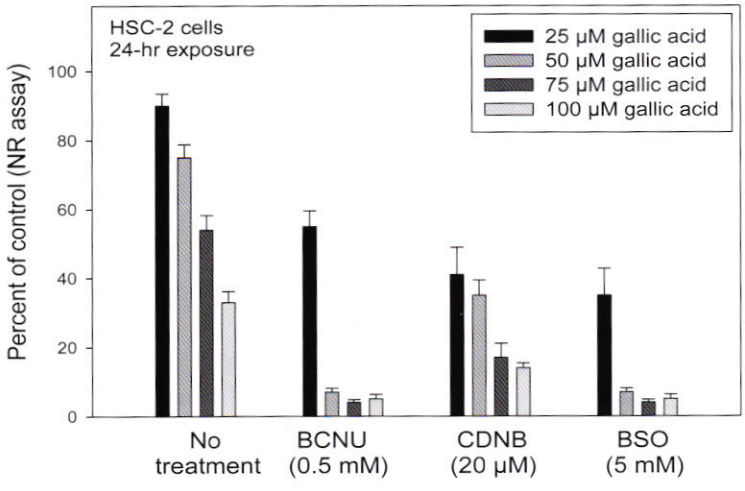

Figure 1. Potentiation of the cytotoxicity of gallic acid to HSC-2 carcinoma cells by co- and pre-exposures to glutathione depleting gents.

To further corroborate data implicating oxidative stress as the mode of cytotoxic action by GA, the HSC-2 carcinoma cells were treated with GA in the presence of catalase, pyruvate, and divalent cobalt, all scavengers of H2O2. The 24-hr cytotoxic potency of GA to the HSC-2 cells was greatly lessened upon exposures in the presence of these scavengers of H_2O_2 and parallel studies with the DHR assay showed greatly reduced levels of H_2O_2 in GA-containing medium co-amended with these scavengers. Apparently, GA cytotoxicity was due, in a large part, to the induction of oxidative stress within the cells.

Oxidative stress has been implicated in cell death via apoptosis. To demonstrate GA induction of apoptotic cell death, HSC-2 cells were treated with GA and after a 24-hr exposure were analyzed with a Guava Easycyte Miniflow Cytometer, using the Guava Viacount reagent to distinguish between viable, nonviable, and apoptotic cells (Figure 2). . Significant levels of apoptotic cells were noted at 100 μM GA and greater. Immunoblot analysis of an apoptotic marker, namely, cleavage of poly(ADP- ribose) polymerase (PARP), also demonstrated GA induction of apoptosis and alleviation of apoptotic cell death in the presence of scavengers of H_2O_2, such as divalent cobalt. (Fig. 2).

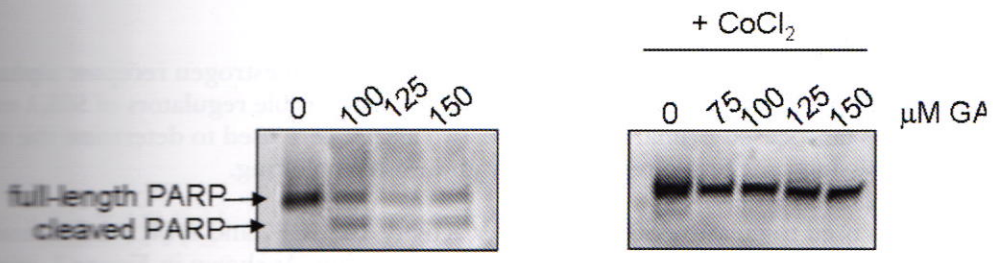

Figure 2. Western blot analysis of PARP cleavage induced by gallic acid in the absence and presence of cobalt, a scavenger of H_2O_2.

Reprinted from Volume 8, 2012, Women in Science, a publication of Stern College for Women.

Student Researchers

Ayelet Berson currently attends Yeshiva University's Stern College for Women, where she is pursuing a major in Biology and a minor in Chemistry. She has assisted Dr. Harvey Babich in research of In Vitro Toxicology as well as in the publication, Jews and Genes in B'or Ha'torah Journal of Science, Art, and Life in the Light of the Torah. Ayelet intends on pursuing a Masters in both Biology and Science Education, after which she plans on becoming a high school biology teacher.

Cancer Biology

S6K1 Regulation in ER-Positive Breast Cancer

by

Batsheva Rosen, Davita Wachsstock, and Marina K. Holz

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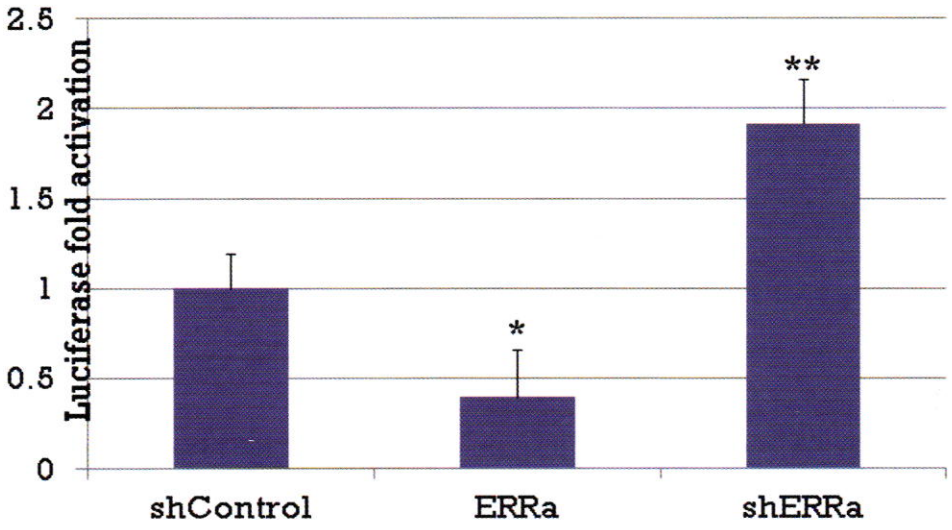
Clinically, up to 60% of breast cancers are Estrogen Receptor (ER)-postive. However, only about half of ER-positive breast cancers respond to endocrine treatments, and resistance often occurs. While mechanisms of resistance are not clear, increased signaling via growth factor pathways such as mTOR (mammalian target of rapamycin) have been observed in these cases. The mTOR pathway regulates such key processes as cell proliferation, growth, survival, and transcription. The current study investigates the molecular mechanisms of escape from endocrine therapy. Elucidating the mechanisms of resistance can lead to better therapies by relying on a combination of targets. One key protein in the mTOR pathway is S6-kinase 1 (S6K1), which is an important regulator of cell proliferation. S6K1 may be important for endocrine sensitivity as it was observed that over-expression of S6K1 occurs in up to 10-30% of breast cancers. Understanding S6K1 regulation may allow it to function as a specific target in combination with endocrine therapy.

Two transcription factors, estrogen-related receptor alpha (ERR*a*), an estrogen receptor alpha activity modulator, and GATA-3, a T-cell development regulator, are possible regulators of S6K1 expression. This study thus far focused primarily on ERR*a*. Two assays were used to determine the role of ERR*a* in S6K1 expression: Luciferase reporter assay and western blotting.

Luciferase assay was used to measure S6K1 promoter activity. In MCF7 and HEK293 cell models, ERR*a* expression was modulated by knockdown or overexpression. As shown in Figure 1, overexpression of ERR*a* resulted in a two-fold downregulation of S6K1 expression. Knockdown of ERR*a* resulted in a two-fold upregulation of S6K1 levels.

Figure 1. S6K1 promoter activity



Western blotting provided validation for the data from the luciferase assay by confirming that the knockdowns and overexpression of ERR*a* indeed resulted in corresponding protein level changes of S6K1 (data not shown).

Future studies will employ RT-qPCR to measure mRNA levels of endogenous S6K1.

Acknowledgements

We would like to thank Yeshiva University, the Elias Genevieve and Georgiana Atol Charitable Trust, National Cancer Center, and National Institutes of Health for providing funding for our research.

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Student Researcher
Batsheva Rosen is currently a junior at Stern College for Women. She is majoring in Biology and Psychology with a concentration in Neuroscience. She hopes to pursue further study in the health sciences.

Student Researcher
Currently a senior in the Honors Program at Stern College, Davita is pursuing a degree in molecular and cellular biology. Although she misses spending time with her five sisters back home, Davita looks forward to involvement in the Torah Activities Council, wishing she could foster stray cats in the dorm, experimental cooking, and peer tutoring for General Chemistry and Statistics. She plans to pursue a Master's in Education in Teaching Science to share her excitement about science with others.

Cancer Biology

Studying DNA Repair Gene Expression and Function in Breast Cancer; One Cell at a Time

by

Eli Grunblatt, Evan Pieri, Sweta Roy, and Sumanta Goswami

Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10033

In recent years it has become evident that cancer progression is not as streamlined a process as normal tissue development. When a normal tissue or organ develops at the embryonic, fetal, infant or child stage, the development process is finely orchestrated by not only the cells in the tissue but by the entire body utilizing different, endocrine, paracrine and autocrine mechanisms. During tumor development on the other hand, there is a very selective growth of only one type of cell in the tissue in an organ. This growth happens with minimal support from the surrounding tissue, quite a far cry from the normal developmental process. However, it has been observed recently that stromal cells, especially macrophages and fibroblasts, play a very crucial role in tumor progression in the breast in a process which is somewhat similar to that of normal mammary gland development.[1] This anomalous growth leads to a very heterogeneous population in the tumor where each cell is quite different from the other. This heterogeneity leads to a unique problem in the cancer clinic, where the bulk of the tumor responds to standard chemotherapy or radiation therapy whereas some cells are resistant to the same. As a result, the cancer often relapses after years of apparent remission. Our lab has been working on trying to identify and characterize these special cells that resist therapy. We have reported that these special cells are highly motile and lead to the spread of cancer resulting in metastasis[2], are resistant to standard chemotherapy[3], have augmented DNA repair and metabolic pathways[3], have shut down their cell cycle, and are anti-apoptotic.[3,4]

Recently in our lab we have started conducting experiments to detect and validate the alteration in DNA repair in individual breast cancer cells by quantifying their mRNA and miRNA expression by in situ hybridization. Additionally, we are studying cell behavior and DNA repair capability at the individual cell level by using the Comet assay. Using these two techniques, we aim to study the diversity of DNA repair in invasive cells and address the root cause of resistance to therapy.

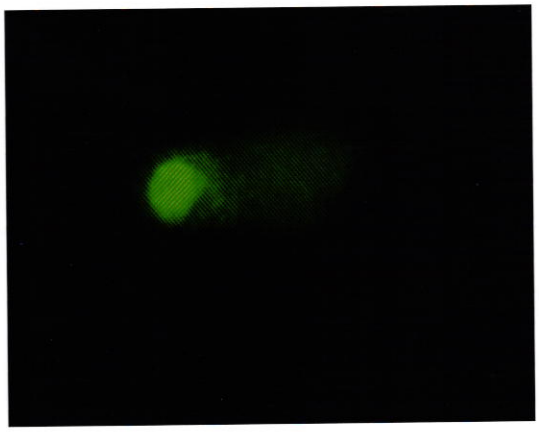

Figure 1. Comet assay of LM2 PBABE cell. 4/24/13

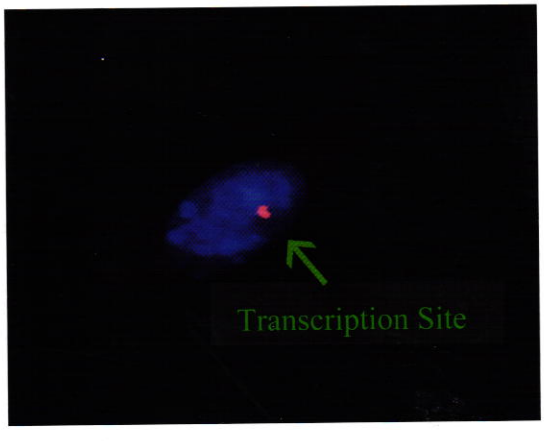

Figure 2. In situ hybridization of MDA-MB-231 cell with probe against p53 (Cy3 labeled) and DAPI counterstain. 3/14/13

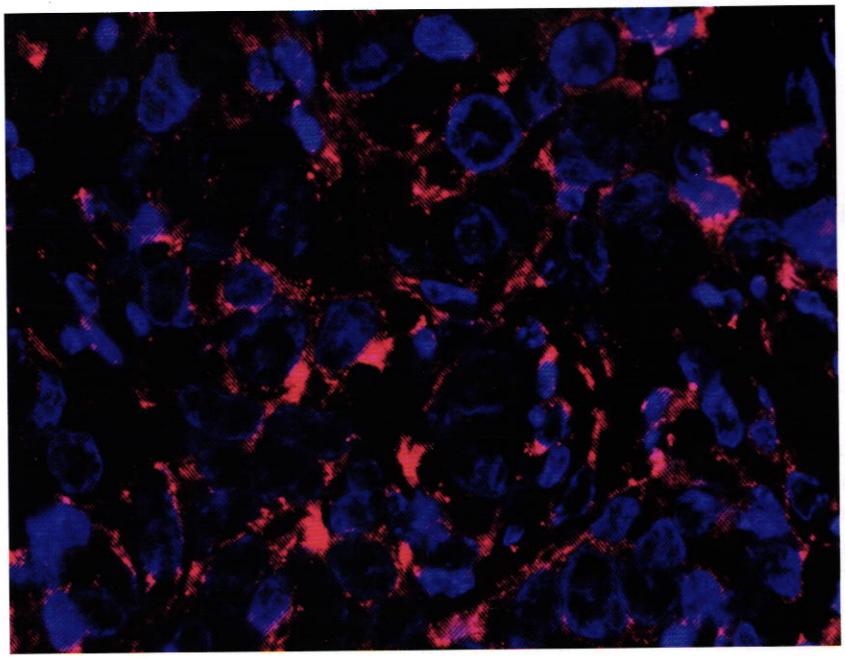

Figure 3. In situ hybridization of breast cancer tissue with probe for p53 (Cy3 labeled) and DAPI counterstain. 3/19/13

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Student researcher

Eli is currently a junior at Yeshiva College majoring in Chemistry and Biology. When he's not working in the lab or in the community, Eli enjoys playing hockey. Following the completion of his undergraduate studies, Eli hopes to pursue a joint M.D./Ph.D. degree in Hematology-Oncology.

Cancer Biology

Stress Gallic Acid, an Inducer of Apoptosis to Human Oral Carcinoma HSC-2 Cells, as Mediated Through Oxidative

by

Robin, Esther F., Wietschner, Jordana R., Weisburg, J.H., Zuckerbraun, H.L., Schuck, A.G., and Babich, H.

Department of Biology, Stern College for Women, New York, NY 10016

Gallic acid (3,4,5-trihydroxybenzoic acid), a polyphenol common in many plants, *e.g.* pomegranate, tea, and grape, has pharmaceutical properties with potential health benefits.
As with most polyphenols, gallic acid exhibits both antioxidant and prooxidant properties.
In vitro studies with human cells in culture have shown that gallic acid is preferentially cytotoxic to cancer cells, as opposed to normal cells, and acts as a prooxidant to induce cell death via apoptosis. As such, gallic acid may be described as a nutraceutical or a natural food product with positive health effects and may be a suitable adjunct to chemotherapeutics in the treatment of cancer.

The connection between gallic acid acting both as a prooxidant and as an apoptosis-inducing agent is ill-defined. The research herein clearly demonstrates a cause-and-effect relationship between gallic acid's production of hydrogen peroxide (H_2O_2) and its subsequent induction of apoptosis to human oral carcinoma HSC-2 cells. Using the FOX assay in a cell-free system, it was shown that Gallic acid is a strong generator of H_2O_2. The diacetate ester of 2',7'-dichlorofluorescein (DCFDA) is a colorless, nonfluorescent, nonpolar molecule that passively diffuses into cells. Within the cell, esterases cleave the two acetates to form DCF, a nonpermeable, polar molecule, which, upon oxidation by intracellular oxidants, principally, H_2O_2, yields a fluorescent product. Intracellular fluorescence, an indication of potential oxidative stress, was noted in HSC-2 cells exposed for 4 hrs. to 100 and 200 μM gallic acid, but not in untreated cells.

Reduced glutathione (GSH), a thiol-containing tripeptide, is the main intracellular antioxidant in a cell's repertoire of defenses against oxidative stress. Depletion of intracellular GSH, a sign of impending oxidative stress, was observed in HSC-2 cells exposed for 4 hrs. to increasing levels of gallic acid (Figure 1). Studies were also performed with gallic acid in the presence of divalent cobalt (as $CoCl_2$). The divalent cobalt cation, acting as a catalyst, decomposes H_2O_2 to water and molecular oxygen. The decrease in intracellular GSH in HSC-2 cells attributable to Gallic acid was greatly reduced by coexposure with 250 μM $CoCl_2$. By scavenging the H_2O_2 generated by gallic acid, Co^{2+} protected the cells from oxidative stress.

Flow cytometric analyses of HSC-2 cells, both untreated and treated with gallic acid, showed that as the concentration of gallic acid was increased, the number of viable cells decreased and the number of apoptotic and dead cells progressively increased. However, in the presence of Co^{2+}, the cells were essentially rescued from apoptotic death. (Figure 2).

These studies showed that the mechanism of apoptotic cell death of cancerous HSC-2 cells exposed to gallic acid is via the induction of oxidative stress.

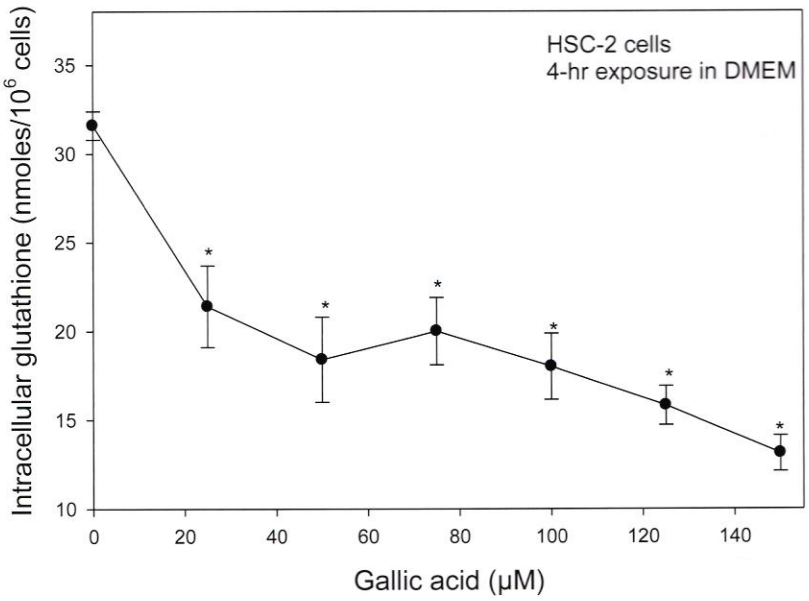

Figure 1. Effect of Gallic acid on intracellular reduced glutathione in HSC-2 cells

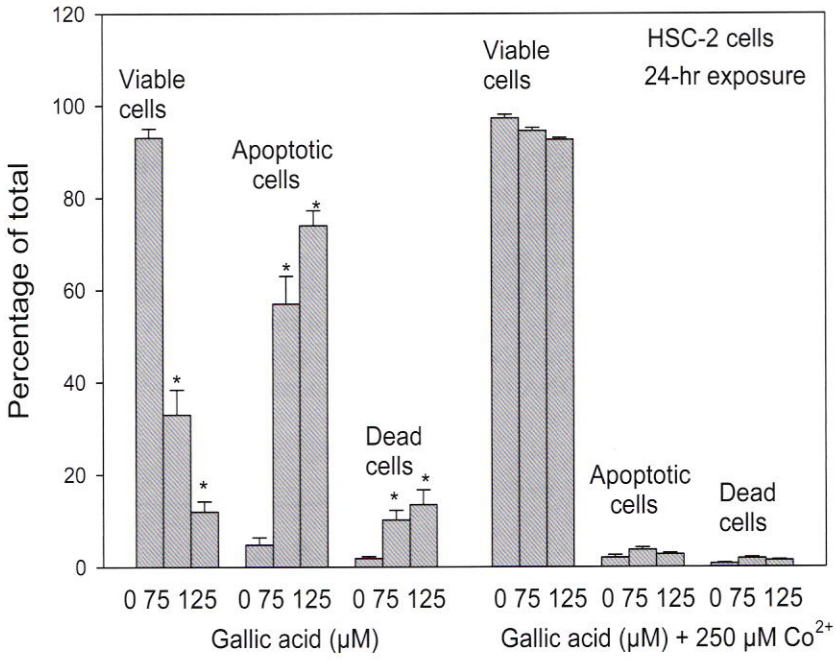

Figure 2. Apoptotic-inducing ability of gallic acid in the absence and presence of Co^{2+}, a scavenger of H_2O_2.

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Student Researcher
Estee is currently a junior at Stern College, majoring in Molecular and Cellular Biology and minoring in Chemistry. She plans to attend medical school after she graduates from Stern. Jordana is also a junior at Stern College, majoring in Biology and she also plans to pursue a career in the health field . Estee and Jordana did research together in July 2012 with Dr. Weisburg at Stern College.

Cancer Biology

Investigating the Role of an Anti-Apoptotic Protein in Breast Cancer Cell DNA Repair

by

Eli Grunblatt, Sweta Roy, Evanka Madan, and Sumanta Goswami

Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10033

Each year, over 40,000 lives are lost to breast cancer in the United States alone.1 According to the American Cancer Society, more than 90% of breast cancer patients who succumb to the condition die as a result of the cancer metastasizing to other areas of the body.2 It has been shown that the presence of a specific migratory subpopulation of breast carcinoma cells, known as invasive tumor cells, is correlated with the prevalence of metastasis. Additionally, this migratory subpopulation is known to be resistant to standard chemotherapy and radiation therapy treatments. We have hypothesized that the chemoresistance and survival of these cancer cells eventually leads to relapse and metastasis following initial treatment with chemotherapeutic agents is achieved by enhanced DNA repair capability in these cells.3

It was observed in our lab that an anti-apoptotic protein ARC is over expressed in the invasive mammary cancer cells that are resistant to standard chemotherapeutic agents.3 Further, we have shown that ARC over expressing cells are resistant to chemotherapy both in vivo and in vitro.4 Although the induction of ARC in human cancers is well established, the functional relevance of this protein to the pathogenesis of any cancer is not known.

In this study, we examined cellular DNA repair signalling pathways in order to delineate the role of ARC in the pathogenesis of breast cancer. Utilizing cell lines in which ARC is either knocked down or overexpressed, we observed a direct correlation of ARC with DNA repair capability both in vivo and in vitro. Single cell electrophoresis assays showed that DNA repair is augmented in cells that over express ARC and diminished in cells that have ARC knocked down. We have reported that in single strand DNA repair pathways, ARC acts by overexpression of the key DNA repair proteins as measured by qRT-PCR. In the double strand DNA repair pathway on the other hand, we observed that ARC causes an over activation of key DNA repair proteins as measured by in cell western analysis using phospho specific antibodies.

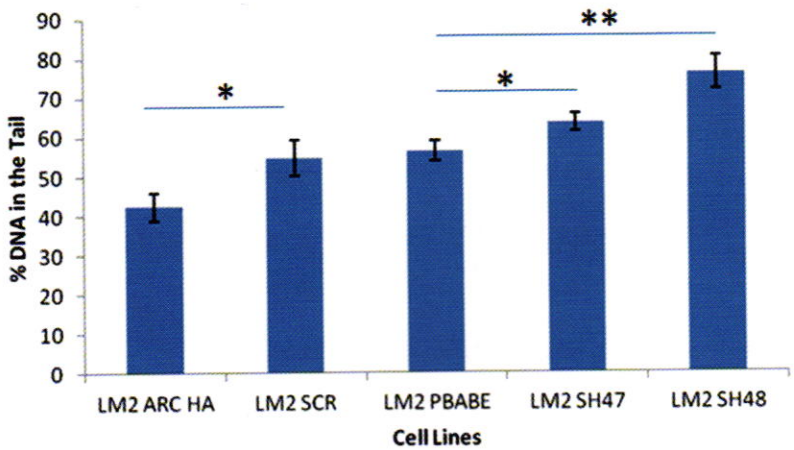

Figure 1. Effect of ARC on Cellular DNA Repair. Various cell lines were generated with ARC modifications on the LM2 background. ARC HA is a vector used to overexpress the intact ARC protein while PBABE is a control vector. SH47 and SH48 indicate treatment with siRNA to knock down ARC expression. SCR indicates scrambled siRNA control. *$p<0.05$, **$p<0.005$

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Student Researchers

Eli is currently a junior at Yeshiva College majoring in Chemistry and Biology. When he's not working in the lab or in the community, Eli enjoys playing hockey. Following the completion of his undergraduate studies, Eli hopes to pursue a joint M.D./Ph.D. degree in Hematology-Oncology.

Cancer Biology

Identification of an Osteosarcoma Progenitor Cell by Analysis of Differential Expression of Cell Surface Receptors of Human Mesenchymal Stem Cells and Mature Chondroblasts

by

Rachel Blinick[1], Sajida Piperdi[2], Amy Y. Park[2], Hua Yi Qu[2], and Richard Gorlick[2]

[2]*Department of Pediatrics Hematology/Oncology, Albert Einstein College of Medicine of Yeshiva University, The Children's Hospital at Montefiore, Bronx, NY 10461*

Osteosarcoma, the most common malignant bone tumor in children and young adults, is thought to originate from a cell at some point along the differentiation pathway of human mesenchymal stem cells (hMSC) to specific cells such as chondroblasts, osteoblasts, and adipocytes. These three cell types are believed to differentiate from a single cell of origin along the differentiation pathway of hMSCs to specific cell types. Identifying changes in surface marker expression throughout the process of differentiation may help characterize the cell of origin as well as the intermediate stages in the differentiation pathway which is crucial to understanding the molecular pathogenesis of osteosarcoma. Looking at the differentiation pathways of hMSC to osteoblasts, chondroblasts and adipocytes may help in identifying the cell of origin that unites all three pathways.

In this study, RNA was extracted from hMSC and mature chondroblasts, and gene expression was measured using microarray on the Affymetrix Gene 1.0 ST array. A list of differentially expressed genes was generated but only genes for cell surface proteins were analyzed for this experiment. hMSCs and chondroblasts were cultured and chondroblasts were characterized using an Alcian Blue Stain. The gene list derived from the microarray will be corroborated with flow cytometry to confirm the differential expression of those surface markers. hMSCs will then be differentiated into chondroblasts, which will be harvested every few days to check for changes in surface marker expression to determine the intermediate stages of the differentiation pathway.

Reprinted from Volume 8, 2012, Women in Science, a publication of Stern College for Women.

Student Researcher

Rachel Blinick recently graduated Stern College with a major in Biology. Currently involved in biomedical research at Mt. Sinai School of Medicine, and having conducted research at Montefiore Medical Center this past summer, Rachel is passionate about the biomedical research world. In her spare time, she enjoys reading, tobogganing and discussing medical ethics with peers and mentors.

Neuroscience

Neuronal Growth and Regeneration

by

Judy Alper[1], Orit Shefi[2], Hadas Schori[2], and Michal Markus[2]

[2]*Department of Biology, Stern College for Women, Yeshiva University, New York, NY 10016;*

[2]*Department of Bio-Engineering, Bar-Ilan University, Ramat Gan, 52900 Israel*

The nervous system is one of the most pivotal systems in the body in that it determines all other forms and functions. Nevertheless, knowledge of the cellular and molecular mechanisms by which the mammalian nervous system operates, develops, and regenerates still needs thorough investigation. Dr. Orit Shefi's lab attempts to gain a better understanding of how neurons acquire their morphology and use these mechanisms to manipulate neuronal growth. This research has the potential to provide insights, which may help enhance neuronal recovery.

I have joined a graduate student, Michal Markus, in a project, which tests the effect of iron oxide nano-particles on the neurite outgrowth in rat pheochromocytoma cells (PC12) in the presence of neuron growth factor (NGF). This entailed the seeding of PC12 cells in vitro together with NGF and iron oxide nano-particles. We followed the neurite outgrowth in six different concentrations of nano-particles, from 0 μg/ml (control) to 40 μg/ml, over a period of three days. We analyzed the data collected using the NeuronJ program. The parameters for analysis of the outgrowth included number of neurites from the soma, number of branches, and average total neurite length. Although we expected to see an increase in neurite outgrowth with increased concentrations of nano-particles as well as with time, the results have been inconsistent. The experiment needs to be repeated in order to establish the verifiability of these results.

In addition to measuring neurite outgrowth in vitro, I have joined my lab manager, Dr. Hadas Schori, in a project, which involves the analysis of neuronal growth in vivo. To this end, we use a simple model of the nervous system- that of the medicinal leech, Hirudo medicinalis. Inspecting neuronal regeneration in the leech involved dissection, so as to expose, remove, and pin the ganglions. The ganglions, which encase the neurons, can then be subjected to experimentation. We have also attempted to perform leech skin transplantations in order to follow the recovery of the skin and the parallel neuronal contact created. Currently, we are working on setting up the technique for skin transplantation.

Both of the projects discussed have allowed us to gain increased knowledge in both the morphology and function of neuronal development and recovery. The results yielded thus far serve as preliminaries to further examinations and can contribute to uncovering new mechanisms by which neurons can grow and develop.

Reprinted from Volume 8, 2012, Women in Science, a publication of Stern College for Women.

Student Researcher

Judy is a junior at Stern College majoring in Physical Sciences. In addition to pursuing a degree in biomedical engineering, she enjoys acting, hiking, and The Lion King.

Neuroscience

Different Route of Administration for Melanocortin Receptor Agonist, Melanotan ii, in the Model of Cryptogenic Infantile Spasms

by

Yosefa Schoor[1], Tamuna Chachua[2], Libor Velisek[2], and Jana Velikskova[2]

[1]*Stern College for Women, Yeshiva University, New York, NY 10016;*

[2]*New York Medical College Valhalla, NY, 10595*

MelanotanII, Melanocortin receptor 3 and 4 agonist, administered intraperitoneally displayed potent effects against spasms in the prenatally primed model of cryptogenic Infantile Spasms (cIS). To confirm the central effects of melanotanII and to understand its true potential as an anti-epileptic drug for Infantile Spasms in humans, a different route of administration was tested in this experiment. The route of intranasal administration, which is less stressful then IP and prevents the peripheral effects seen in drugs like ACTH (the first line drug for cIS) was utilized. Due to its small size (ten amino acids) melanotanII was delivered intranasally and tested for its effect against spasms in prenatally betamethasone-primed animals. A concentration of 10μg of melanotanII in 6μl was administered through nostrils (3μl per nostril) in 15 days old rats. Control animals received saline instead of melanotanII. Collected data did not yield significant differences between intranasally melanotanII - and saline-delivered groups.

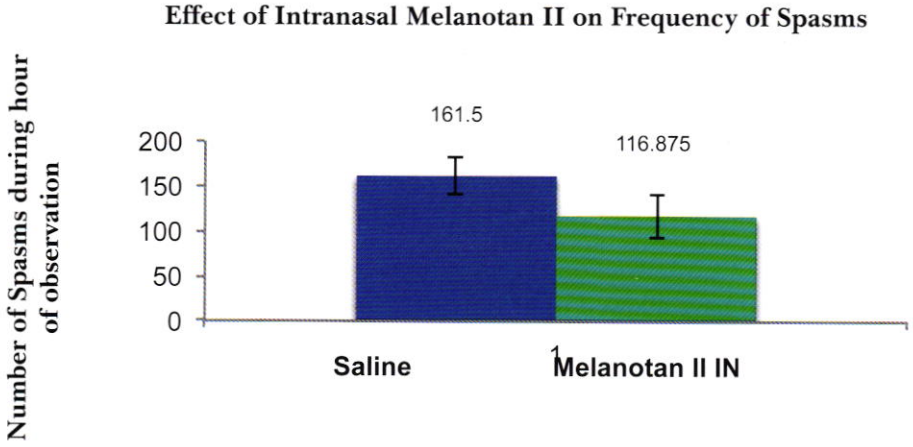


Figure 1. No significant difference in frequency of spasms was detected between saline and intranasal Melanotan II treated groups.

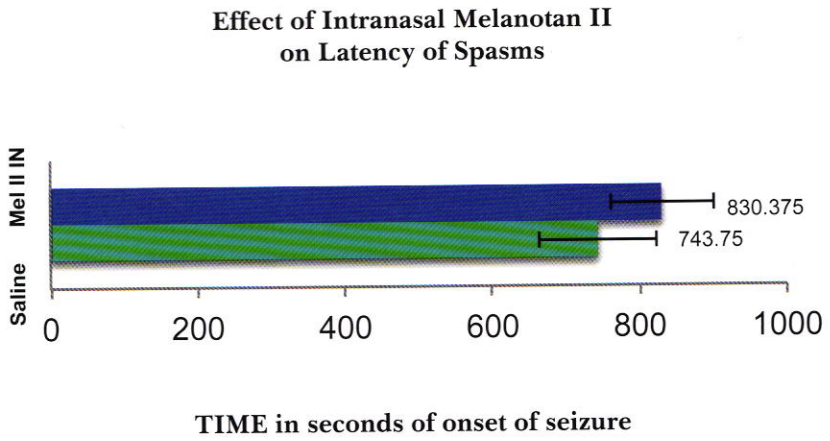


Figure 2. No significant difference in latency of spasms was detected between saline and intranasal Melanotan II treated groups.

Reprinted from Volume 8, 2012, Women in Science, a publication of Stern College for Women.

Student Researcher

Raised on a farm in Monsey, New York, Yosefa Schoor has always been intrigued by the inner workings of the body and especially the brain. After doing research at an fMRI unit at Columbia, a neuroscience lab at The Rockefeller University, and an epilepsy lab at New York Medical College, she saw the practical applications of science. However, when observing and interacting with doctors and patients, she recognized the necessity to view it within a context of a humane value system, the guiding light of medical ethics. As President of the Medical Ethics Society she has been motivated to spread these ideals and awareness to fellow students and the community at large. She plans on continuing her involvement in Yeshiva University's project TEACH, project START, SURGE, and Neuroscience Society.

Neuroscience

The Establishment of Transgenic Fish that Express Synaptic Markers on MCT8-positive Cells

by

Mordechai Smith[1] and Lior Appelbaum[2]

[1]*Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10033;* [2]*The Faculty of Life Sciences and The Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan 52900 Israel*

Allen-Herndon-Dudley syndrome (AHDS) is an X-linked psychomotor retardation that is characterized by hypotonia (low muscle tone), muscle hypoplasia (low number of muscle cells), paroxysmal dyskinesia (sudden episodes of abnormal involuntary movements), and severe cognitive impairment. AHDS symptoms also include abnormal levels of thyroid hormone (TH), specifically, high serum T3 levels and low serum T4 levels. AHDS is associated with mutations in the trans-membrane transporter protein monocarboxylate transporter 8 (MCT8). In this project we used the zebrafish (Danio rerio) model to visualize MCT8 expression cells with fluorescent markers. The zebrafish is a powerful vertebrate model with conserved organization of the central nervous system (CNS). The Mct8 gene is highly conserved in zebrafish with its mammalian ortholog (shares 56-57% homology).

Dr. Appelbaum's lab is seeking to understand the neurological mechanism underlying AHDS. Because neurological impairment in AHDS is rooted in MCT8 deficiency, we wanted to check synaptic activity as loss of MCT8 may affect synaptogenesis and synaptic plasticity and ultimately affect neuron function. In order to do so, DNA constructs containing mct8 promoters that drive the expression of the coding sequences of either the presynaptic protein SYP or the post-synaptic proteins PSD95 and GPHN fused to EGFP (green fluorescence) or tagRFP (red fluorescence), were injected into one-cell-stage-embryos. These embryos (F0) were raised to adulthood and, in this project, F0 fish were screened to isolate stable transgenic lines.

To find a transgenic fish, we must first assure that the F0 fish has incorporated the transgene into its germline cells. Germline cells are progenitors to gametes such as eggs and sperm. Only if a F0 fish has incorporated the new gene into its germline will its progeny have the modified gene.

My project was to screen all F0 fish for the presence of several transgenes in the germline. Screening is done in two steps. First, I outcrossed all F0 transgenic fish with wild type fish. I then purified DNA from the ensuing batch of embryos (F1). From the DNA, I amplified the region of the transgene (EGFP or tagRFP) using Polymerase Chain Reaction (PCR). The resulting product was run through a gel electrophoresis which allowed me to screen for the presence of the transgene. If the F1 DNA contained the transgene, I was able to ascertain that the F0 fish had incorporated the transgene into its germline. The second step in screening required re-crossing the positive F0 fish and observing the F1 for actual fluorescence. A fluorescent binocular was used to observe the fish and any fish that showed positive signs of the fusion protein was considered a line.

I outcrossed 23 mct8:GPHN-tRFP fish, 16 mct8:PSD95-EGFP fish, and 4 mct8:SYP-EGFP fish. I received a positive PCR result in 3 mct8:PSD95-EGFP fish, 3 mct8:GHPN-tRFP fish, and 2 mct8:SYP-EGFP fish. Of those fish, two mct8:PSD95-EGFP fish have shown fluorescence and may be raised for further analysis of MCT8 function. These lines may also shed light on the neurological mechanism of AHDS.

Student Researcher

Mordechai Smith was born in Boston, Massachusetts, and after living in Israel for seven years, he currently lives in Lawrence, NY. He just finished his third year at YU where he is majoring in Biology, minoring in Public Health and pursuing a career in medicine. He is currently the Executive Director of the YU Student Medical Ethics Society (MES). In addition to being involved in MES, Mordechai is the President of the Biology Majors Board. Over the last couple of years, Mordechai has tutored math in the local middle school, PS 143, as a member of the Literacy Program and tutored Biology at the YU campus. He is also very involved in Project START, a program that teaches science modules to students in local elementary schools.

Shifting Trends of Ragweed (Ambrosia) Measurements During a 22 Year Period in Northern and Southern New Jersey

by

Jonathan Maik[1], Yong Zhang[2], Donald Dvorin[3], Panos Georgopoulos[4], and Leonard Bielory[5]

[1]*Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10033;*

[2]*Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, NJ 08854;*

[3]*Drexel University College of Medicine, Philadelphia, PA 19129;* [4]*Robert Wood Johnson Medical School, Piscataway, NJ 08854;* [5]*Center for Environmental Prediction, Rutgers University, New Brunswick, NJ 08901*

Rationale: Ragweed is a clinically significant aeroallergen. Total pollen production (TPD), pollen season start dates (PSSD), peak dates (PPD), season duration (PSD), count annual mean (PCAM), and peak values (PPV) for Ragweed changed over a 22 year period.

Methods: Ragweed pollen was collected from Northern (Newark; [N]) and Southern (Cherry Hill; [CH]) New Jersey regions using a volumetric sampling device according to the NAB standard. TPD= count values for a given year; PSSD= date in which 5% of pollen production of that year had been reached (n=days into year). PPD= date with highest pollen count, (n=days into year). PSD= amount of days between start date and end date for each species. (End date= day in which 95% of pollen production was reached). PCAM= arithmetic mean of pollen count values from the entire year. PPV= highest pollen count value for the entire year.

Results: Over the 22 year span; the arithmetic mean of the last five years was compared to the arithmetic mean of the first five years (N:CH). TPD decreased 76.6% vs 44.0%; PSSD decreased .1% vs 2.7%; PPD increased 2% vs 3.7%; PCAM decreased 70.9% vs 54.8%; PPV decreased 50.4% vs 23.9%; PSD decreased 21.8% vs an increase of 19.7%.

Conclusions: Ambrosia in two locations NJ (70 miles apart) demonstrated similar decreasing trends for TPD, PCAM, PPD, PSSD, and PPV while PSD demonstrated a dichotomy.

Student Researcher

Jonathan is a junior majoring in Biology at Yeshiva College and lives in Livingston New Jersey. Jonathan is the President of the Yeshiva University Public Health Club, and is currently involved in aeroallergen research. He is especially appreciative to his parents who always support his endeavors and to Dr. Bielory for his guidance with the research.

Environmental Science

Effect of Desert Coastal Dune Plants' Ecophysiological Adaptations on Free-Living Soil Nematode Communities in Yavne, Israel

by

Nathan Japhet[1] and Yosef Steinberger[2]

[1]*Department of Biology, Yeshiva College, Yeshiva University, New York, NY, 10033;*

[2]*Terrestrial Ecology Laboratory of Bar-Ilan University, Ramat Gan, 52900 Israel*

Plants are associated with dune stabilization and are bio-indicators of a dune's relative stability. Due to nutrient source limitation, development of different ecophysiological adaptations among plant communities generates distinct microhabitats underneath plant species, which will determine the density, distribution and composition of soil organisms. The aim of the study was to determine the effect of plant ecophysiological adaptations on soil nematode communities in the desert coastal dune ecosystem. Samples were collected in June 2012 from underneath three perennial plants with significantly different ecophysiological adaptations: *Echium angustifolium*, a shrub thought to have anti-nematode properties; *Stipagrostis lanata*, a low-lying grass and indicator of dune stability; and *Artemisia monosperma*, a low sand-fixing shrub and indicator of dune mobility. An inter-plant area was used as a control.

The results demonstrated that soil water content (SWC) and pH were significantly different under different plants and inter-plant areas, with the highest values found under *Echium angustifolium* (pH) and *Stipagrostis lanata* (SWC). SWC and pH were positively correlated with nematode community density, which was significantly higher under *Echium angustifolium* than other locations; the lowest density of nematode communities was under *Artemisia monosperma* and control samples. In previous studies, however, SWC has been shown to negatively correlate with the density of soil nematode communities due to excess water in soil pore caves reducing predator-prey interactions. It seems that SWC is only positively correlated with nematode density in the short term. Nematode density was not significantly different among soil depths in *Echium angustifolium* (P= 0.96) and *Artemisia monosperma* (P= 0.95) locations; demonstrating those plants' ecophysiological adaptations effect is more significant than soil depth. Nematode density under *Stipagrostis lanata* and control locations did vary significantly by depth due to the lack of adequate plant cover of the surface soil layer. The anti-nematode properties of the *Echium* shrub did not have the expected effect on nematode density and further research is needed into its anti-nematode properties.

Table 1. Univariate analysis of variance (ANOVA) for soil properties under different plants and inter-plant area in Negev desert near Yavne, Israel.

	Plants		Depths		Plants*Depths	
	F-Test	P-value	F-Test	P-value	F-Test	P-value
Soil properties						
Soil water content (SWC)	5.81	0.0024	0.42	NS	1.39	NS
Total organic carbon (Corg)	2.33	NS	2.38	NS	1.13	NS
pH	54.75	<0.0001	7.04	0.0026	6.13	0.0002
Conductivity	1.46	NS	0.41	NS	0.72	NS
Na	0.24	NS	0.92	NS	1.29	NS
K	7.65	0.0004	1.68	NS	1.41	NS
Ca	0.52	NS	0.45	NS	1.58	NS
Total nematodes (Tnem)	6.63	0.0011	0.79	NS	0.61	NS

Table 2. Descriptive statistics for the investigated components of soil for sampling period

	E. angustifolium	*S. lanata*	*A. monosperma*	*Control*
pH	7.36±0.11	7.35±0.07	7.09±0.05	7.22±0.08
Cond (µS)	99.37±13.03	91.96±7.03	101.03±14.83	95.39±8.38
SM (%)	0.3±0.13	0.31±0.20	0.14±0.08	0.14±0.11
OM (%)	0.25±0.12	0.30±0.10	0.38±0.10	0.3±0.10
Ca	22.77±6.43	23.92±3.21	25±6.74	25.83±6.69
K	1.57±2.13	-.05±1.16	0.33±0.71	-1.23±0.88
Na	1.43±1.43	0.77±1.98	1.68±4.35	1.53±2.09

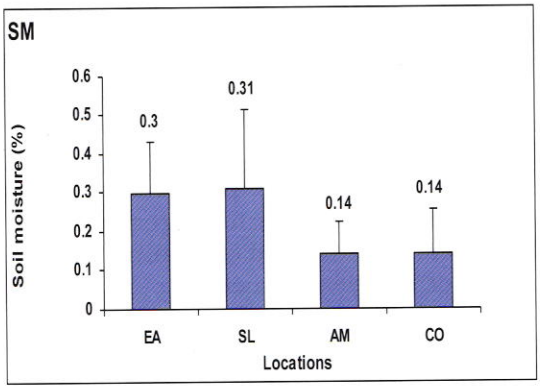


Figure 1. Soil Moisture between Locations

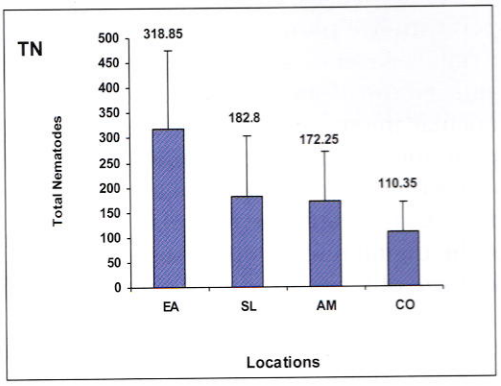
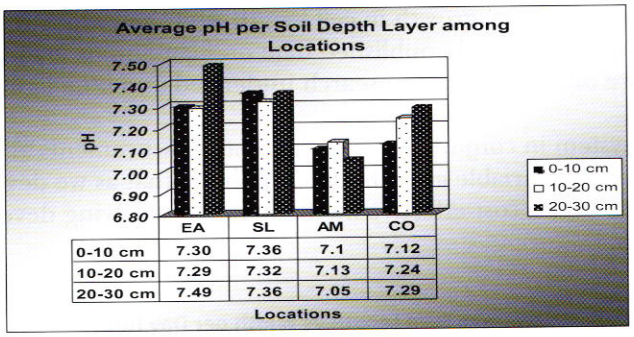


Figure 2. Average Total Nematode Density between Locations



	EA	SL	AM	CO
0-10 cm	7.30	7.36	7.1	7.12
10-20 cm	7.29	7.32	7.13	7.24
20-30 cm	7.49	7.36	7.05	7.29

Figure 3. Average pH per Soil Depth Layer among Locations

References:

Pen-Mouratov, S., Hu, C., Hindin, E. and Steinberger, Y. (2011) Soil microbial activity and a free-living nematode community in the playa and in the sandy biological crust soil formations of the Negev Desert. Biology and Fertility of Soil 47: 363-375.

Student Researcher

Nathan is a senior in Yeshiva College majoring in Biology. His research interests are in the natural processes of the environment, especially the ecological field; including, but not limited, to an interest in the biogeological cycles, pteridology, soil ecology, and clean technology. He currently is involved in research that examines the growth patterns of several species of fern gametophytes and uses a digital microscopy system to create time-lapse photography of the growing plants. Nathan has conducted research in the past at the Clinical Molecular Biology laboratory of Rhode Island Hospital where he worked on the optimization of a procedure that tested for microsatellite instability in clinical tumor samples. He has also worked in a research program between Bar-Ilan University and Yeshiva University where he conducted research on the vertical distribution of free-living nematode species in the sand dunes of Yavne, Israel in Bar-Ilan's Terrestrial Ecology Laboratory.

A Correlation Study of Fern Gametophyte Growth Using Ocular Micrometers Compared to a Software-Controlled Digital Microscopy System (Moticam 352)

by

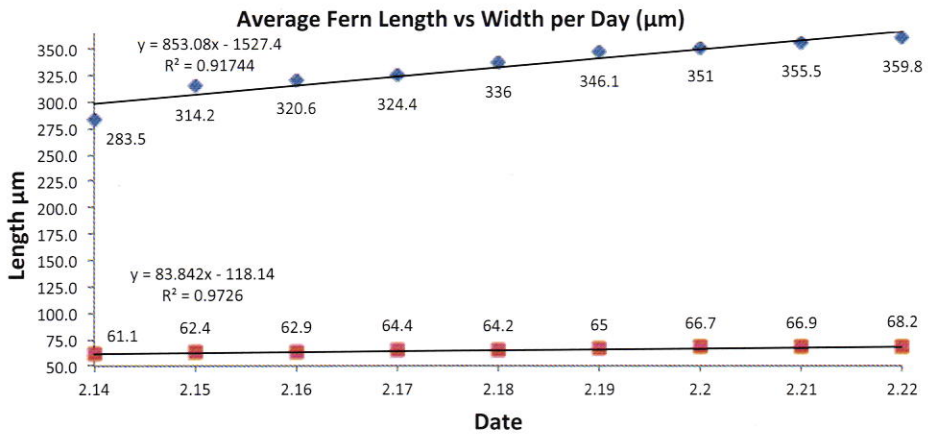
Nathan Japhet, Brian Goodman, Ilya Gorelick, Yaakov Chein,
Aitan Magence, and VJ Chiappetta

Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10333

The use of inexpensive digital cameras simultaneously attached to microscopes and computers, equipped with live photo-capture technology, can be used to study whole organism development and/or cellular events. These systems allow for continuous time-lapse imaging on the computer. This study utilized the Moticam 352 system. The standard methodology for fern cell measurement is to use an ocular micrometer to measure the cells. In comparison, this digital microscopy system was adopted to increase the precision of measurement of the fern cells. The system, in addition, allows continuous time-lapse imaging of a specific fern gametophyte. These more precise measurements will enable us to determine the relative accuracy of our ocular micrometer measurements. The drawback of the digital microscopy system is that with the camera's limited field of capture, the available sampling size of ferns is reduced compared to that of the ocular measurements.

We focused on the early developmental events of single-celled layered *Dryopteris erythrosora* fern gametophytes- including germination, cell division, and filamentous growth. The software technology was utilized to measure the length and width of each cell of the developing gametophyte from the filamentous to the 2-D prothallus stage, as well as the total length of the fern. This allowed us to trace the variable growth rates of fern gametophytes in standard white light conditions. We found that the filamentous stage displayed primary growth in cell length while cell width remained, on the average, stable. This is consistent with previously published data on filamentous growth in other species. We are now going to compare our system with research under red and blue light growth conditions.

This digital microscopy system in conjunction with manual measurements allows researchers a cost-effective method of measuring variable growth rates. We hope that as we develop the digital microscopy system, this will introduce a cost-effective methodology of studying developmental changes in fern gametophyte studies.



Graph 1. This compares total fern length to average fern cell width in one of the Moticam 352 system measured gametophytes. The blue line represents the best-fit line for the growth of the averaged length of all the cells of the fern per day. The red line represents the best-fit line for the growth of the averaged width of all the cells of the fern per day.

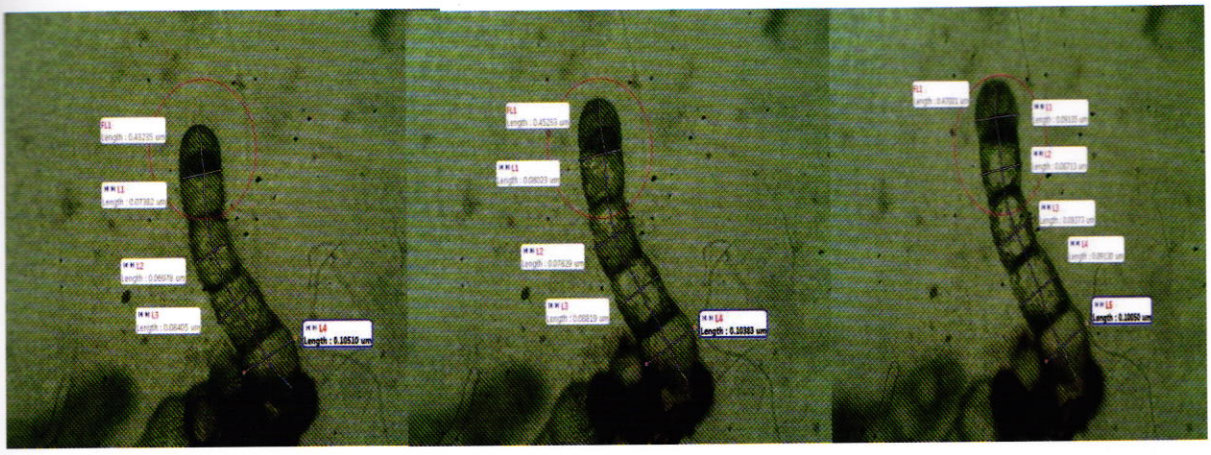


Figure 1. Examples of Moticam 352 Measured Fern Gametophyte Displaying Time-Lapse Growth

References:

Mills, D.A., Kelley, K. & Jones, M. (2001). Use of a digital camera to document student observations in a microbiology laboratory class. The American Biology Teacher, 63(2), 119-- 123.

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Kiss, Helen G, Kiss, John Z. (2005). Sensing Red, White & Blue Using Spores of the Sensitive Fern To Introduce Important Concepts in Biology. The American Biology Teacher, 67 (9), 549-555.

Student Researchers

Nathan is a senior in Yeshiva College majoring in Biology. His research interests are in the natural processes of the environment, especially the ecological field; including, but not limited, to an interest in the biogeological cycles, pteridology, soil ecology, and clean technology. He currently is involved in research that examines the growth patterns of several species of fern gametophytes and uses a digital microscopy system to create time-lapse photography of the growing plants. Nathan has conducted research in the past at the Clinical Molecular Biology laboratory of Rhode Island Hospital where he worked on the optimization of a procedure that tested for microsatellite instability in clinical tumor samples. He has also worked in a research program between Bar-Ilan University and Yeshiva University where he conducted research on the vertical distribution of free-living nematode species in the sand dunes of Yavne, Israel in Bar-Ilan's Terrestrial Ecology Laboratory.

Genetics

Lipid Signaling Between Soma and Germline May be Required for Drosophila Spermatogenesis

by

Geulah S. Ben-David and Josefa Steinhauer

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Lysophospholipids are single fatty acid chain phospholipids that can promote proliferation, motility, and survival in cultured cells. In mammals, lysophospholipid signaling has been linked to cancer progression and has been implicated in normal physiology and development. Mechanisms that regulate lysophospholipid levels in vivo are not well understood. One pathway by which lysophospholipids are generated is the Lands cycle, in which phospholipase A_2 (PLA_2) converts membrane phospholipids to lysophospolipids by removal of a fatty acid chain (deacylation). PLA_2 activity is counterbalanced by the activity of membrane-bound O-acyltransferase (MBOAT) family enzymes, which catalyze the reacylation of lysophospholipids into phospholipids (Figure 1). Oysgedart (Oys) and Nessy (Nes) are Drosophila MBOAT family lysophospholipid acyltransferases. Adult male *oys nes* mutants are sterile with a complete block in spermatid individualization. RNA in situ hybridization shows that *oys* and *nes* are expressed in the testis (Figure 2). The spermatogenesis defect of *oys nes* mutants can be rescued by expression of Oys cDNA in the somatic cells of the testis but not the germline, and the defect can be phenocopied by RNAi-mediated knock-down of *oys* and *nes* in the somatic cells. In *oys nes* mutants, molecular markers of somatic cell development are expressed normally, and somatic cell membranes appear normal with a fluorescent membrane marker. Additionally, five of the ten Drosophila PLA_2 genes are expressed in the testis (Figure 3), and overexpression of PLA_2 in the somatic cells causes individualization defects. Together, our data suggest that the Lands cycle mediates cell communication between soma and germline in the Drosophila testis, by regulating the availability of lysophospholipid signals. These studies provide a novel context for investigating the roles of lysophospholipid signals in cell communication and fertility.

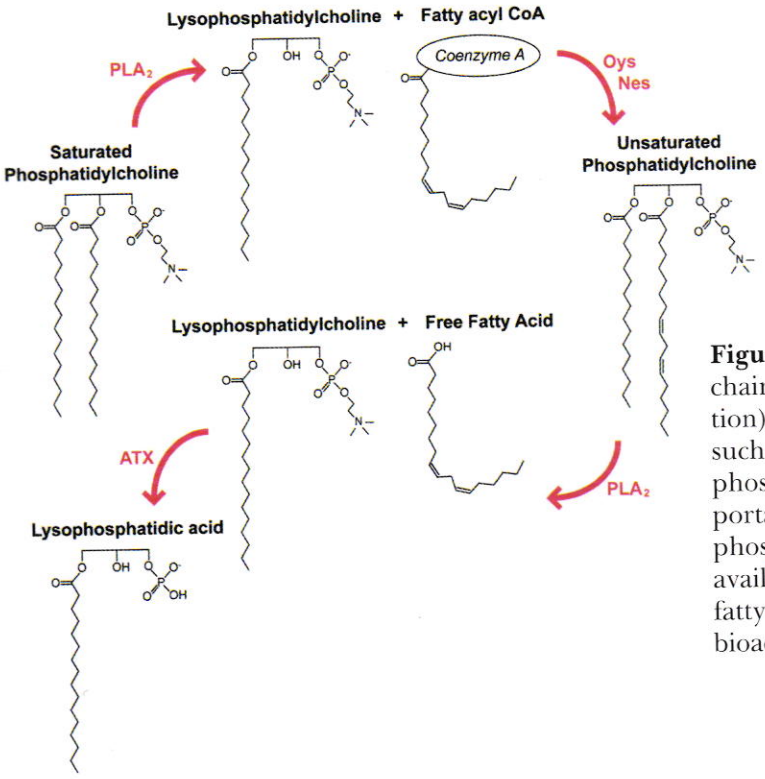

Figure 1. PLA_2s remove fatty acid chains from phospholipids (deacylation), while MBOAT family LPLATs such as Oys and Nes reacylate lysophospholipids. The Lands cycle is important for remodeling of membrane phospholipids but also regulates the availability of lysophospholipids and fatty acids, which can act as bioactive lipid signals between cells.

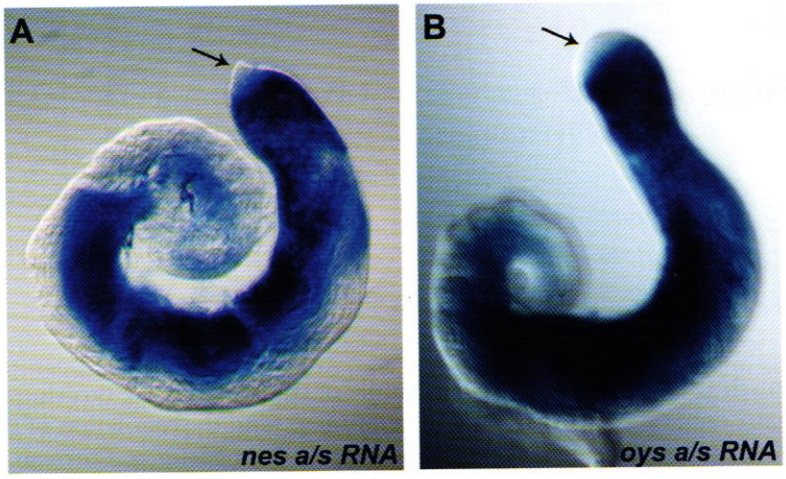

Figure 2. RNA in situ hybridization reveals *nes* (A, blue) and *oys* (B, blue) expression in the Drosophila testis. Both transcripts are expressed in dividing cysts but not in the germinal proliferation center (arrows).

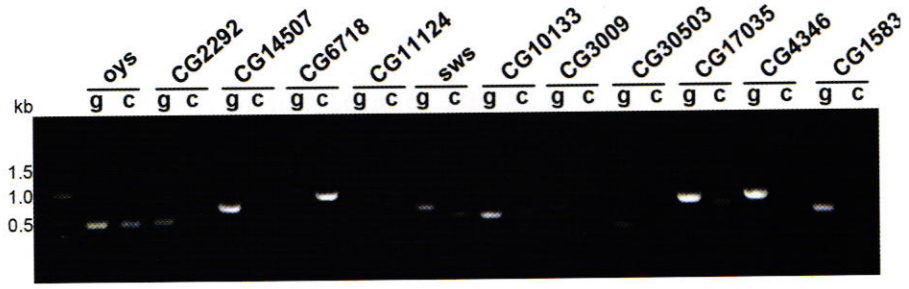

Figure 3. RT-PCR on wild-type testis cDNA indicates that predicted PLA_2 genes CG10133, CG17035, CG14507, CG6718, and sws are expressed in testes. Additionally, the putative ATX homolog encoded by CG2292 also is expressed.

Student Researcher

Geulah graduated last May from Stern with a degree in Biology. She is currently working as a Research Assistant in Dr. Steinhauer's Lab at Yeshiva College with the Drosophila model organism. In her spare time, Geulah enjoys traveling and experiencing art and culture.

Genetics

Processing and Presentation of the Drosophila Epidermal Growth Factor Receptor Ligand, Spitz

by

Eli Miller[1], Josefa Steinhauer[1], and Jessica E. Treisman[2]

[1]*Department of Biology, Yeshiva College, New York, NY 10033;*

[2]*Skirball Institute for Biomolecular Medicine, New York, NY 10016*

The Epidermal Growth Factor Receptor (EGFR) family of transmembrane tyrosine kinase receptors is utilized in many contexts during animal development, and dysregulation of this pathway has been implicated in numerous human cancers. Drosophila melanogaster has proven to be a valuable model for studying EGFR regulation in vivo. Like human EGFR ligands, the predominant *Drosophila* EGFR ligand Spitz (Spi) is produced as a type I transmembrane pro-protein. Maturation to the active ligand requires proteolysis within its transmembrane domain to release the soluble extracellular domain, called sSpi. sSpi is palmitoylated at its N-terminus, and palmitoylation mediates membrane association at the cell surface following secretion. Spi pro-protein is not active in vivo. This stands in contrast to mammalian EGFR ligand pro-proteins, which often are active EGFR ligands themselves; however, their activity often differs from that of the processed ligands. To understand why the Spi transmembrane pro-protein is inactive while membrane tethering via palmitoylation promotes activity, a panel of chimeric transmembrane Spi constructs was generated by fusing the Spi extracellular region to the transmembrane proteins Neurotactin (Nrt), Gliotactin (Gli), or CD2 (Figure 1A). The Spi palmitoylation site was mutated in all three constructs. In the Nrt-Spi chimera, the type II transmembrane protein Nrt was fused to the sSpi N-terminus, mimicking the orientation of wild-type palmityolated sSpi. In the Spi-Gli chimera, sSpi was fused at its C-terminus to the type I transmembrane protein Gli, reversing the orientation of sSpi with respect to the membrane. In Spi-CD2, sSpi was fused at its C-terminus to the type I transmembrane domain from rat CD2, producing a shortened extracellular domain that mimics the Spi pro-protein. We also generated a fourth chimera, Spi-Gli-Spi, in which the Spi cytoplasmic domain replaced the Gliotactin cytoplasmic domain in Spi-Gli.

The activity of the four constructs was measured in the imaginal wing disc using a *lacZ* reporter for EGFR signaling. Nrt-Spi and Spi-Gli both induced strong EGFR pathway activity, whereas Spi-CD2 and Spi-Gli-Spi induced weak pathway activity. Co-expression with the Spi trafficking factor Star appeared to have no measureable effect on the activity of Spi-Gli or Spi-CD2 (Figure 1B, C, D, E), whereas it enhanced the activity of Spi-Gli-Spi (Figure 2). Together, these data reveal that Spi can activate the EGFR when tethered to the membrane, that the orientation of sSpi with respect to the membrane does not affect signaling capacity, that reducing the distance between the membrane and sSpi does not prevent signaling, and that the Spi cytoplasmic domain mediates dependence on the trafficking factor Star. Although they differ only in their transmembrane and cytoplasmic domains, Spi-CD2 activates the EGFR while the Spi pro-protein does not. Gaining a better understanding of how ligand processing potentiates ligand activity will shed light on the formation and development of cancers in humans and can open doors to further investigation of paracrine signaling in general

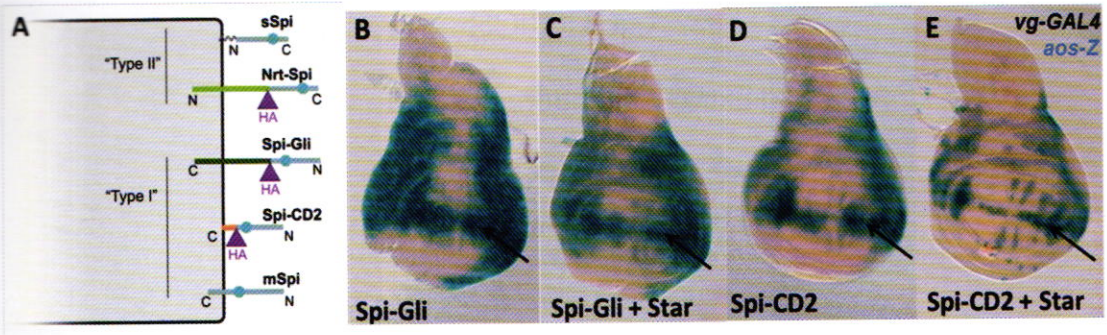

Figure 1. Co-expression with Star appears to have no measureable effect on the activity of Spi-Gli or Spi-CD2. (A) Transmembrane Spi chimeras were generated by fusing sSpi to exogenous proteins. Nrt is illustrated in light green, Gli in dark green, and CD2 in orange. Palmitate is represented by the zigzag. N- and C- termini are indicated. All chimeras were tagged with an HA epitope. The structures of Spi pro-protein (mSpi) and processed sSpi are shown. (B,C,D,E) Spi-Gli and Spi-CD2 induced ectopic argos-lacZ in wing imaginal discs when expressed with vg-GAL4 either alone (B,D) or with co-expressed Star (C,E), but induction was not stronger when co-expressed with Star. B, C, D, and E were stained and imaged in parallel.

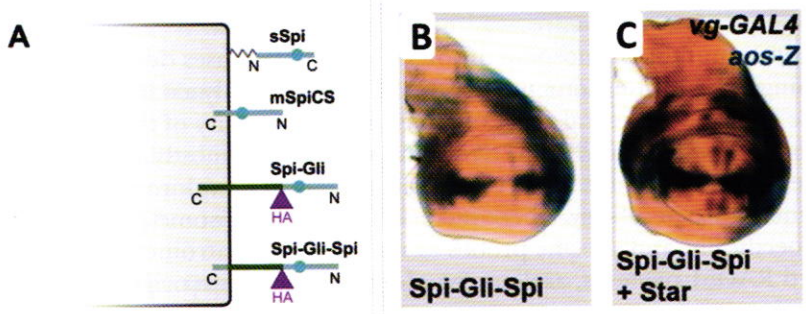

Figure 2. Spi-Gli-Spi activity depends on Star. (A) The Gli cytoplasmic domain in Spi-Gli was replaced with the Spi cytoplasmic domain to generate Spi-Gli-Spi. (B,C) Spi-Gli-Spi induced ectopic argos-lacZ in wing imaginal discs when expressed with vg-GAL4 either alone (B) or with co-expressed Star (C), but induction was stronger when co-expressed with Star. B and C were stained and imaged in parallel.

Student Researcher
Eli Miller is a senior at Yeshiva College majoring in Biology and minoring in Chemistry. He will continue his research at Yeshiva College under Dr. Steinhauer throughout the next academic year after which he plans to attend medical school.

Genetics

Exploring Extra Pericentromeres and Telomeres

by

Naomi Schwartz[1], Yinghui Song[2], Jidong Shan[2], Tae Moon Kim[4], Paul Hasty[4], and Cristina Montagna[2], [3]

[1]*Department of Biology, Stern College for Women, Yeshiva University, New York, NY 10016.*

[2]*Department of Genetics and* [3]*Pathology, Albert Einstein College of Medicine of Yeshiva University, Bronx, NY 10461.*

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Inefficient DNA repair is a major cause of genetic instability and chromosome abnormalities, common characteristics of cancer cells. Proper genome maintenance is critical to the cell's well-being, and thus, several repair pathways have evolved to cope with DNA damage. One of such pathways includes the homologous recombination protein RAD51, a RecA recombinase important for replication fork maintenance. Proper ATP binding is critical for RAD51 function: when RAD51's lysine K133 (an important ATP binding factor) is mutated into its defective K133A form, chromosomal rearrangements occur within the cell. Previous research identified a hitherto undescribed chromosomal abnormality, Extra Pericentromeres and Telomeres (EPTs), that appears within these mutated cells, yet there has been no further study of these novel rearrangements. This study focuses on EPTs specifically: how many occur, which chromosomes they affect, and whether they affect single chromosome duplication or multi-chromosome fusion. Mouse metaphases derived from K133A cells were visualized using Spectral Karyotyping. Of the 33 spreads analyzed, 63 EPTs were located, as well as a multitude of other structural rearrangements. The majority of the EPTs visualized affected three specific chromosomes: 1 and 11 (mostly duplicated), and 8 (mostly fused to chromosome 11). In order to ensure that these results are accurate, and to further explore the complexity of EPTs, additional experiments are necessary. These include using chromosome-painting probes to visualize chromosome 11 specifically, and specific probes to visualize the centromeres and telomeres. EPTs are formed by mutated RAD51 proteins, and are far more complex than originally thought, requiring much additional study.

Acknowledgements

I would like to thank the Molecular Cytogenetic Core at Albert Einstein College of Medicine for assisting me with the execution of the SKY hybridizations, image acquisition, and analysis. I would also like to thank the members of the Montagna and Hasty labs for providing support and sharing reagents. Additional thanks go to the Summer Undergraduate Research Program at Albert Einstein College of Medicine, for the funding allowing me the opportunity to carry out this research summer project, as well as to NIH CA013330-38 to I.D. Goldman and ACS 120025 to C. Montagna for additional funding.

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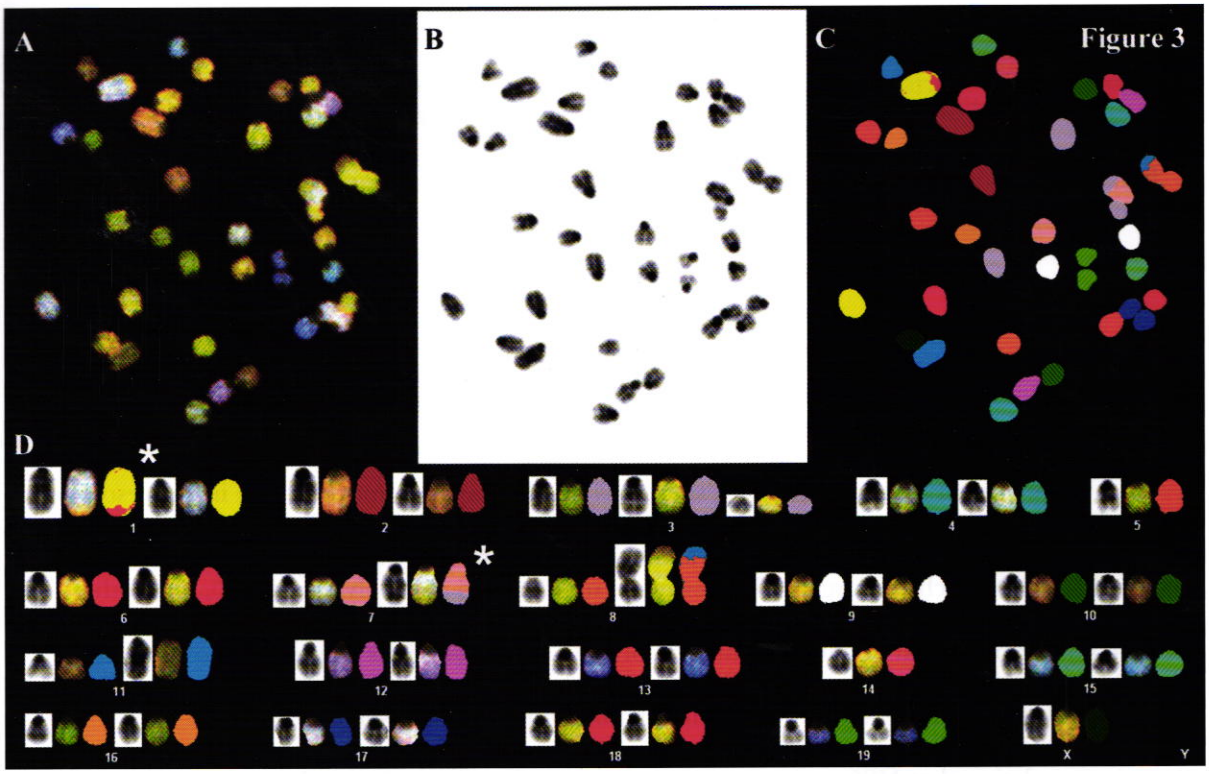

Spectral Karyotyping of HsRAD51^{K133A} mouse metaphases.

(A) Metaphase spreads visualized in red, blue, and green through spectral pixel analysis
(B) DAPI staining of the chromosome bands
(C) Metaphase spreads visualized in their computer assigned pseudo-colors to help the classification process
(D) Karyogram containing the spectral, DAPI, and pseudo-color classifications

Note the EPTs common in chromosomes 1, 8, and 11 (see asterisks), which can be identified through their distinctive stacked arrangements (telomere-to-centromere attachments).

Student Researchers
Naomi Schwartz is a junior at Stern College for Women of Yeshiva University. She is majoring in Molecular and Cellular Biology, and hopes to attend medical school in the future.

Pulmonology

Resolution of Lung Inflammation with MSC and Aspirin to Cure ARDS

by

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[2]*Harvard Institutes of Medicine, Boston, Massachusetts 02115*

This summer I was fortunate to work in a lab under the supervision of Dr. Bruce Levy MD of Harvard Medical Institutes and Brigham and Womens Hospital in Boston. I was able to take part in two separate studies, The UCSF Project and the LIPS-A Study.

Recent studies suggest that mesenchymal stem cells (MSC) play an important role in the resolution of lung inflammation. When a human lung is exposed to bacterial endotoxins, (a toxin contained within the bacterial cell wall which has the ability to cause disease, synonymous with Lipopolysaccharides (LPS) which are large molecules made up of a lipid and polysaccharide), or another injury-related stimulus, an inflammatory response characterized by increased permeability of lung endothelium or pulmonary edema (a build up of fluid in the alveoli) is triggered. However, if the injured lung is then treated with either MSC or its cultured media, pulmonary edema is reduced, the endothelium barrier is restored, and the inflammatory state is resolved.

There is speculation that MSC promotes the resolution of inflammation and tissue repair through the secretion of paracrine signaling molecules, such as lipoxins. In our human *in vitro* study called the UCSF Project, we investigated the effects of the interactions between MSC and alveolar type 2 cells (ATII) on Lipoxin A_4 (LXA_4) secretion. To do so, ATII cells were grown with MSC in media, either in the same or separate cell chambers, with pro-inflammatory cytokines (signaling molecules). LXA_4 levels in these media samples were then quantified with an ELISA assay. We were determined to see if the LXA_4 is one of the paracrine compounds that MSC secrete and if LXA_4 plays a role in the MSC-mediated pro-resolving and tissue-repairing effects.

My particular role in this study was to perform lipid extractions and ELISAs to measures the LXA_4 levels. This was done in order to see if the levels of LXA_4 changed between ATII cells and MSC versus ATII cells with regular fibroblasts (cells that play a role in wound healing.)

We conducted an additional study called LIPS-A which focused on a particular disease called Acute Respiratory Distress Syndrome (ARDS). ARDS is a leading cause of mortality in patients with pulmonary abnormalities. Initial development of ARDS involves vascular endothelial dysfunction and increased permeability of the alveolar-capillary barrier, both of which are associated with an inflammatory state. As result of these changes, fluids accumulate in the alveoli of the lungs (both due to higher influx and lower clearance of fluids). As alveoli are filled with fluids, less oxygen are exchanged between alveoli and the bloodstream. At this stage, patients often suffer from hypoxemia (low oxygen levels in the blood), organ failures, and death. Aspirin is known to have anti-inflammatory and pro-resolving properties. Given that early stages of ARDS involve the development of an inflammatory state in the vasculature (blood vessel walls), treatment with regular doses of aspirin for at-risk patients may reduce the risks leading to the onset of ARDS. The LIPS-A score was recently developed

to predict the risk of ARDS development (and this was how the risks of ARDS are quantified). In our study, the "Levy Lab" is partially investigating whether aspirin significantly reduces lung inflammation and if so, what are the effects of aspirin on the blood concentration of various eiconsanoids such as Thromboxane B2 (TXB2) and 15-epi-LXA_4.

To aid to this study, I performed lipid extractions and ELISAs to measure the levels of TXB2 and 15-epi-LXA_4 to see if the levels were different between ARDS taking aspirin compared to patients who did not take the medicine.

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Student Researcher
Jennifer Herskowitz is a junior at Stern College for Women majoring in Biology. In her free time, Jennifer enjoys to paint. She is the oldest of five children and her dream is to pursue a career in Dermatology.

Biophysics

Conformations of 2-methyl-2,4-pentanediol in Protein Crystals

by

Dahniel Sastow[a,b], Ariel Axelbaum[a,b], Jean Jakoncic[c], Jerome Karp[a,b], Sergey V. Buldyrev[a], Bruce J. Hrnjez[d], and Neer Asherie[a,b]

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[b]*Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10033;*

[c]*National Synchrotron Light Source, Brookhaven National Laboratory, Upton, NY 11973;*

[d]*Collegiate School, New York, NY 10024*

One of the most common organic additives in protein crystallization is the chiral molecule 2-methyl-2,4-pentanediol (MPD). We have recently found that when MPD is used to crystallize lysozyme, the resolution and disorder of the protein crystals are affected by which enantiomer is used. In order to understand this chiral effect, it is essential to assign properly any MPD molecules present in the crystal structure, i.e., to select the conformer(s) and enantiomers(s) of the molecule that best fit the electron density.

To guide our selection, we examined the conformations of (*R*)- and (*S*)-MPD found in the RCSB Protein Data Bank and the Cambridge Structural Database. In addition, we carried out quantum chemical and molecular dynamics simulations to characterize the possible conformers of MPD. We find that the most stable conformer is the one where the two torsion angles that characterize the five-carbon backbone are both approximately 180°; other conformers are significantly less stable. The stability of this conformer is due to the favourable arrangement of the substituents on adjacent carbons and the formation of an intramolecular hydrogen bond. Our results illustrate the usefulness of determining the allowed conformers of small molecules in order to validate models for protein-ligand complexes.

Student Researcher

Dahniel is in his first year on campus at Yeshiva University, after spending a year in Israel, and is majoring in Biology. When he isn't in the lab or studying, Dahniel enjoys playing basketball and watching TV shows.

Biophysics

Crystallization of Lysozyme with (R)-, (S)- and (RS)-2-methyl-2,4-pentanediol

by

Ariel Axelbaum[1,2], Jean Jakoncic[3], Mark Stauber[1,2], Jacob Berger[1,2], and Neer Asherie[1,2]

[1]*Department of Physics, Yeshiva College, Yeshiva University, New York, NY 10033;*

[2]*Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10033;*

[3]*National Synchrotron Light Source, Brookhaven National Laboratory, Upton, NY 11973*

We are investigating an aspect of protein-precipitant interactions that is relatively unexplored in the context of protein crystallization: chirality. Here we discuss the crystal structures of lysozyme with the chiral precipitant 2-methyl-2,4-pentanediol (MPD). We chose this protein-precipitant pair for three reasons. First, lysozyme is the most widely examined protein in crystallization and structural analysis studies. Second, MPD is a chiral molecule that is one of the most common additives in protein crystallization, though until now it has been used exclusively in the racemic form. Third, lysozyme has been previously crystallized with (*RS*)-MPD, but the results of these investigations are contradictory: Weiss et al. [1] find only (*R*)-MPD in the crystal, while Michaux *et al.* [2] find only (*S*)-MPD.

We find that (*R*)- and (*S*)-MPD interact differently with the protein. The resolution and disorder of the crystals vary with the precipitant used: the highest quality crystals produced with (*R*)-MPD. When (*RS*)-MPD is the precipitant, only (*R*)-MPD molecules are observed in the crystal and they are at the same locations found for pure (*R*)-MPD. As the structure of the protein is essentially identical for all precipitants used, our work shows that the chirality of precipitants provides an additionally way to affect protein crystallization.

[1] Weiss, M.S., Palm, G.J. & Hilgenfeld R. (2000) Acta Cryst. D 56, 952.
[2] Michaux, C., Pouyez, J., Wouters, J. & Prive G.G. (2008) BMC Struct. Biol. 8, 29.

Student Researcher

Ariel Axelbaum is a senior and chemistry major in Yeshiva University and has been doing research for Professor Neer Asherie since March 2010. Ariel is pursuing a career in medicine and enjoys swimming and playing tennis during his free time. His research focuses on the interactions between proteins and chiral precipitants. Ariel and his research partner, Dahniel Sastow, have recently finished a comprehensive analysis of the conformations of the precipitant 2-methyl-2,4-pentanediol (MPD) in protein structures with resolution of 1.50Å or better.

Bioengineering

Photonic Crystal Biosensor Device

by

Leedan Cohen[1] and Deniz Aydin[2,3]

[1]*Department of Biology, Stern College for Women, Yeshiva University, New York, NY 10016;*

[2]*The Edward S. Rogers Sr. Department of Electrical and Computer Engineering, University of Toronto, Toronto, Canada;*

[3]*Institute of Biomaterials and Bioengineering, University of Toronto, Toronto, Canada*

The purpose of this project is to demonstrate biodetection using a biosensor which is sensitive to the shifts in the refractive index (RI) of the medium surrounding the sensor. Refractive index change can be due to changes in the bulk fluid, or due to binding of analytes to the functionalized sensor surface. The goal is to ultimately create a quick method of diagnosis through using an unprocessed blood sample.

A biosensing chip is cut from a silicon wafer, which will later hold photonic crystals made up of mesas. Using a Plasma Enhanced Chemical Vapor Deposition (PECVD), a 20nm oxide layer is deposited onto the silicon surface in order to allow adherence of the polymer layer. The polymer will not adhere to the nitride because the nitride lacks hydroxyl groups. An ellipsometery measurement is used to confirm that the oxide has been deposited. To prepare for the functionalization of the APTMS polymer, the silicon chip is placed in a dichloromethane (CH_2Cl_2) solution. RCA 1 cleaning, consisting of NH_3, H_2O_2, and deionized H_2O in a ratio of 1:1:5, will create a clean and even oxide surface. The APTMS polymer is then dissolved in toluene and is deposited onto the chips using a reflux system. The goal is to obtain a monolayer coating of APTMS. The coating properties will depend on reaction conditions such as time, temperature, and the concentration of reagents. In order to determine whether a monolayer was obtained, the surface must be characterized. To that end, we used FTIR (Fourier Transform Infrared Spectrometry) to determine the functional groups on the surface, AFM (Atomic Force Microscopy) to give a topological view of the surface, and XPS (X-ray Photoelectron Spectroscopy) to determine the elemental and chemical composition. After the functionalization of the APTMS, microfluidic PDMS (Polydimethylsiloxane) channels are made to allow the solutions to flow over the chip.

This biosensor uses a PDMS T-junction (Figure 1, Courtesy of Ryan Schilling), which has openings for inlets and outlets so that the solutions can be inserted via ferrules and needle tips to flow over the mesas. PDMS is used because it is optically transparent and therefore has no effect on laser measurements. PMMA (Polymethyl methacrylate) clamps are used to hold the PDMS and the silicon chip tightly together to avoid solution leakages. When screwed together, the clamps squeeze the PDMS and the silicon chip tightly together. The screws also allow for the entire device to be attached to the optical holder. The window in the clamp reveals the mesas, which allows the solution to flow between the PDMS and the crystals. This window also allows the detection laser to be shone through the photonic crystal mesas. Our focus has been to use this method, as it is reversible, allowing for the reuse of the PMMA clamps, the PDMS microfluidic channel, and the silicon chip. An AutoCAD design of the PMMA clamp can be seen in Figure 2. A sample of a PDMS T-junction attached to a SiOx chip is displayed in Figure 3 (inlets/outlets highlighted).

Once the lasers are aligned and the silicon samples are functionalized, the desired testing solutions can be introduced into the microfluidic channel through the inlets, allowing the fluid to flow over the mesas. A Peltier cooler is used to prevent the temperature from fluctuating. Measurements of the refractive index shift are taken and the results will determine if binding has occurred. A clamped sample between the PMMA which is attached to the optical holder with inlets and outlets can be seen in Figure 4a,b.

After APTMS is functionalized on the surface, a 10 mM gluteraldehyde, 10 mM sodium cyanoborohydridein 1xPBS is used to treat the surface in order to immobilize the proteins. Streptavidin is

added to the surface. Biotin then binds to the streptavidin and BSA is added in order to avoid binding between other proteins and the remaining aldehydes. An outline of the production process of the biosensor chip can be seen in Figure 5. A similar procedure in functionalizing the silicon chip can be used for fluorescent biosensors where fluorescent biotin is added to the surface. These completed samples are analyzed using a fluorescent microscope (In Vitro Imaging System IVIS). Presence and uniformity of fluorescence is used to qualitatively determine goodness of functionalization.

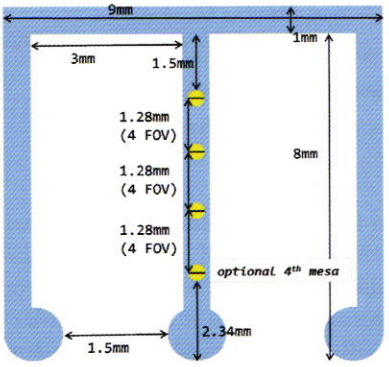

Figure 1: T-Junction

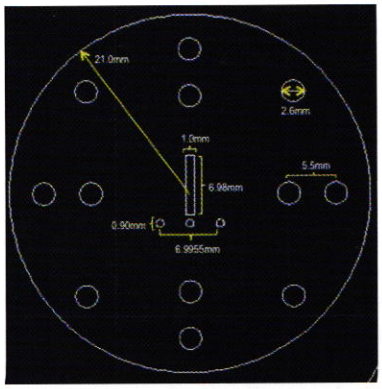

Figure 2: PMMA Clamp Design

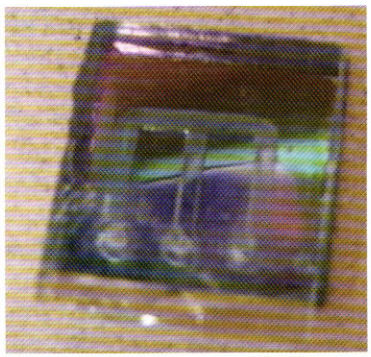

Figure 3: SiOx and mounted PMMA

Figure 4a,b: Biosensor device; top view, side view

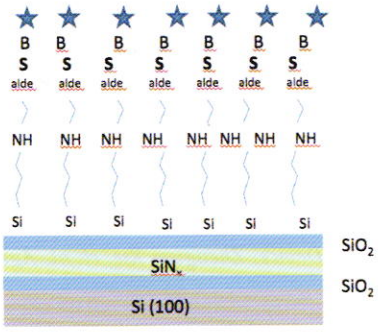

Figure 5: Surface Chemistry

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Student Researcher
Leedan Cohen is in her second year at Yeshiva University, majoring in Biology. In her free time, she loves water skiing, listening to '80's music, and reading a good book. She is the chapter leader of Project Sunshine and is the treasurer for the Pre-Med Club. Leedan is greatly involved with project START in New York, and is currently expanding the program internationally, founding a new chapter in Toronto, Canada. Leedan has a passion for research; she spent last summer at the University of Toronto researching Biophotonics and Microfluidics. In the coming summer she will be doing Breast Cancer Research at Sunnybrook Hospital.

Bioengineering

Identifying the Aging Gene in Yeast through the Use of a Microfluidic Device

by

Dahlia Pasik[1], Maria Cher[2], Orshay Gabay[2], and Doron Gerber[2]

[1]*Stern College for Women, Yeshiva University, New York, NY 10033;*

[2]*The Mina & Everard Goodman Faculty of Life Sciences, Bar-Ilan Institute of Nanotechnology and Advanced Materials, Ramat-Gan, 52900 Israel*

The budding of yeast serves as an important model organism for aging research. However, it is difficult to observe the aging pattern in yeast through the classical approach of micromanipulation. The development of the microfluidic system has enabled us to track individual mother cells throughout their lifespan allowing direct observation of cell cycle dynamics and various other molecular markers. The purpose of the microfluidic system is to retain the mother yeast cells in the device while the budding daughter cells are flushed away. The mother yeast cells adhere to the device by chemically modifying the yeast cells and the glass surface of the device. Sulfo-NHS-LC-biotin is added to the yeast cells and biotinylated-BSA, followed by neutravidin, is added to the glass surface. Through the formation of the biotin-avidin complex between the mother yeast cells and the device, the mother cells stay on the device while the daughter cells flush away. The device is made up of two layers. The first layer, the flow layer, connects the network of reaction chambers. The second layer, the control layer, controls the flow of the liquid within the reaction chambers. During the experiment, we found that yeast flow is sensitive to the height of the chamber. When using the microfluidic device with a chamber height of 14 μm, the yeast cells aggregated within the inputs. However, when the height of the chamber was enlarged to 25 μm, we succeeded to obtain a continuous flow of yeast within the microfluidic device. With the view of a light microscope, we were able to observe a sufficient amount of yeast cells within all of the reaction chambers. Next, we checked the immobilization of the mother yeast cells to the device through the biotin-avidin complex. When yeast was attached to Sulfo-NHS-LC-biotin, it adhered to the avidin that was present on the device. However, yeast aggregates did form when the concentration of 106 was used. This perhaps was due to a high yeast concentration or of the concentration of the NHS attached to the yeast. The next step will be to optimize the concentration, supply food for the yeast, and visualize the budding process of the yeast. Although we currently can only screen yeast sequentially, the long-term goal that can be achieved with the microfluidic device is the screening of a library of yeast in parallel.[1]

References:

[1]*Molecular Phenotyping of Aging in Yeast Cells Using a Novel Microfluidic Device. Zhengwei Xie, et. al. Aging Cell, (2012) 11, pp599-606.*

Reprinted from Volume 8, 2012, Women in Science, a publication of Stern College for Women.

Student Researcher

Dahlia is currently a junior at Stern College majoring in Molecular and Cellular Biology. She enjoys her biology courses, but also enjoyed seeing science come to life when she worked at a Nanotechnology lab at Bar Ilan University. During her spring semester, she continued following her interest in research and worked in the lab of Dr. Vigodner. She has an interest in medicine, and especially loves her weekly job as a HASC counselor where she deals with adults with various types ofspecial needs.

Stem Cell Biology

Effects of Water Transporters on Lung Progenitor Cell Differentiation

by

Mark Weingarten[1], Namita Sen[1], and Yakov Peter[1,2]

[1]*Department of Biology, Yeshiva College, Yeshiva University, New York, NY 10033;*

[2]*Department of Pulmonary Medicine, Albert Einstein College of Medicine, New York, NY 10467*

Aquaporins (AQPs) are a family of water transporter proteins expressed in developing embryonic and adult cells. AQPs act to maintain hydrostatic balance and to mediate progenitor cell proliferation as well as differentiation in numerous tissues. In order to investigate the role of water transport in the progressive development of lung progenitor cells in culture, we examined the expression of AQP isoforms within a population of lung anchorage-independent cell (AIC) progenitors, a cell subset first reported by our laboratory. Comparative measurements of AIC mean fluorescent intensity by flow cytometry indicated a robust increase in cell volume over a three week period. The observed hypertrophy during differentiation can be explained by a surge in AQP-mediated cellular water content. Real-time polymerase chain reaction was implemented to determine AQP family transcript expression in AICs over this time frame. With the exception of AQP7, no significant changes in AQP1-9 expression were found. The increase in AQP 7, a member of the aquaglyceroprotein family, is significant as aquaglyceroproteins transport both water and glycerol molecules. Glycerol is an important source of energy and a required component in the biosynthesis of cellular lipids and lung surfactants. Therefore, these findings suggest a link between AQP7, water and glycerol transport, as well as pathways of lung progenitor energy production, biogenesis and hypertrophic differentiation. Findings from this study may suggest future repositioning or new indications for existing agents to treat hydrodynamic lung diseases.

Student Researcher

Mark Weingarten is currently in his second year at Yeshiva University. Prior to commencing his undergraduate education, he attended DRS Yeshiva High School in Woodmere, followed by two years of study at Yeshivat Kerem B'Yavneh in Israel. Weingarten plans to start Semicha at RIETS this fall. A Kressel Scholar, he is currently pursuing a concentration in history and biology.

Cell Biology

Separation of Different Types of Testicular Cells from Mouse Testis; Studies of Sumoylation

by

Miriam Andrusier, Elisheva Markov, Yuxuan Xiao, and Margarita Vigodner

Department of Biology, Stern College for Women, Yeshiva University, New York, NY 10016

Background and Introduction

Spermatogenesis consists of divisions of spermatogonia, meiosis of spermatocytes and differentiation of spermatids. This process is supported by hormones and growth factors produced by testicular somatic cells such as Sertoli and Leydig cells.

In humans, infertility affects many couples worldwide and in the US. The male partner is responsible for infertility in at least half of all cases and about half of infertile men have idiopathic infertility (infertility with an unknown cause or origin.) Therefore, it is important to study new previously non-characterized proteins during spermatogenesis in order to better understand normal spermatogenesis and possible causes of infertility.

Sumoylation (a recently discovered type of covalent modification by Small Ubiquitin-like Modifiers or SUMO proteins) is an important regulatory event in cell function; however, its role during spermatogenesis is largely unknown. The aim of the project in Dr. Vigodner's laboratory is to identify and initially characterize specific targets of sumoylation in different types of testicular cells. Because testicular tissue is complex and multi cellular in nature, to achieve the aim of the project, populations enriched for specific cell types need to be obtained from mouse testes.

Materials and Methods

Mice were sacrificed and their testes were removed and de-capsulated. The testes then underwent two enzymatic digestions to isolate interstitial Leydig cells and to obtain cell suspension. The cells were separated using STAPUT technique which is based on separation of different cell types by using gravity sedimentation. A density gradient was created by a gradual mixing of 2% and 4% BSA solutions. The testicular cells were loaded on top of the density gradient and allowed to sediment. Different cells migrated through the gradient and stopped at the point at which the density of the BSA solution equaled to their own. After several hours, 12 ml fractions were collected into tubes and analyzed microscopically using accepted morphology criteria and antibodies specific for different cell types.

Once immunofluorescence has been done and the fractions were determined to be pure, immunoprecipitation is performed using anti-SUMO antibodies followed by a Mass spectrometry analysis to identify the SUMO-modifying proteins.

Results

STAPUT was determined to be a good method of separating cells and immunofluorescence proved that the samples were indeed enriched for specific cell types. Using those techniques, we succeeded to separate fractions of meiotic spermatocytes and spermatids (figures below) which may be very important in future studies of meiosis and spermatid differentiation.

One of our concerns was a possible loss of sumoylated proteins from the cells following a prolonged separation procedure. However, immunofluorescent staining of the fractions using anti-SUMO antibodies revealed a bright SUMO signal in spermatocytes and spermatids. The SUMO localization pattern was similar to that previously reported for those cells (please see the figures below). Fractions from different separations are now being collected in order to have enough protein lysates for successful immunoprecipitation experiments.

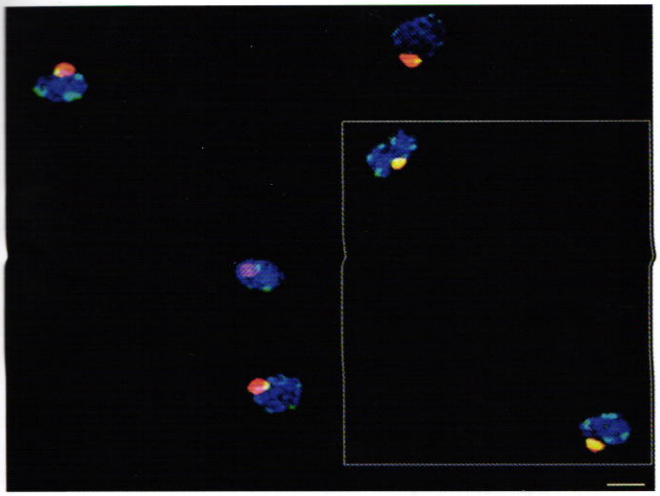

Figure 1. Spermatocyte fraction after STAPUT separation. Gamma H2AX (red) is a marker of spermaticytes and is localized to the XY body. SUMO (green) is concentrated in the centromeric heterochromatin and XY body, *as previously described; DNA is stained* by DAPI (blue);

Insert is another microscopic field from the same slide; Scale bar is 10 microns.

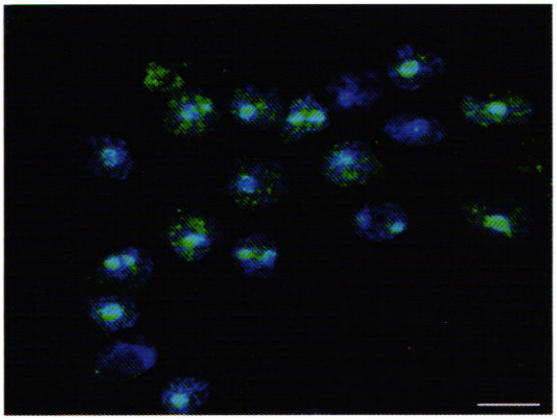

Figure 2. Round spermatid fraction after STAPUT seapration. SUMO (green) is concentrated in the centromeric heterochromatin and is also seen throughout the nucleus, as previously described; DNA is stained by DAPI (blue); Scale bar is 10 microns.

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Student Researcher
Miriam is a junior at Stern College who is majoring in Biology. She is working toward fulfilling her dream of becoming a reproductive endocrinologist and has been working in Dr. Margarita Vigodner's male infertility research lab.

Molecular Biology

The Role of the De-ubiquitinase UBP10 in DNA Double Strand Breaks Repair in Saccharomyces Cerevisiae

by

Aliza Y. Loshinsky[1], Yifat Zuckerman[2], and Shay Ben Aroya[2]

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Chromosomal instability, the loss or gain of large chromosomal segments, leading to aneuploidy or gross chromosomal rearrangement has been discovered in the vast majority of malignancies and tumors. Gross chromosomal rearrangements can be caused by double strand breaks (DSBs) in the DNA that are not repaired.

Evidence has shown that proteasome-mediated degradation is involved in the repair of DSBs. Previously, a screen was carried out in the lab to find the proteins that need to be degraded by the proteasome for a successful completion of the repair process. One of the hits was Ubp10, a deubiquinase that de-ubiquitinates histone H2B. Although Ubp10 was not found to be a target of the proteasome, the overexpression of Ubp10 in media containing DNA damaging agents caused severe growth defects. Previous studies have shown a direct link between the ubiquitilation of histone H2B and the timely and successful repair of DSBs in human cells. The goal of this project is to further understand how the over production of de-ubiquininases, which results in their gain of function, will affects the repair of a specifically induced DSB. The baker yeast Saccharomyces cerevisiae is used as a model system.

A homologous recombination assay was performed using two samples of cells from the MK203 strain, one sample of the wild type cells and one sample of cells that was transformed with a GAL1-UBP10 plasmid. The MK203 strain contains two alleles of the *URA3* gene. One allele, on chromosome V, contains a cut site for the galactose-induced HO endonuclease. Thus, transferring the cells to a galactose media induces a single DSB in chromosome V. The cells then use the mechanism of homologous recombination to repair the DSB, using the other allele of the *URA3* gene, on chromosome II, as a template for repair. The allele of the *URA3* on chromosome II differs slightly from the allele on chromosome V in that it does not have a HO endonuclease cut site and it does contains restriction sites for the restriction enzymes E*co*RI and B*am*HI. Thus, the repaired chromosome will not have an HO cut site and but will include restriction sites for B*am*HI and E*co*RI.

After the yeast cells were induced with a DSB, a sample of cells was taken every 30 minutes. When all the samples were obtained, the region of the DNA where the DSB was induced was amplified. The samples were then treated with the restriction enzyme B*am*HI to discover the extent which DNA repair occurred by homologous recombination and gene conversion. The cells that did successfully repair the DSB are expected to show two smaller bands of DNA when run on a gel, compared to the cells that did not undergo DNA repair and gene conversion and are expected to show one large band. If the overexpression of Ubp10 does inhibit timely DSB repair, it is expected that the cells overexpressing Ubp10 will show one large band for more samples, indicating that the cells require a longer period of time to undergo DNA repair and gene conversion. At this time, the results of the study are not yet conclusive.

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Student Researcher

Aliza Loshinsky is a senior in Stern College majoring in Biology. She plans on pursuing a career in optometry. Her previous research interests have included ocular diseases, the genetics of chromosomal instability and the effect of nutraceuticals on normal and cancer cells.

Molecular Biology

Exploring the role of Huntingtin protein in regulation of MacroH2A1

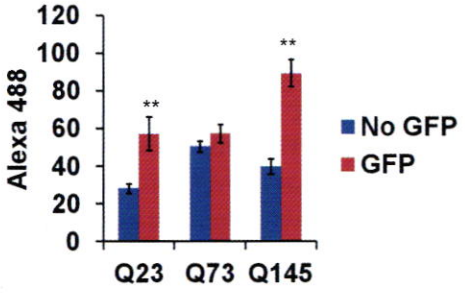
by

Erica Hasten, Matthew Gamble, and Leonid Novikov

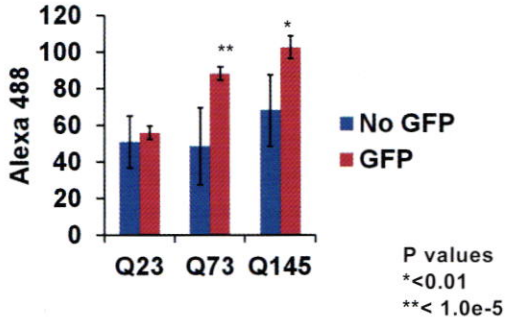
Department of Molecular Pharmacology, Albert Einstein College of Medicine, Yeshiva University, New York, NY 10461

Huntington's disease (HD) is an autosomal dominant genetic disorder that involves an expansion of a polyglutamine (polyQ) track near the N terminus of huntingtin protein (HTT), which leads to the aggregation of this protein in the cells. While HTT is ubiquitously expressed, HD manifests clinically as a progressive central nervous system neurodegenerative disorder. A recent study has linked increased expression of the histone variant macroH2A1 to HD progression. MacroH2A1 incorporation into the nucleosome—or DNA packaging proteins to replace nucleosome protein H2A—has been linked to both positive and negative regulation of transcription. There have been several links found between HD and transcriptional disregulation. Here, we explored the possible mechanisms by which mutant HTT might regulate macroH2A1 expression. First we determined the level of macroH2A1 in mouse neuronal precursor cells with wild type or mutant humanized HTT exon 1. To explore the possible role of wild type HTT in macroH2A1 expression we depleted HTT from IMR90 human fibroblast cell lines using lentiviral shRNA constructs. To determine the role of the polyQ track in triggering macroH2A1 overexpression, we expressed N-terminal HTT-GFP fusion proteins harboring different numbers of glutamine repeats in A549 and HEK cell lines. We used immunofluorescence to monitor macroH2A1 levels in the transfected cells. Together, our findings suggest that HTT polyQ track length may indeed play a role in regulating the expression of macroH2A1. Our results leave the open possibility that macroH2A1 may play a role in the molecular pathology of HD.

Immunofluorescence of A549 Cells transfected with huntingtin over-expression plasmids



Immunofluorescence of HEK Cells transfected with huntingtin over-expression plasmids



Data indicates that there was an increase in macroH2A1 levels in the cells that had the longest poly Q repeats. This suggests that these two proteins are connected on a molecular level.

Student Researcher

Erica Hasten is a senior at Stern College majoring in Biology with a concentration in Molecular and Cellular biology. When she isn't explaining her very long titled major to her curious colleagues, she can be found playing soccer on the lady macs soccer team or can be found dancing and singing in the school musical. She will begin to pursue a PhD from Albert Einstein College of Medicine next year.

Immunology

Calibration of Primary and Secondary Antibodies for Ideal Immunofluorescence Staining in Neurons and Other Cell Types

by

Sarina Miller[1], Anna Sloutskin[2], and Ronald S. Goldstein[2]

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[2]*Department of Life Sciences, Bar Ilan University, Ramat Gan, 52900 Israel*

Illnesses caused by human neurotrophic viruses have been difficult to study because of the limited availability of human neurons for experimentation. Human embryonic stem cells (hESC) are pluripotent cells that can be differentiated into neurons, thereby providing a potentially unlimited source of this previously difficult to obtain cell type. Since cultures of differentiating hESC contain many cell types, it is important to be able to identify which cells are neurons. In addition, it is important to know which subtypes of neurons are produced by the differentiation method developed in our lab[1].

hESC-derived neurons were recently shown to be a useful tool for the study of Varicella Zoster virus (VZV), the cause of Varicella Zoster (chicken pox) and Herpes Zoster (shingles). VZV is a human specific neurotrophic virus that infects peripheral neurons. In order to use these neurons as a model to study VZV, we must confirm that they (as well as other types of cells) were infected with VZV. While antibodies often stain specifically antigens in non-neuronal cells (such as in MeWo and Arpe cells), the same antibodies often react with neurons in a non-specific manner, requiring additional testing.

Indirect immunofluorescence staining is a technique using antibodies to detect specific molecules found in a cell and to thereby identify and characterize its phenotype. Our work involved determining ideal dilutions of primary and secondary antibodies to produce strong staining that is easily visible and has minimal non-specific background staining. Antibodies can be raised against antigens that indicate different stages of neural development or viral infection. Primary antibodies added to cells bind to the antigen, and are detected with a fluorophore-tagged secondary antibody for visualization with a fluorescence microscope.

24-well-plates containing coverslips with various cell lines[2] were fixed with 4% paraformaldehyde when they reached approximately 80% confluence. These coverslips were blocked to prevent non-specific antibody binding, and exposed to primary antibodies at varying dilutions for 1 hour (room temperature) to overnight . The coverslips were subsequently exposed to various[3] dilutions of a secondary antibody for 40 minutes, counterstained with Hoechst (specific to nuclei), mounted on slides, and analyzed using a fluorescence microscope. The dilutions tested ranged from 1:5 to 1:50,000.

Primary antibodies calibrated included antibodies specific for neurofilament-m subunit (polyclonal, 1:1000), E7 specific to microtubules (1:100), Tau specific to axons (polyclonal 1:350, monoclonal 1:100), Brn3a specific to transcription factors in the nuclei of peripheral sensory neurons (polyclonal and monoclonal, 1:250), and a monoclonal IgM antibody specific to actin (1:5). Antibodies to VZV proteins that we calibrated included polyclonal ORF62, ORF63, and ORF4 regulatory proteins, the gE membrane protein (1:10,000), and monoclonal ORF61, ORF62 and ORF63 (1:10,000). The VZV antibodies were kindly provided by Prof. Paul Kinchington (University of Pittsburgh, USA).

Secondary antibodies calibrated included 488 donkey anti mouse (green fluorescence, 1:250), 488 streptavidin (green, 1:1000), Cy2 goat anti mouse (green, 1:500), and Texas red IgM anti mouse (red, 1:100).

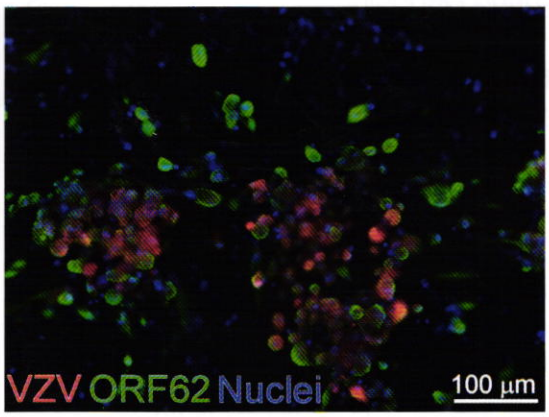

Figure 1. MeWo cells infected with VZV expressing ORF66-bound RFP (red) and stained with antibody against ORF62 (green) at a dilution of 1:10,000. Nuclei are stained with Hoechst (blue). The figure shows the specific staining of the ORF62 antibody to the membranes of the infected cells.

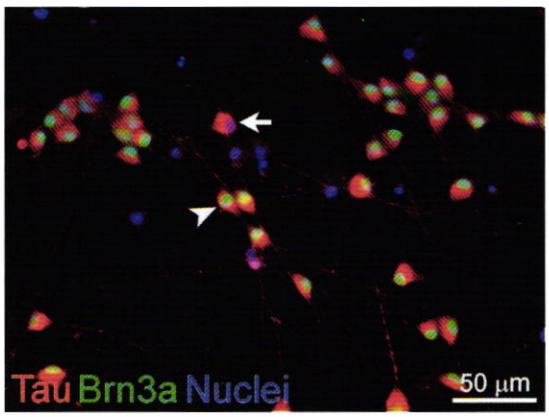

Figure 2. hESC derived neurons stained with the axonal marker Tau (red) and Brn3a (green) primary antibodies. The nuclei of the neurons are stained with Hoechst (blue). Brn3a detects a transcription factor and can therefore be seen prominently in the nuclei of the cells. The presence of a Brn3a stain indicates that the neuron may be a sensory neuron. The arrow is pointing to a neuron lacking Brn3a, in contrast to the neuron indicated by the arrowhead that was stained by Brn3a.

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[1]*Pomp O., Brokhman I., Ben-Dor I., Reubinoff B., Goldstein R. S.. 2005.Generation of peripheral sensory and sympathetic neurons and neural crest cells from human embryonic stem cells. Stem Cells 23:923–930.*

[2]*Cell lines used for experiments included MeWo (human melanoma line), Arpe ARPE-19 (human retinal pigmented epithelial cells), Vero (green monkey kidney epithelial cells), PA6 (mouse stromal cells), and human neurons derived from the H9 cell line.*

[3]*For most experiments, only one antibody was calibrated, and the other was maintained at a constant previously tested dilution.*

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Student Researcher

Sarina Miller is a senior at Stern College majoring in Biology and Jewish Studies with the goal of becoming a high school biology teacher in Israel. She can often be found sitting in on too many classes for her own good, and enjoys photography, tap dancing, and singing with the B'notes (Stern's a cappella group).

Developmental Biology

Identification of DNA Repair Genes Required During Denucleation of Lens Fiber Cells

by

Bella Wolf[1],Tiphaine Chevalier[2], Ales Cvekl[2,3], and Jian Sun[2]

[1]*Stern College for Women, Yeshiva University, 245 Lexington Avenue, New York, NY 10016;*

[2]*Department of Genetics, Albert Einstein College of Medicine, Bronx, NY 10461;*

[3]*Department of Opthamology and Visual Science, Albert Einstein College of Medicine, Bronx, NY 10461*

The mammalian ocular lens is a structure that refracts light on to the retina. In order to achieve this, it is of crucial importance that lens transparency is maintained. Subcellular organelles such as the nucleus reduce transparency of the lens fiber cells and hinder refraction of light. Therefore, one critical step in ocular lens development is the degradation of the nucleus in lens fiber cells in a process called denucleation. Failure to execute denucleation leads to abnormal lens fiber cell differentiation and cataract formation.

As the denucleation process occurs, double stranded DNA breaks form and chromatin degrades. Therefore previous research in our laboratory has indicated that in order to counteract this and ensure that apoptosis, which would produce optical irregularities and scattering of light, does not occur, DNA repair enzymes are mobilized.

The purpose of this experiment is to identify the functional DNA repair enzymes participating in the denucleation process. The mRNA levels of embryonic stage 15.5 mice lens, which have not yet undergone denucleation in the lens fiber cells, is compared through the use of real time PCR to that of embryonic stage 17.5 mice lens, the approximate stage in which denucleation occurs.
Results show that most DNA repair enzymes do not show a significant change from E15.5 to E17.5; however, several DNA repair pathway genes (eg. Nbn (Nbs1), Mlh1, Xpa, Mpg) show a considerable up-regulation. These results encourage the current hypothesis that there is a significant participation of certain DNA repair enzymes during the denucleation process.

Acknowledgements

This work is supported by NIH grants, 95261482, University Undergraduate Summer Research Scholars Program, Summer Undergraduate Research Program, and an unrestricted grant from RPB to the Department of Ophthalmology and Visual Sciences. I would like to thank Dr. Ales Cvekl, Jian Sun, and Tiphaine Chevalier for all of their help, guidance, and encouragement during this program.

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Student Researcher

Bella Wolf is currently a Junior at Stern College for Women. She is in the S. Daniel Abraham Honors program at Stern and is also the co-president of SURGE, a club devoted to presenting the various research experiences that the student body at Stern has.

Nutritional Biology

Manual or Automatic Defrost Freezers Differ in Human Milk Preservation

by

Joseph Aharon[1], Ali Faraghi Ahrabi[1,2], Deepali Handa[1,2], Champa N Codipilly[1,2], Debra Potak[2] and Richard J Schanler[1,2,3]

[1]*Lilling Family Neonatal Research Lab, Feinstein Institute for Medical Research, Manhasset, NY 11030;*

[2]*Department of Neonatal-Perinatal Medicine, Cohen Children's Medical Center of New York, New Hyde Park, NY 11042;*

[3]*Department of Pediatrics, Hofstra North Shore-LIJ School of Medicine, Hempstead, NY 11549*

Freezer storage of expressed human milk is the usual practice for mothers of infants in the Neonatal Intensive Care Unit (NICU) as well as those at home and/or returning to the workplace. However, there is a paucity of data on the quality of milk stored for months in a freezer. The automatic defrost type freezer features a freeze-thaw cycle that potentially might alter the constituents of the milk during storage. No studies have examined the effects of alternating freezer temperatures on the integrity of human milk.

Our objective was to determine if automatic defrost freezers (AD) differentially affect human milk properties compared with manual defrost freezers (MD). To answer our question, 30 ml of freshly expressed human milk were obtained from NICU mothers (n=20). After a time 0 sample was examined, milk samples were stored at -20°C in both AD and MD freezers and control samples were stored frozen at -80°C. Samples were removed at 4, 8, and 12 weeks and were analyzed for pH and bacterial colony counts (total, TBCC; Gram positive, GPCC; and Gram negative, GNCC). Data were analyzed using repeated measures ANOVA.

The results of our studies were as follows. The milk pH did not change significantly in -80°C freezer over time. Milk pH declined in MD, but significantly more so in AD over time, $p<0.05$. TBCC declined significantly in AD over time as compared to MD and -80°C, $p<0.001$. GPCC declined over time more in AD than in MD or -80°C, $p=0.002$. GNCC (present only in 7 samples) declined more so in AD compared to MD and -80°C freezers over time but this change was not statistically significant, $p=0.10$.

Upon conclusion of our experiment, we found that the type of freezer used to store human milk has a significant effect on milk constituents. MD and -80°C freezers are associated with the least change in milk constituents in comparison to AD freezers. Antibacterial properties of human milk continue to manifest some activity during storage in AD freezers. Guidelines involving long-term storage of human milk should indicate type of freezer.

Student Researcher

Joseph Aharon is a second year Computer Science major in Yeshiva College. He grew up in Queens, NY and studied at Yeshivat Har Etzion for one year before beginning his undergraduate studies. His favorite activities include sports, cooking, and watching animated films. He plans to pursue a career in software development.

Chemical Engineering

Infrared-Emitting Organic LEDs

by

Hudi Jacobson[1] and Yaakov R. Tischler[2]

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[2]*Dept. of Chemistry, Bar-Ilan University; Ramat Gan, 52900 Israel*

Organic Light Emitting Diodes (OLEDs) are part of a new generation of lighting and display technology. They consist of thin layers of organic materials with unique optical and electronic properties sandwiched between two electrodes. These materials can be deposited on numerous substrates and are thus easily stored and carried around1. When an OLED is electrically excited, the organic molecules vibrate and their electrons get excited, jumping up to higher energy levels. Eventually, the excitons (excited electrons) relax from their high energy states and fall back to lower levels, emitting radiation.

The cavity in an OLED is comprised of the film of organic material in between the two electrodes. The focus of our experiment was to design the cavity structure for Infrared-Emitting OLEDs by determining which material should be used and how thick the layer should be. An ideal material is one that absorbs and emits in the IR. We test IR absorbance using an FTIR (Fourier Transform Infrared) spectrometer (see Figure 1).

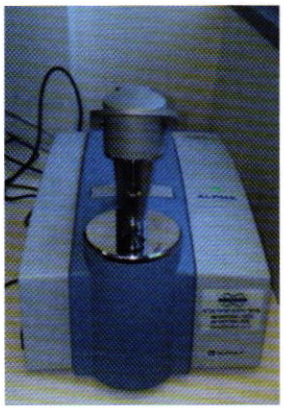

Figure 1. BRUKER FTIR spectrometer used in our analysis

We spin-casted thin films of Polystyrene and Polymethyl Methacrylate with varying concentrations in order to achieve a thickness similar to the size of a wavelength of infrared light. The data showed that Polystyrene displayed good absorbance peaks in the IR at wavenumbers which are multiples of 700 cm^{-1} (see Figure 2), similar to what we found in the literature2. We therefore decided to work with Polystyrene and to concentrate on making a film that was thick enough for our cavity.

We made several solutions of Polystyrene in Chloroform and constructed a spin curve (see Figure 3) to decide which speed and which concentration yield a film that of optimal thickness for our experiment.

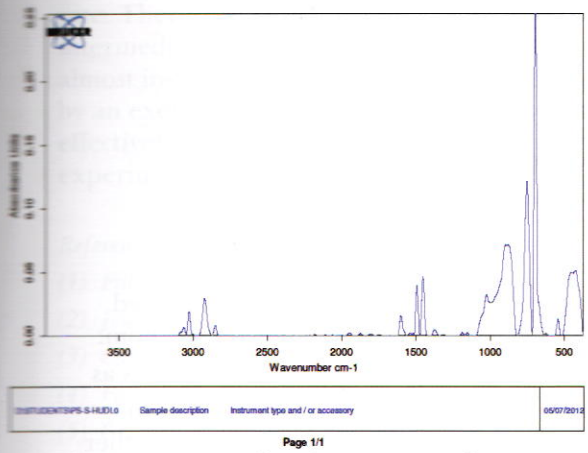

Figure 2. FTIR absorbance curve for Polystyrene

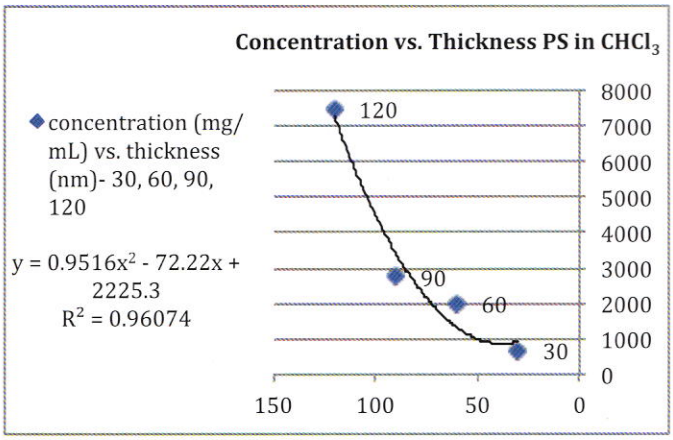

Figure 3. Spin curve for various concentrations of Polystyrene in Chloroform

The ideal film thickness was determined to be approximately 4.6 microns, based on Bragg's Law, $d=\lambda/2n$, where d is the film thickness and n is the index of refraction of our material.

Current work involves constructing diodes using Potassium Bromide as a substrate, since this material is almost completely transparent in the IR wavelength range of interest. Our diode will be composed of a round disk of KBr, two 20 nm-thick silver electrodes and an optimally thick organic layer of Polystyrene spin-casted from Chloroform with a ratio of 105mg/mL. We plan to test the IR emission of the diodes using a SPEX 270M monochromator and an IR detector.

Eventually, we hope to use this model to create inexpensive IR-emitting OLEDs, which can be used for chemical sensing, as well as in solid state IR lasers.

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[2]*Structural and thermal behavior of polystyrene thin films using ATR–FTIR–NanoDSC measurements. Paul Bernazzani, Rachel F. Sanchez J Therm Anal Calorim (2009) 96:727–732*

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Student Researcher

Hudi is a junior at Stern College (second year on campus) who was previously a Chemistry major, but recently switched to Economics. She hopes to enter the field of Audiology.

Organometallic Chemistry

Palladium-Catalyzed Aryl Fluorination

by

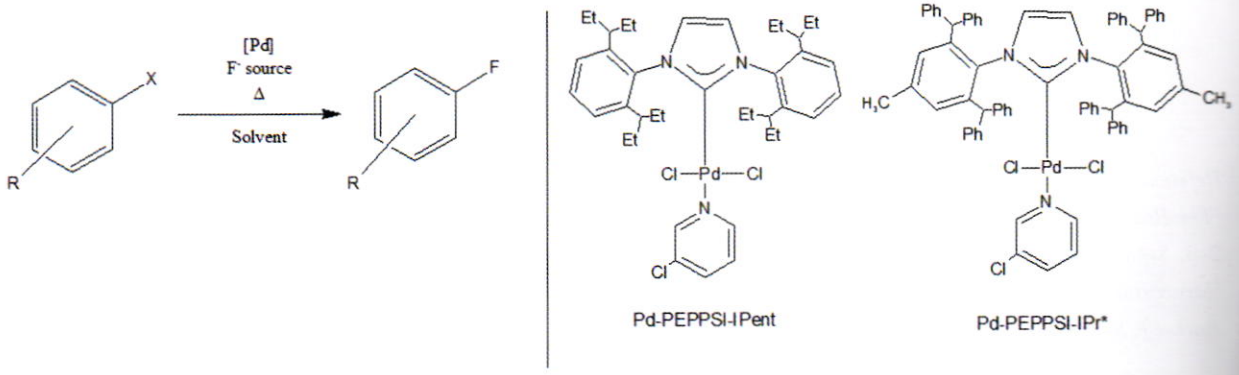
Ari Cuperfain and Fabiola Barrios-Landeros

Department of Chemistry, Yeshiva College, Yeshiva University, New York, NY 10033

Fluorinated compounds have an extensive role in modern chemical applications.[1,2] An estimated 20% of all pharmaceuticals and 30% of synthetic agrochemicals contain at least one fluorine atom. Furthermore, radioactive ^{18}F-labeled molecules are increasingly utilized for diagnostic purposes as contrast agents in PET scans.[3] Despite the wide use of fluorinated compounds, few synthetic approaches are known that can incorporate fluorine atoms into aromatic rings, especially when other functional groups are present. This is a limiting factor to the development of novel PET tracers that could theoretically enhance the detection of physiological disorders. Many current fluorination techniques require harsh reaction conditions, long reaction times, or stoichiometric amounts of rare reactants.[4] These syntheses are generally expensive and harmful to the environment.

The ability to catalyze these fluorination reactions from aryl halide precursors by the more moderate d-block transition metals through cross-coupling reactions has historically met limited success.[5] The common phosphine ligands used to stabilize the palladium metal are prone to interact with the fluorine in an undesired fashion. However, a relatively new class of ligands, N-heterocyclic carbenes (NHC), have been used successfully in other transformations,[6,7] yet have remained largely uninvestigated with respect to aryl fluorination. In this study, we synthesized the ligands and complexes shown to assess the efficacy of bulky NHC-stabilized palladium catalysts in facilitating the substitution of an aryl halide with a fluorine anion (Scheme 1).

Scheme 1.



Thus far, we have found minor conversion into the fluorinated compound using both of these catalysts with silver fluoride as the fluoride source. We also identified that oxidative addition of the aryl halide to the metal, which is the first step in the transformation, is not occurring at a reasonable

rate. There are currently two hypotheses to explain these observed results: either (1) the LPd(Ar)(X) intermediate is highly unstable and in the absence of an outlet such as the desired product, it reverts almost instantaneously back to the original starting material, or (2) the catalyst requires activation by an exogenous species – such as a base or amine – in order to perform the oxidative addition step effectively. However, more investigation is required and our lab is currently conducting additional experiments to elucidate further this mechanism of oxidative addition.

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(1) Filler, R.; Saha, R. Future 2009, 1, 777.

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(7) Valente, C.; Calimsiz, S.; Hoi, K. H.; Mallik, D.; Sayah, M.; Organ, M. G. Angew. Chem. Int. Ed. 2012, 51, 3314.

Student Researcher

Ari is a fourth year student finishing his major in Chemistry and minor in Biology. He will be pursuing a graduate degree in Chemistry next year where he hopes to continue investigating the chemistry of transition metals and their applications towards biological activity.

Organometallic Chemistry

Using Metal Catalysis to React Carboxylic Acids with Isonitriles under Mild Conditions

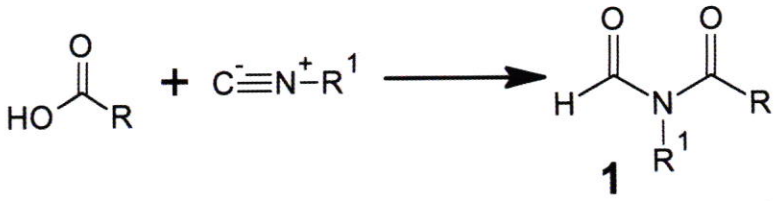
by

Joshua Fluss and James Camara

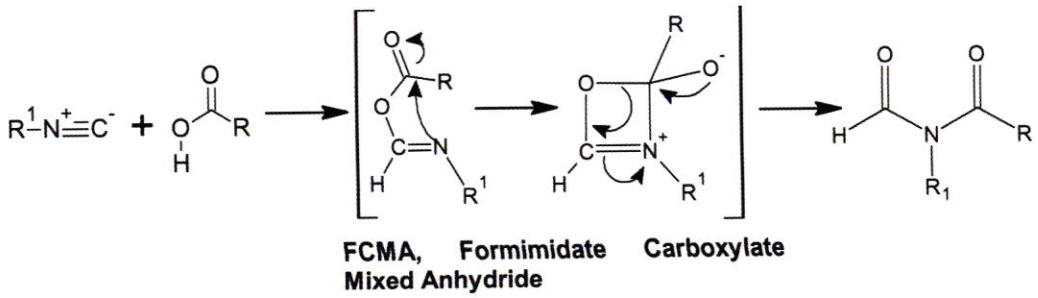
Department of Chemistry, Yeshiva College, Yeshiva University, 10033

Glycoconjugates have a large number of therapeutic applications. The uses of glycoconjugates include treatments for HIV/AIDS, cancer, diabetes, influenza, targeted drug delivery systems, among many others (1). One possible method of constructing a glyconjugate is by coupling of the glycoprotein with a therapeutic agent through a peptide bond (2). Previous research has shown that simple carboxylic acids and isonitriles would react to produce an N-formylamide (1), (3) with such a peptide bond. The general reaction scheme and a suggested mechanism are shown below in Reaction 1 and Scheme 2.

Reaction 1. *Reaction of carboxylic acid with isonitrile (4)*



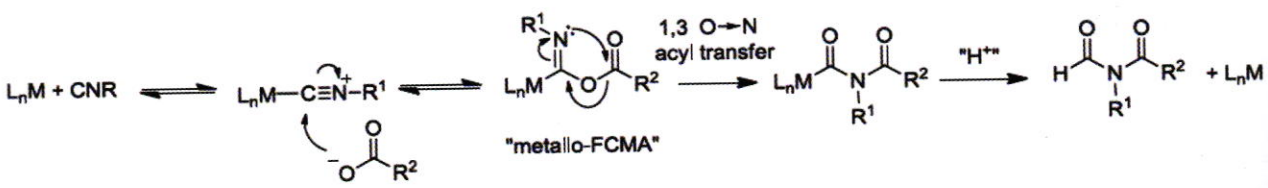
Scheme 2. Proposed mechanism for Reaction 1 (5)



This simple two-component coupling (2cc) reaction has a number of promising features. However, activating the reaction required heating the reaction mixture in a microwave to 150 °C. These conditions limit the variety of functional groups that can participate in the reaction.

Our research proposed to use an Iron-based catalyst to enable the reaction of carboxylic acid and isonitrile to proceed under mild conditions. A proposed pathway is shown in Scheme 3.

Scheme 3.



Scheme 3. Proposed pathway for the nucleophilic attack of carboxylate on a coordinated isonitrile

$[CpFe(CO)_3]^+$ is an attractive starting complex, as the stepwise installation of up to three different ligands has already been demonstrated in the literature (6), allowing for facile variation of the electronic and steric properties of the metal. Additionally, half-sandwich complexes of this form usually show reversible electrochemistry. This may allow further tuning of the electronic properties of the metal by oxidizing Iron to Fe^{3+}.

Another feature in our catalyst is the potential for intramolecular stabilization of the transition state of the 1,3 O*a*N acyl transfer. One promising method of stabilization is the incorporation of Hydrogen-bonding residues into the ligands to assist in stabilizing the transition state. A Hydrogen bond to the acyl group of the metallo-FCMA would activate it toward 1,3-O*a*N acyl transfer. Additionally, carefully choosing the site of the Hydrogen-bond may lock the geometry of FCMA into the transition state of 1,3-O*a*N acyl transfer. In this aim, we coordinated 3-pyradine-diphenylphosphine, a ligand that is capable of Hydrogen-bonding.

We synthesized $[CpFe(PMe_3)(3\text{-}pyPPh_2)(MeNC)]PF_6$, and are currently testing the reactivity of the catalyst with carboxylates. We hope that studies of reaction scope will show that this compound is more effective at synthesizing N-formylamides than the 2cc reaction, as well as the Iron complex without the Hydrogen bonding residue.

Student Researcher
Joshua Fluss is a senior in Yeshiva College, graduating in May with a degree in Chemistry and Economics. He is currently the Chairman of the Honors Student Council, and remains involved with USRP, the YC Chemistry Club, and Project START. Joshua hopes to apply to Ph.D. programs in chemistry in the coming year, with the goal of working in the pharmaceutical industry.

Computational Chemistry

The Effect of Cation-Pi Interactions on Lysine Methylation

by

Elizabeth Goldberger and Chaya Rapp

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A large part of protein diversity stems from post-translational modifications, whereby chemical groups such as phosphates, sulfates, methyl groups, and acetyl groups are covalently added to existing amino acids. These sites of structural modification then serve as sites of interaction with other proteins. Lysine is one amino acid that regularly undergoes modifications, and lysine methylation is a particularly common modification in histone proteins. The basic amino group on the lysine side chain can undergo various degrees of methylation, ranging from monomethylation to dimethylation to trimethylation, each of which has a unique effect on the binding affinity of the protein towards other proteins and may result in different physiological consequences.

The occurrence of lysine methylation in histone proteins has epigenetic implications in that it directs transcriptional regulation via recruitment of specific reader proteins that bind only to specifically methylated lysine residues. Also, as a direct consequence of the increased bulkiness that results from additional methyl groups, histone packing is often altered. In terms of pathologies, many tumor-suppressing proteins bind selectively to proteins modified by lysine methylation.

Methyl binding specificity, or the affinity of a binding protein to a particular methylation state, is a result of several factors. These include hydrophobic desolvation, hydrogen bonding, steric strain, and cation-pi interactions. The cation-pi interaction refers to interactions between the positively charged methyl lysine side chain and the pi electrons of aromatic residues, such as tyrosine, phenylalanine and tryptophan. Our study focused on cation-pi interactions and how the strength of these interactions vary with differing methylation states and different orientations of the methylated group with respect to surrounding residues.

To study cation-pi interactions, we performed quantum mechanical calculations on representative systems in which benzene was used as a model for an aromatic residue, and an ammonium ion with one, two, three, or four attached methyl groups was used to model unmodified lysine, mono-, di-, and tri-methyl lysine respectively. As a starting point, the cation was placed directly above the center of the benzene ring, on the perpendicular line from the ion to the benzene plane, and then subsequently moved away from the perpendicular in increasing 30° increments. Calculations were also performed using increasing distances between the center of the benzene ring and the cation. These alterations of structure served to yield insight into the influence of angles and distances on cation-pi interaction energy trends, which were quantified via quantum mechanics using Jaguar software.

Results showed that for all five cations, the most energetically favorable orientation was the one in which the cation was directly above the center of the benzene ring (referred to as the 0_0 geometry); a sample plot showing interaction energy vs. geometry for the dimethylated state is shown in Figure 1. Cations of higher methylation states formed weaker interactions than those with lower methylation states. Also, interactions in systems having the cation in the plane of the benzene ring were relatively unfavorable. In most cases the structures in which the cation was placed between two benzene carbons had lower interaction energies than those structures with the cation directly above a benzene carbon. It is hoped that our results will lead to a greater understanding of methyl-lysine binding interactions, and the development of more accurate models to simulate lysine methylated systems.

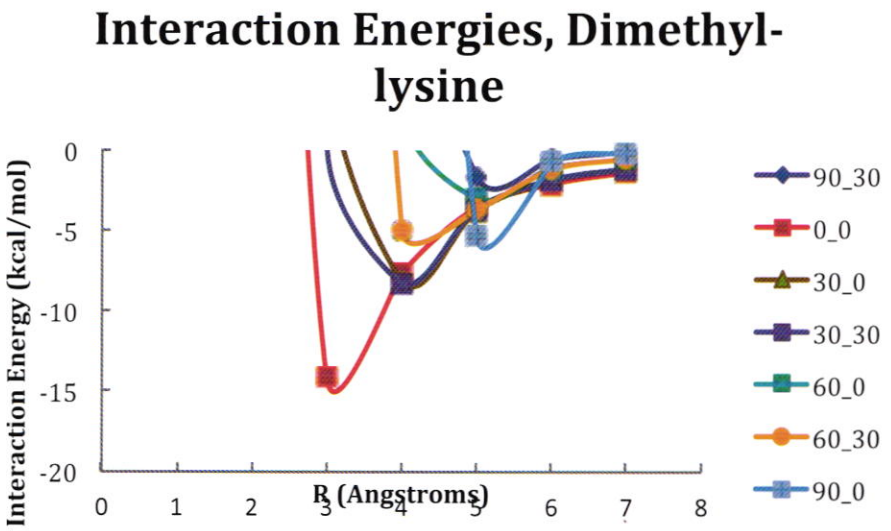

Figure 1. Interaction energies of seven different model systems as functions of the distance of the dimethylammonium cation from the center of a benzene ring. The 0_0 structure represents a cation directly above the ring's center; the 30_0 structure represents a cation at an angle of 30° from the vertical and in line with a benzene carbon, while the 30_30 structure represents a cation at the same vertical angle but in line with the midpoint between two benzene carbons, and so on.

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Student Researcher
Elizabeth Goldberger is a Chemistry major at Stern College who will be attending medical school in the Fall. She has recently completed her senior thesis on the subject matter described here, and she is thrilled to have her research published in the Undergraduate Research Abstracts Journal.

Artificial Intelligence

Linguistic Classification of Biblical Texts Using Supervised Machine Learning

by

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Among the first questions that scholars of the Bible need to ask when studying a book of the Bible is "when was this written?" The dating of a text provides important information about the context in which it was written and can be crucial for understanding the historical setting and meaning of the text.

Biblicists have used a variety of techniques to attempt to date biblical texts, one of the most useful of which is the analysis of linguistic features. The basic premise of linguistic dating is that the Bible was written over the span of many centuries, and ancient Hebrew, as languages are wont to do, developed substantially over the course of that time period. As such, it should be possible to date a book of the Bible based on the type of Hebrew used in that book.

It is generally agreed that there are two major strata of biblical Hebrew: Early (classical) Biblical Hebrew and Late (post-exilic) Biblical Hebrew. Some books, like Joshua, Samuel, and Kings, are generally presumed to be written in Early Biblical Hebrew, while other works, such as Ezra, Daniel, Nehemiah, and Chronicles are said to be written in Late Biblical Hebrew. There are, however, a number of books in the Hebrew Bible whose linguistic classification is ambiguous and/or disputed. As it happens, this problem--of classifying texts as belonging to one historical period of Hebrew or another-- is a question that lends itself to be resolved by an algorithmic process known as supervised machine learning.

Supervised machine learning algorithms for text categorization operate as follows: For each possible class to which a text could be assigned, we find a set of training texts which we already know to belong to that category. In our case, we would gather two sets of texts: one that belongs to Early Biblical Hebrew and one that belongs to Late Biblical Hebrew. Each text in both sets is then represented by a list of numbers which represent a certain quantifiable aspect of the text. For example, to classify documents by word unigrams (the frequencies with which individual words appear in a text), we turn each document into a vector (list) of numbers corresponding to the number of times each word appears in that class. These feature vectors are then used to create a mathematical model that can be used to classify other texts. For our research, we used models constructed from our training sets using unigrams and bigrams of Hebrew words as well as unigrams of morphological encodings of each word in our training sets. In each case, our models used a Bayesian multinomial regression algorithm to classify the query documents.

The reliability of a particular classification model can be ascertained by performing K-fold cross-verification, wherein the training texts are divided into K parts, K-1 of which are used to create a model and 1 of which is used as a query set. This process is repeated K times, each iteration using a different part of the training corpus as the query set. The accuracy of the K-fold cross-verification helps predict how accurately the algorithm will be able to classify a query text whose classification is currently unknown. In our experiments, we showed that cross-verification gives us an accuracy of about 85% for the models that used morphology and word bigrams and about 93% when using simple word unigram frequency.

We used our models to classify every book in the Bible and every chapter in the book of Psalms, and we also performed an in-depth case study on the book of Joel. In each case, we use each model (word unigram, word bigram, morphology unigram) to independently classify the query texts. In many cases, the results of all three classifications were the same, but there were also a significant number of cases in which there were discrepancies between the results from different models. In some cases, this may be because the query texts do not neatly fit into either the Early Biblical Hebrew or Late Biblical Hebrew categories but are instead representative of a transition period between these two strata of Biblical Hebrew. In any event, it is apparent that supervised machine learning can be a very effective tool to linguistically classify and date biblical texts.

Student Researcher
Toviah Moldwin is a senior at Yeshiva College, majoring in Computer Science and Mathematics. His research interests include artificial intelligence and computational neuroscience, which he intends to continue to pursue after he graduates. When he isn't coding, Toviah enjoys playing guitar, writing, and running.

Cake Cutting: Bounding the Maximum Degradation of Social Welfare Due to Fairness Criteria in Chore Division Scenarios

by

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Introduction. The classic "cake-cutting" problem is as follows: There are n players who intend on fairly dividing a "cake" amongst themselves. Each of these players has his/her own valuation of which parts of the cake he/she prefers. The goal is to create a division that maximizes social welfare, while taking into account fairness requirements. We aim to provide bounds on the maximum sacrifice of social welfare caused by these fairness constraints. Previous works have dealt with the division of goods, where players have a utility function and like parts of the "cake." Here, we focus on the division of chores, where players have disutility functions and dislike parts of the "cake." Although these scenarios are similar, many of the ratios and proofs that hold true for goods fall apart when dealing with chores. We consider cases with an additional requirement that each player receives one contiguous piece. Other works have investigated cases in which players can receive any number of pieces from anywhere in the cake, but to our knowledge no one has yet looked at cases with this constraint.

Fairness Criteria. It is important to look at social welfare when trying to decide how to split up a cake. After all, we want to maximize the total happiness. But there is also an aspect of fairness to each individual player. We consider the three major fairness requirements:

- Proportionality – each player gets at most 1/n of the cake (by his/her own valuation)
- Envy-Freeness – no player prefers getting the piece allotted to any of the other players
- Equitability – all of the players get the exact same disutility (by their own valuations)

Social Welfare Functions. There are also different ways of assessing social welfare. The utilitarian social welfare is the total disutility of all of the players combined. Maximizing this type of welfare ensures that we have the most happiness overall, but it may sacrifice the happiness of individuals. Egalitarian social welfare addresses this issue by only taking into account the disutility of the player who is worst off. We consider these two types of social welfare functions.

Price of Fairness. In order to quantify the degradation of social welfare due to the different fairness requirements, we define the notion of Price of Fairness, in its three forms – Price of Proportionality, Price of Envy-Freeness, and Price of Equitability, defined as follows. The Price of Proportionality (resp. Envy-Freeness, Equitability) of a cake-cutting instance I, with respect to some social welfare function, is defined as the ratio between the minimum disutility attainable when divisions must be proportional (resp. envy-free, resp. equitable) and the minimum possible disutility for the instance, taken over all possible divisions. For example, if $X_{EF} \subseteq X$ is the set of all (connected) envy-free divisions of an instance, the egalitarian Price of Envy-Freeness for this instance is:

$$\frac{min_{y \in X_{EF}}\, eg(y)}{min_{x \in X}\, eg(x)}$$

Results. We aim to show bounds on the maximum utilitarian and egalitarian Prices of Proportionality, Envy-Freeness, and Equitability of any instance. Our results for chores, along with the previous results for goods, are summarized in Table 1, where n is the number of players. An upper bound

means that the respective price of fairness of any instance in the class is never greater than the bound; a lower bound means that there exists an example of an instance with at least this price of fairness. A bound is tight when the lower bound exactly matches the upper bound.

Price of:	Proportionality	Envy-Freeness	Equitability	
Utilitarian	n	∞	n	Chores (this work)
Egalitarian	1	∞	1	
Utilitarian	UB: $\frac{\sqrt{n}}{2}+1-o(1)$ LB: $\frac{\sqrt{n}}{2}$		UB: n LB: $n-1+\frac{1}{n}$	Goods (previous work)
Egalitarian	1	$\frac{n}{2}$	1	

Table 1: All Results

We provide a tight bound of n on the utilitarian Prices of Proportionality and Equitability. We show that the Price of Envy-Freeness, using either the utilitarian or the egalitarian social welfare function, is unbounded (for n>3), meaning that there is no maximum amount of social welfare that may have to be forfeited for the sake of envy-freeness. Additionally, we demonstrate that the egalitarian Prices of Proportionality and Equitability are 1, which means that no amount of social welfare is lost for the sake of proportionality or equitability.

Student Researcher
Yosef Hoffman is graduating from Yeshiva College in May 2013 with a BA in Computer Science and Mathematics. He spent the Summer of 2012 doing theoretical computer science research in Bar Ilan University, the results of which can be found in this journal. After he graduates, he plans on pursuing a career in software development and living in New York with his amazing soon-to-be wife Sonia.

Algebraic Geometry

Enumeration of Standard Young Tableaux of Certain Truncated Shapes, Continued

by

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[2]*Department of Mathematics, Bar-Ilan University, Ramat-Gan, 52900 Israel*

A standard Young tableau (SYT) consists of a table with n boxes, each filled with one of the numbers between 1 and n such that numbers increase along both rows and columns (see Figure 1). Standard Young tableaux have numerous applications in combinatorics, representation theory, and algebraic geometry. As an example, it can be shown that the number of SYT on a given standard shape of size n is equivalent to the dimension of a related representation of Sn [3]. An SYT is said to be in a standard shape if the shape is aligned on the left and row length is weakly decreasing (less than or equal to the previous row) from top to bottom (see Figures 2 and 3). In such a scenario, there exists a well-known "hook-length formula" to enumerate all possible SYT of a given shape ([2], p. 214). When a standard shape is truncated, however, no general formula is known.

In [1], Adin and Roichman began exploring specific truncated shapes, such as squares and rectangles with one or two boxes removed from the northeastern corner (Figure 4). Similar studies were carried out by Panova [4]. We continued this project by researching conjectured formulas for shapes of the form (n ^ 2) \ (n – 2) (Figure 5), (n ^ 2) \ (n – 3) (Figure 6), and n(n + 1) \ (n – 2) (Figure 7). In addition, we sought to understand in which scenarios we could expect a product formula, and in which scenarios no such formula exists.

To discover a conjectured formula, Adin and Roichman developed a bijection between a large truncated shape and a combination of two smaller standard shapes. This allows us to count the number of standard Young tableaux (NSYT) by counting all the possible combinations of smaller shapes in the range of the bijection via the already known hook-length formula. If NSYT consistently contains only relatively small prime factors (at most the size of the shape), this indicates the existence of a product formula.

After applying this method to the shapes mentioned above, we obtained positive results for those shapes with a first row of length 2, and negative results for shapes with a first row of length 3. We conjecture that for n > 7, the largest prime factor of NSYT for the shape (n ^ 2) \ (n -2) is the largest prime number less than n ^ 2. We further conjecture a generalized formula for any shape of the form of a k by n rectangle with a row of two squares appended to its NW corner to be (F(k) F(n) (kn-k)! (kn+n)!) / (F(n+k) (kn+n-k)!), where k is the number of rows (excluding the appended row of length 2), n is the number of columns, and F(m) is defined as the product of the factorials of x for x in range(1, m). This formula has been proven analytically for k = 2,3, and verified computationally for all rectangles between the sizes of 2 by 2 and 20 by 20.

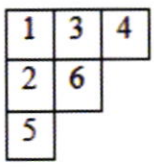

Figure 1. A standard Young tableau

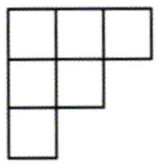

Figure 2. A standard shape

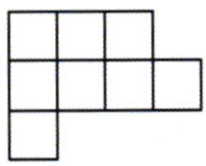

Figure 3. A non-standard shape (row 2 is greater in length than row 1)

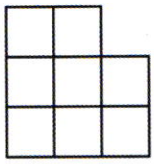

Figure 4. A truncated square shape, with one box removed from the NE corner

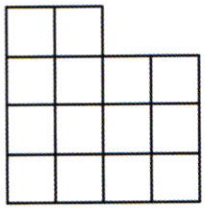

Figure 5. The shape (n ^ 2) \ (n – 2) for n = 4

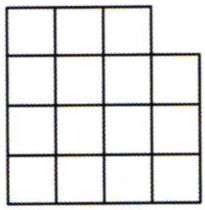

Figure 6. The shape (n ^ 2) \ (n – 3) for n = 4

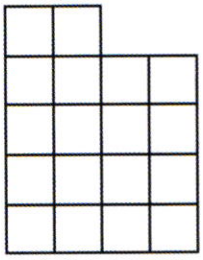

Figure 7. The shape (n*(n + 1)) \ (n – 2) for n = 4

Acknowledgements

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Student Researcher

Zachary Goldstein is a senior at Yeshiva College majoring in Chemistry. He is from South Bend, Indiana and will be applying to medical school this summer.

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Set Valued Functions

Eigenvalues, Adjoints, and Conjugates of Set-Valued Sublinear Functions

by

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One of the most basic functions in mathematical analysis is the linear function. The question arises if one can find an analogue of the linear function in set-valued analysis, i.e. a set-valued function that resembles a linear function as much as possible. The crucial difficulty lies with the fact that the set of all subsets of a linear space is no longer a linear space. In particular, there is no inverse for the 'element-wise' addition of sets, i.e. no 'difference' for sets.

Rockafellar in 1970[1] introduced the concept of the convex process, which he believed was this analogue. Recently, a new notion has been proposed by Hamel[2]: the conlinear function.

In this paper, we expound upon this conlinear function. After presenting some important background concepts, we define an A-sublinear, a set-valued sublinear function that is also additive. We subsequently provide equivalent conditions for an A-sublinear function to become a conlinear function. Given that this function is also convex, we build upon notions in set-valued convex analysis, mainly duality and differentiability, discussed by Hamel and Schrage[3,4]. Specifically, we attend to set-valued conjugates, directional derivatives, subdifferentials, and supports, and link them to convex and adjoint processes. It turns out that set-valued sublinear functions and convex processes are basically the same concept. Moreover, the (classical) adjoint process of a sublinear set-valued function (understood as a convex process) coincides with the support (the set of all conlinear-affine minorants) of the sublinear function. This generates new insights into the relationships between recently introduced notions, such as directional derivatives and subdifferentials, for convex set-valued functions.

We finally discuss the set-valued eigenvalue problem, previously considered by Seeger and others[5,6,7], in the context of our conlinear setting.

With this conlinear function, one has the means to tackle many problems in optimization theory. In particular, it can be used in many applied fields, including mathematical finance and economics where set-valued coherent risk measures[8] provide excellent examples for set-valued sublinear functions.

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Student Researcher

Uri Carl is a fourth-year student majoring in mathematics and minoring in philosophy at Yeshiva College. He enjoys thinking about abstract mathematical entities and spaces, as well as tackling fundamental issues in philosophy. He additionally finds listening to various genres of music, ranging from classical to classic rock, soothing and focusing. After graduating from YU, he plans on pursuing a Ph.D. in operations research.

Biophysics

DNA Rotation Studies Using Tethered Particle Motion

by

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[2]*Physics Department and Nanotechnology Institute, Bar-Ilan University, Ramat Gan, 52900 Israel*

Single-molecule experiments studying the biophysical properties of DNA have revealed many molecular interactions and sub-processes not observable in ensemble studies. An elegant method called Tethered Particle Motion works by conjugating one end of the DNA with a bright particle which can be observed under a microscope. The other edge is fixed to a surface, and the end-to-end distance is easily extracted. Our research group used gold nanobeads (diameter 80 nm) and darkfield microscopy to allow for high image contrast and resolution. Observing how the DNA's diffusion in the surrounding liquid moved the bright gold nanoparticle allowed for the calculation of the DNA strand's spring constant and persistence length, while the mechanical effect of the presence of specific proteins in the liquid could be easily studied.

The current project involves the use of gold nanorods, one-dimensional sticks of microscopic gold, in place of the spherical nanobeads. Though the added dimension is too small to be directly detected by the microscope, the rod's rotational position can be extrapolated from the microscope's image based on plasmon physics. As extensive study of the optical properties of metals has shown, the polarization of light reflected off of cylindrical shapes depends on the orientation of the incident light, the metal, and the reflection. By gathering data on the DNA's twisting motion in addition to its position, we hope to learn more about how strands of DNA stretch, fold, and twist, both by themselves and in the presence of various enzymes.

Student Researcher

Gilad Barach is a third-year student in Yeshiva College, majoring in Physics and Mathematics. He keeps himself busy with research and an assortment of extracurricular clubs and activities. Once he's had his fill of YU, he hopes to go to graduate school in physics so he can spend his career developing cool things in the hi-tech industry.

Complex Networks

Cascading Failures: Distribution of Betweenness in Networks Failing by Overload

by

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Much of modern technology relies heavily upon the interactions between disparate elements across some form of network. The internet, electrical power grids and social media interactions are only some of the many realizations of network theory in the contemporary world. We seek to identify the nature of the reactions of somewhat abstracted versions of these types of networks to random, large-scale attacks.

We study the Motter and Lai model of cascading failures based on the betweenness centrality of the nodes, for a random regular network (1). After removing a fraction of the nodes, we study the size of the giant component at the end of the cascade of failures, as a function of the fraction of the nodes that survived the initial attack. We find that the type of transition by which the network disintegrates changes from first order to second order as the maximum capacity of the nodes increases. As we would expect, we find that the point of transition depends heavily on the tolerance factor built into the system, and we attempt to define a model to describe the connection between the fraction of transition and the tolerance.

We examine the distribution of betweenness of the nodes both before and after the initial attack, and find that it is both predictable and well-behaved. By extracting the maximum values of betweenness from the distribution and scaling the results for various levels of tolerance, we find that our method of analyzing the network through its betweenness distribution mirrors the results that we find when examining both the final size of the giant component and the length of cascades. We further demonstrate that we may analytically describe the behavior of the transition point in relation to varying tolerances.

References:

[1]*A. Motter, Y. Lai, "Cascade-based attacks on complex networks," Phys. Rev. E 66, 065102(R) (2002)*

Student Researcher

Yaakov Tuchman is a junior in Yeshiva College majoring in Physics, with a Pre-Engineering major added on for fun. When he is not busy learning, Yaakov spends some of his spare time teaching science in a local public school to share his enthusiasm for science with others. He intends to pursue a degree in Materials Science in pursuit of a fuller appreciation of the structure of matter.

Complex Networks

Cascading Failures in Networks with Proximate Dependent Nodes

by

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Many real networks, such as the communications and internet networks, are interdependent. A failure in one network can cause failures in the other. This can lead to the sudden collapse of both networks. In the real world, it is unlikely that an internet server in New York will depend on a power plant in California. Therefore, we introduce a notion of distance to explore the effects of the proximity of interdependent nodes in the cascade of failures after an initial attack. In our model, we build two identical random regular networks, A and B, each of whose nodes are labeled $1 \ldots N$. These nodes are randomly connected by links to exactly k other nodes. We then create bidirectional dependency links, requiring that the links connect nodes in the second network that have the same index as a nearby node.

We destroy a fraction $(1-p)$ of randomly selected nodes in A. The nodes in B that are dependent on the destroyed nodes fail, isolating some of their neighbors. These neighbors also fail, causing the nodes dependent on them in A to fail. The repetition of this process leads to a cascade of failures, which may result in a set of surviving nodes, with no further failures, which spans the entire network. This set is called the mutual giant component. As p decreases, the size of the giant component also decreases and, at a certain value of p, the giant component completely disappears. We call this value, p-critical, or p_c. We will denote the p_c for a degree k and distance d as p_c (k,d). We show how p_c varies as a function of k and d (Figure 1). The networks to the left of the blue line undergo second order transitions while those on the right side undergo first order transitions. The one point, which is circled, p_c (8,1), undergoes a transition which is neither purely first nor second order.

We offer an analytic solution for p_c for the case of $d=1$. While this is the simplest non-trivial case, as the connectivity increases, these networks exhibit an interesting shift in the type of transition, from second order to first order. In order to calculate p_c, we need to evaluate the fraction of indices in which A_i is dependent on B_i. We denote this fraction as m, and refer to them as monomers. This problem is a version of Rényi's parking problem[1] that applies to a discrete graph. After analyzing the probabilities of links leaving assigned and unassigned nodes, we are able to analytically calculate the ratio of monomers in the network.

We further define a node as "supported" if its dependent node is connected to its own giant component. This definition will allow us to isolate the effects of failures in one network. Using an analog to the equation of basic percolation theory, $a=(1-p)+p*[P(x \cap y)]$. We define a as the probability that a given link that leaves from a supported node does not lead to the giant cluster. The expression stems from the fact that there is a probability $(1-p)$ that the link leads to a destroyed node and thus will not lead to the giant cluster. However, if this link leads to a possibly alive node, x represents the event that this node does not lead to the giant component. If the link leads to any node that survived the initial attack, y represents the event that the node's dependent node does not connect to its own giant component. Therefore, $[P(x \cap y)]$ represents the probability that the adjacent node is not connected to the giant cluster. We then construct five equations which follow this structure and through an iterative process, are able to analytically solve for p_c and see the nature of the two types of transitions (Figure 2). The odd behavior of for p_c (8,1) can now be better understood. We first see behavior characteristic of a second order transition, but it then changes to that of a first order transition.

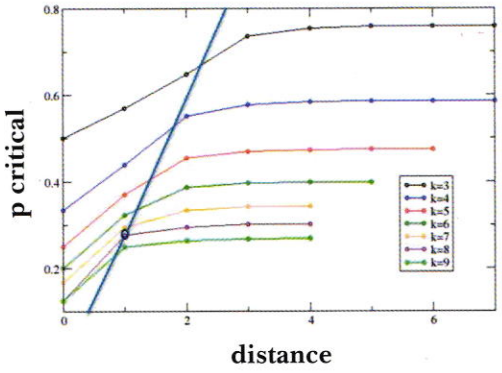

Figure 1. Numerical results of p_c vs. distance obtained by averaging 100 realizations of networks consisting of $N=10\hat{}6$ nodes, for different degrees of connectivity (k). It can be seen that for each value of k, the p_c rises monotonically.

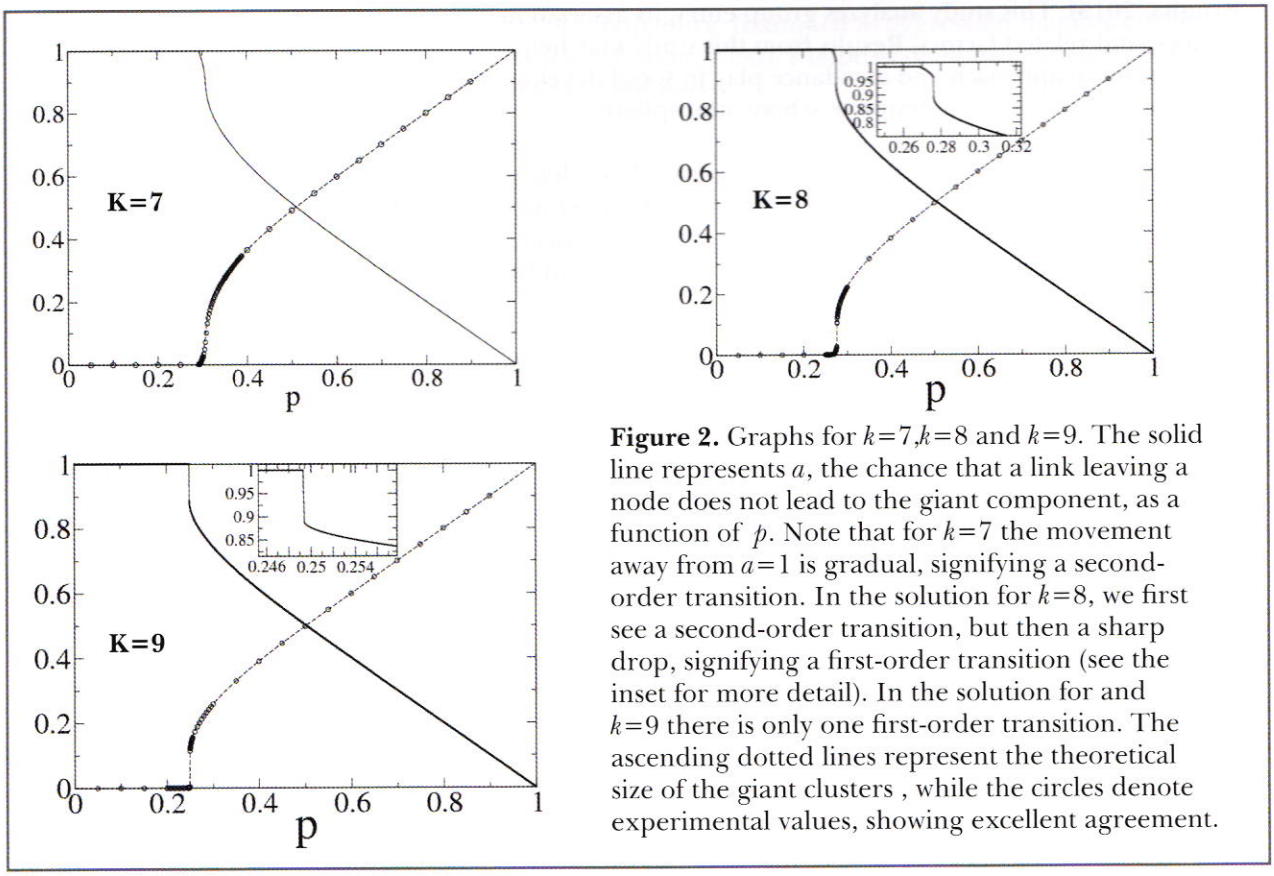

Figure 2. Graphs for $k=7$,$k=8$ and $k=9$. The solid line represents a, the chance that a link leaving a node does not lead to the giant component, as a function of p. Note that for $k=7$ the movement away from $a=1$ is gradual, signifying a second-order transition. In the solution for $k=8$, we first see a second-order transition, but then a sharp drop, signifying a first-order transition (see the inset for more detail). In the solution for and $k=9$ there is only one first-order transition. The ascending dotted lines represent the theoretical size of the giant clusters , while the circles denote experimental values, showing excellent agreement.

References:

[1]A. Rényi, Publ. Math. Inst. Hung. Acad Sci. 3 109-127 (1958)

Student Researcher

Hailing from Teaneck, NJ, Yosef Kornbluth is a double major in Physics and Math. Part of the Class of 2015, he will be doing research into network theory for the next two years as a Kressel Scholar. After graduation, he plans to join a Ph.D. program in Physics or Engineering.

Student Researcher

Steven Lowinger, from Queens, NY, is currently majoring in Physics and minoring in Mathematics. He began doing research in network theory last summer and hopes to continue until he graduates in 2014. After graduation he plans on pursuing a Masters degree in Engineering.

Social Psychology

Investigating Group Entry's Link to Conduct and Status in School Peer Groups

by

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The latest wave of school violence highlights the need for rigorous, empirical study of relationships among youth. Roots of longterm adult difficulties lie in childhood struggles with peers (Fryers & Brugha, 2013). This study analyzes group entry, its association with prosocial and delinquent behaviors, and related factors. Results from this study may help to improve our understanding of the role that social approach and avoidance play in social development. The study may also help inform better tools for creating a desirable school atmosphere.

Relevant research has focused on adults, yet crucial developmental changes stress the need to study youth. Time spent with peers increases, concerns for peer acceptance at the group level soar, and bullying and victimization surge. Aggressors are less physical, relying more on verbal and relational aggression and find specific targets. Prosocial behavior and healthy relations also change (Dodge, Coie, & Lynam, 2007).

Group entry is a critical social task that relies on proper emotion regulation and social skills (Waters & Sroufe, 1983). Rejection inevitable for those with poor group entry styles results in many negative correlates such as lower school performance, aspiration level, vocational competence, participation in social activities, negative attitudes toward school and higher rates of conduct disorder, substance abuse, criminal offences, and behavioral problems than non-rejected peers (Bagwell, Newcomb, & Bukowski, 1998; Ollendick, Weist, Borden, & Greene, 1992).

Negative outcomes may not be due to social rejection alone; rather, I hope to demonstrate that they work in concert with different types of group entry styles. A dominant style indicates high levels of approach and relates to less sensitivity to signs of punishment and less ability to inhibit actions when results are negative (Keltner, Gruenfeld, & Anderson, 2003). Approach is the "direction of behavior toward positive stimuli," and contrasts to avoidance, the "direction of behavior away from negative stimuli" (Elliot, 2006, p. 112).

In the current study, I will collect data from all the children in each class at a school, which will allow me to examine the entirety of this small social environment. An interested school has approximately 300 5th-12th grade students. In order to yield a richer understanding of each child (such as when a child's perception of their behavior reflects reality) the study combines self-report and peer-nomination surveys.

I will measure group entry with a self-report questionnaire that will identify which children employ a dominant group entry style using disruptive and aggressive tactics to attract attention, which passively hover around the group in a withdrawn fashion, and which choose an assertive middle ground. The study will also ask participants to report on the group entry styles of their peers, I will use sociometric procedures, a widely used method that assesses popularity by having children identify who they like to spend time with the most and those they like to spend time with the least. I expect to replicate the findings that popular children tend to employ an assertive but not dominant strategy, whereas less popular children approach groups in a dominant or withdrawn fashion (Dodge, Schlundt, Schocken & Delugach, 1983).

Moreover, I hope to show that social rejection works in concert with different types of group entry styles to produce negative outcomes. Identified with sociometric procedures, rejected children are low in social preference (often voted liked least and rarely voted liked most). The combination of rejection and higher approach makes those who employ dominant group entry more susceptible to engaging in externalizing and delinquent behavior than their withdrawn, rejected counterparts. I will measure externalizing behavior with peer reports of aggressive behavior and delinquency with a self-report of involvement in a variety of delinquent behaviors (e.g., drinking, cutting class, law breaking, etc.).

Finally, I will explore how group entry relates to social power and aggression. In order to measure power, the study will combine self and peer report on influence in the peer group. Power is a known correlate of approach behavior and profligate activity (Keltner et al,, 2003). Thus, I expect power to be linked to assertive and dominant styles of group entry. Inasmuch as aggression manifests differently in various group entry situations (Crick & Dodge, 1996), I hope to demonstrate the differential associations between aggression and styles of group entry.

If the expected results materialize, this study will contribute to the growing knowledge of children's peer groups and successfully expand the research on social power to children, providing insight on crucial forces in both positive and negative social development. Hopefully, this new information can help foster a healthier school environment in which children can safely explore their social worlds.

Student Researcher
Aaron Cherniak is a senior studying Psychology at Yeshiva College as part of the Jay and Jeannie Schottenstein Honors Program. During his two years conducting research with Dr. Eliezer Schnall and Dr. Jenny Isaacs, he has contributed to numerous research articles and presented research. Aaron serves as the Association of Psychological Science Campus Representative for Yeshiva University.

Social Psychology

Men and Their Religious Family Member's Letters to Religious Leaders.

by

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Religion is a major organizing tool of cultural practice, meaning-making, and development throughout human history. Religion often creates cultural meaning for relationships and interpersonal activities as individuals and societies interact and mutually develop (Etengoff & Daiute, 2012). Throughout history and in times of acute change, some religious structures and communities have evolved in response to the contexts of modernity. However, the course of change for certain subgroups within Judaism and Christianity has been limited, although specific relational practices such as sexuality and love have become redefined in modern sociopolitical terms and the lived experience of individuals. This research therefore specifically aims to understand the lived experience of how gay men and their religious relatives negotiate the contexts of modernity and sexuality, religion, and family in their letters to religious leaders.

The proposed research presents a systematic inquiry of individual and family development around issues of sexual preference disclosure and its aftermath within the context of Jewish and Christian contexts. Sixteen gay men from religious backgrounds (8 Christian *M Age*= 25, *SD*=3, 8 Jewish *M Age*= 24, SD=3) and nine of their religious family allies (6 Christian *M Age*= 52, *SD*=11, 3 Jewish *M Age*= 47, *SD*=20) from across the United States were recruited via list serves, relevant organizations, and snowball sampling. Participants wrote letters to religious leaders about their community's current policies related to gay men. Letters were written on average four years since the first family member disclosure event (*SD*= 3). This method of narrative analysis was selected as it empowers participants to be actors of change as opposed to only observers and it encourages participants to report issues within realistic sociocultural contexts.

A total of 93 problems (*M*= 4) and 75 solutions (*M*= 3) were discussed in the 25 letters of gay men and their religious family allies. Participants wrote about problems in the following domain categories: community, family, sexual and romantic fulfillment, scriptural interpretation, religious faith and institution, social friendships and interactions, politics, and personal anguish. The scopes of the problems discussed were focused on technical, systemic, community specific, personal, and family issues.

Although both gay men and religious family allies acknowledged on average a similar number of difficulties and solutions, a Cultural-Historical Activity Theory based process of analysis indicates that the interactions between gay men and their religious activity system differs from that of their religious family allies. For example, a greater percentage of gay men, as compared to their religious family allies, wrote letters about explicit problems (e.g., *"...it is hard to be accepted simply for who I am from the people around me."*) as opposed to implicit problems (e.g., *"Our children need to feel safe to disclose who they really are."*). In addition, gay men were more likely to write about problems experienced on the religious community level than their religious relatives.

Moreover, a greater percentage of gay men, as compared to their religious family allies wrote about community problems while simultaneously praising their religious leader for their other efforts. For example, a 22 year-old Mormon participant shared *"I love you, Bishop. You, and people like you, make my life easier every time I pause to remember the blessings you've provided. Unfortunately, I choose to pay more attention to those who make my life more difficult..."* It is possible that religious family allies are less likely to praise religious leaders than critique them, as they feel more secure within their religious activity system. This hypothesis is supported by the data indicating that religious family allies used religious

values and faith more frequently than their gay relatives to mediate their conflicts between religion and sexuality (Family Members 89%, Gay Men 38%, 1, N=25, p=.013). For example, although a Jewish sister wrote that homosexuality *"remains a conflict within the Orthodox world"* due to the commandment to procreate heterosexually, she also referenced the religious values of communal unity in her argument not *"to stray those who are homosexual away."* A similar strategy was used by a Methodist mother from the South who began her letter by asking *"What would Jesus say?...Spiritual love between two people seems to never be portrayed as a sin -- love your neighbor as yourself."*

The aim of this research is to tell a story of how parents' and children's letters focused on critiques of their socioreligious system in different ways. Although both groups wrote letters about problems and what they would like to see changed, the arguments that they crafted differed in content and tone. For example, gay men were more likely than their religious allies to explicitly mention problems and praise their religious leaders for their efforts. In addition, religious family allies were more likely to use religious values as tools of their argument. Such results suggests that gay men and their religious family allies have different perceptions of the difficulties and their daily methods of navigating these difficulties perhaps due to their respective structural locations..

Although this study is one of the first pieces of psychological research to present family *units'* perspectives regarding the mediation of sexuality, family, and religion, there are still some sampling limitations. Firstly, future research should expand the general sample size as well as that of religious and regional subgroups. Secondly, the generalizability of this study is limited as the participants recruited were already engaged in mediational strategies such as support groups and blogging. Therefore, researchers and clinicians should proceed with caution before applying these results to different religious and regional and groups that are not already engaged in mediational strategies.

In addition to being one of the first studies to explore the conflicts experienced by both gay men and their religious family allies, this qualitative study approaches the question of how these conflicts are navigated from a positive psychology perspective. This analysis of the different positive strategies that are used in their letters to religious leaders can be used to develop clinical interventions focusing on the unique structural location and needs of the two populations.

Student Researcher
Shira (Kandel) Donath is a senior at Stern College for Women, majoring in Psychology and minoring in Business. Her appreciation for data-driven decision making has guided her in both research and student leadership positions. Over the past two years, Shira has worked together with the administration to enhance the undergraduate environment at Yeshiva University as part of the Student Academic Affairs Committee. She hopes to pursue a career in Applied Research, which will utilize her understanding of research methodologies, as well as suggest its implications for future practice.

Social Psychology

Religious Affiliation and the Parent-Sibling Relationship in Families with a Child with Special Needs

by

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The presence of a child with special needs may have a negative impact on the relationships between family members. The purpose of this study was to analyze the influence of religious commitment on the parent-sibling relationship in a family with a child with special needs. Twenty-three parents of children with special needs were administered a questionnaire regarding their faith and affiliation with religious organizations. The Parent Adolescent Relationship Questionnaire was administered to evaluate the parent-sibling relationship. Results indicated that parents with less religious affiliation scored higher on the Global Distress scale reflecting more dissatisfaction and conflict in the parent's relationship with the sibling. Parents with less religious affiliation scored higher on the Communication scale reflecting more negative communication, more intense arguments and a lack of consideration for each other's feelings. These results suggest that religious support may improve interactions between family members, particularly between the parent and sibling.

Student Researcher

Jessica Listhaus is a senior at Stern College and will be graduating in May 2013 with a major in Psychology. She plans to attend the Kean Occupational Therapy Master's Degree Program in Fall 2013. As the younger sibling of a child with special needs, Jessica is interested in studying the impact of having a family member with special needs on the relationships of other family members. In addition to this research, Jessica is conducting research on the impact of birth order and personality on the Parent-Sibling relationship.

Cognitive Psychology

'Can Your Eyes Define You? A Correlation of Dissociative Capacity to Personality Traits and Learning Styles.'

by

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Dissociation is the conscious or unconscious ability to separate memory, perception or motor response from awareness. The ability to dissociate is biologically determined and is reflected in specific physical signs. Previous research has demonstrated that the eye-roll sign, which is vertical mobility of the eyes, defined as the amount of sclera visible between the lower eyelid and the bottom of the cornea when a person looks straight up, is a biological finding correlating with dissociative capacity. The hypothesis of this current study is that in mentally healthy subjects, the eye-roll sign will correlate with specific measures of learning styles and mindstyle characteristics. Eye-roll was measured as the amount of sclera seen when the subject looks up, personality using the Mindstyles Questionnaire and learning styles using the Memletics Learning Style Inventory (MLSI). Associations between mindstyle and eye-roll were calculated. Correlations between eye-roll and learning styles of visual, aural, verbal, physical and logical were evaluated. A significant correlation was found between the eye-roll sign and mindstyle category. A strong correlation also emerged between the eye-roll category and learning styles. It is exciting to consider that a relatively quick and simple and quick physical assessment can offer such insight into both a person's personality and learning styles.

Student Researcher

Adam is an incoming freshman who will be entering into the Sy Syms Business Honors program next semester and will be double-majoring in Marketing and Management. He conducted this research while in high school, beginning in the 10th Grade. Psychology has and always will be a great interest of Adam's, both for its fascinating and stimulating attributes as well as its applicability towards the business world and how people interact with each other.

Cognitive Psychology

Perspective Taking Reduces Egocentric Errors in Simple Communication Tasks

by

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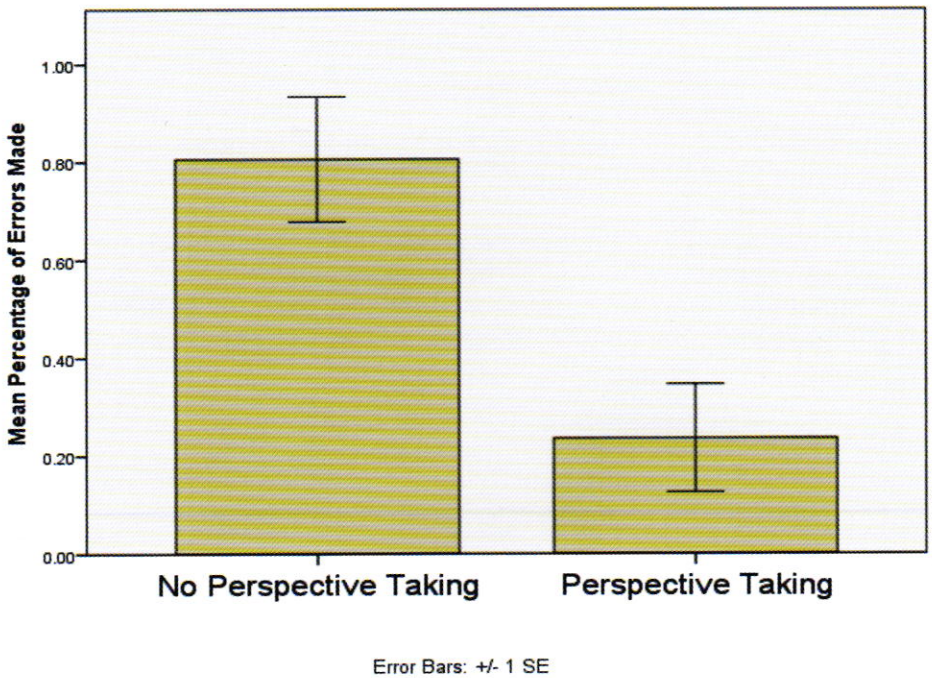
Keysar (2007) suggested that everyday human communication can be hindered by the failure to take another's point of view into account. Such egocentrism has been demonstrated both in simple communication tasks - such as when an experimenter asks a participant to move items around a set of shelves (Referential Communication Game) - and in more complex communication tasks, such as negotiation tasks.

Egocentrism in complex communication tasks can be reduced by inducing participants to take another's point of view (Perspective Taking, PT). However, it is not clear whether PT can be induced to assist in simple communication tasks such as the Referential Communication Game.

We argue that the standard Referential Communication Game actually contains a PT manipulation, but nobody thus far has contrasted it with a neutral condition. In this study, we used the standard Referential Communication Game with the inclusion of a neutral (No-PT) condition and found that PT improved communication.

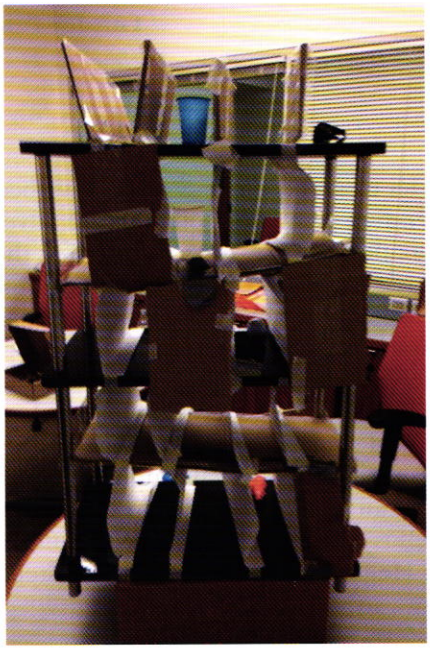
This research was conducted under the guidance of Professor Bruno Galantucci as part of course in experimental psychology.

Figure 1. The results of our study



Participants in the No-PT condition made 80% of possible egocentric errors. Participants in the PT condition made 20% of all possible egocentric errors.

Participant's View



Experimenter's View

Figure 2. The apparatus used for the referential communication game in our study In the game, the experimenter instructs the participant to moves items around the shelves

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Student Researcher
Yoel Epstein is a senior at YC majoring in Psychology and the lab manager of Professor Ariel Malka's research lab. He enjoys watching Ted Talks on topics of psychology and looks forward to the day that YC faculty members will make their Ted Talks debut. After graduation, he hopes to return to full-time Talmud study and to eventually pursue a doctorate in Clinical or School Psychology.

Student Researcher
Asher Lindenbaum is a senior at YC majoring in Psychology and a Research Assistant in Professor Ariel Malka's research lab. In his spare time, he enjoys singing, playing guitar, and loves to cook. After graduation, he will be attending the Accelerated Master's Program in the Azrieli School of Education and hopes to eventually pursue a doctorate in Clinical Psychology.

Political Science

Political Presence: Using the Self-Expansion Model as an Accurate Predictor of Close Presidential Elections in Modern American History

by

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What decides close elections? Studies have been done on a wide variety of factors, such as a campaign's spending or reliance on negative advertising, a voter's past turnout rate or marital status, and a population's density or stability. This thesis argues that in close elections, candidate appraisal decides voting preference among conflicted voters. The Self-Expansion Model, which so far has only been used in the context of interpersonal relationships, is used to measure this hypothesis. This psychological model rests on two assumptions, namely that self-efficacy is a core human drive and that people achieve self-efficacy by broadening their sense of self to include others cognitively, behaviorally and/or affectively. The psychological world offers no comprehensive definition of "self," though myriad studies have been done on the self-concept's functionality. A review of 63 great political thinkers revealed two recurring themes, however: persistence and corporeality. Thus, only four kinds of self can exist, as founded by Plato (the self is persistent but not corporeal), Niccolo Machiavelli (the self is corporeal but not persistent), John Locke (the self is both persistent and corporeal), and Georg Hegel (the self is neither persistent nor corporeal).

It is hypothesized that conflicted voters prefer the candidate who triggers the most expansion from these selves. But what has past scholarship said about why people vote? Two literature reviews (one political and one psychological) about voter turnout are reviewed. These literature reviews investigate past studies on everything from registration barriers or concurrent elections to a voter's income or patience, but both neglect to mention candidate appraisal. This hesitance arises from the fear that such studies are not objective and from these studies' lack of unification. Because these studies as so focused on certain candidate features, such as personality or age, they are unfocused as a group. The Voter/Candidate Relationship is proposed as a unifying model for studies on candidate appraisal, arguing that this parasocial relationship is ongoing, affective, interdependent and meaningful – like any other relationship.

To test this hypothesis, individuals around Central Park were approached on October 28, 2012, until 36 respondents were obtained, 18 males and 18 females. The interaction consisted of an oral interview begun with an interview request ("Good morning/afternoon, can I give you a short political survey?"), one sentence of instruction ("Of the two main presidential candidates, which one do you feel is more..."), then seven short questions. Four questions primed respondents to consider the traits of the two major candidates, one question addressed who the respondents believed would most likely win, a question offered the Inclusion of the Other in the Self Scale (IONSS), and the last question asked for candidate preference. Age and gender were used as controls. Two separate 2-Sample Z Test for Proportions revealed that neither age nor gender correlated to candidate preference or the strength or candidate preference among the voters. A regression analysis on the IONSS showed

a statistically significant correlation (r^2=.8515) between reported self-expansion, candidate preference and the strength of candidate preference among conflicted voters and unconflicted voters. It is thus recommended that polling organizations consider adding Self-Expansion to their repertoire of survey tools for the next presidential election, where the divisive political environment and lack of an incumbent is likely to produce another close electoral race.

Student Researcher
Gurney is a senior with a passion in political science, psychology and music. Next year, he will attend the University of Colorado at Boulder for law school.

Developmental Psychology

Remediating Academic Impacts of Early Neglect

by

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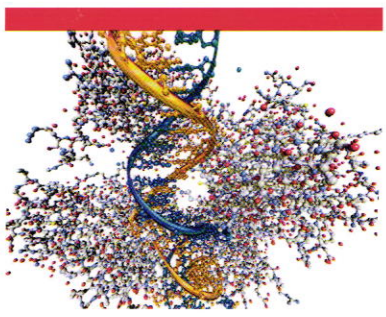
In 2011 there were 3.4 million reports of child maltreatment in the U.S. Of these, 78.5% children were neglected, that is, they did not receive age-appropriate care by their caregivers. About half of these children were five years of age or younger. Numerous studies have found a correlation between early childhood neglect and poor academic performance and delays in language development. Recent research has identified under development of the prefrontal cortex as a potential cause for the link between neglect and poor academic performance. The prefrontal cortex is responsible for executive functions, including the ability to engage in goal-directed behavior, working memory, and inhibitory control, which positively correlate with academic achievement. Interventions with parents and educators to promote cognitive functioning in those areas governed by the prefrontal cortex may improve academic success in neglected children.

Student Researcher

Shira (Kandel) Donath is a senior at Stern College for Women, majoring in Psychology and minoring in Business. Her appreciation for data-driven decision making has guided her in both research and student leadership positions. Over the past two years, Shira has worked together with the administration to enhance the undergraduate environment at Yeshiva University as part of the Student Academic Affairs Committee. She hopes to pursue a career in Applied Research, which will utilize her understanding of research methodologies, as well as suggest its implications for future practice.



Yeshiva University