Stern College for Women
Yeshiva University

2005-2006
2004-2005
2003-2004

WOMEN IN SCIENCE

Undergraduate Achievements in Biology, Chemistry and Physics

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Introductory Remarks

The Departments of Biology, Chemistry, and Physics, each unique in its specific discipline, share a proactive approach in promoting the academic success of students at Stern College for Women (SCW) and to helping them achieve their career goals. The spectrum of career choices in the biomedical, health, and natural sciences is varied, with our students entering graduate programs in medicine, dentistry, osteopathy, optometry, physical therapy, occupational therapy, physician assistant, nursing, genetic counseling, nutrition, and diagnostic medical imaging; masters programs in biotechnology and bioinformatics; and doctoral programs in the biomedical sciences and in chemistry. Education in physics and engineering sciences are stepping stones toward careers in research and education in technology-oriented fields, including nanoscience and nanotechnology. (See the Student Accomplishments section for a more detailed listing).

The departments direct students to stretch beyond the classroom experience by their involvement in scientific research. Both during the academic year and the summer, students may work one-to-one with on-campus faculty. During the summer, the research laboratories at our Albert Einstein College of Medicine (AECOM) provide additional opportunities through the Roth Institute Program. Summer internship opportunities for students of all the science majors are available at the world renown facilities of Brookhaven National Laboratory (BNL) and Stony Brook University (SBU), through collaborative research with YU, BNL, and SBU. Furthermore, the faculty actively encourages science majors to apply for competitive undergraduate research internships, both nationally and in Israel. In the summer of 2006, about 35 SCW students were involved in research, either at SCW, AECOM (See Roth Scholars), or at external research facilities, including The Rockefeller University, Bellevue Hospital, Yale University, Harvard Medical School, Hackensack University Medical Center, the University of California at San Francisco, BNL, SBU, and Citroil Enterprises, as well as in St. Michael's Hospital (Canada), the Rambam Hospital (Haifa), and the Forensics Division of the National Police (Jerusalem). (See the "Abstract Booklets of Student Research" section for a descriptive analysis of the various projects and the section and "Student Accomplishments" for a detailed listing of student internships.)

Our students' impressive record as coauthors on scientific articles in peer-reviewed journals, as well as on research abstracts of work presented at national meetings of scientific societies (See "Student Publications") is indicative of the quality of their input and of the high regard the sponsoring laboratories have for our students.

A specific objective of the science departments at SCW, in addition to nurturing the highest level of academic achievement, is to provide students with opportunities for leadership roles. Upper level students may be appointed to positions as Teaching Assistants (TAs) for laboratory courses and as Recitation Instructors to review materials for the lecture portion of science courses. Student-led clubs, such as the Biology Club, the Chemistry Club, the Physics Club, the Pre-Med Club, the Pre-Dent Club, the OT Club, etc., provide opportunities for students to gain skills in organizing events and in coordinating social functions.

SURGE, the Student Undergraduate Research Group Exchange, a faculty-sponsored, student-led club gives students the forum to present their research as a seminar before their colleagues and the science faculty. The goal of this faculty-initiated club is to encourage and foster research and the exchange of research information. Meetings are held once a month, usually with two or three students presenting power-point professional seminars. Faculty members also use these meetings to inform students of upcoming internships and fellowship opportunities. In the 2005-2006 academic year, the following students presented seminars:

Frida Fridman:	Inhibitor screening for human purine nucleoside phosphorylase, bovine xanthine oxidase, and *E. coli* thymidine phosphorylase
Michaella Goldberg:	Correlation of gene expression and sporulation efficiency in *S. cerevisiae*
Yelena Kozirovsky:	VEGF and avastin
Helen Nissim:	Regulation of Mts1 binding by myosin-IIA heavy chain phosphorylation
Elisheva Levine:	An implicit solvent study of phosphorylation in protein molecules
Ilana Pister:	Analysis of immune response to *Trypanosoma cruzi*
Yardanna Platt:	Urinary matrix metalloproteinases in patients with pulmonary arterial hypertension
Louisette Soussan:	Thiol-stabilized palladium nanoparticles: size control and hydrogenation.
Shani Snyder:	Role of cAMP pathway in *Toxoplasma gondii* differentiation.
Dinah Zaghi:	pH sensitivity in talin

Each fall semester, the science departments jointly sponsor a poster presentation contest. Students present their work and discuss the research with attending faculty. The posters, and more importantly the student's understanding of the project and the extent of her hands-on participation, are evaluated by the science faculty. Three to five winners are selected to present at a national meeting of the American Chemical Society (ACS). The costs of attending the meeting, including transportation and hotel, are underwritten by the Dean's Office, SCW. In the spring of 2006, Jessica Feig, Frida Fridman, Michelle Goldberg, Elisheva Levine, and Louisette Soussan attended the 231st National Meeting of the ACS, held in Atlanta, GA. (See "Abstract Booklets of Student Research.")

In 1991, with the support of Dr. Ira Kukin, a member of the Board of Trustees of Yeshiva University, an annual chemistry lecture series was established. The invited speakers are distinguished scientists, many of them Nobel Laureates, who direct their talks to the undergraduate students. Prior to the lecture, students have the opportunity to interact with the speakers, and after the lecture, to participate in a question session. This annual lecture is attended by the undergraduate science students of Yeshiva University, selected high school students, science faculty, administrators, invited scientists from the New York area and Dr. Ira Kukin and his

family. In the spring term, 2006, Dr. Martha Greenblatt, Rutgers University, spoke on the topic, "The beauty and fascination of solids." Student comments such as, "I appreciated the *chizuk* to those of us who wish to pursue a career in science," are often enunciated after these lecturers. By attending the Kukin lectures throughout their undergraduate career, they realize their progressive advancement in science by their increased understanding of the lectures. These lectures serve as an encouragement to chose a career in science.(See "Kukin Lecture Series.")

SCW graduates who will be attending AECOM for their medical education are eligible to apply for Anne Scheiber Fellowships. This unique award provides up to full tuition scholarships based on need for four years of medical training. (See "Anne Scheiber Fellowship.") Students considering careers in various Allied Health fields (for example, occupational and physical therapy) or in engineering may wish to consider one of our several combined degree programs with other universities (See "Combined Degree Programs in the Sciences.")

An important focus of SCW is to educate the next generation of Jewish women for leadership positions in their professions and communities. Our commitment to the Yeshiva University mission of *Torah U'Madda* is mirrored in the daily lifestyles of our students and thereafter in their future roles as professionals. Stern College students have academic strengths in both general and Jewish studies; the fusion of these worlds is evident in the student publication, *Derech HaTeva, a Journal of Torah and Science*. This SCW publication is distributed nationally and internationally and has received much praise for its level of Torah/science scholarship. (See *Derech HaTeva* section for a listing of articles that have appeared in volumes 1 through 10). The 2005-2006 academic year saw the publication of the new journal, *Science and Ethics: a Joint Perspective*. This journal discusses bioethical and biomedical issues of current interest, again relying of the unique strengths of our students - their combination of Torah and secular studies. (See *Science and Ethics: a Joint Perspective*, for a listing of articles in volume 1.)

The Departments of Biology, Chemistry, and Physics share much in common, yet each has its own distinct approach and style to educating and to stimulating learning. To become better acquainted which the sciences at SCW, the reader is directed to the specific subsections for each department.

Department of Biology

Faculty: Harvey Babich, Ph.D.; Bill Bassman, M.S.; Joseph DeSantis, Ph.D.; Emil Gernert, Ph.D.; Brenda Loewy, Ph.D.; Jeffrey Mollin, M.S.; Alyssa Schuck, Ph.D,; Margarita Vigodner, Ph.D.; Jeffrey Weisburg, Ph.D.; Richard Weiss, M.D.; Harriet Zuckerbraun, Ph.D.

The Biology Department offers a wide range of courses giving students a thorough grounding in the fundamentals of modern biology as well as exposing them to some of the cutting edge areas of biomedical research. Offerings include Cell Biology, Developmental Biology, Ecology, Genetics, Immunology, Microbiology, Molecular Biology, Pharmacology, Physiology, Neurobiology, Neuroendocrinology, the Epidemiology of Bioterrorism, and Women's Health.

In recent years, innovative classes using the journal club approach have been introduced. In these courses students read original scientific articles, present oral seminars, and develop the analytical skills for critical interpretation of experimental data. These journal clubs, led by adjunct faculty from neighboring institutions (Mount Sinai School of Medicine, New York University Medical Center, and the Albert Einstein College of Medicine), have addressed the following topics: Stem Cell Research; Cancer Research; Apoptosis; and Mouse Models of Cancer. The analytical proficiency that students develop through these journal clubs helps promote success on entrance tests for professional and graduate schools and is fundamental to the appreciation of scientific research.

During early June of 2006, nine biology majors with special interests in Marine Sciences participated in a two-week intensive course in Marine Biology. Taught by Dr. Joseph DeSantis and partially funded through the S. Daniel Abraham Honors Program, the course included a week of lectures at the Beren Campus followed by a week of field work at the Darling Marine Center (DMC), Walpole, Maine. Activities included field collecting offshore and from mud flats and original behavioral research within a modern wet-lab facility. Students spent Shabbat in Providence, Rhode Island as guests of the Jewish community.

SCW students learning about tides and marine life.

Stern women working the mudflats

Students bringing nature to the lab

Aware of the need to maintain state-of-the-art technology, the Biology Department constantly upgrades equipment for use in courses and for in-house research. For example, in the 2005-2006 academic year, five VIS/UV spectrophotometers and five inverted microscopes were added. However, equipment by itself is not adequate to stay current, new ideas come with new faculty. The Biology Department was most fortunate to recruit two additional scientists for 06-07: Dr. Margarita Vigodner from The Rockefeller University and Dr. Alyssa Schuck from New York University Medical Center. As an introductory note to our new faculty, we provide brief geographical sketches, as well as some information on their research agendas for Biology Department.

Born in Saint Petersburg, Russia, at the age of 18, Dr. Vigodner and her family moved to Israel. In Israel, she obtained a B.S. in Chemistry from Ben-Gurion University, a M.S. in Cell Biology and Histology from Tel-Aviv University (TAU),

and a Ph.D. from the Department of Clinical Biochemistry, TAU. Her research focused on the development of novel methods for monitoring germ cell development, using flow-cytometry and confocal microscopy. Prior to joining SCW, Dr. Vigodner, as a postdoctoral fellow at The Rockefeller University, was actively involved in a research focusing on the role of small ubiquitin-related modifiers (SUMO, members of a family of ubiquitin-related proteins) in chromatin modification during meiosis. Her graduate and postgraduate studies resulted in manuscripts published in peer reviewed scientific journals, including *Developmental Biology* and the *America Journal of Physiology*. To quote Dr. Vigodner, "I am looking forward to setting up my research at SCW and to involving students in my projects." At TAU, Dr. Vigodner taught Cell Biology and Histology and, later, as adjunct faculty at Baruch College, she taught the laboratory section of Genetics. In the Fall term, 2006, Dr. Vigodner's courses included Cell Biology (lecture + lab) and Reproduction Biology (lecture).

Dr. Alyssa Schuck, an alumus of Stern College for Women, earned a B.A. in Biology. While an undergraduate, Dr. Schuck (nee, Reisbaum) published ascientific research article in the journal, *Toxicology Letters*, as well as the manuscript, "Tumors in Tanach and Talmud," in *Derech HaTeva*, 3:28-29 1999. In graduate school at New York University, her initial year of research focused on the response of epidermal proteins to ultraviolet light and resulted in a publication in *FASEB J.* As a graduate student at NYU, Dr. Schuck also instructed a laboratory section in Principles of Biology at SCW. She redirected her research project to study the regulatory mechanism of an essential bacterial enzyme. This later project was the topic of her doctoral dissertation and in July, 2006, Dr. Schuck received her Ph.D. in microbiology from NYU. As adjunct faculty member in the Biology Department at SCW, Dr. Schuck initiated a research program, primarily geared to Biology majors in the Honors Program, to introduce them to state-of-the-art biomedical techniques.

Various members of the Department provide openings for students to participate in their research activities. For example, Dr. Weisburg, studying human cancer cells resistant to chemotherapeutics, and Drs. Babich and Zuckerbraun, studying the differential sensitivities between malignant and normal human cells to green and black teas, include students in their research projects. On-campus research opportunities are expected to increase dramatically with the arrival of Dr. Vigodner and Dr. Schuck Off-campus research placements abound, including the Roth Scholars Program at AECOM and other research internships sponsored by Yeshiva University. For example, Nilly Brodt, was awarded a YU-sponsored research internship for the Summer, 2006, to work in the laboratory of Dr. Marina Kaufman-Holz, Harvard Medical School, Boston, MA. Dr. Holz will join the faculty of the Biology Department in the Spring term, 2007. In an e-mail to the Biology Department to update her progress, Nilly commented, "From the very first day, we plunged into our incredibly interesting project and ever since, we have been trusted to carry out procedures I had never heard or read of before." ... "I have done everything from inoculating bacteria, transfecting cells with plasmid DNA, infecting cells with viral supernatant to gels onto nitrocellulose membranes etc." "I cannot even express how much I have learnt in such a short period of time and the caliber of research in our lab still astounds me." "So, I extend the biggest thank you for granting me this wonderful opportunity. I have no doubt this summer will prove rewarding for

the rest of my career in the sciences." (For additional information, See "Abstract Booklets of Student Research" and "Student Publications").

The Department hosts a spectrum of interesting seminars. Programs in the 2005-2006 academic year included a seminar by Dr. Nathan Aviezer, head of the Department of Physics, Bar-Ilan University, on the topic, "On contradictions between Torah and science; the creation of the universe," and a seminar by Rabbi Gideon Weitzman, head of the English Department of the Puah Institute, on the topic, "Infertility in the Jewish community: potential solutions." Dr. Brenda Loewy, the college's Pre-Health Advisor who guides students interested in Medicine, Dentistry and the Allied Health fields through the application process, organizes a series of wide-ranging seminars. Programs in the 2005-2006 academic year included seminars by Noreen Keerigan (Assistant Dean of Admissions, AECOM), Dr. Edward Burns (Associate Dean for Academic Affairs, AECOM), Dr. David Muller (Dean of Medical Education, Mount Sinai School of Medicine), Michele Dojer (New York College of Osteopathic Medicine), Dr. Paul Alexander (American Program in the Technion, Israel), and Marjorie Fass (Sr. Associate Director, Johns Hopkins School of Nursing). Dr. Jeffrey Weisburg, the advisor for the Biology Club, was instrumental in organizing various events, including a trip to the Bodies Exhibit at South Street Seaport and a seminar hosted by Dr. Robert Marion, AECOM and Blythedale Children's Hospital. Dr. Marion, a pediatric geneticist, discussed the surgical operations to separate the conjoined twin, Carl and Clarence Aguirre.

In the summer of 2005, President Richard Joel initiated the "Summer at YU" program for high school students who had completed their 11th grade. The program provided Beit Midrash style Jewish Studies in the morning with a liberal arts/science or business option in the afternoon. For the program's second year, the Biology Department provided a hands-on laboratory course in tissue culture, microbiology, and molecular biology. The students worked with bacteria, yeast, fruit flies, plants, and human cells in culture and employed a variety of sophisticated techniques including cell counting with a hemacytometer, staining of eucaryotic chromosomes; UV spectrophotometry to quantify DNA, DNA extraction, DNA agarose gel electrophoresis, and photodocumentation. By introducing young students to some of the powerful techniques of modern biology, the faculty hoped to inspire a whole new generation of future scientists. Their science-oriented trips, included the Bodies Exhibit, the Laboratory Animal Research Center of The Rockefeller University, and the Albert Einstein College of Medicine, as well as a trip to a local zoo, led by Rabbi Natan Slifkin, affectionately known as the "Zoo Rabbi."

Department of Chemistry

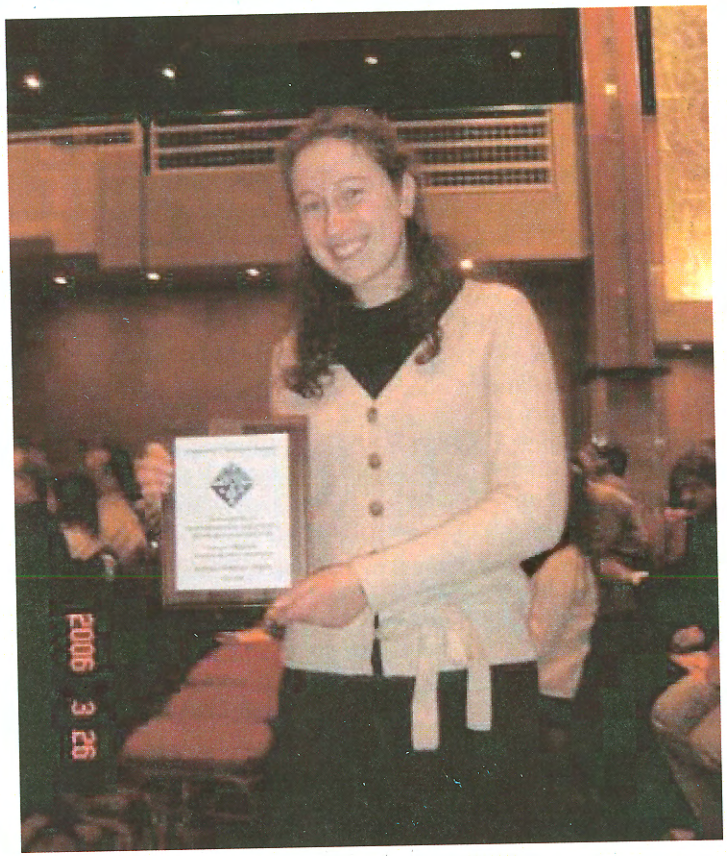
Faculty: Lea Blau, Ph.D.; Cecily Dobin, M.S.; Donald Estes, Ph.D.; Chaya Rapp, Ph.D.; Lance Silverman, Ph.D.

In keeping with the approach to science education at SCW, the Chemistry Department offers a series of high level courses, opportunities for undergraduate research, and extracurricular programming to foster an enthusiasm for science and an interest in scientific research.

Recent on campus research in which students have participated include the development of a biophysical chemistry experiment for the *Physical Chemistry On-Line Consortium* in collaboration with Dr. Don Estes and Dr. Lea Blau; and two projects in collaboration with Dr. Chaya Rapp in computational chemistry that have appeared in the *Journal of Physical Chemistry* and *Proteins*. (See "Student Publications" for details). Summer research student (2005) Elisheva Levine, together with Dr. Chaya Rapp, has contributed to a manuscript on implicit solvent treatment of electrostatic forces, recently submitted to the *Journal of the American Chemical Society* by researchers at the University of California, San Francisco. Dinah Zaghi and Reina Eisner have spent summers 2005 and 2006 at the University of California's Department of Pharmaceutical Chemistry, as part of an ongoing collaboration between Dr. Matt Jacobson (UCSF) and Dr. Chaya Rapp. In the past three years, the Stern College Chemistry Club, a student affiliate of the American Chemical Society (ACS), has earned two Innovative Activities Grants. These grants have enabled the students to create a lecture series and to organize field trips to museum exhibits, pharmaceutical companies and the offices of the Food and Drug Administration. For science and non-science students alike, the highlight of the year is a colorful magic show in the chemistry laboratories, directed by Mrs. Cecily Dobin and performed by members of the Club. In recognition of its various accomplishments, the Club has been presented with Commendable, Honorable Mention and Green Chemistry awards at ACS national meetings over the past seven consecutive years.

Sarah Guigui, a research intern in the chemistry department, performing measurements.

In recent years, the number of students enrolled in chemistry courses has increased significantly. To expand our course offerings and to enhance courses on all levels, an NMR spectrometer has been purchased and a search for new faculty is in progress. In response to students who have expressed greater interest in chemistry as it pertains to the life sciences, the Biology and Chemistry Departments have collaborated in the initiation of a Biochemistry major. Since its inception, interest in the Biochemistry major has grown impressively with 17 graduates who have gone on to medical, dental and optometry school, as well as to graduate programs in the sciences.



Elisheva Levine with the award presented to Stern College by the ACS.

Department of Physics

Anatoly Frenkel, Ph.D. Associate Professor
Dennis Engel, Ph.D., Adjunct Lecturer
Sergey Buldyrev, Ph.D., Professor
Alexander Teperev, Scientific equipment engineer

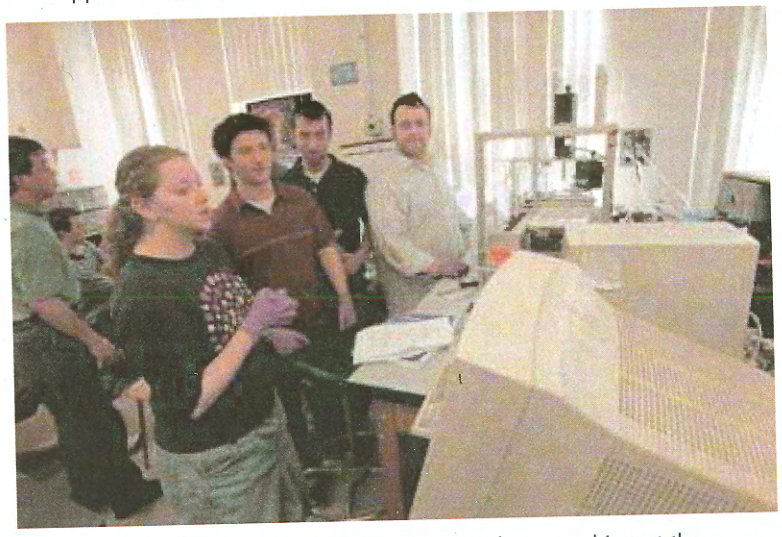
Because of its emphasis on a "research and discovery approach" to education, the Physics Department at Stern College for Women (SCW) has been steadily gaining interest among incoming freshmen. Enrollment in the calculus-based freshman physics course grew from three to four students in 1999-2002 to thirteen students in the 2005-2006 academic year. Enrollment in the algebra-based freshman physics course was also at an all-time high of 35 students in 2005-2006. Many talented students now aspire to physics professions due to the opportunities created by the Physics Department over the last few years. Students have access to the state-of-the-art experimental facilities in the Brookhaven National Laboratory (BNL) and at other major research centers through collaborative research and education programs developed by the Physics Departments at SCW and Yeshiva College (YC). Two years ago the Physics Department at SCW offered a minor in Physics. However, since the 2005-2006 academic year, a new B.A. Physics program is offered for incoming freshmen. At present, four students have declared Physics as their major.

In the 2005-2006 academic year, course offerings in physics included General Physics (calculus based), Introductory Physics (algebra based), Classical Mechanics, and Electromagnetic Theory. In Summer 2006, two honors courses in Nanoscience were offered by the Department (more details below). Starting in the Fall 2006, a new honors course, Intermediate Physics Laboratory (3 credits) for physics majors, was offered. A very successful version of this course, developed at YC by Dr. F. Zypman, was used as its prototype. During the 2005-2006 academic year, Dr. Zypman, in a truly intercollegial spirit, collaborated with Dr. Frenkel in the design of the course. The new experiments, developed during the Spring and Summer 2006, include advanced optics experiments (microwave optics; atomic spectra; blackbody radiation; interferometry) and electromagnetism (wave propagation; electric circuits).

In Fall 2006, Yeshiva University (YU) physics professor, Dr. Sergey Buldyrev, offered Thermodynamics and Statistical Mechanics at SCW, designed for physics majors.

To accommodate the new Intermediate Physics Laboratory course, in Summer 2006 the Physics Department added two more rooms to its laboratory space. A new passageway was constructed from the existing freshman physics laboratory to the two rooms designated for the Intermediate Physics Laboratory. New equipment was installed and tested during the Summer 2006, with the skillful help of Mr. Alexander Teperev, our scientific equipment engineer.

One aspect of our success story is the development of strong ties with SUNY/Stony Brook's Materials Research Science and Engineering Center (MRSEC), funded by the National Science Foundation (NSF). NSF MRSEC is a regional center, under the direction of Dr. Miriam Rafailovich, attracting college undergraduates and high school students from the tri-state area and beyond. The Center offers summer programs in which the students, guided by faculty mentors and visiting scientists, work on individual research projects of their choice. In the summers of 2003 and 2006, NSF MRSEC was the first stop of the honors courses Experiments in Modern Physics: Discover Nanoscience; and Nanoscience for Poets, co-created by YU physics professors Drs. Frenkel, Cwilich, and Zypman. In these courses both SCW and YC undergraduates studied modern physics at the BNL on Long Island. The ties between the two universities strengthened further, as several of the high school students who did summer research at MRSEC subsequently enrolled at SCW and YC. These students continued their collaboration with MRSEC through the joint research program between the SCW Physics Department and the research facilities at MRSEC. In Summer 2006, SCW and SUNY Garcia MRSEC collaborated on the variety of projects, including the synthesis and characterization of Au, Pd, Pt nanoparticles and their investigation by synchrotron x-ray spectroscopy methods and their applications as fuel cell catalysts and hydrogen storage materials.



Michelle Simpser (SCW) and YC students working at the Stony Brook University Garcia MRSEC.

Since its inception in 2004 at SCW, Dr. Frenkel and his students continuously operate their own Nanoparticle Factory, in which they synthesize ligand-protected, gold and palladium nanoparticles and study their unique properties. More information about our group research is on the Stern Physics Department website: www.yu.edu/stern/physics (follow the link to Student Research).

Leah Kanner, Sarah Azran and Dina Turetsky involved in nanoparticle synthesis at SCW's Nanoscience Factory.

Throughout the year, faculty and SCW students enjoy multiple trips to the BNL's National Synchrotron Light Source. For some projects, competitive research needs to be done at the world's best synchrotron source and, thus, trips are made to the Argonne National Laboratory's Advanced Photon Source. Faculty trips are supported by research grants and student trips are generously supported by the Office of the Vice President for Academic Affairs. New research grants awarded to Dr. Frenkel by the Department of Energy (DOE) allow for the hiring of up to six students for summer internships, to do cutting edge research in the fields of condensed matter physics, nanoscience, catalysis, biophysics, and in cross-disciplinary fields. Dr. Frenkel, in conjunction with students and associates, conducts research in the fields of nanoparticle synthesis and characterization by synchrotron techniques (funded by DOE) and performs studies of metal-to-insulator transition in chromium-doped vanadium oxides (DOE funded). Dr. Frenkel is also a founding director of a newly established Synchrotron Catalysis Consortium at BNL (DOE funded). Many research activities involving SCW and YC students take place at the consortium facilities. Such exposures to first class science and to an atmosphere of discoveries play major roles in shaping the career plans of undergraduates.

Dina Turetsky (left) and Nina Bursky-Tammam at BNL in the Summer, 2006.

SCW physics students are active in research in the summer and throughout the year. Their research is presented at highly visible national and international meetings and at seminar presentations. Several of the physics students gave oral presentations at the regular sessions of meetings of scientific societies. SCW students are listed as coauthors on refereed articles published in prestigious physics, chemistry, and materials science journals.

Our in-house research has benefited much from inter-collegial collaboration with YC. Since 2003, Drs. Cwilich and Zypman (YC) have partnered with Dr. Frenkel in developing advanced honors courses in physics. The latest courses, Discover Nanoscience and Nanoscience for Poets, attracted students with and without a science background. In 2006, the SCW students, Sarah Azran (Speech Therapy) and Dina Turetsky (Psychology), participated in the course, along with students from YC. Nina Bursky-Tammam, Leah Kanner, Yardanna Platt, Michelle Simpser, and Ariella Bram, members of Dr. Frenkel's nanoscience research group, served as course assistants and role models for the other students enrolled in the course. For the first time in the history of courses in the Honors Program, the research project, which was the focus of the course, resulted in an abstract submitted for an oral presentation at the Fall meeting of the Materials Research Society in Boston, 2006. All students in the course, as well as the course assistants, were listed as coauthors in this presentation.

Students of the Summer 2006 honors courses: Nanoscience for Poets and Discover Nanoscience at BNL's National Synchrotron Light Source.

The Physics Department is always seeking new students interested in doing first class research in a variety of applied fields.

STERN COLLEGE FOR WOMEN COMBINED DEGREE PROGRAMS

The following are the basic elements of the combined degree programs for the sciences offered at SCW. These programs are competitive and final admissions decisions are made by the cooperating institutions.

Dentistry - B.A./D.D.S.
Qualified students may be recommended to a combined degree program between Stern College and New York University College of Dentistry. Three years at SCW, during which prerequisites and college requirements are met, are followed by four years at NYU College of Dentistry. The student receives the B.A. degree after the first year at NYU, and the D.D.S. degree after completing the four years at NYU.

Engineering - B.A./B.S. or B.A./M.S.
Stern College offers several combined plans in Engineering with Columbia University and Stony Brook University (SBU). Students in joint YU-Colubmia 3+2 plans attend SCW for 3 years, take the prescribed coursework and, with recommendation of the Pre-Engineering advisor, may be admitted to Columbia University's School of Engineering and Applied Science (SEAS). After successful completion of the 2-year program at Colubmia, SCW awards the B.A. in Pre-Engineering, and Columbia awards the B.S. in Engineering. In addition, students can fulfill requirements for minor in physics at SCW.

Under the 4+2 plan, the student completes a B.A. degree at SCW, while fulfilling prerequisites for SEAS. After two additional years of study at Columbia, the student receives the M.S., bypassing the bachelor's degree in Engineering.

Students in joint YU- SBU 3+2 program start their education at SCW and finish at SBU's College of Engineering and Applied Sciences (CEAS). After spending 3 years at SCW, students will have an option to either graduate with B.S. degree in Engineering from SBU or take graduate level courses during their second year at CEAS and graduate with MS degree, also in 2 years.

Nursing - B.A./B.S.N./M.S.N.
Stern College offers a combined program in nursing with Johns Hopkins University. Students spend three years at Stern College completing college requirements and pre-requisite courses for a total of 111 credits, followed by a one-year accelerated program at Johns Hopkins. Upon successful completion of these studies, students earn a B.A. from Stern College and a B.S.N. from Johns Hopkins. Students may then continue on for a Masters degree. Depending on the major selected, these additional studies leading to the MSN may take one or two years.

Occupational Therapy - B.A./M.S.
Stern College offers a combined program in Occupational Therapy with Columbia University. During the first three years at SCW, students complete college requirements and prerequisites for Columbia's OT program. They apply to the 2-year Columbia program during the fall semester of their junior year. Students are awarded the B.A. from Stern College after the first year at Columbia, and the M.S. upon completion of the program.

Optometry - B.A./O.D.
Stern College and the State University of New York State College of Optometry offer an affiliation program to qualified students through which they can receive an undergraduate degree and a Doctor of Optometry degree in seven years. Students accepted into this program attend SCW for three years while they complete college requirements and prerequisites for the College of Optometry. After the first year at SUNY College of Optometry, students receive the B.A. degree. The O.D. degree is awarded after completing the four years at SUNY College of Optometry.

Physical Therapy - B.A./D.P.T.
Stern College offers combined programs in Physical Therapy with New York Medical College Graduate School of Health Sciences and the University of Medicine and Dentistry of N. J. During the first three years at Stern College, students complete college requirements and prerequisites for the Doctorate of Physical Therapy Program. Students are awarded the B.A. after completing the first year at the professional school, and the D.P.T. at the completion of the 3-year program.

Physician Assistant - B.A./M.P.S.
Stern College offers a combined program in Physician Assistant Studies with Mercy College. During the first three years, students complete college requirements and prerequisites for Mercy College's M.P.S. program. After completing 111 credits with a minimum GPA of 3.0, and with at least a "B" in prerequisite courses, qualified students continue at Mercy College. After the first year at Mercy College, students receive the B.A. degree from Stern College. The M.P.S. degree is awarded after completing two years and three months at Mercy.

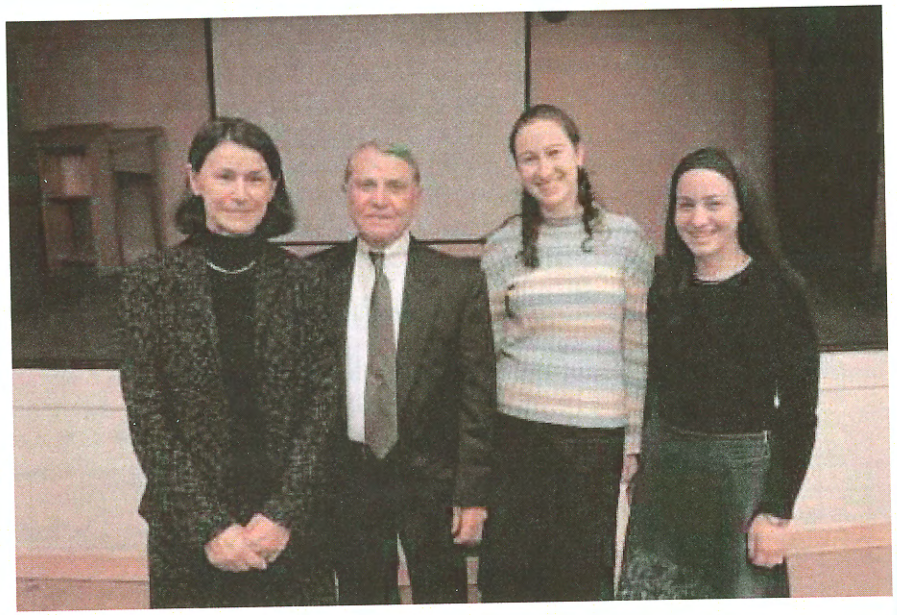
Podiatry - B.A./D.P.M.
Stern College and the New York College of Podiatric Medicine offer a combined program in Podiatry. During the first three years, students recommended to the program complete college requirements and prerequisites for the NY College of Podiatric Medicine. After the first year at NYCPM, SCW awards the B.A. NYCPM awards the D.P.M. at the completion of the program.

KUKIN LECTURES

In 1991, with the support of Dr. Ira Kukin, a member of the Board of Trustees of Yeshiva University, an annual chemistry lecture series was established. The invited speakers are distinguished scientists, many of them Nobel Laureates, who direct their talks to the undergraduate students. Prior to the lecture many students have the opportunity to interact with the speakers and after the lecture to participate in a question session.

This annual lecture is attended by the undergraduate science students of Yeshiva University, selected high school students, science faculty, administrators, invited scientists from the New York area, and Dr. Ira Kukin and his family.

	Date	Guest Lecturer	Title of Lecture	Affiliation
1	November 5, 1991	Roald Hoffmann*	Logical Structure of Modern Chemistry	Cornell
2	November 4, 1992	Jerold Meinwald	The Chemistry of Everyday Insect Life	Cornell
3	December 7, 1993	Elias J. Corey*	Molecular Robots, Small Molecules as Enzyme-Like Catalysts	*Harvard*
4	October 10, 1994	Derek Barton*	*How to Win the Nobel Prize*	Texas A&M
5	December 6, 1995	Ephraim Katchalski Katzir	A Scientist as State President: Experiences and Expectations	Weizmann Institute
6	November 4, 1996	Alfred Bader	*The Chemist as Entrepreneur*	
7	November 19, 1997	William N. Lipscomb*	Chemistry of the 20th Century: The Structure-Function Relationship	Harvard
8	October 28, 1998	Dudley Herschbach*	The Impossible Takes a Little Longer	Harvard
9	December 1, 1999	Sylvia Ceyer	The Unique Chemistry at Surfaces: Splats, Hammers, and Sinkholes	MIT
10	November 1, 2000	Julius Axelrod*	Neurotransmitters and Psychoactive Drugs	NIH
11	November 12, 2001	Mary Good	Science and Technology Policy: Why You Should Care	U. of Arkansas
12	October 29, 2002	Mario Molina*	The Antarctic Ozone Hole	MIT
13	November 12, 2003	Ronald Breslow	The Chemistry-Biology Interface	Columbia
14	October 11, 2004	Jacqueline K. Barton	DNA Charge Transport: Chemistry and Biology	California Institute of Technology
15	December 13, 2005	Dr. Martha Greenblatt	The Beauty and Fascination of Solids	Rutgers University
		* Nobel Laureates		



Martha Greenblatt, the 2005 Kukin lecturer, with Ira Kukin, the sponsor of the lecture series, with students.

Martha Greenblatt, the 2005 Kukin lecturer, talking with students after the lecture.

Student Accomplishments

The Departments of Biology, Chemistry and Physics take a very active role in guiding students seeking careers in basic research and the health sciences. The first section delineates the graduate/professional schools our students have entered in pursuit of their advanced degrees. Thereafter, is a listing of research internships in which our students have participated; many, if not all, of these internships are highly competitive. The students learn and develop state-of-the-art laboratory skills and techniques in our college's science courses. Thus, our track record for placing students in prestigious external research laboratory facilities is most impressive.

Student Accomplishments, SCW
Academic Year, 2005-2006; Summer, 2006
Graduating Seniors

Discipline	Number of students entered	Professional/ Graduate Schools
Medicine	10	AECOM; Sackler; Technion; Ben-Gurion Univ./Columbia Univ. Program
Dentistry	3	UMDNJ; Nova Southeastern Univ.
School of Pharmacy	1	Nova Southeastern Univ.
Ph.D/M.D. program	1	AECOM/ Sue Golding
Occupational Therapy	14	Columbia Univ.; NYU; Kean Univ.; Touro College; SUNY Downstate
Physical Therapy	8	Hunter College; Columbia Univ.; UMDNJ; NYU; Emory Univ.; Touro College
Nursing	19	Columbia Univ.; NYU; Johns Hopkins; SUNY Downstate
M.S. program	1	Biomedical Sciences,UMDNJ
Diagnostic Medical Imaging	1	SUNY Downstate
Teaching Positions	1	Ma'ayanot High School

Note: Most students were accepted to more than one professional/graduate school; the specific programs identified in the table only identify the particular program selected by the student.

Research Internships:

Fall, 2005 & Spring, 2005:

Jessica Feig: Cardiopulmonary Rehabilitation, NYU Medical Center

Esther Fischer: AECOM, Neurosciences (Dr. Abrams)

Sara (Rosine) Knafo: Department of Physics, YC (Dr. Asherie)

Yelena (Leah) Kozirovsky: The Beth Israel Cancer Center, Health Research Training Program, NYC Department of Health and Mental Hygiene

Malka Krupka: Department of Cell Biology and Neurology, Skirball Institute of Biomolecular Medicine, Laboratory of Dr. J. Salzer and AECOM, Department of Neurology, Laboratory of Dr. Mehler

Elisheva Levine: Dept. of Chemistry, SCW (Chaya Rapp)

Abigail Rabinowitz: Montefiore Hospital

Elizabeth Ravkin: Biology Department, SCW (Dr. Babich) and Genome Imaging Facility, AECOM, Laboratory of Dr. C. Montagna

Pesia Soloveichik: Department of Pharmacology and Biological Chemistry; Mt. Sinai School of Medicine, Laboratory of Dr. Shelly Rackovsky

Temima Strauss: Dept. of Chemistry, SCW (Chaya Rapp)

Dinah Zaghi: The Beth Israel Cancer Center, Health Research Training Program, NYC Department of Health and Mental Hygiene

Summer 2006:

Judy Alkoby: Rambam Hospital, Haifa, Israel (Dr. Bentur)

Ariella Bram: Department of Physics (SCW) and Brookhaven Lab (Dr. A. Frenkel)

Zahava Brodt: Harvard Medical School (Dr. M. Kaufmán-Holz)

Nina Bursky-Tammam: Department of Physics (SCW) and Brookhaven Lab (Dr. A. Frenkel)

Sarah Guigui: Dept. of Chemistry, SCW (Dr. L. Blau and Dr. D. Estes)

Ariella Cohen: Citroil Enterprises (Carlstadt, NJ)

Michelle Cohen: Roth Scholar, AECOM

Maggie Dweck: Rusk Institute of Rehabilitation Medicine (Nursing)

Reina Eisner: Department. of Pharmaceutical Chemistry, University of California San Francisco (Laboratory of Dr. M. Jacobson)

Ilana Erlich: St. Michael's Hospital Summer Student Internship, University of Toronto, Canada (Laboratory of Dr. Bradley Strauss)

Jessica Feig: Roth Scholar, AECOM (Dr. M. Mehler)

Esther Fischer: AECOM, Neurosciences (Dr. Abrams)

Elana Goldberg: Forensics division, National Police (Israel)

Michelle Goldberg: University Scholar, AECOM

Shawna Joyce: Yale University, Laboratory of Reproductive Sciences

Gila Kanal: Yavneh Olami Summer Program in Nursing/Midwifery, Israel

Leah Kanner: Department of Physics (SCW) and Brookhaven Lab (Dr. A. Frenkel)

Elana Kessel: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Yelena (Leah) Kozirovsky: University Scholar, AECOM

Elisheva Levine: Chemistry Department, Stern College for Women (Dr. C. Rapp)

Rebecca Marmor: Bellevue Hospital, PAVERS Program summer internship in the Emergency Room

Eliana Muskin: Rusk Institute of Rehabilitation Medicine (Medical oncology)

Shira Pasternak: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Deena Perles: Rusk Institute of Rehabilitation Medicine (Physical therapy)

Yardanna Platt: Department of Physics (SCW) and Brookhaven Lab (Dr. A. Frenkel)

Elizabeth Ravkin: Roth Scholar, AECOM

Avital Rosenbaum: Careers in Medicine Program, Hackensack University Medical Ctr.

Zahava Schmukler: The Rockefeller University (Dr. J. Rappoport)

Michelle Simpser: Department of Physics (SCW) and Brookhaven Lab (Dr. A. Frenkel)

Louisette Soussan: Roth Scholar, AECOM

Amanda Weiss: The Rockefeller University (Dr. J. Rappoport)

Rachel Yamnik: Harvard Medical School (Dr. M. Kaufman-Holz)

Dinah Zaghi: Department of Pharmaceutical Chemistry, Univ. California - San Francisco.

Student Accomplishments, SCW
Academic year, 2004-2005; Summer, 2005
Graduating Seniors

Discipline	Number of students entered	Professional/ Graduate Schools
Medicine	5	AECOM; Wayne State Univ.; Drexel; Touro-Technion
Dentistry	7	Univ. of Penn; UMDNJ; Baltimore College of Dentistry; NYU
Optometry	1	SUNY
Occupational Therapy	12	Columbia Univ.; NYU; Ontario Univ.
Physical Therapy	7	UMDNJ; Hunter College; Touro College
Physician Assistant	3	Touro College; UMDNJ; Towson Univ.
Nursing	12	Columbia Univ.; UMDNJ; NYU; Villanova; Johns Hopkins
Genetic Counseling	1	Sarah Lawrence
Nutrition	3	Hunter College; LIU; Columbia Univ.
Public health	1	Columbia University

Note: Most students were accepted to more than one professional/graduate school; the specific programs identified in the table only identify the particular program selected by the student.

Research Internships:

Fall, 2004 & Spring, 2005:

Rachel Avner: Health Research Training Program, Environmental - Food Borne Illnesses; NYC Dept of Health & Mental Hygiene

Nomi BenZvi: Department of Chemistry, SCW (Dr. L. Blau and Dr. D. Estes)

Jessica Feig: Department of Biology, SCW (Dr. Weisburg)

Esther Flaschner-Berko: Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, Laboratory of Dr. M.F. Mehler

Jessica Chernack: Department of Biology, SCW (Dr. Weisburg)

Frida Fridman: Cornell Medical College, Department of Immunology and Infectious Disease, Laboratory of Dr. S. Witkin

Sarah Guigi: Department of Chemistry, SCW (Dr. Rapp)

Malka Krupka: NYU School of Medicine, Department of Cell Biology and Neurology, Skirball Institute of Biomolecular Medicine, Laboratory of Dr. J. Salzer

Yardena Mandel: Department of Biology, SCW (Dr. Weisburg)

Eliana Muskin: Department of Biology, SCW (Dr. Babich)

Sarah Nemzer: Department of Physics, SCW and Brookhaven National Laboratory (Dr. Frenkel)

Ilana Pister: Department of Physics, SCW and Brookhaven National Laboratory (Dr. Frenkel)

Alissa Selevan: Department of Biology, SCW (Dr. Babich)

Aviva Shafner: Department of Biology, SCW (Dr. Weisburg)

Zahava Sinensky: Department of Biology, SCW (Dr. Babich)

Louisette Soussan: Department of Physics, SCW and Brookhaven National Laboratory (Dr. Frenkel); Department of Chemistry, SCW (Dr. Rapp)

Shoshana Ungar: Department of Biology, SCW (Dr. Babich)

Sarah Weinerman: Department of Biology, SCW (Dr. Babich)

Rachel Yamnik: Haskins Laboratory

Dinah Zaghi: Department of Chemistry, SCW (Dr. Rapp)

Summer, 2005:

Nathalie Abitbol: Department of Physics, SCW and Brookhaven National Laboratory (Dr. Frenkel)

Claudia Amzallag: Mt. Sinai School of Medicine; Oncology

Ariella Babich: Rusk Institute of Rehabilitation Medicine (PreSchool)

Tiffany Brown: Rusk Institute of Rehabilitation Medicine (Physical therapy)

Yadina Ebrani: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Elana Ehrlich: Mt. Sinai School of medicine (PROP = Pre-med Research Opportunities)

Jessica Feig: NYU Medical Center, Cardiopulmonary Laboratory

Frida Fridman: AECOM (Roth Scholar)

Jessica Gilson: Rusk Institute of Rehabilitation Medicine (Physical therapy)

Ronit Gold: Mount Sinai School of Medicine

Tamar Gold: AECOM (Roth Scholar)

Giti Gross: Rusk Institute of Rehabilitation Medicine (Nursing)

Yonit Gross: The Mount Sinai Hospital - Mount Sinai School of Medicine

Sara (Rosine) Knafo: Department of Physics, YC (Dr. Asherie)

Michal Konigsberg: Rusk Institute of Rehabilitation Medicine (Medical oncology)

Yelena (Leah) Kozirovsky: AECOM, Developmental Molecular Biology Laboratory

Rachel Laker: Rusk Institute of Rehabilitation Medicine (Physical therapy)

Elisheva Levine: Department of Chemistry, SCW (Dr. Rapp)

Elana Meyersdorf: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Eliana Muskin: Department of Physics, SCW (Dr. Frenkel) and Stony Brook

Helen Nissim: AECOM (Roth Scholar)

Ilana Pister: AECOM (Roth Scholar)

Yardanna Platt: Folkman Laboratory, Children's Hospital, Boston, MA

Elizabeth Ravkin: Vira Bioscience, CA

Yael Saden-Barach: AECOM (Roth Scholar)

Alissa Selevan: Department of Biology, SCW (Dr. Babich)

Ariela Sherman: UMDNJ, Neurobiology Laboratory

Suzanne Snyder: AECOM (Roth Scholar).

Louisette Soussan, Department of Physics, SCW and Brookhaven National Laboratory (Dr. Frenkel)

Esther Spiegelman: Yavneh Olami (Israel), Herzog Hospital (Occupational therapy)

Tehilla Stepansky: AECOM (Roth Scholar)

Temima Strauss: Department of Chemistry, SCW (Dr. Rapp)

Shoshana Ungar: Mt. Sinai School of Medicine

Aliza Weg: Department of Biology, SCW (Dr. Weisburg)

Sarah Weinerman: AECOM (Roth Scholar)

Elisheva Weinstein: AECOM, Genetics Laboratory

Rachel Yamnik: Yavneh Olami (Israel), research in a biomedical company

Dinah Zaghi: Department of Pharmaceutical Chemistry, UCSF

Student Accomplishments, SCW
Academic year, 2003-2004; Summer, 2004
Graduating Seniors

Discipline	Number of students entered	Professional/ Graduate Schools
Medicine	10	AECOM; NYU Sackler; UMDNJ
Dentistry	5	UMDNJ; Nova Southeastern Univ.; Univ. of Toronto
Optometry	1	SUNY
Osteopathic Medicine	4	NY College of Osteopathic Medicine
Podiatry	1	NY College of Podiatry
Ph.D. programs	5	Sue Golding, AECOM; Univ. of Penn.; CUNY
Occupational Therapy	11	Columbia Univ.; NYU; Univ. of Illinois
Physical Therapy	7	Hunter College; Columbia; NY Medical College
Physician Assistant	7	UMDNJ; Mercy College; Barry Univ.; Nova Univ.
Nursing	9	Columbia Univ.; NYU; Johns Hopkins; Univ. of Penn.
Diagnostic Medical Imaging	1	SUNY Downstate

Note: Most students were accepted to more than one professional/graduate school; the specific programs identified in the table only identify the particular program selected by the student.

Research Internships:

Spring, 2004:

Frida Fridman: Cornell Medical College, Department of Immunology and Infectious Disease, Dr. Steven Witkin

Tova Gavrilova: Health Research Training Program, NYC Dept of Health & Mental Hygiene

Eliza Moskowitz: Health Research Training Program, NYC Dept of Health & Mental Hygiene

Karyn Winkler: Health Research Training Program, NYC Dept of Health & Mental Hygiene

Summer, 2004:

Shoshana Bacon: Rusk Institute of Rehabilitation Medicine: Neurosurgery

Leora Cohn: AECOM, Summer Undergraduate Research Program

Michelle Faber: Henry Ford Hospital, Neurology Laboratory, head - Dr. C. Chopp; Detroit, Michigan

Deborah Fein: Rusk Institute of Rehabilitation Medicine (Physical therapy)

Rebecca Feiner: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Esther Flaschner: Roth Scholar, AECOM

Frida Fridman: Cornell Medical College, Department of Immunology and Infectious Disease, Dr. Steven Witkin

Jessica Geisler: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Dana Glasner: Undergraduate Summer Research in Molecular Biophysics, Princeton University

Ronit Gold: Stern College for Women, Department of Biology

Tamar Gold: Stern College for Women, Department of Biology

Sara Keschner: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Malka Krupka: Roth Scholar, AECOM

Diane Liebman: Rusk Institute of Rehabilitation Medicine: Rehabilitation Medicine

Gitty Mandel: Rusk Institute of Rehabilitation Medicine: Neurosurgery

Shevie Moskowitz: University of Colorado Hospital (laboratory of Dr. M. Levi)

Ellie Pinter: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Pesi Porat: Roth Scholar, AECOM

Avigayil Rosen: Sloan-Kettering (Dr. Zelessky)

Reina Roth: Roth Scholar, AECOM

Debbie Rybak: Roth Scholar, AECOM

Vivi Stahl: AECOM, CCI Administration

Aliza Strassman: Rusk Institute of Rehabilitation Medicine (Occupational therapy)

Aliza Weg: Stern College for Women, Biology Department (Dr. Weisburg)

Irina Yadgarova: Rusk Institute of Rehabilitation Medicine: Radiation Oncology

Abstract Booklets

SCW students are accepted as summer undergraduate research interns in a variety of institutions, ranging from in-house research laboratories at SCW to research facilities at Albert Einstein College of Medicine and other prestigious institutions (see Student Accomplishments). Many of these summer undergraduate research internships are highly competitive. As we are proud of our students' accomplishments, the Departments of Biology, Chemistry, and Physics publish our own in-house Abstract Booklet describing the many projects in which our students have participated.

ABSTRACT BOOKLET

STUDENT RESEARCH - 2006

Stern College for Women
Yeshiva University

Department of Biology
Department of Chemistry
Department of Physics

Table of Contents

Effect of Hydrogenation on the Local Structure of Palladium Nanoparticles: Comparative XAFS and TEM Study

by

Ariella Bram,[1] J. Zhou,[2] M. Rafailovich,[2] and A. I. Frenkel[1]

[1]Deparment of Physics, Stern College for Women, Yeshiva University, New York, NY; [2]Department of Materials Science and Engineering, State University of New York at Stony Brook, Stony Brook, NY

In this experiment we compared the effect of hydrogenation on palladium nanoparticles with different ratios of palladium and sulfur. The three concentrations used were 5:1, 3:1 and 2:1. The two methods used for analysis were XAFS and TEM. We used beamline X11A at Brookhaven National Laboratory to measure XAFS in order to examine the effect of hydrogenation on the structure of the nanoparticles. We took TEM images to see the size of the nanoparticles before hydrogenation. Using the TEM to see size-change in hydrogenated nanoparticles is not practical because the error of the resolution would encompass the change due to hydrogenation.

Our results showed that unlike previously reported, hydrogenation in palladium nanoparticles uses not only the inner structure, but also the outer bonds to hold hydrogen. In the case of the inner structure, this is noticed by an overall increase in the bond length that makes up the lattice structure of the nanoparticles. Usually there are sulfur atoms attached to the outside of the palladium nanoparticles, but after hydrogenation the number of sulfur bonds decreases which shows that the sulfur bonds are replaces with hydrogen bonds. We tested our samples before hydrogenation, as soon as possible after hydrogenation and several hours after that in order to see changes in the structure after time. Out of our three samples, the 5:1 ratio retained the hydrogen that replaced the outer sulfur bonds, but not the hydrogen in inner core. The 3:1 ratio showed both ways of storing hydrogen but retained neither, and the 2:1 ratio only showed hydrogen replacing sulfur bonds but did not retain it. These results show that palladium 5:1 nanoparticles were best suited for hydrogenation.

After looking at the TEM pictures we concluded that palladium 5:1 nanoparticles were the largest particles of our three samples (~ 4 nm, as opposed to ~ 2.5 nm). This may be the distinguishing character that allows the 5:1 sample to retain its hydrogen for longer.

Synthesis and Characterization of Pd Nanocatalysts for Fuel Cell Membranes

by

Nina Bursky-Tammam,[1] Yardanna Platt,[1] Juan Zhou,[2] and Anatoly Frenkel[1]

[1]Physics Department, Stern College for Women, Yeshiva University, New York, NY; [2]Materials Science and Engineering, Stony Brook University, Stony Brook, NY

The burgeoning of nanocatalysis into a popular field is a corollary of the failure of our depleting fuel resources to provide us with efficient and economical sources of energy. We studied metal nanoparticles as catalysts for fuel cell reactions because of their large surface area to volume ratio, which creates many possibilities for interactions with other molecules. Additionally, palladium nanoparticles could absorb hydrogen which makes them an attractive component for proton exchange membranes in fuel cells. In order to study the relationship between nanoparticles' size, their hydrogenation property and the overall efficiency in fuel cells, we investigated the possibility to control the size of thiol-stabilized palladium and gold nanoparticles by manipulating the metal to thiol ratio. We were interested in synthesizing both gold and palladium nanoparticles because gold nanoparticles do not adsorb hydrogen, and can be used as a control.

To synthesize the nanoparticles we used the two-phase method: metal precursor in water was added to phase transfer reagent in toluene. After the metal complexes were transferred to toluene (top layer), the thiols and the reductant were then added. The samples were purified by centrifuging with ethanol, dried, and deposited on adhesive tape for x-ray synchrotron experiments. X-ray absorption experiment results (Fig. 1) demonstrated that the sample's structure changed systematically with the Pd:S ratio, from the smaller Pd-Pd coordination to the larger one as Pd:thiol concentration increased. Thus, the nanoparticles's size and structure can be controlled by varying just one parameter: metal to thiol ratio.

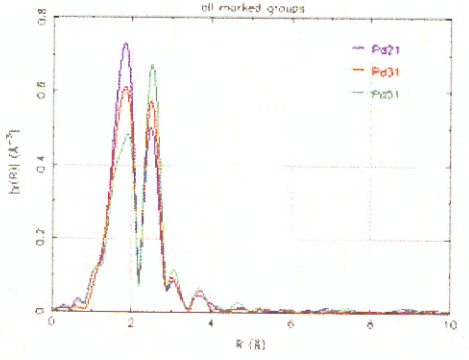


Figure 1: This graph shows the R-space of Pd 2:1 (blue), Pd 3:1 (red) and Pd 5:1 (green). The first peak in each graph is the first Pd-S bond; the second peak is the first Pd-Pd bond. The intensity of the peak is proportionate to the ratios of Pd to S. For example, Pd 2:1 has more sulfur in its sample than Pd 5:1, therefore the first peak in Pd 2:1 is higher (more intense) than the first peak in Pd 5:1.

Using Antibody Arrays as a Tool to Search for Cx43 Binding Partners

by

Michal Cohen,[1] Christina Chrisman,[2] David C. Spray,[2] Eliana Scemes,[2] and Sylvia O. Suadicani[2]

[1]Department of Biology, Stern College for Women, Yeshiva University, New York, NY;
[2]Dominick P. Purpura Department of Neuroscience, Albert Einstein College of Medicine, Bronx, NY

Protein-protein interactions play key roles in the regulation of cellular function. Various techniques, such as affinity purification, immunoprecipitation and yeast two-hybrid screening, have been used to identify the binding partners of a particular protein. Antibody arrays provide an alternative method. Based on the use of various antibodies generated against diverse proteins, the antibody array provides a high throughput method to screen and identify multiple binding partners.

The goal of this study was to implement this new method to search for and identify proteins that bind to connexin43 (Cx43), the main astrocytic gap junction forming protein. Gap junctions are intercellular channels that connect adjacent cells and allow direct cytosol-to-cytosol exchange of ions and small molecules. It has been previously shown that this form of intercellular signaling is regulated by connexin-associated proteins (Examples of proteins known to interact with Cx43 are those forming cytoskeleton (e.g., tubulin, actin) and zonula occludens-1 (ZO-1). In addition, the interaction of c-Src and v-Src with Cx43 has been shown to inhibit gap junction mediated communication.

The results of the array study suggest possible interaction of Vinculin and GFAP with Cx43. These results were supported by immunoprecipitation, providing further evidence that the antibody array is a valid technique for determining protein-protein interactions. One of the newly identified Cx43 binding partners, Vinculin, is a membrane-cytoskeletal protein that controls cytoskeletal mechanics and cell spreading through regulation of focal adhesion function and structure. Another, glial fibrillary acidic protein (GFAP), forms intermediate filaments and is thought to play a role in the interaction of astrocytes with other cells and to be involved in controlling astrocyte shape and movement. Both Vinculin and GFAP are known to be expressed in astrocytes of the central nervous system, allowing for possible interaction with Cx43.

Identification and Characterization of an Allosteric Site in Mammalian 15-Lipoxygenase

by

Reina A. Eisner,[1] Matthew P. Jacobson,[2] and Chakrapani Kalyanaraman[2]

[1]Department of Chemistry, Stern College for Women, Yeshiva University, New York, NY;
[2]Department of Pharmaceutical Chemistry, University of California Graduate Division, San Francisco, CA

Allosteric sites of proteins are important in the inhibition of protein function. These sites could be critical to the regulation of the protein activity by suppressing the enzyme, activating the enzyme, and targeting protein inhibitors. Active binding sites are the obvious sites of protein-ligand interactions, however, experiments by the Holman Laboratory, UCSC, using a synthesized inhibitor to lipoxygenase, revealed that the inhibitor did not block the active site and that an allosteric site was present on 15-lipoxygenase. Lipoxygenases are iron containing enzymes found in plants and animals. Lipoxygenase isozymes are involved in uncontrolled cell growth and regulation. Products of lipoxygenase are precursors of hormones, such as leukotrienes and lipoxins, which play a key role in inflammatory responses. Inhibitors of lipoxygenase have potential as anti-cancer agents because they have shown to suppress tumor formation. Our objective was to identify and characterize the allosteric site on the N-terminal ß-barrel domain of mammalian 15-lipoxygenase. A further objective was to elucidate the geometry of the ligand and to estimate the size of the largest molecule that could fit into the site. Characterization of the allosteric site included its location and the size of binding ligands. Our method used Glide as the docking program. Based on the electrostatic/steric component and geometry, seven molecules were constructed and then docked to the allosteric site of the protein. The location of the allosteric site on the N-terminal ß-barrel domain was hypothesized and identified by the docking program through residue numbers. Future analysis will focus on the ligand-protein complex structures and will run molecular dynamic simulations to determine whether this binding site is indeed an allosteric binding site. Molecular dynamics can be performed as an indirect methodology of examining a structure in solution. Further experiments, performed where the N-terminal ß-barrel domain of lipoxygenase was removed from the protein, showed that the overall activity of the protein increased. These results are consistent with the terminal acting as a modulator of lipoxygenase activity. If the site is indeed an allosteric site it could prove successful in drug design as an alternative site for inhibition.

Proliferation and Cell Cycle Exit Abnormalities in the Developing Striatum of Huntington's Disease Knock-In Mice

by

Jessica Feig,[1] A. Molero,[2] S. Gokhan,[2] and M.F. Mehler[2]

[1]Stern College for Women, Yeshiva University, New York, NY;
[2] Dominick P. Purpura Department of Neuroscience, Albert Einstein College of Medicine, Bronx, NY

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder resulting in motor and cognitive dysfunction mostly related to the late-onset death of striatal medium spiny projection neurons. The mutation responsible for this late-onset disease consists of an abnormal expansion of the trinucleotide (CAG) repeats within the gene that encodes huntingtin. Although huntingtin's function and mechanism of action are presently unknown, the altered protein ultimately is responsible for specific regional profiles of neuronal loss. Our studies suggest that huntingtin may, in fact, have crucial functions during brain development, some of which are related to dynamic regulation of cell cycle kinetics in neural stem cells (NSCs) and in more lineage-restricted precursor species. To further examine these findings, BrdU labeling assays were used to study the pattern of proliferation and cell cycle exit for different neuronal subtypes within the developing striatum in a HD knock-in (KI) mouse [WT (Hdh-Q18) and mutant (Hdh-Q111)] model. Preliminary results show that the Hdh-Q111 embryonic mouse exhibits an increase in the number of proliferating cells in the stem cell generative zones and further alterations in the expression pattern of developmental stage-specific neural lineage species by cells that have undergone cell cycle exit, suggesting abnormalities in the progression from symmetric to asymmetric cell division. Although the association of cellular proliferation and degeneration may at first seem counterintuitive, these findings indicate that specific stem and progenitor cells of the evolving striatum continue to divide, but do not properly differentiate into neurons, thereby impeding the normal development of this structure and increasing the propensity of inadequately differentiated vulnerable neurons to undergo selective regional neurodegeneration at later stages of adult life.

Searching for Connexin Binding Partners

by

Esther Fischer,[1] Mona Freidin,[2] and Charles Abrams[2]

[1]Stern College for Women, Yeshiva University, New York, NY,
[2]Department of Neuroscience, Albert Einstein College of Medicine, Bronx, NY

Gap junctions are channels comprised of proteins that allow for intercellular communication by the exchange of ions and small molecules. At the light microscopy level, the morphologic correlate of a gap junction is a plaque, which is an area of intense staining between two cells. A gap junction is composed of two apposed connexons (hemichannels) from two adjacent cells. Each hemichannel is made up of six connexin subunits. The hemichannels may be comprised of the same type of connexin (homotypic cell-cell channels) or different types of connexins (heterotypic cell-cell channels). Similarly, the hemichannel may be comprised of six identical connexin subunits (a homomeric hemichnanel) or of more than one type of connexin subunit (a heteromeric hemichannel). In humans, most tissues express a small subset of the greater than 20 identified connexins. Mutations in the gene encoding Cx32 lead to the X-linked form of Charcot Marie Tooth Disease (CMT). (CMT is a group of inherited disorders affecting predominantly or exclusively the peripheral nervous system (PNS) Although Cx32 is expressed in the myelinating glia of both the PNS and central nervous system (CNS), most patients show abnormalities only in the PNS . This leads to the hypothesis that another connexin may be taking over the function of Cx32 in the CNS. As a first step to investigate this hypothesis, we have identified CNS glial connexins which can interact with Cx32 to form heterotypic channels.. . We labeled the astrocytic connexins Cx30 and Cx43 and the oligodendrocyte connexins Cx32 and Cx47 with EGFP (enhanced green fluorescent protein) or DS-Red Monomer (a monomeric red fluorescent protein) and expressed each of these connexins alone in Neuro2a cells. We then performed dual-color fluorescence confocal microscopy to determine heterotyic compatibility. We found that plaques efficiently formed between cells expressing Cx32 and Cx30, but did not form between Cx32 and Cx43. In addition no heterotypic plaques were seen between cells expressing Cx32 and Cx47. Dual whole cell patch clamp recordings have substantially confirmed these results. These results provide a preliminary indication of the type of functional gap junctions that may be present between CNS glial cells and specifically the role of Cx32 in glial coupling. Experiments to examine the roles of disease causing mutations in Cx32 in disrupting these interactions are planned.

Haplotype Analysis of 22q11.2 Deletions in VCFS Patients

by

Michelle S. Goldberg,[1] A. Blonska,[2] M. Babcock,[2] and B.E. Morrow[2]

[1]Department of Biology, Stern College for Women, Yeshiva University, New York, NY;
[2]Department of Molecular Genetics, Albert Einstein College of Medicine, Bronx, NY

VCFS is a congenital anomaly disorder caused by a deletion of chromosome 22 at 22q11.2 that occurs in 1:2,000 to 1:4,000 live births. This disorder is associated with over 180 clinical features, including cleft palate, heart defects, characteristic facial features, immune deficiency, learning disabilities and psychiatric illness. Although most VCFS patients have the same 3 Mb deletion, the expressivity of the disorder is highly variable. We are planning a whole genome association study to correlate genotypes and phenotypes among VCFS patients in order to identify genetic modifiers that affect the severity of the disorder. To ensure internal consistency, only patients with the common 3 Mb deletion will be included in the future genetic modifier study. In the current study, VCFS patient samples were genotyped and analyzed to determine the size and origin of the deletion. A total of 119 patients with 3.0 Mb deletions were identified to be used in the genetic modifier study. A number of patients with unusual chromosomal rearrangements were also identified, and although they will not be included in the genetic modifier study, these individuals may be interesting to study in more detail in the future. The 3 Mb deletion was found in 93% of our samples and the 1.5 Mb deletion was found in 7%. Deletions were found to occur at approximately equal rates in maternal and paternal chromosomes. These data corroborate previously published findings.

DNA's Stability: Composition vs. Sequence

by

Sarah Guigui, Donald Estes, and Lea Blau

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

The stability of the DNA double helix was originally attributed to hydrogen bonding of complementary bases. However, upon denaturation, these hydrogen bonds are broken and replaced by hydrogen bonds between the bases and the water molecules in the solvent. The energy change arising from the differential hydrogen bonds is small. The unwinding of the double helix, as a result of heating, was monitored by UV spectroscopy. The melting temperatures of several oligonucleotides with identical base composition but different base sequence were determined. The dependence of the melting temperature on strand concentration was analyzed to yield thermodynamic data ($\triangle H^\circ$, $\triangle S^\circ$, $\triangle G^\circ$). The experimental results were compared to those predicted from the nearest neighbor model. Nonaqueous solvent effect studies were then carried out to examine the role of hydrogen bonds and interactions between the bases as a result of base stacking. In our work, it was shown that the stability of the DNA duplex is a sequence dependent phenomenon arising from base stacking or hydrophobic interactions.

Altered SPRR2A, SPRR2B, and Filaggrin Expression in Eosinophilic Esophagitis

by

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Eosinophilic esophagitis (EE) is a disease of the esophageal mucosa characterized by eosinophilic inflammation and epithelial cell hyperplasia (proliferation). Previous results using microarray analysis demonstrated that the genes in the Skin Epidermal Differentiation Complex (EDC) were dramatically decreased in EE biopsies. We aimed to confirm the down regulation of filaggrin and other in genes in the EDC in EE esophageal biopsy samples. We also aimed to examine the expression of these genes in vitro, in the esophageal epithelial cell line TE7, as a function of their proliferation and differentiation. Forward and reverse primers for Filaggrin and SPRR2A were designed for use in real time Polymerase Chain Reaction (PCR). After RNA isolation and reverse transcription (RT), cDNA derived from the esophageal epithelial cell line (TE7) and cDNA derived from patient biopsies were submitted to real-time PCR. The primers were designed and tested by PCR. The expected band sizes for SPRR2A, SPRR2B and Filaggrin (199bp, 210bp, and 335bp) were observed. Filaggrin mRNA expression was down regulated 6.3-fold in EE patient biopsies compared to normal biopsy samples. We demonstrated in vitro that the expression of these genes correlated with the differentiation of esophageal epithelial cell line cells. In conclusion, Filaggrin down regulation could be used as a marker of EE. Also gene expression of the skin differentiation markers, SPRR2A, SPRR2B, and Filaggrin, correlate to cell differentiation in esophageal epithelial cells in vitro. The decreased epithelial cell differentiation marker expression in EE may result in increased vulnerability of the esophagus, possibly due to loss of the protective functions associated with the keratinization process, such as barrier function. Future Directions include to quantify and localize the protein expression of these genes in EE patient biopsies and to find the factors that regulate SPRR2A, SPRR2B, and Filaggrin expression.

The Effect of Antiphospholipid Antibodies on First Trimester Trophoblast Cells

by

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Antiphospholipid syndrome (APS) is associated with increased levels of circulating antiphospholipid antibodies. In addition thrombosis and rheumatological disease, this syndrome is associated with higher incidences of recurrent spontaneous abortion, preeclampsia, and preterm labor. These pregnancy complications are associated with shallow invasion and increased levels of neutrophils in the decidua. Trophoblast cells are unusual in that they express phospholipids, such as cardiolipin and/or B2GP1, on their cell surface, and thus are targets for antiphospholipid antibodies. It has been shown that trophoblast cells can recruit macrophages and NK cells through chemokine production. The presence of these immune cells are thought to aid trophoblast invasion and successful placentation. We hypothesize that antiphospholipid antibodies affect trophoblast function leading to an altered immune cell profile at the maternal-fetal interface. We used two mouse anti-human B2GP1 monoclonal antibodies, ID2 and IIC5, and evaluated their effects on a human first trimester trophoblast cell line (H8). H8 cells were incubated with and without ID2 or IIC5 at various concentrations and times. Binding was determined by immunocytochemistry, and the effect of the antibodies on trophoblast cell death and apoptosis was determined by i) celltiter viability assay; ii) Hoescht staining; and iii) Caspase-Glo assay. Cytokine production was evaluated by Luminex analysis. We found that ID2 binding was significantly weaker than IIC5 binding. At high doses both antibodies induced cell death, but did not trigger caspase activation. At low levels of antibody concentration there was induction of cytokines and chemokines. ID2 increased trophoblast secretion of GRO-? and IL-6, while IIC5 increased trophoblast secretion of GRO-?? IL-6, and IL-8. This suggests that low levels of antiphospholipid antibodies may cause recruitment of immune cells, such as neutrophils, while at high levels trophoblast apoptosis may occur in a caspase-independent manner. Together these finding suggest that antiphospholipid antibodies may cause placental dysfunction through their direct effects on trophoblast function.

X-ray Absorption Studies of Molecular Nanomagnets

by

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Mn12-acetate, a single-molecule magnet, is intriguing because its strong magnetization reorients in discrete increments under external magnetic field at low temperatures (below 3K). It demonstrates the phenomenon known in quantum physics as resonant tunneling of magnetization. Among the many properties of this molecular magnet that are still unknown is the effect of the external magnetic field on the local structure around Mn atoms in the Mn12-acetate molecule. Another puzzle is whether the solvent disorder, caused by the interaction between Mn atoms and acetate complexes can influence magnetic properties in this system.

Two x-ray absorption fine-structure experiments were conducted to provide a deeper look into the structure-property relationship of Mn12-acetate. Manganese K-edge absorption spectra were collected at 2.3 K and magnetic fields of 0T, 5T, and after reversal to 0T, to determine whether a change in magnetic field would result in a change in the local structure around Mn. Samples of Mn12-acetate were also measured with/without solvent at room temperature. These experiments were conducted at the NSLS X18B beamline at Brookhaven National Laboratory. XAFS spectroscopy, due to its short range order sensitivity, is uniquely suited for determination of the atomic-level structure of a compound. Structural changes could be linked to changes in magnetization or other properties.

Preliminary analysis has not shown significant differences between their structures. The variations we obtained seem insignificant and are within the noise level. Further analysis is underway to determine whether in fact these slight variations may indicate an actual change in structure.

In summary, we obtained that there is little or no coupling between the Mn12 acetate lattice and magnetic field. This result is in striking contrast between this system and its ferroelectric counterparts where reversal of external electric field causes significant atomic displacement within the unit cell.

Receptor Localization Controlled by Three Amino Acids in the Carboxyl Terminal Domain of the Gastrin Releasing Peptide Receptor

by

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Many cell types are polarized. Polarized cells contain distinct regions that perform specific cellular functions. The targeting of specific molecules to their appropriate regions within the cell dictates cellular function in polarized cells. These molecules include cell surface receptors, receptor binding proteins and other signaling molecules. Thus, it is crucial that these cells have their receptors in the appropriate region and at the proper time to facilitate ligand binding and signal transduction. Gastrin releasing peptide receptor (GRPr) is a seven transmembrane G protein coupled receptor (GPCR). The Kroog laboratory recently determined that wild type mouse GRPr is targeted to the basolateral surface of polarized Madin-Darby canine kidney (MDCK) cells, a well-studied polarized cell model. The lab previously identified the region within the GRPr that controls receptor localization. Using a truncation mutant, the carboxyl terminal domain (CTD) was determined to govern GRPr localization within the cell. A series of truncation mutants within the CTD region were used to isolate the amino acid sequence that was responsible for receptor localization. GRPr truncation at serine-372 eliminated basolateral targeting, yet GRPr truncation at arginine-376 did not produce receptor mislocalization to the apical region. Hence, the amino acid sequence necessary for receptor localization involves a small region of GRPr (372SLINR376). This led to the analysis of the specific amino acids that determine receptor localization. Mutation of leucine-373 and isoleucine-374 to alanine led to loss of basolateral targeting. Serine-372 was previously identified in the lab as being a candidate phosphorylation site. To test the role of ser-372 phosphorylation in GRPr targeting, serine-372 was mutated to asparagine (S372N) in order to maintain a polar residue but remove the phosphorylation site. We treated cells transfected with wild type GRPr or S372N with phorbol ester (TPA) to stimulate phosphorylation by protein kinase C. In cells with low GRPr expression, TPA-stimulated wild type GRPr relocated to the apical region of the cell. However, upon treatment with TPA, the S372N localization was unchanged. This indicates that phosphorylation of serine-372 regulates localization of the receptor. I tested whether mutation in this region of GRPr affected other cellular functions, and found no negative effect on GRPr binding affinity or agonist-stimulated internalization. The evidence derived from these studies suggests that a specific motif containing a phosphorylation site and several branched chain amino acids produces basolateral GRPr localization in polarized cells. I also found that a similar motif is seen in several other GPCR where a candidate phosphorylation site is directly followed by two hydrophobic amino acids such as leucine, isoleucine, valine and phenylalanine in the CTD region. Based on my observation, this motif may be common to several members of the GPCR superfamily.

Prediction of pKa Values of Histidine Side Chains

by

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Acidic and basic amino acids are critical to protein function, as in acid-base catalysis which occurs in the ribonuclease enzyme. When subject to the pH of the solvent, these amino acids can be protonated or deprotonated depending on their acidity, measured by pKa values. The pKa value of a particular amino acid is strongly dependent on its electrostatic environment within a protein. Thus, the determination of pKa values is an integral part of protein structure prediction.

The PLOP (Protein Local Optimization Program) predicts protein structure using the all-atom OPLS force field and the Generated Born-Surface Area (GBSA) solvation model for the calculation of energies. As a recently included feature, the pKa of an amino acid can be predicted by sampling protonation states during the process of structure optimization. The free energy cost of protonation, ? Gprot, is used as the criteria by which a given protonation state is accepted or rejected. To assess the effectiveness of pka prediction, we created a test set including all histidine side chains in 36 high resolution crystal structures from the Protein Data Bank (PDB). Histidine residues are generally titrated at pH values close to physiological pH and can exist in three different protonation states: 1) protonation of the delta nitrogen (HID) 2) protonation of the epsilon nitrogen (HIE) and 3) protonation of both nitrogens (HIP). We ran structural predictions on the test set of 116 histidines using both arbitrary protonation states, as a control, and employing the pKa prediction protocol.

Results showed that using pKa prediction does not achieve superior results for the prediction of histidine side chains. Average RMSD values, which measure how close a predicted structure is to the crystal structure, were almost identical (0.44 angstroms with pKa prediction and 0.43 angstroms without), for the two sets of predicted structures. The development of improved methodology for pKa prediction is ongoing.

Incidence of Rotavirus in Stool Samples from Hospitalized Adults

by

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Rotavirus is known as one of the most common childhood diseases, striking most children around the world by age five. It causes some of the most severe acute gastroenteritis in children resulting in many hospitalizations and even death. Not much is known about the causes of acute gastroenteritis in adults. Our study sought to determine the incidence of Rotavirus as the etiology as a pathogen for acute gastroenteritis in the adult population. Our study involved multiple means of detection of viral presence in specimens of adult fecal material from patients over the age of eighteen hospitalized due to complications of gastroenteritis. The specimens were analyzed for the presence of rotavirus through the use of ImmunoCard Stat! Assay and Rotaclone EIA. The ImmunoCard Stat! Assay is an immunogold based technology. The Roaclone EIA is an enzyme immunoassay, which is considered to be the gold standard in rotavirus detection. PCR was used on positive samples in order to determine the genotype of the rotavirus strain present. Preliminary data suggests some seasonality, and an incidence of rotavirus in approximately six percent of cases. Application of this research may be useful in determining the need for and assisting in the development of vaccines to benefit adult patients.

Generation of Septin 9 (SEPT9) Isoform v3 Construct and an NIH3T3 Stable Transfectant

by

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The septin family of genes represents a highly redundant and conserved family of GTP binding proteins that assemble into filaments and are associated with diverse processes in dividing and non-dividing cells. In mammals the septin family has 13 orthologs that have been shown to be involved in multiple cellular processes, including cell migration, apoptosis and signal transduction. One member of this gene family, Septin 9 (SEPT9), has been identified as a novel oncogene implicated in breast tumorigenesis. The SEPT9 locus maps to 17q25. Cytogenetic and molecular genetic data show that SEPT9 is amplified and overexpressed in mouse models for breast cancer and in human breast carcinoma cell lines; suggesting that an oncogenic function for SEPT9 is necessary to promote breast tumor growth. One aspect of my project was to perform Real Time PCR on cDNA synthesized from RNA extracted from tumor samples of fifty breast cancer patients. Our findings suggest that less aggressive tumors overexpress SEPT9 to a greater extent than more malignant tumors do.

The SEPT9 locus encodes for 18 possible transcript variants. Six different N-terminal isoforms (v1-v2-v3-v4-v4* and v5) and 3 C-terminal isoforms (V1-V2 and V3) have been successfully amplified in ovarian cell lines. In order to begin to understand the role of SEPT9 in carcinogenesis, it is necessary to characterize its complex expression pattern. The first goal of my project was to construct a vector with the v3 isoform of SEPT9. The 2.5 kbp v3 sequence was cloned into a CMV promoter containing pcDNA3.1/myc-His A vector in-frame with the C-terminal myc tag. The vector was then sequenced to confirm proper insertion of the SEPT9 gene. My second goal was to create an NIH3T3 stable transfectant. This was accomplished using Fugene 6 Transfectant reagent; positive cells were selected for by coincubation with Geneticin. Real Time PCR was conducted on transfected cell lines and a significant increase of mRNA expression was observed. Likewise, immunocytochemistry indicated filamentous cytoplasmic overexpression of the SEPT9 protein.

The Effect of Mutant Endocytic Proteins on Cell Motility

by

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The internalization of extracellular cargo (endocytosis) is accomplished by a complex group of processes regulated by different groups of proteins. Clathrin-mediated endocytosis is responsible for the entry of specific cargo ranging from nutrients to viruses. The nascent vesicle is encased in a clathrin coat, and additional proteins that play a role in the process include adaptors, that bind cargo, and accessory proteins, which assist in the progression of endocytosis. One well studied accessory protein is dynamin, which is involved in cleaving the nascent clathrin-coated vesicle from the plasma membrane. The mutation of any of these endocytic proteins impairs internalization or completely prevents the process from occurring. Previous research has been done to correlate the expression of dominant negative mutant variants of endocytic proteins tagged with the green fluorescent protein (GFP) with inhibition of endocytosis. Similar studies done with cells expressing wild-type GFP-tagged proteins showed no inhibition. Moreover, research has shown a correlation between membrane-trafficking processes, such as endocytosis, and cell motility. We, therefore, developed an assay system in which MDCK (Madin-Darby canine kidney) epithelial cells were plated to confluence and subsequently wounded. Migratory cells on the wound edge were microinjected with either wild-type GFP-tagged dynamin2 or GFP-tagged dominant negative dynamin2 (K44A), previously shown to inhibit endocytosis. The migratory rate of the GFP-expressing cells was measured and compared to one another. Following an evaluation of twenty-nine wild type and thirty-one mutant cells in at least seven studies, a forty-two percent inhibition of migration was observed in the cells expressing the dynamin mutant (K44A) relative to the cells expressing the wild-type protein. These observations demonstrate a correlation between the processes of endocytosis and cell motility. As dynamin is also known to regulate other processes potentially relevant to cell motility, future experiments will involve analysis of mutant variants of other adaptors and accessory proteins in the same assay system. Additionally, the quantitative amount of expression of dynamin and other proteins can be relatively calculated by their varying fluorescence. This can allow for a direct link between amount of mutant DNA expressed and amount of migration inhibition, elucidating the importance of the protein's role in endocytosis and cell motility.

Fuel Cell Catalysts: Synthesis, Deposition onto Membranes, Application and Characterization

by

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Today's world is a world with growing energy expenditures. As our limited supplies of fossil fuels are slowly being depleted the search for alternative energy sources has entered the limelight of top edge research. One such alternative that has caught the public eye is fuel cells. These cells are essentially electrochemical cells which take readily available gases, hydrogen and oxygen, and makes them useful by converting chemical energy into electrical energy. Hydrogen gas is oxidized at a platinum anode, producing hydrogen ions and electrons. There is a polyelectrolyte membrane which allows hydrogen ions to pass through, however this membrane is impermeable to the negatively charged electrons. The electrons are forced to go through circuitry connected to the cell, thereby generating electricity. The hydrogen ions pass through the membrane to reach the cathode where oxygen is reduced and recombine with the hydrogen ions to make water, an environmentally safe product. One disadvantage to this alternative is that each cell is not an efficient energy source, thereby forcing one to use multiple cells at a time. Therefore, we proposed a system that would increase the power efficiency of each individual fuel cell.

We suggested that certain metal nanoparticles, such as Pd, would increase power output of a fuel cell if they were coated onto the polyelectrolyte membrane. Nanoparticles have a large surface area to volume ratio, thereby creating many possibilities for interactions with other molecules. Metals are used as catalysts, especially in reduction reactions, by adsorbing hydrogen onto its surface. Therefore we postulated that these metal nanoparticles might increase power output by increasing the amount of hydrogen maintained in a cell at one time. We therefore synthesized thiol functionalized nanoparticles, both Pd and Au of various sizes through a two phase synthesis. The sizes were controlled based on their metal-thiol ratio. These nanoparticles were hydrophobic and therefore were able to be lifted onto the polyelectrolyte membrane using a Langmuir-Blodgett trough. We tested our nanoparticle-coated membranes against an uncoated control membrane and discovered that there was a significant increase in the voltages and currents produced by the fuel cell. Accordingly, the power output of these coated cells was higher than those of a non-coated cell. Au was used as an additional type of control, to determine if the chemistry of the nanoparticles used was significant. Another point of discussion was the particle size. We therefore compared the different effects the size of Pd nanoparticles might have on the energy output, which will continue to be studied.

Determining the Topography of Focal Adhesions using Laser Feedback Interference Microscopy

by

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Cell motility is a complex phenomenon which requires the protrusion of lamellipodium at the leading edge of the cell, producing adhesions between the bottom of the cell and the substratum called focal contacts or focal adhesions. The goal of this research is to try to resolve the distance between the cell and the substratum at focal adhesions, thus determining the topography of the surface of the cell. YFP-paxillin, a focal adhesion protein found at the leading edge of a cell, was transfected into rat mammary cancer cells. Images obtained from a fluorescent microscope showed that paxillin was mostly concentrated at the edges. The height of cell surface and the reflectivity of the cells were measured using phase shifting laser feedback interferometry coupled with a high numerical aperture inverted microscope. Before taking any measurements from the cell, we first calibrated the instrument using a known reference standard. Scans of the empty glass bottom MatTek dishes confirm that the dish is essentially flat. Our results demonstrate that laser feedback interferometry can be used to provide a measure of the distance between the cell and the substratum. We have obtained both a map of the surface shape of a cell as well as its reflectivity. Finally, we have quantified the ventral surface topology at focal adhesions and we have shown that these changes are correlated with YFP-paxillin.

Analysis of Clathrin Mediated Endocytosis in Different Model Organisms

by

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Clathrin mediated endocytosis is a process by which a cell internalizes extracellular components via inward budding of the plasma membrane containing receptor sites specific to the cargo being internalized. In many cases, the cargo to be internalized acts as a ligand and binds to the plasma membrane spanning receptor. In some instances, this signals a self-polymerizing molecule, clathrin, to bind to and coat the membrane, leading to invagination of the membrane and the formation of a clathrin coated vesicle (CCV). In other cases, those receptors activated by ligand binding are targeted to preformed clathrin coated pits. Regardless of coating method, the clathrin has been bound or binds to the membrane and forms the CCV with the help of adaptor and accessory proteins. The clathrin coating acts to stabilize the curvature and increase deformation of the invaginating membrane. Once internalized, the CCV releases its clathrin coat. As of yet, it remains unclear as to whether uncoated vesicles combine to form an endosome de novo or fuse to endosomes that already exist for processing within the cell. Clathrin and its corresponding endocytosis process can be imaged in a number of ways. Immunocytochemistry involving fluorescent-labelled antibodies and confocal microscopy imaging is one method, but does not allow for live-cell imaging. Another method, whereby the clathrin protein is tagged with a fluorescent protein, such as GFP, allows for live-cell imaging with a fluorescence microscope. In several single-celled protozoan organisms (Trypanosome, Paramecium and Tetrahymena) the plasma membrane at the base of cilia and flagella are thought to be "hot spots" for endocytotic events. However, clathrin has been identified in the human centriolar proteome and a basal body proteome of Chlamydomonas reinhardtii, a well-studied motile single celled alga with two flagella. Basal bodies are centrioles that move to the cell periphery and anchor and control the direction and movement of the cilia and flagella. In order to evaluate whether localization of clathrin to the flagella base is a genetically conserved finding, and to determine whether it marks sites of endocytosis or possibly a structural role at the basal body, we have begun evaluating several genetically disparate organisms. Preliminary data from the lab suggests that clathrin localizes to the base of the flagella in mouse sperm and C. reinhardtii. To further study the role of clathrin, we have attempted to introduce GFP-tagged clathrin to both C. reinhardtii and the nematode, C. elegans for live-cell imaging. Transformation of C. reinhardtii with GFP-tagged clathrin did not produce any GFP-positive cells. However, we have been successful with GFP-tagging in C. elegans and have seen what appears to be basal body clathrin localized to the base of cilia in the C. elegans sensory neurons.

Increased S6K1 Protein Expression Confers Proliferative Advantage and Rapamycin Sensitivity to Human Mammary Cancer Cells

by

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Each cycle of cellular division, combined with the biosynthesis of macromolecules which directly precedes it, results in the doubling of DNA content and cell mass. The generic term for this highly complex process is cell growth. Cell growth is regulated by many factors, including Target of Rapamycin, (TOR or mTOR in mammalian cells), a large protein kinase whose gene has been located in every eukaryotic genome investigated to date (reviewed in Fingar and Blenis, 2004). Rapamycin is a naturally-occurring bacterially-derived drug which inhibits TOR, thereby restricting cell cycle progression and causing cell size reduction. Due to these effects, rapamycin possesses immunosuppressive activity and has great potential in inhibiting growth of tumors. Through the integration of environmental cues, such as nutrient signals and growth factors, mTOR acts as a central coordinator of cell proliferation and cell division. mTOR mediates growth through increased protein synthesis by phosphorylating several proteins, the two most notable of which are the S6 Kinase1 (S6K1) and 4E-Binding Protein 1 (4E-BP1). We focus on S6K1, which has emerged as a crucial regulator of protein translation, cell proliferation and cell size control. S6K1's best-characterized target is the S6 protein within the 40S ribosomal protein subunit. S6K1's signaling pathway represents a vital moderator of mTOR-dependent cell cycle control. (Fingar et al., 2004). We examined growth of mammary cell lines expressing different levels of S6K1 and now report that high S6K1 expression correlates to a difference in cell proliferation, depending on the imposed surrounding conditions.

Our findings suggest that cell lines' S6K1 expression level will profoundly affect their growth and proliferation rate. While high levels of S6K1 do not confer proliferative advantage in the absence of serum or in full serum, S6K1 overexpression correlates to increased proliferation in conditions of low serum and to a growth hindrance when rapamycin is introduced into the media.

Our future direction of research includes the assessment of the proliferation capacity of cancerous mammary cell lines exhibiting S6K1 knock down in varying growth conditions. Incorporating our various findings, we hypothesize that cell lines expressing high levels of S6K1 have developed an addiction to this protein's signaling and that, by successfully targeting their S6K1 expression, it is possible to significantly hinder cell proliferation. These studies have considerable potential for future clinical application and are especially relevant to cancer therapy. The drug industry could develop treatments with specific S6K1 knock down capabilities, which, contrary to medicines currently available, such as rapamycin derivatives, would leave the remainder of the critical mTOR pathways undisturbed.

Administrating such a drug to breast cancer patients whose mammary tumor cells exhibit high levels of S6K1 ensures an even greater specialization of treatment. Furthermore, inhibition of S6K1 activity by pharmacological means could be combined with conventional chemotherapies in hope that these would act synergistically to prevent tumor proliferation and metastasis, strengthening the medical communities' fight against cancer, and offering even greater hope to all those affected by the terminal disease.

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[1]These authors contributed equally to this work.

ABSTRACT BOOKLET

STUDENT RESEARCH - 2005

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DEPARTMENT OF PHYSICS

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Local Structural Studies around V and Cr in Chromium Doped V2O3 across the Metal-Insulator Transition Boundaries

by

Agnes (Nathalie) Abitbol[1], P. Shanthakumar[2], T. Huang[2], D. M. Pease[2], and A. I. Frenkel[1]

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At a temperature of 155K, pure V_2O_3 experiences a metal insulator transition on cooling, from a paramagnetic metal (PM) to antiferromagnetic insulator phase (AFI).

Pure V_2O_3 in its PM phase has a trigonal structure while it has a monoclinic one when in its AFI phase. However, at room temperature-which is above the transition temperature- at Cr concentration x exceeding ca. 1%, Cr- doped V_2O_3 is a paramagnetic insulator (PI) but has trigonal structure. To understand the changes in the local structures around Cr and V and investigate their effect on the electronic properties, we undertook their investigation by X-ray-absorption fine structure (XAFS) spectroscopy. This technique allows to investigate the details of the atomic environment (number of neighbors, their identity, geometry of nearest neighboring bonds) separately around V and Cr atoms in this system. For example, one of the most intriguing questions that theorists need to be answered experimentally is how Cr enters the V_2O_3 lattice.

Since the amount of Cr is so low (the samples were prepared with $x = 0.00365$ to 0.0523), Cr K-edge measurements were not possible with conventional detectors because V absorption dominates the background, and the signal to noise ratio in the Cr XAFS is very poor. To amplify the Cr signal, we employed the recently developed log-spiral of revolution detector that filters out the fluorescence rays of Cr from the entire emission spectrum from the sample.

We performed V K-edge XAFS at the National Synchrotron Light Source at Brookhaven National Laboratory, and Cr K-edge XAFS at the Advanced Photon Source at Argonne National Laboratory. The two figures below demonstrate that Cr enters the V_2O_3 lattice substitutionally on the both sides of the MIT (since the polarization dependent Cr-V bonds behave similar to V-V bonds in pure V_2O_3). These results demonstrate, for the first time, that the local environment around Cr is similar to that around V, at all concentrations of Cr, in both metallic and insulating phases.

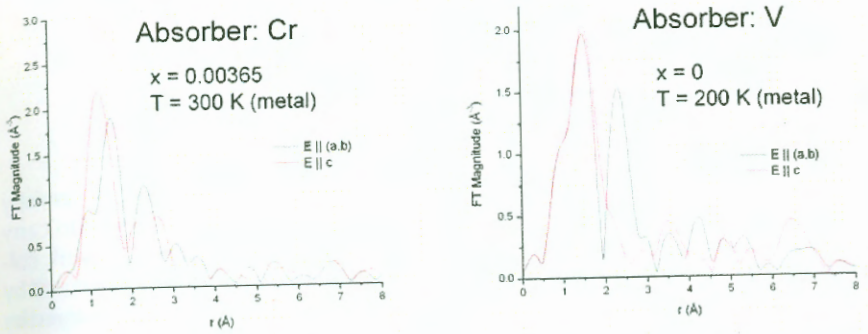

Figure 1: Comparison between the Cr data and V data in metallic phases of single crystals $(Cr_xV_{1-x})_2O_3$ and pure V_2O_3, respectively.

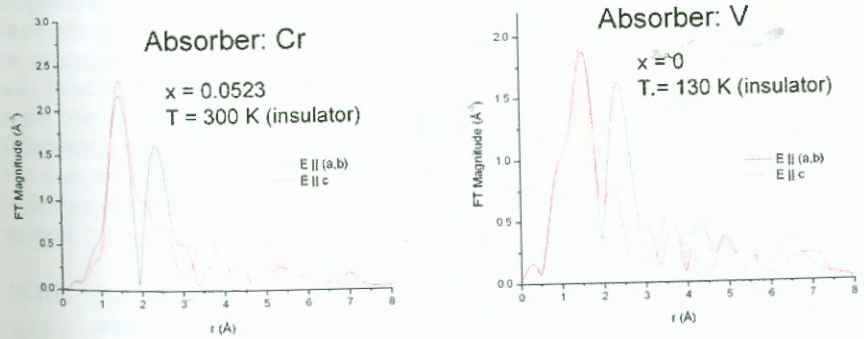

Figure 2: Comparison between the Cr data and V data in the insulating phases of single crystals $(Cr_xV_{1-x})_2O_3$ and pure V_2O_3, respectively.

The DNA Melt: Composition, Sequence, and Thermodynamics

by

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A new module, the DNA Melt, has been developed for the Physical Chemistry On-Line (PCOL) Consortium. PCOL is a multi-university, multi-faculty effort to carry out physical chemistry projects on-line. One goal is to allow students to work collaboratively from remote sites. In this module, a short DNA duplex is denatured by heating. The transition from double-stranded to single-stranded DNA is monitored by UV spectroscopy.

The dominant forces of interaction are determined in the helical structure by varying the base sequence and/or base composition. he effect of solvent composition, including ionic strength, on the melting temperature is also investigated. The dependence of the melting temperature on strand concentration is analyzed to yield thermodynamic data ($\Delta G°$, $\Delta H°$, $\Delta S°$). The experimental thermodynamic data are compared to those predicted from the nearest-neighbor model. The structural dependence of DNA melting is important for several molecular biology techniques including the polymerase chain reaction in which primers are attached to the melted target strands to make additional copies of DNA of complementary structure.

The Generation and Characterization of Antibodies Specific for ART-27, a Novel Coactivator with Tumor Suppressor Function in the Prostate

by

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The androgen-receptor (AR) is a transcriptional regulatory protein that transduces the signaling information conveyed by androgens. When androgens bind, the hormone-AR complex enters the nucleus, associates with specific DNA sequences, and modulates transcription initiation from nearby promoters. Recently, androgen receptor trapped clone-27 (ART-27) was identified and found to be a coactivator that binds to the N-terminus of the androgen receptor. Since studies have shown that activation of AR is essential for the development of the prostate gland in the adult male, we investigated the role ART-27 plays in this gland. Androgen receptor mutations in prostate cancer prevent ART-27 from functioning properly suggesting an important relationship between AR and ART-27. Immunohistochemical studies indicated that under normal conditions, ART-27 just like AR, is expressed in luminal epithelial cells but not in the stroma. It was also shown that ART-27 expression was reduced in human prostate cancer cells suggesting that this coactivator may be a tumor-suppressor. In order to further examine the specific role of ART-27 in the prostate, transgenic mice over-expressing this coactivator has been generated. We have successfully characterized antibodies specific for ART-27 using immunohistochemistry and western blot, which will serve as a powerful tool to study the global effects on the transcription of many important genes known to be involved in regulating prostate growth.

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Correlation of Gene Expression and Sporulation Efficiency in *S. cerevisiae*

by

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Complex genetic traits controlled by multiple loci account for much of natural variation. Despite their importance, few complex traits are understood at the molecular level. We studied sporulation efficiency in *S. cerevisiae* to both determine the role of gene expression and identify causal polymorphisms governing this trait. Analysis of microarray-based gene expression data from two strains with distinct sporulation efficiencies revealed significant expression differences, including up-regulation of mitochondrial genes in the high sporulating strain. We hypothesized that in a cross between these two strains, sporulation efficiency would co-segregate with the expression of genes associated with the mitochondria. Although gene expression data were only available for four cross segregants at the time of publication, we already have evidence to disprove the hypothesis that expression of mitochondrial genes correlates with sporulation efficiency. Future analysis will focus on identifying other genes whose expression patterns co-segregate with sporulation efficiency. Identifying differentially expressed genes, as well as causal polymorphisms, will enhance our understanding of the full molecular picture of sporulation efficiency, allowing us to address broader questions such as the extent to which gene expression affects heritable variation in complex traits.

The Ability of the Microbicide Pro2000 to Inhibit Infection and Transmission of the HIV Virus to Target Cells

by

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HIV is a retrovirus, which infects cells, incorporates viral DNA into its host's genome and produces viral particles in the body. The glycoprotein gp120, located on HIV's virion, binds to CD4 and two chemokine receptors, CCR5 and CXCR4, found on human cells. Because of these receptors, HIV targets CD4+ lymphocytes cells thereby destroying these cells together with the body's immune ability. Immature dendritic cells are located on the vaginal mucosa and submucosa. These cells will first come in contact with the virus where it will replicate or be carried to CD4+ T cells. This research involved the study of the drug PRO2000 and its affect on dendritic cells in the presence of HIV. The drug is designed to stop gp120 on HIV from binding to CD4 and inhibit the uptake and infection of dendritic cells as well as prevent the transmission of HIV from dendritic cells to T cells. This drug is being developed as a topical vaginal microbicide to be used by women to reduce the sexual transmission of HIV.

In the experiments preformed, dendritic cells were incubated with Pro2000, washed and infected with a pseudotyped virus and examined to see if the virus was transmitted to HeLa cells. In this case, the virus was not inhibited indicating that the drug does not strongly bind to cells. However, when the drug was incubated with the virus and then incubated with dendritic cells, there was an inhibition of the virus. This indicates that the drug binds to the virus and prevents its uptake. Consequently, this drug could be useful in protecting women from getting HIV during intercourse by blocking the critical first interaction of the virus with the cells in the vaginal mucosa.

Energetics of Phosphate/Carboxylate Substitution

by

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Post-translational phosphorylation plays a major role in cellular regulation with the phosphorylated residue generally being a serine or threonine. Phosphorylated residues are stabilized by interaction with positively charged residues such as lysine or arginine. A question relevant to protein engineering is whether the interaction between a phosphorylated residue and a positively charged amino acid can be reproduced by the presence of a negatively charged amino acid residue in place of the phosphate. We used the *Spartan* molecular modeling program to construct systems of glutamic acid interacting with lysine (GLU/LYS), and phosphorylated-serine interacting with lysine (SER-P/LYS), at hydrogen bond distances ranging from 2.5 to 10 angstroms. The OPLS all atom force field and the Generalized-Born implicit solvation model were used to calculate the energies of the various systems. Our results show contact minima between five and six angstroms for both systems, and a much deeper energy minimum for the phosphorylated system.

Oct-1 Proximal Cooperating Elements for Gata-2 Transcription

by

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The Gata-2 gene codes for a transcription factor necessary for early ectoderm and mesoderm development, and later in multiple cell specific expression programs. The Gata-2 gene is dependent on Bone Morphogenetic Protein (BMP) signaling pathway. However, the mechanism for Gata-2 activation is not known. In this study the Gata-2 promoter is tested for its reaction towards BMP downstream signaling in early embryogenesis in order to determine its mechanistic pathway. Testing results indicate that Gata-2 activation is dependent on Smad , due to the ability of smad-6 to inhibit BMP activation and Smad-1's ability to substitute for BMP. Once signaling reaches the promoter there is a region situated between -819 and -443 base pairs that is imperative for activation. In this region there are two key binding sites referred to as BMP response elements 1 and 2 (BRE) that cooperatively facilitate Gata-2 transcription. The Oct-1 protein binds BRE1 which is composed of a 5'-ATGCAAAT-3' sequence that is situated between -819 and -751 base pairs. However, the protein binding constitution of BRE2 is yet to be determined. It is believed that the main candidates for this site are Mix.1, Vent and Smad proteins. All of these candidates are downstream from BMP and possess strong inter-regulatory effects with Gata-2 or with each other. Interestingly, vents, particularly, Vent-2 possess an absolutely necessary binding sequence of TAAT. This sequence is also found along the BRE2 site positioned between -666 and -646 base pairs. Furthermore, zebrafish vent and vent related homeobox gene vox are inactivated by mutation, show reduced expression of Gata-2 at mid gastrula stage. The BRE2 candidates may bind to the BRE2 site independently, cooperatively or in certain combinations with each other, so that in cooperation with Oct-1 Gata-2 can be transcribed.

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An Implicit Solvent Study of Phosphorylation in Protein Molecules

by

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We studied the energetics of hydrogen bonds between charged groups in proteins, including the amino acids, arginine, lysine and glutamic acid, and the phosphate group introduced in posttranslational phosphorylation. Calculations were performed using the Delphi implicit solvent model, a finite difference Poisson-Boltzmann solver. We investigated the potentially most stable separations and orientations for oppositely charged residues, as well as the question of what extent negatively charged amino acids can reproduce the effects of a phosphate group. Our results show contact minima ranging from 3.75 to 5 angstroms and that phosphates can be substituted with carboxylates in one third of cases, especially when the phosphate carried a single negative charge. Finally, we compared our results to those produced by molecular dynamics calculations in explicit solvent to determine which aspects of the energy landscape were accurately represented by implicit solvent methods. Our findings show that Poisson-Boltzmann results were within 1-3 kcal of explicit solvent results and produced an underestimation of energy in cases where the hydrogen bond donor was arginine or the hydrogen bond acceptor was a phosphate.

The Effects of Titanium Dioxide Nanoparticles on Human Cells

by

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Titanium dioxide nanoparticles are used in sun protection products, yet there has been very little research on the effects of these nanoparticles on human cells. We therefore studied the effects of Titanium Dioxide nanoparticles on human glial nerve cells and dermal fibroblasts. In order to visualize the effects, migration assays were carried out, as well as imaging studies with Confocal, Atomic Force, and Phase Contrast microscopes. Three types of Titanium Dioxide nanoparticles were used in the migration assay; amino acid treated Nano-TiO_2 rutile (k-1), amino acid treated Nano-TiO_2 rutile (11), and ultra fine granular shaped rutile Titanium (14nm). Nanoparticles of various concentrations were added to the cells and it was found that concentrations above 0.2mg/ml were lethal to the glial cells. Imaging using a Phase Contrast microscope showed that glial cells incubated with nanoparticles (11) had the smallest average migration distance, thus the largest cell death. Glial cells incubated with K-1 nanoparticles had a marginal effect compared to the control, demonstrating a large average migration distance. TiO_2 nanoparticles had a greater effect on the dermal fibroblast cells, than on the glial cells. In order to better understand the interactions between nanoparticles and cells, the structure of actin in the cells was examined using the Confocal microscope. The actin fibers were thick and elongated in cells without nanoparticles. However, the actin fibers were thinner and deformed in cells that contained nanoparticles. Thus, it appeared that TiO_2 nanoparticles had an effect on the structure and amount of actin in the cells.

X-Ray Absorption X-Ray Fine Structure (XAFS) is a premiere structural technique used to study the nanoparticle-cell interaction, due to its sensitivity to the local environment of the x-ray absorbing atom. XAFS experiments were carried out on dermal fibroblasts and glial cells, using Titanium Dioxide (TiO_2), Palladium Citrate (PdCt + BH4), and Platinum (K2PtCl + NaBH4) nanoparticles. The experiments were performed at the National Synchrotron Light Source at Brookhaven National Laboratory, Beamlines X11A, B. The purpose of these experiments was to compare the surface structure of the nanoparticles inside and outside of the cells. We were able to detect Ti K-edge XAFS in the most concentrated sample of TiO_2 nanoparticles, (the sample without cells) as a baseline control. The original samples of nanoparticles and cells were supported in an agarose gel, however they were too dilute for detection. We therefore, created a method of mounting a few thin samples of agarose onto an adhesive tape, to create a more dilute sample. XAFS analysis on this type of systems is a novel approach, which had not been used previously under these experimental conditions. Additional experiments will be performed using the same conditions with more concentrated samples. Further research will be conducted on various nanoparticles and their effect on human cells using enhanced conditions for XAFS measurements. In summary, these experiments were able to detect some specific effects of nanoparticles on human cells.

Regulation of Mts1 Binding by Myosin-IIA Heavy Chain Phosphorylation

by

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Mts1, which is a member of the Ca^{2+}-regulated S100 family of proteins, has been characterized as a metastasis factor and is thought to regulate the motility and invasiveness of cancer cells. In previous studies, we demonstrated that mts1 specifically binds to nonmuscle myosin-IIA on residues 1909-1924 of the heavy chain and promotes the unassembled state. Although this region contains a PKC phosphorylation site at Ser1917, mts1 binding is not affected by PKC phosphorylation. Rather, phosphorylation on Ser1944 by CK2, which is located 20 residues downstream of the mts1 binding site, inhibits mts1 binding and protects against mts1-induced destabilization of myosin-IIA filaments. To examine the regulation of mts1 binding by heavy chain phosphorylation in vivo, we created A, D or E substitutions at Ser1944 in the full-length myosin-IIA heavy chain and in myosin-IIA rod fragments. Biochemical assays using the myosin-IIA rod fragments are being performed to evaluate how these amino acid substitutions effect myosin-IIA assembly and mts1 binding.

The Role of AKT and FOXO1 in Hematopoiesis can be Studied through Loss of Function Experiments Using RNA Interference

by

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Vital to the survival, proliferation, and differentiation of many cells types are AKT, a serine threonine kinase, and FOXO1, a transcription factor downstream of AKT which is phosphorylated and inhibited by AKT. To better understand the role of AKT and FOXO1 in hematopoiesis and mature erythroid cells, we designed experiments to study the loss of function of these two proteins. One method of inducing loss of function is RNA interference, a phenomenon in which the translation of a given gene is inhibited. Duplices of short interfering RNAs (siRNAs) specific for AKT were annealed and these oligonucleotides were tested in 293T cells. The siRNAs which inhibited AKT production were identified and short hairpin RNAs (shRNAs) were designed based on the sequences of these siRNAs. The shRNAs were cloned into a Lentiviral plasmid and Lentivirus can now introduce the shRNAs targeting AKT into G1ER cells. Additionally, siRNAs targeting FOXO1 were identified by transfecting NIH/3T3 cells with four different siRNA sequences. These results can now be used to identify shRNAs that can inhibit FOXO1 expression. The inhibition of AKT and FOXO1 through the use of shRNAs can help us understand the role of these two proteins in hematopoiesis.

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In vitro Cytotoxicity of a Theaflavin Mixture from Black Tea to Malignant, Immortalized, and Normal Cells from the Human Oral Cavity

by

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The growth inhibitory effects of a theaflavin mixture from black tea were more pronounced to malignant (CAL27; HSC-2; HSG1) and immortalized (S-G; GT1) cells than to normal (HGF-2) cells from the human oral cavity. Studies with malignant carcinoma CAL27 cells and immortalized GT1 fibroblasts showed that cytotoxicity of the theaflavin mixture was enhanced as the exposure time was increased, with the tumor CAL27 cells more sensitive than the GT1 cells. Hydrogen peroxide (H_2O_2) was detected in cell culture medium amended with the theaflavin mixture. The level of H_2O_2 in cell culture medium amended with the theaflavin mixture was lessened in the presence of catalase and $CoCl_2$; the level of authentic H_2O_2 was also lessened in the presence of $CoCl_2$, suggesting that Co^{2+} led to the rapid catalytic decomposition of H_2O_2. The cytotoxicity of the theaflavin mixture was due, in part, to the generation in the cell culture medium of hydrogen peroxide (H_2O_2), which lessened the intracellular levels of glutathione in the CAL27 cells and, to a lesser extent, in the GT1 cells. For both cell types, coexposures of the theaflavin mixture with catalase or $CoCl_2$ afforded protection.

The Effects of *Trypanosoma cruzi* on the Spleen

by

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Chagas' disease, caused by *Trypanosoma cruzi* is a potentially lethal disease. Infection causes an immune response that may be overactive, leading to tissue damage. Here we demonstrate the effects of two molecules involved in the immune response, NOS3 and NOS2 (nitric oxide synthase isoforms produced by endothelial cells and macrophages, respectively). The abdominal region and gastrointestinal tracts of *T. cruzi* infected mice were studied and compared with uninfected mice. Spleens of infected mice were found to be significantly larger than those of uninfected mice. Infected wild type mice spleens appeared to be larger than those in knockout mice, supporting the idea that an alteration in the immune system can hinder the negative effects of *T. cruzi*. Magnetic resonance imaging allows for the comparison and analysis of tissue prior to and post disease and distress. It is a particularly attractive tool for translational research, as results from studies of mouse models of human disease can be applied in the clinical setting.

Urinary Matrix Metalloproteinases in Patients with Pulmonary Arterial Hypertension

by

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Pulmonary arterial hypertension (PAH) is an obliterative vasculopathy of the small vessels of the lung associated with endothelial and smooth muscle cell proliferation. Alteration of the vascular extracellular matrix has a role in experimental PAH. We examined whether matrix metalloproteinases (MMP) are similarly upregulated in vivo in patients with PAH. We studied a cohort of 53 patients with PAH and 47 age-matched and sex-matched controls and performed substrate gel electrophoresis supported by immunoblot analysis using monospecific antibodies on urine samples to detect MMP activity patterns. In addition, we studied 13 lung tissue samples from patients with PAH and 3 controls for presence and localization of MMPs by immunohistochemistry. At least one urinary MMP species was detected in a significantly greater proportion of patients affected by PAH (72%) in comparison to controls (17%, $P < 0.001$). Four MMP species were highly expressed in patients with PAH compared to controls: a >150 kDa species, a 140 kDa species, a 92 kDa species (MMP-9) and a 72 kDa species (MMP-2). The 72 kDa (MMP-2) species was an independent predictor of idiopathic iPAH ($P < 0.001$) but not associated PAH (APAH). MMP-9 immunostaining was observed in a higher proportion of lungs affected by PAH compared to controls and localized to the endothelial cells and smooth muscle cells of affected lesions. MMP-2 expression was only observed in cases of iPAH and localized to plexiform lesions. Pulmonary arterial hypertension is associated with the increased expression of MMPs in the pulmonary vascular lesions seen in this disease. We report, for the first time, the detection of specific, biologically active species of MMPs in the urine of patients with PAH. The urine MMP pattern is correlated with disease-specific etiology.

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MTT Assay on Novel Encoded Particle Technology that Enables Simultaneous Interrogation of Multiple Cell Types

by

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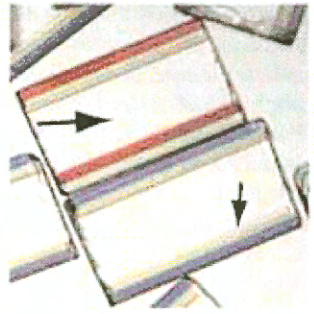
A cell analysis platform, based on encoded microcarriers, enables multiplexed analysis of a diverse range of cellular assays. At the core of this technology are classes of microcarriers that have unique, identifiable codes that are deciphered using CCD-based imaging and subsequent image analysis.



The encoded particles are shown above. These particles are roughly 350 µm x 550 µm in size and are 90µm thick. There are 2 pairs of colored coding bands (small arrow) on either side of an optically clear section (big arrow). The code is determined by the combination of colors at each of the 4 positions. The platform is compatible with a wide variety of cellular imaging-based assays, including calcium flux, reporter gene activation, cytotoxicity, and proliferation. In addition, the platform is compatible with both colorimetric and fluorescent readouts. Notably, this technology has the unique ability to multiplex different cell lines in a single microplate well.

The goal of my research was to develop a protocol for the application of the MTT assay to the Cell Card system for Drug Discovery. The nature of the MTT assay is such that it presents several unique challenges for the Cell Card platform. The MTT cell proliferation assay relies on mitochondrial enzymes to cleave the pale yellow MTT into dark blue formazan crystals which then accumulate in healthy cells. The number of viable cells is directly proportional to the formazan product and the color intensity. It is necessary to adjust the proper dose of MTT, as well as, the proper time of incubation so that all cells are stained, but not stained so darkly that they conceal the carrier codes making image analysis impossible. This is additionally complicated by the differential staining intensity exhibited by various cell lines. Thus, it is necessary to group cells into light, medium and dark staining categories and to develop a different set of staining conditions for each group. Another factor is the variable doubling speed of different cell lines. Different seeding densities must be chosen for cells that grow very quickly as these cell lines will completely obscure the microcarrier and it code if seeded too heavily.

Interneuron Diversity in the CA1 of the Hippocampus

by

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The hippocampus contains diverse interneuron subtypes which synapse in different areas within the hippocampus and perform different functions. Some interneurons fire spontaneously, contributing to oscillating patterns of activity in the hippocampus. One such pattern is the theta frequency. These rhythmic oscillations are thought to be involved in various cognitive tasks and disruptions of their pattern have been implicated in epilepsy. Activation of an interneuron's kainate receptors (KAR) has been found to increase the cell's firing rate, so it is thought that KAR may play a role in the disruptions in brain rhythms associated with epilepsy. In order to further understand the role of KAR in interneuron function we have mapped the KAR distribution over *stratum oriens* interneurons. We have also classified interneuron subtype based on their dendritic and axonal termination patterns. We find three types of KAR distributions, which correspond to specific subtypes of interneurons.

In vitro Cytotoxicity of Green Tea Polyphenol Extract and Sanguinarine Chloride to Cells of the Human Oral Cavity: Lack of Synergistic Interaction

by

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The neutral red cytotoxicity assay was used to assess the relative 24-hr cytotoxicities of a green tea polyphenol extract and sanguinarine chloride to cell lines isolated from the human oral cavity. For both the green tea polyphenol extract and the sanguinarine chloride the sequence of sensitivity was, carcinoma HSC-2 cells > immortalized GT1 gingival fibroblasts > normal HGF-2 gingival fibroblasts. Extensive cytoplasmic vacuolization was noted in all cell lines exposed to cytotoxic levels of the green tea polyphenol extract. Exposure to cytotoxic levels of sanguinarine chloride induced cytoplasmic vacuolization in HSC-2 cells, micronuclei in GT1 cells, and cell shriveling in HGF-2 cells. In addition, upon exposure of the GT1 fibroblasts to 2.25 μM sanguinarine chloride for 24 hrs, the nucleoplasm became clustered with circular spaces and the nuclear envelope was distinctly visible (Fig. 1). In cell culture medium, green tea polyphenol extract, but not sanguinarine chloride, generated hydrogen peroxide. Synergistic interactions in toxicity were not noted for combinations of green tea polyphenol extract + sanguinarine chloride.

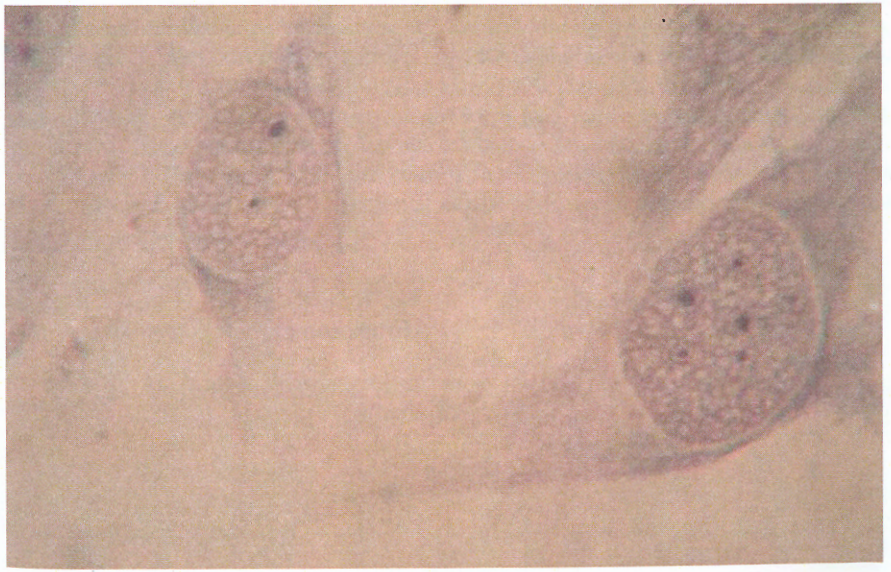

Figure 1. GT1 fibroblasts exposed for 24 hrs to 2.25 μM sanguinarine chloride. Original magnification, 1,000X; Giemsa stain

Toxicity of Dental Products Evaluated with the Allium Assay

by

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The *Allium* assay is an easy and sensitive tool for measuring overt cytotoxicity and subtle genotoxicity of chemical test agents. Small onion bulbs were cultivated in test tubes containing spring water amended with varied concentrations of test agents. Overt cytotoxicity was expressed by the inhibition of root growth and subtle genotoxicity by cytologic studies of the effects of the test agents on nuclear and mitotic chromosome morphologies. The *Allium* assay was used to evaluate the toxicities of two dental products, bisphenol A used in dental sealants and chlorhexidine digluconate, an antimicrobial agent used in mouth rinses.

Onion bulbs were exposed to chlorhexidine digluconate, at concentrations ranging from 0.00001 to 0.001%, for 7 days, after which measurements of root lengths were performed. A concentration-response toxicity response was noted. Concentrations from 0.0001 to 0.00075%, used to evaluate genotoxicity, revealed the presence of hypercondensed nuclei (Fig. 1) and an occasional broken mitotic chromosome. Exposure to bisphenol A revealed a variety of chromosomal aberrations, including vagrant and sticky chromosomes (Fig. 2), as well as enlarged nuclei (Fig. 3), possibly reflecting endoreduplication.

Fig. 1. Hypercondensed nuclei (left) and normal nuclei (right)

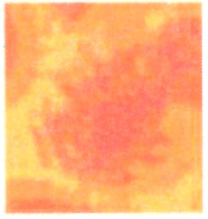


Fig. 2. Sticky chromosomes

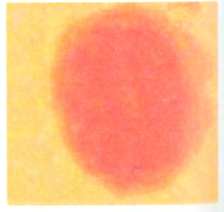
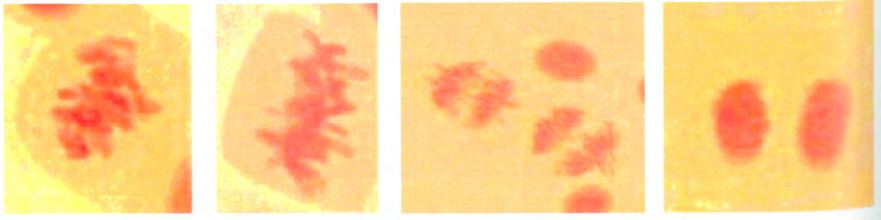


Fig. 3. Enlarged nucleus



Normal Mitosis

Prophase Metaphase Anaphase Telophase

Role of cAMP Pathway in *Toxoplasma gondii* Differentiation

by

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The cAMP pathway, specifically cAMP dependant protein kinase (PKA), has been implicated in the differentiation of *Toxoplasma gondii*. During its asexual cycle *T. gondii* undergoes an interconversion between bradyzoite and tachyzoite that is crucial for pathogenesis. A cDNA microarray was used to measure transcriptional changes in the *T. gondii* genome when differentiation was induced by drugs that target the PKA pathway (H89, SNP, and C1). The sequences of ten genes that were up or down regulated were unknown. To determine whether or not these genes are involved in differentiation, the genes were amplified in preparation for sequencing. To prepare DNA for sequencing PCR was performed or directly on frozen phage or after phage was produced from infected bacteria or using rapid excision assay to prepare plasmid DNA containing the cDNA sequence. Sequences revealed were BLASTed against the *T. gondii* genomic database, protein database, and EST databases. A high mobility group (HMG) protein generally involved in transcription was among the protein matches found. To investigate expression of HMG in *T. gondii*, the HMG gene was cloned into an expression vector and transfected into the RH strain of *T. gondii*. Preliminary results show probable expression of HMG in the nucleus but further experiments are needed to validate these findings and observe the effects of HMG on differentiation. The PKA pathway was also studied, to investigate if two of its catalytic subunit's isoforms, PKAc1 and PKAc2, interact with each other. HA-tagged proteins were extracted from two stable transfections of the PLK strain of *T. gondii* and then purified using HA-magnetic beads. Western blot analyses showed clearly that two PKAc1 and PKAc2 interacted with each other and that PKAc2 interacted with PKAr. Additional experiments are needed to investigate other possible protein interactions.

Thiol-stabilized Palladium Nanoparticles: Size Control and Hydrogenation

by

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Ligand-stabilized nanoparticles represent an interesting nano-scale system that has tunable electronic, structural and catalytic properties which makes it important for applications such as catalysis or hydrogen storage. We investigated the possibility to control the size of the thiol-stabilized palladium nanoparticles by just one parameter: the palladium/thiol ratio. We also studied the effect of hydrogenation on the thin Pd nanoparticle films made by the Langmuir Blodgett (LB) technique. While hydrogen incorporation in Pd lattice has been heavily studied, using nanoparticles for hydrogenation is a relatively new research field. Since nanoparticles have much more surface and subsurface sites than bulk metals, one expects unique absorption properties may be revealed due to the change in absorption caused by the surface-specific and nano-scale effects.

Several samples of palladium nanoparticles were prepared by using a two-phase method developed by Brust *et al.* This method uses water and toluene as the inorganic and organic solvents respectively, a reducing agent and a phase transfer reagent. All the samples were made the exact same way. The only difference was the amount of thiol added. The particles were prepared at the Nanoparticle Factory located at the Stern College for Women's Chemistry laboratory.

We used two different techniques to find the size and structure of the palladium nanoparticles: Transmission Electron Microscopy (TEM) and Extended X-Ray Absorption Fine Structure (EXAFS). TEM measures the size distribution of the nanoparticles. EXAFS measures coordination numbers of Pd-S and Pd-Pd bonds in the nanoparticles. This information allows to estimate the size of the particles when a cuboctahedral model of their structure is assumed. Both EXAFS and TEM demonstrated that the size of free-standing nanoparticles decreased as the thiol concentration increased. Interestingly, we obtained that the size stabilized at the smallest values for the 1:1 ratio of Pd to thiol. This effect is similar to what we previously observed for thiol-stabilized Au nanoparticles, where it was attributed to the increasingly larger role of thiol-thiol repulsion as the Au/thiol ratio decreased.

We then used the Langmuir-Blodgett technique to deposited nanoparticles on Kapton film substrate. It consists of a trough that needs to be filled with distilled water, and two barriers that compress the film spread over the water. We spread nanoparticles in the trough and performed the pressure-area curve measurement to find the pressure at which the films were lifted. About 750 layers were stacked together in order to have a sample thick enough for EXAFS. We found that the Kapton-supported nanoparticles retained their structure. EXAFS measurements were performed on the 1:1 and 3:1 samples before and after their exposure to hydrogen. We obtained that the structure of the hydrogenated samples had enhanced disorder which we attribute to the defects caused by hydrogen incorporating into the Pd lattice.

Regulation and Subcellular Localization of S100A3

by

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The S100 family is the largest super family of proteins carrying calcium binding EF-hand sites. These S100 proteins are small, acidic proteins of 10-12kDa and were found to be involved in a variety of cellular processes, such as cell cycle regulation, cell growth, differentiation, and motility. Various diseases like cardiomyopathies, neurodegenerative and inflammatory disorders, and cancer are linked with altered S100 protein levels. S100 proteins form homo- and heterodimers, and upon calcium binding, they undergo a conformational change which exposes a hydrophobic cleft. This cleft is the interaction site of S100 proteins with their target proteins. We have recently identified that S100A3 is regulated by transcription factor NFAT.

NFAT, the nuclear factor of activated T cell, was first recognized as an important transcriptional factor that regulated cytokine gene expression in immune cells, specifically T cells. NFAT is now recognized as a transcriptional factor in regulating gene expression in numerous cell types. NFAT activity has been shown in cardiac hypertrophy, adipocyte differentiation, and in learning memory. When the cells are treated with ionomycin and PMA, phophatase calcineurin is activated which then dephosphorylates NFAT. Upon its dephosporylation, NFAT becomes functional and passes through the pores in the nuclear membrane where it controls gene expression.

The focus of my research is to understand the regulation of S100A3. I asked how does NFAT regulate S100A3 and where is S100A3 located inside the cell.

To address the first question, a luciferase reporter assay was employed. There were five different constructs used in the experiment: 1) A known NFAT-responsive luciferase reporter construct, which was used as the positive control. 2) A plasmid contains only the luciferase reporter which was used as a negative control. 3) Three different constructs, contain various lengths of the S100A3 promoter region right in front of the luciferase. One clone included -1kb, another contained -0.6kb, and the third plamid had -0.3 kb of the S100A3 promoter. After measuring the luciferase activity and normalizing the data with the co-transfected B-gal, the following conclusions were drawn- in the untreated state, the -0.6kb region had the highest luciferase activity, implying that the 400 bp that were deleted from the -1kb to -0.6kb region were repressing transcription. The level of luciferase activity in the -0.3kb region dropped significantly, suggesting that the 300 bp that were removed from -0.6kb to the -0.3kb were stimulatory. However, when the cells were treated with ionomycin and PMA, which activates NFAT, the only region that had a significant increase in luciferase activity was the -1kb promoter region. The average fold of induction for the -1kb region was almost three times higher than when the cells were

left untreated. These data indicate that -0.6 to -1kb region is NFAT-responsive.

For the second area of the research project in where locating the S100A3 was the goal, I subcloned three constructs. Two constructs were ligated with GFP, green fluorescent protein, and one construct contains a FLAG epitope target at the N-terminus of S100A3. In one construct, the S100A3 was at the N-terminus followed by GFP, and the other construct S100A3 is at the C-terminus. Two days after transfecting the BHK cell line with these constructs, the cells were viewed under a fluorescence microscope. When a green fluorescence was sighted, that would indicate the location of the S100A3 -GFP fusion protein. Indirect immunofluorescence is used to detect Flag-S100A3 in cell. S100A3 is found mainly in the nucleus. S100A3 may also present in endovesicular compartment, suggesting that S100A3 may be secreted into the extracellular space.

In conclusion, the 400 bp region from the -1kb to -0.6kb of the S100A3 promoter is NFAT responsive. And, S100A3 is localized in the nucleus. Additional experiments will be required to understand the regulation and function of S100A3.

Prediction of Protein Loops in Solution

by

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The ability to determine the structure of a protein in solution is a critical tool for structural biology, as proteins in their native state are found in aqueous environments. We demonstrated the ability to predict the structure of loops in solution by validating predicted loops against restraints determined by NMR experiment. Predictions were run on structures from the Protein Databank (PDB) determined by NMR experiment (native), and the same structures that were refined in explicit solvent (cns). Using two sets of structures allowed us to test whether prediction accuracy depends on the quality of the experimental structures used. Our results showed successful prediction of loops in solution with average RMSD for predicted loops in the native set of 0.50, 0.93 and 1.49 angstroms, for loops of 4-6 residues in length, and a percentage of restraints violated of 3.60%, 10.59%, and 16.1%. Our results further showed dependence of prediction performance on structural quality with decreases in average RMSD of 0.06, 0.20 and 0.60 angstroms for loops of 4-6 residues in length, and a difference in percentage of restraints violated of 0.19%, 4.67%, and 11.4% for the refined set compared to the native set of structures.

P-Glycoprotein Expression Protects Multidrug Resistant Cells from Reactive Oxygen Species and Reactive Nitrogen Species

by

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Cellular resistance to a wide spectrum of cytotoxic agents (chemotherapeutics, immunotoxins, and radiation) has been a subject of increasing interest to those concerned with the clinical treatment of a wide variety of cancers. Of the various forms of resistance, the phenomenon of multidrug resistance has received the most attention. In many cases, multidrug resistant is due to the overexpression of the transmembrane protein called P-glycoprotein. Presently, few if any groups have researched the effects of reactive oxygen species (ROS) and reactive nitrogen species (RNS) on P-glycoprotein-expressing cancer cells. ROS, which includes hydrogen peroxide, and RNS, which include nitric oxide, are cytotoxic to the cell as they attack the DNA of the cell and cause double strand breaks and damage many types of proteins especially the functions of enzymes and structural proteins. The cell is unable to repair the damage and undergoes apoptosis, programmed cell death. Many cancer treatments, such as chemotherapeutics and radiation, use ROS to kill the cells. Using the human promyeloid leukemia cell line, HL60, and its P-glycoprotein expressing variant, RV+ cells, it was determined that the RV+ cells, as compared to the HL60 cells, were more than10 times resistant to hydrogen peroxide and 5 times resistant to nitric oxide. This resistance maybe due to the fact that upon exposure to ROS and RNS, the RV+ cells were able to generate more glutathione as compared to HL60 in the presence of ROS and RNS. HL60 cells and RV+ cells in the absence of ROS and RNS basically express the same levels of glutathione. Another mechanism for resistance may be due to RV+ cells expressing twice as much ROS basally as compared to the HL60 cells. Elucidating the pathway that has been altered to protect the resistant cells from ROS and RNS is paramount, as it may be able to improve the therapies provided to patients with resistant forms of cancer due to the over-expression of P-glycoprotein.

The Optimization of the *In vitro* Production of Red Blood Cells from Cord Blood Derived Hematopoietic Stem Cells

by

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The ability to produce red blood cells *in vitro* from hematopoietic stem cells will improve our understanding of erythropoiesis and hemoglobin regulation, and development of effective gene therapy treatments for several hematopoietic diseases. Our goal was to increase the efficiency of the differentiation of cord blood derived $CD34^+$ stem cells into erythrocytes. Firstly, CD34+ cells were grown in liquid media (Stem Span) with cytokines until day 9. Secondly, they were co-cultured on a feeder layer in Stem Span with erythropoietin (Epo) until day 15. Thirdly, they were co-cultured without Epo until day 24. We aimed to optimize the differentiation process by testing three variables from the time the cells were transferred to a feeder layer: 1. feeder layer cell line (MS-5 or FHB), 2. incubation oxygen level (pO_2 of 21 or 5%), and 3. initial cell concentration ($2.5x10^4$ or $5.0x10^4$ cells/ml). We assessed the amount of erythropoiesis by comparing the quantity, morphology, hemoglobin content, and percent enucleation of cells at three day intervals. Optimal erythropoiesis occurred when $CD34^+$ cells were co-cultured on FHB cells at a concentration of $5.0x10^4$ cells/ml and incubated at 5% oxygen.

Cytotoxicity of Catechin Gallate to S-G cells

by

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Tea, one of the most widely consumed beverages in the world, has diverse pharmacological activities, including chemopreventive properties against cancer. Green tea, consumed at high levels in Asian countries, is derived from leaves of *Camellia sinesis*. In the production of green tea, fresh tea leaves are pan-fried or steamed and dried to inactivate polyphenol oxidase, thereby preserving the polyphenolic constituents in the tea. The polyphenols in green tea include epigallocatechin gallate (EGCG), the major component and thought to be an anticarcinogen, epicatechin gallate (ECG), epigallocatechin (EGC), catechin gallate (CG), and, to lesser extents, gallocatechin gallate (GCG), epicatechin (EC), and catechin (C). This study evaluated toxicity of CG to S-G cells, an immortalized epithelioid cell line derived from the human oral cavity. Initial studies showed that the sequence of toxicity to the above-noted polyphenols to S-G cells, based on a 3-day exposure and evaluated with the neutral red cytotoxicity assay, was ECG> CG, GCG > EGCG >> EGC >> EC, C. The cytotoxicity of CG to various cell lines was also evaluated. The growth inhibitory effects of a CG were more pronounced to the S-G cells and to malignant (CAL27; HSC-2; HSG1) cells than to normal (HGF-1; HGF-2) fibroblasts from the human oral cavity. Increasing the exposure time to CG increased its cytotoxicity, with NR_{50} values of 127 μM for a 1-day exposure, of 67 μM for a 2-day exposure, and of 58 μM for a 3-day exposure. As noted with ECG, compared with EGCG, CG was a poorer generator of H_2O_2 in tissue culture medium. This apparently explained the lack of glutathione depletion in cells exposed to 50 to 250 μM CG for 3 hr and the lack of protection by coexposure to 100 Units/ml catalase. Although CG by itself did not induce lipid peroxidation in S-G cells, it synergized lipid peroxidation induced by treatment with Fe^{2+}. Preliminary studies indicate that CG, albeit at high concentrations, may induce apoptosis. Although the mechanism of cytotoxicity of CG needs more elucidation, the studies herein showed that its cytotoxicity is comparable to that of EGCG, the main anticarcinogen in green tea, and that it is preferentially cytotoxic to malignant cell lines.

Mutational Analysis of Notch 3 in Human Breast, Colon, and Prostate Cancers

by

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Mutational activation of the Notch 1 receptor gene has been implicated in human T cell acute lymphoblastic leukemia (T-ALL). The mammalian genome has four different Notch genes (Notch 1-4), all of which are involved in controlling normal development. The mature Notch receptor is composed of two noncovalently associated subunits, the Notch extracellular (NEC) and Notch transmembrane (NTM) fragments, which interact through heterodimerization domains in each polypeptide (HD). Physiological activation of Notch signalling occurs when Serrate/Jagged and Delta family ligands bind to NEC, initiating a series of proteolytic cleavages in NTM. This results in the generation of an intracellular Notch (ICN) fragment, which acts as a transcription factor in the nucleus. Point mutations in the Notch 1 HD and PEST domains (part of NTM) have been shown to act as oncogenic mutations in Notch 1 (over 50% of human T-ALL's have activating mutations within the HD and/or PEST domains of Notch 1).

Our lab has found that Notch 3 is highly expressed in some human tumours. Therefore, to test for similar activating mutations in Notch 3, I have been isolating and purifying gene segments of Notch 3 obtained from breast, colon, and prostate tumour samples. These gene segments are being sequenced and compared to wild type sequences to determine if point mutations are present in the HD and PEST domains of Notch 3 from tumour samples, as found in the Notch 1 gene from T-ALL cells. Results from our mutational analysis will be presented.

pH Sensitivity in Talin

by

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Studies show that cells can use intracellular pH to regulate actin-based motility. This investigation aims to determine how this process occurs at a molecular level. Our study demonstrated a correlation between pH changes and the structure of talin, an actin binding protein. Talin is one protein involved in binding actin microfilaments found in actin cytoskeletons. Actin cytoskeletons are cross-linked with intergrins, which are transmembrane proteins that interact with the extracellular matrix. At a pH of 6.4 it was found that there was a high affinity of Talin to bind to actin, whereas at a pH of 7.4 there was a reduced probability of actin binding to the protein. Computational methods were used to investigate how pH might regulate talin-actin binding. A homology model of the C terminal region of the I/LWEQ domain of talin was created based on the established structure HIP1R. In the modeled structure of five helices, five side chains were predicted to have pKa's near the cellular range of pH. These were found grouped together at one end of the protein and included one histidine and four aspartic glutamic acids with strongly shifted pKa's. Constant-pH molecular dynamic simulations then revealed how changes in protonation state between pH 6 and 7.5 were coupled to conformational changes. The titratable residues functioned as a pH sensor, which caused one of the helices to bind less tightly to the other four at higher pH, probably exposing a "cryptic" actin binding site. At a lower pH we were able to confirm results with experimental results, where there was an increase an exposure to the actin binding site as the fist helix, otherwise known as the USH, travels away from the other helices.

ABSTRACT BOOKLET

STUDENT RESEARCH - 2004

Stern College for Women
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DEPARTMENT OF BIOLOGY
DEPARTMENT OF CHEMISTRY
DEPARTMENT OF PHYSICS

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Neurogenin 1 Mediates Erythropoietin Enhanced Neurogenesis in Adult Stroke Brain

by

Faber, M.[1], Wang, L.[2], Zhang, Z.G.[2], Jiao, Z.X.[2], Zhang, R.L.[2], and Chopp, M.[2,3]

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Previously, we demonstrated that erythropoietin (EPO) enhances neurogenesis in stroke brain of the adult rat. In the present study, we examined the effects of EPO on expression of the pro-neuronal basic helix-loop-helix (bHLH) transcription factor, neurogenin 1(Ngn1), as a mediator of neurogenesis. For the *in vivo* study, male Wistar adult rats (n=3) were treated with recombinant human EPO (rhEPO, 5000U/kg) starting 24h after embolic middle cerebral artery occlision (MCAo). For the *in vitro* study, neurospheres derived from the subventricular zone of the adult rats (n=6) were transfected with small interfering RNA (siRNA) specific for rat Ngn1 and were then treated with rhEPO (10U). Ngn1 mRNA levels were measured using real-time reverse transcriptase-polymerase chain (RT-PCR). The total number of TuJ1 positive cells and the length of neurites in TuJ1 positive cells were measured. Treatment with rhEPO significantly increased brain Ngn1 mRNA levels to 3.8 fold in EPO treated rats (n=3) compared with stroke only rats (n=3). Ngn1 mRNA was expressed in neurospheres and treatment with rhEPO significantly increased Ngn1 mRNA (1.9 fold at 2h, 5.7 fold at 24h compared with control) as well as increased the numbers of TuJ1 positive cells (17.2±4.1% vs 9.4 ±2.9% in the control group, $p<0.05$). Silencing of Ngn1 by means of siRNA blocked rhEPO elevated Ngn1 mRNA by 45% and significantly reduced rhEPO-increased TuJ1 positive cells (9.6±1.8 vs 17.2±4.1% in rhEPO only group), whereas scrambled cassettes did not block Ngn1 mRNA and numbers of TuJ1 positive cells. In addition, silencing of Ngn1 significantly reduced EPO enhanced neurite outgrowth (65±9.2μm vs 91±8.9 μm in rhEPO only group, $p<0.05$). These data demonstrate that Ngn1 mediates EPO enhanced neurogenesis in brain of the adult rat.

PS1 Mutation Causes Increased Cell Death, with Selective Ensuing Proliferation, in Adult Brains

by

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Mutations in the protein PS1 have been implicated in causing Familial Alzheimer's Disease (FAD), although the exact mechanism of action has not yet been determined. PS1 is involved in many complex developmental pathways, regulating cell fate decisions and maintenance of neuronal subpopulations, and subtle developmental abnormalities may facilitate later onset of the disease. In this study, we investigated the effect of the PS1 M146V mutation on neurogenesis and cell death in adult knock-in mice. The brains revealed increased cell death in selective neuronal populations of the adult knock-in, as predicted by expected pathology of FAD tissue. In addition, the knock-ins also demonstrated increased cellular proliferation in these sections. Interestingly, the knock-in cortex displayed high levels of cellular death. The relationship between cells undergoing cell death and adjacent cells undergoing proliferation has yet to be defined. However, the proximity of these two cell populations suggests that either there is an aborted attempt of stem or progenitor cells to rescue cells that are dying, or ultimately cell cycle response may represent a homeostatic mechanism to prevent irrevocable cell injury or death. Why this population is selectively dying is not yet understood, and further research may provide key insights into the susceptibility of neuronal pools to FAD.

Interleukin-6 and Interleukin-1 Receptor Antagonist in Cord Blood of Infants with Varying Pregnancy Outcomes

by

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Objective: Investigation of the association between interleukin (IL)-6 and interleukin-1 receptor antagonist (IL-1ra) cord blood concentrations and pregnancy outcomes and ethnic variations in their production.

Study Design: Blood samples were obtained from the fetal side of the umbilical cord of 471 infants immediately after delivery. The quantitative analysis of cytokine in sera was performed using IL-1ra Cytoscreen kit and IL-6 ELISA kit. The clinical data of pregnancy outcomes was obtained after the completion of testing.

Results: IL-1ra concentrations were positively associated with gestational age ($P<.0001$). IL-1ra levels were also significantly lower in pregnancies complicated by preterm premature rupture of the fetal membranes (PPROM) than in term births ($P<.001$). The infants with respiratory distress syndrome (RDS) and those with the need for neonatal intensive care unit (NICU) had lower levels of IL-1ra ($P<.03$ and $P<.0069$ respectively) than healthy newborns. Infants conceived with assistive reproductive technology (ART) had lower levels of IL-1ra than infants conceived spontaneously. Correlations between gestational age and ART, NICU and RDS were highly significant ($P<.0001$). The IL-6 level in cord blood of infants with chorioamnionitis was much higher ($P<.0069$) than that of healthy newborns. Comparison of IL-6 production within different ethnic groups showed that blacks have a significantly lower IL-6 ($P<.0069$) production than any other ethnicity.

Conclusion: The higher concentration of IL-6 in umbilical venous blood of patients with chorioamnionitis is indicative of intrauterine inflammation due to infection. The varying production of IL-6 among different ethnic groups demonstrates the variability in immune response to infection which in turn may influence an individual's susceptibility to preterm labor and its complications. The reduced concentration of IL-1ra in cord blood of patients with PROM, RDS, in need of NICU, and those conceived with the help of ART suggests that reduction in the concentration of this anti-inflammatory cytokine may increase susceptibility to various birth complications.

Mediation of the *In Vitro* Cytotoxicity of Green and Black Tea Polyphenols by Cobalt Chloride

by

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The effects of Co^{2+} (as $CoCl_2$) on the cytotoxicity of green tea polyphenol (GTP) and black tea polyphenol (BTP) extracts towards proliferation of immortalized human gingival epithelial-like S-G cells were studied. The 24-hr potencies of GTP and BTP extracts, as determined with the neutral red (NR) cell viability assay, were greatly reduced in the presence of 250, but not of 50, μM Co^{2+}. The cytotoxicities of the GTP and BTP extracts were due, in part, to their generation of hydrogen peroxide (H_2O_2) in the cell culture medium (DMEM). Progressively increasing the concentration of Co^{2+} in the tea polyphenol-amended cell culture medium resulted in a lowering of the level of H_2O_2. The cytotoxicity of freshly added H_2O_2 to S-G cells was abolished in the presence of 250 μM Co^{2+} and the level of freshly added H_2O_2 to cell culture medium was progressively lowered as the concentration of Co^{2+} was increased. Apparently, under the conditions of these studies, the decreases in the cytotoxicity of GTP and BTP extracts in the presence of $CoCl_2$ were due to the rapid catalytic decomposition by Co^{2+} of the H_2O_2 generated in the tea polyphenol-amended cell culture medium.

Neurogenesis Following Transient Retinal Ischemia

by

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The adult mammalian brain contains neural stem and progenitor cells that can proliferate, self-renew, and generate all of the elements of the mature brain, including neurons. Techniques have been developed which have made it possible to isolate and expand cells with properties characteristic of early neural multipotent progenitor cells (MPCs). These techniques have opened possibilities for the use of these cells for CNS transplantation, neural replacement and repair. More recently, the identification of stem cells in the rodent eye has been demonstrated. The purpose of this study was to bring the rapidly expanding area of progenitor cell biology to bear on the problems of retinal ganglion cell degeneration as a consequence of transient retinal ischemia.

The anterior chamber of Sprague Dawley rats was raised to an intraocular pressure (IOP) of 120 mm Hg in order to exceed systemic arterial blood pressure. After completion of either 15 or 45 minutes of ischemia the needle was withdrawn and the IOP normalized. The rats received IP injections of BrdU for 13 days following ischemia. At the completion of 1, 2, 4, or 8 weeks after ischemia, the eyes were enucleated and their histoarchitecture was evaluated by light microscopy. Measurements of the thickness of the retinal layers were performed, in addition to anti-BrdU staining.

The data demonstrated that chronic elevation of IOP results in cellular proliferation following ischemic injury. Enhanced neurogenesis in the retina may be a compensatory mechanism in response to elevated IOP and may promote visual functional recovery in retinal ischemia. Furthermore, strategies aimed at activating endogenous MPC populations may be developed as a therapeutic strategy to improve the functional outcome in patients with retinal ischemia.

Differential *In Vitro* Cytotoxicity of (-)-Epicatechin Gallate (ECG) to Cancer and Normal Cells from the Human Oral Cavity

by

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This study evaluated the biologic activity of epicatechin gallate (ECG), a polyphenol in tea, to carcinoma HSC-2 cells and normal HGF-2 fibroblasts cells from the human oral cavity. The relative cytotoxicity of ECG, as compared to five other polyphenols in tea, was evaluated. For the HSC-2 carcinoma cells, ECG, catechin gallate (CG), and epigallocatechin gallate (EGCG) grouped as highly toxic, epigallocatechin (EGC) as moderately toxic, and catechin (C) and epicatechin (EC) as least toxic. For the HGF-2 fibroblasts, ECG and CG grouped as highly toxic, EGCG as moderately toxic, and EGC, C, and EC as least toxic. The cytotoxic effects of the polyphenols were more pronounced to the carcinoma, than to the normal, cells. The addition of ECG to cell culture medium led to the generation of hydrogen peroxide (H_2O_2). However, ECG, as compared to EGCG, was a poor generator of H_2O_2 and, hence, the cytotoxicity of ECG was unaffected by the presence of the antioxidants, N-acetyl cysteine and glutathione, and catalase. The cytotoxicity of ECG was unaffected by a metabolic activating system, i.e., a hepatic microsomal S-9 mix. DNA fragmentation, caspase-3 activity, and nuclear staining, both with acridine orange and the TUNEL procedure, were used to assess ECG-induced apoptosis. ECG induced apoptosis in the carcinoma HSC-2 cells, but not in the normal HGF-2 fibroblasts. This research supports those studies suggesting that tea green is an effective chemopreventive agent of oral carcinoma.

Dietary Saturated Fats Induce Increased Expression of SREBPs and Glomerulosclerosis in Obesity Prone C57BL/6 Mice but Not in Obesity Resistant A/J Mice

by

Moskowitz, S.[1], Jiang, T.[2], Wang, Z.[2], Liebman, S.[2], Proctor, G.[2], Rogers, T.[5], Lucia, S.[3], Li, J.[2], and Levi, M.[2,4]

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We have shown that in animals with type 1 diabetes mellitus there is upregulation of the renal expression of the transcriptional factor sterol regulatory element binding protein-1 (SREBP-1) that results in increased fatty acid synthesis, accumulation of lipids and increased expression of growth factors resulting in accumulation of extracellular matrix proteins, glomerulosclerosis, and proteinuria. The purpose of this study was to determine if there is altered renal expression of SREBPs in a model of diet induced obesity and insulin resistance. Compared to mice that are fed a 10 kcal % fat diet C57Bl/6 mice that are fed a 45 kcal % saturated (lard) diet are susceptible to obesity whereas A/J mice are resistant to obesity when fed the same diet. In C57Bl/6 mice there are significant increases in renal SREBP-1 and SREBP-2 mRNA (real time PCR) and protein (western blotting of nuclear extracts) abundance, whereas in A/J mice there are no changes in SREBP-1 or SREBP-2 mRNA or protein abundance. The increases in SREBP-1 and SREBP-2 expression in the C57Bl/6 mice results in renal accumulation of triglycerides and cholesterol. There are also significant increases in the renal expression of plasminogen activator inhibitor-1 (PAI-1) and vascular endothelial growth factor (VEGF), type IV collagen and fibronectin, resulting in glomerulosclerosis and proteinuria. In mouse mesangial cells grown in the presence of saturated fatty acids there are significant increases in SREBP-1 and SREBP-2 expression which indicates a direct role for saturated fatty acids in the upregulation of SREBP-1 and SREBP-2 expression. Our results indicate that in a model of diet-induced obesity in the mice there is upregulation of renal SREBP-1 and SREBP-2 expression, which most likely plays an important role in mediating the glomerulosclerosis and proteinuria.

Characterizing Nanoparticle Sizes using EXAFS and TEM

by

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The objective of this project was to compare the two methods, Extended X-Ray Absorption Fine-Structure (EXAFS) and Transmission Electron Microscopy (TEM) in size and shape characterizations of thiol-stabilized gold nanoparticles. Several samples of gold nanoparticles were measured, each synthesized by either a one- or two-phase method and varying gold-thiol ratios. Contrast image analysis of TEM data demonstrated that the synthesis method and the gold-thiol ratio affected the average nanoparticle size. EXAFS data was analyzed to determine the average coordination number and average Au-Au bond length of each sample. Close-packed structure of the smallest clusters (11.3 Å in diameter) and their cuboctahedral shape was suggested by comparing the results for coordination numbers (7.5±0.7) obtained for these clusters against existing models. The diameters of the nanoclusters were then calculated using the Au-Au bond lengths obtained from EXAFS. Results from TEM and EXAFS agree, within their uncertainties, though TEM yields an average size weighted toward larger particles and EXAFS yields an average size weighted toward smaller particles. Our method of EXAFS analysis allows effective characterization of nanoparticle size and shape, even for sizes smaller than the resolution limit of TEM.

Comparison of One-Phase and Two-Phase Methods of Synthesizing Alkanethiol-Stabilized Gold Nanoparticles

by

Pister, I.[1], Harris, T.[1], Soussan, L.[1], Nemzer, S.[1], Sun, Y.[2], Rafailovich, M.[2], and Frenkel, A.[1]

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Two methods of synthesis were used to synthesize alkanethiol-stabilized gold nanoparticles. The one-phase synthesis used an organic phase with tetrahydrofuran (THF) as the solvent and Super-Hydride solution (1.0 M lithium triethylborohydride in tetrahydrofuran) as the reducing agent. The two-phase synthesis used water and toluene as the inorganic and organic solvents. $[N(C_8H_{17})_4]Br$ is used as the phase transfer reagent and NaBH4 is used as the reducing agent. Both methods used 1-Dodecanethiol ($C_{12}H_{25}SH$) for the alkanethiol chains. The particles were examined using Transmission Electron Microscopy (TEM) and Extended X-Ray Absorption Fine-Structure (EXAFS). Both analyses concluded that the two-phase method resulted in smaller particles than the one-phase method. We suggest that this difference may be caused by the details of reduction of gold that are different in these two methods. In the two-phase method the reduction of the particles and their coating by the alkanethiol chains occurred at the interface of the organic and inorganic layers, since the gold and the alkanethiol chains are in the organic phase while the reducing agent is in the inorganic phase. In the one-phase preparation, all components (gold, reductant and thiols) are located in the same volume with organic solvent. Therefore, reduction in the one-phase method occurs throughout the volume, i.e., faster than in the two-phase method where the reduction occurs at the interface between the organic and inorganic layers. This, in turn, leads to the faster rate of agglomeration of gold atoms and formation of bigger particles prepared by the one-phase method compared to the two-phase method.

Phosphate Stabilization in Phosphorylated Protein Structures

by

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One of the mechanisms employed by the cell to regulate its activities is post-translational phosphorylation in which a protein is covalently modified by the addition of a phosphate group. Regulation is accomplished through a change in protein conformation which is induced by the introduction of the doubly charged phosphate group. Using a set of experimental protein structures drawn from the Protein Databank, we compared the interactions which stabilize the newly introduced phosphate group, with those that typically stabilize the side chains of negatively charged aspartic acid and glutamic acid residues. Interaction energies were calculated using a physical chemistry based energy function and a continuum salvation model. Our findings show the two major sources of negative charge stabilization to be hydrogen bonds with the amide backbone (21% of phosphate groups, 46% of Asp residues and 28% of Glu residues) and salt bridges with positively charged Arg side chains (47% of phosphate groups, 19% of Asp residues and 28% of Glu residues). Hydrogen bonds with Ser and Thr side chains account for stabilization of 17% of phosphate groups, and 9% of both Glu and Asp residues. Salt bridges with positively charged Lys side chains appear much less frequently than those with Arg (6% of phosphate groups, 6% of asp residues and 11% of glu residues), while positively charged His side chains almost never stabilize phosphate groups and account for a small minority of interactions with Asp and Glu residues (4% and 2% respectively). Similarly, Gln and Asn side chains do not typically stabilize phosphate groups while they account for hydrogen bonds with 7% and 6% of Asp and Glu residues respectively. Water mediated salt bridges with negatively charged Asp and Glu residues, and hydrogen bonds with several other side chains, account for the remainder of interactions. This study contributes to an understanding of charge stabilization in proteins, and the relationship between changes in structure and function.

Examination of Alternative Splicing in SGCE Gene

by

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Myoclonus dystonia (M-D) is a movement disorder characterized by lightening-like jerks (myoclonus) and sustained twisting and repetitive movements, resulting in abnormal postures (dystonia). The phenotype of this disease also has psychiatric symptoms such as obsessive-compulsive behavior, alcohol dependence, and panic attacks. Recently, mutations in the Epsilon Sarcoglican (SGCE) gene have been shown to be associated with this disease. This gene is a type one transmembrane glycoprotein and a component of the dystrophin-glycoprotein complex that links the cytoskeleton to the extracellular matrix in muscle. It is widely expressed throughout a variety of tissue including striated muscle, smooth muscle, lung, liver, kidney, spleen, testis, sciatic nerve, as well as brain, but its function in brain is unknown. Originally when this gene was discovered only twelve exons were identified. These twelve exons were analyzed for mutations in our lab and twenty-four mutations were found in different exons throughout the gene in M-D patients. Recently a thirteenth exon called exon 11b, located between exons 11 and 12, was identified and determined to be brain specific in mice (Nishiyama, 2004). Two isoforms of the SGCE gene were found in mouse brain due to alternate splicing. Using Polymerase Chain Reaction (PCR) and Sequencing we examined 55 patients without mutations in the SGCE gene but did not find any new mutations in this thirteenth exon. Because M-D is a neurologic disorder we wanted to examine this brain specific exon in both normal and affected human brains to determine if there was differential expression of the various isoforms. Using RT- PCR and quantitative PCR we were able to identify these two isoforms. Various brain regions showed different amounts of the isoforms in normal tissue. Further differences were identified between the affected and normal tissue whereby the predominant isoform in normal showed a lower level of expression in the affected or vise versa. A third isoform was found in various brain regions from one of the patients but the significance of this is unclear at this time. The difference in isoforms distribution between affected and normal brain regions suggests that these isoforms may play a role in the disease however understanding the normal function of this gene is necessary before we can clarify the importance of these isoforms.

Size Control of Thiol-Stabilized Gold Nanoparticles

by

Soussan, L.[1], Nemzer, S.[1], Harris, T.[1], Pister, I.[1], Sun, Y.[2], Rafailovich, M.[2], and Frenkel, A.[1]

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The goal of this research was to investigate the possibility to control the size of the thiol-stabilized gold nanoparticles by a gold/thiol ratio. Several samples of gold nanoparticles stabilized by dodecanethiol chains were prepared at Stern College by using a two-phase method. This synthetic technique involves the use of water as the inorganic solvent, toluene as the organic solvent, NaBH4 as the reducing agent and $[N(C_8H_{17})_4]Br$ as the phase transfer agent. The only difference between the seven samples analyzed was the gold/thiol ratio. The samples were analyzed by using two techniques, Extended X-Ray Absorption Fine Structure (EXAFS) and Transmission Electron Microscopy (TEM).

The results of these two techniques demonstrate that as the gold-thiol ratio decreases, the average size of the particle decreases as well. Surprisingly, we obtained that at the values of the gold/thiol ratio less than 1:2, the cluster size stabilizes. The smallest clusters were obtained by EXAFS analysis to be cuboctahedral in shape where Au atoms occupy close packed structure positions. The size of the clusters was ca. 11 Å, corresponding to a 55 atom regular cuboctahedron. Due to a finite distribution of sizes obtained by TEM, we conclude that the significant amount of clusters were the 13 atom clusters, i.e., the smallest possible regular polyhedral clusters. This result explains why the further decrease of the Au/thiol ratio (below 1:2) does not change the average cluster size. Another possible interpretation can be that the increase of the thiol concentration does not help to constrain the growth of Au particles because of steric repulsion of thiol chains. The latter becomes significant at small Au/thiol ratios.

The Multidrug Resistance Phenotype Confers Resistance to the Green Tea Extract Epigallocatechin Gallate

by

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Mutildrug resistance (MDR), which is due, in part to the overexpression of P-glycoprotein, confers resistance to a variety of natural product chemotherapeutic agents such as daunorubicin, vincristine, and colchicine. Cells which express the MDR phenotype also are resistant to immunotherapies like complement mediated cytotoxicity and immunotoxins. RV+ cells, a P-glycoprotein overexpressing variant of the HL60 myeloid leukemia cell line, displayed a relative resistance to the green tea extract (-)-epigallocatechin gallate (EGCG). EGCG, which has been shown to be more toxic to tumorigenic cells than to normal cells, kills by forming hydrogen peroxide in the presence of cell culture media causing oxidative stress and DNA damage of the cell, ultimately resulting in apoptosis and/or necrosis. Intracellular hydrogen peroxide formation was found to be decreased in the RV+ cells as compared to the HL60 cells. Interestingly, flow cytometry experiments to determine when apoptosis was occurring in the two cell lines after exposure to EGCG revealed that HL60 cells were being killed by two mechanisms, apoptosis and necrosis, while any RV+ cells that were being killed were only by apoptosis. The observations demonstrate how the mechanisms of death differ between cancer cells that are sensitive to the therapy and the resistant cells. Also these results may have implications in cancer cells that are able to survive radiation therapy, which kills similarly to EGCG.

Student Publications and Presentations

SCW undergraduates are listed as coauthors on two types of scientific publications: (a) on research publications submitted to peer-reviewed scientific journals and (b) on abstracts, published by scientific societies as part of their national meetings. Inclusion as coauthors is reflective of their meaningful involvements in the projects.

Each Fall, the Departments of Biology, Chemistry and Physics hold in-house student scientific poster presentations. Students prepare professional posters of their research. Members of the science faculties evaluate the projects and select students to present their scientific data at a national meeting of a scientific society. Abstracts of the research are published as part of proceedings of the scientific society. Travel and hotel accommodations for attending these scientific meetings are provided by SCW.

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Student Presentations at the National Conference of Undergraduate Research

1998: **Malka Skiba** and **Cheryl Younger**
1995: **Lauren Insel** and **Judy Ehrenberg**
1994: **Yaffa Cheslow**, **Debbie Friedman**, and **Stacey Tuckman**

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Helen Nissim — Ilana Pister — Tehilla Stepansky
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University Undergraduate Summer Research Scholar
Suzanne Snyder

Summer, 2004

Roth Scholars
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Debbie Rybak — Reina Roth

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Meryl Sava — Anna Sedletcaia

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Summer, 1996

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The Anne Scheiber Fellowship Program provides scholarship support to Stern College undergraduates as well as graduates pursuing their advanced training at the Albert Einstein College of Medicine. The program, established by Ms. Scheiber through a twenty two million dollar bequest, seeks to support high achieving women with financial need to realize their academic and professional goals. Stern College graduates who attend the University's Albert Einstein's College of Medicine may apply for awards up to full tuition for their four years of medical training. We proudly salute the Anne Scheiber Fellows who are fulfilling Ms. Scheiber's dream:

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Derech HaTeva, a Journal of Torah and Science

Derech HaTeva is an undergraduate publication of Stern College for Women. Articles are authored primarily by science majors, although students in other majors are encouraged to submit manuscripts. The manuscripts are a synthesis of Torah and science thoughts and thus represent the unique intellectual strengths and talents of our students. This journal is catalogued in the National Library of Congress

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An Orthopedic Analysis of Jacob's Injury

by
Abigail Rabinowitz

This article has been reprinted from Derech HaTevah Volume 10, pages 41-42, 2006

For centuries, children and adults alike have enjoyed the stories of the Bible, which relay exciting narratives involving angels, giants, and, of course, supernatural events. With the help of biblical commentaries and modern day knowledge of science, however, we are able to delve deeper and gain a greater understanding of the substance behind these fairy-tale-like stories.

Bereishit (chapter 32) relates the incident in which after Jacob crossed the Jordan River with his family, he returned to the other side. Rabbi Shlomoh ben Yitzchak, a medieval French commentator (known as, Rashi), suggested that Jacob returned to retrieve some jugs. There he was, standing at the bank of the river, when Jacob confronted by a man, who, according to the Jewish sages, was the guardian angel of Jacob's estranged brother, Esau. This confrontation led to a fight, which is described in the following verses:
Bereishit: chapter 32; verses 25-33:

25. And Jacob was left alone and a man wrestled with him
until the break of dawn.
26. When he perceived that he could not overcome him,
he struck the ball of his thighbone; and the ball of Jacob's thighbone
became dislocated as he wrestled with him...
32. The sun rose for him as he passed Penuel and he was limping on his hip.
33. Therefore the Children of Israel are not to eat the displaced
sinew on the ball of the thighbone to this day, because he
struck the ball of Jacob's thighbone on the displaced sinew. [1]

The Bible itself does not provide the readers with any details regarding the actual injury that Jacob suffered, only that his thigh was hurt and that he subsequently suffered from a limp. The Biblical commentators provide a variety of opinions, albeit, conflicting at times, to explain the nature of Jacob's injury. More recently, Dr L.J. Hoenig, a physician, reexamined Jacob's injury in light of current medical knowledge. He provides suggestions as to the possible modes of injury and the accompanying neurological and musculoskeletal damage [2].

Biblical commentators offer several different possibilities as to how the injury itself was inflicted upon Jacob. In the language of the Bible, the angel's contact with Jacob's thigh is indicated by the word *"vayigah"*, "and he touched." Very often, when commentators are unsure of the precise translation of a Biblical word in a specific context, it is deciphered by looking for other instances using the same word. With this technique, Rabbi Samson Raphael Hirsch, a 19th-century commentator, noted that *"vayigah"* generally conveys an improper touching or a violent gripping [3]. He explained that the angel gripped Jacob's hip-joint and when Jacob resisted, the muscle was torn from its ligaments, disabling the use of his leg and causing him to limp [3]. On his commentary on the Talmud tractate, Chullin (91a), Rashi suggested that the angel, standing behind Jacob, repeatedly hit him in the buttocks area until he was injured. However, Rabbi Bahya ben Asher, a 14th-century commentator, suggested the injury was inflicted by a blow close to Jacob's genitalia [4].

Rabbi Moses ben Maimon (Maimonides), a 12th-century commentator and physician, took a very different approach. He suggested that the injury was not inflicted through physical means, but rather, Jacob prophetically envisioned this battle with the angel [5]. Isaac Abravanel, a 15th-century commentator, maintained that although the battle did not physically occur, Jacob did sustain a real injury [6]. He postulated that Jacob may have suffered from a musculoskeletal hip injury due to a sudden, intense bodily reaction to a terrifying prophetic vision [6]. It is interesting to note that in accordance with Maimonides' supernatural approach, Bereishit Rabbah, a 3rd-century exegesis on the Bible, suggested that when *"the sun rose for him,"* it was to heal his limp; "it was a miraculous healing"[1]. Isaac Abravanel held that initially Jacob was unable to move and he subsequently developed a limp as he recovered [6].

Within Bereishit Rabbah there are several different positions as to what kind of damage Jacob actually sustained, based on their interpretations of the word *"vataykah,"* "strained." According to Rabbi Berekiah and Rabbi Eleazar, Jacob's hip was "flattened" by the angel, suggesting some sort of anatomical distortion to the area [7]. Rav Assi translated "strained" to mean "split" open "like a fish," suggesting that Jacob suffered from some sort of laceration, or open wound [7]. Rav Nahman believed that Jacob's hip was dislocated.

A possible diagnosis for Jacob's injury may be a femoral neck fracture, which is a break right below the hip joint [8]. This would explain why Jacob suffered from a limp after the incident. The first position in Bereishit Rabbah, suggesting that Jacob's hip was "flattened," might refer an impaction of the femoral neck.

Aside from the musculoskeletal damage inflicted by the fight, Jacob also appears to have suffered from a peripheral nerve injury. The Talmud in Chullin indicates that the site of Jacob's injury was at the *"gid hanashe,"* the "sinew of the thigh bone," which, according to Jewish tradition, is the sciatic nerve. It is called the *"gid hanashe"* because it popped out of its place and moved upward (*nasha,* literally, jumped) [1].

The biblical text does not confirm for a fact that it was the sciatic nerve that was injured, but Hoenig believes that the nature of the injury, based on Rashi in Chullin, would lead to that conclusion [2]. When a peripheral nerve is damaged, there may be interference between the brain and the area that the nerve serves. This could result in an inability to move certain muscles or to feel normal sensations [9]. The sciatic nerve has control over the muscles of the back of the knee and lower leg and provides sensation to the back of the thigh, part of the lower leg, and the sole of the foot [10]. Because peripheral nerves are so easily dam-

aged [9], if Jacob was in fact hit from behind in the buttocks area, causing a posterior hip dislocation like Rav Nahman bar Jacob suggested, it is very likely that his sciatic nerve was injured and that he was left immobilized or limping [2]. Hoenig also suggests that Jacob may have suffered from a limited neurapraxia of the sciatic nerve, indicated when a nerve temporarily fails to conduct properly [11], because as noted by Bereishit Rabbah, Jacob later regained complete usage of his hip.

Hoenig postulates other possible neurological injuries sustained by Jacob, such as radicular low back pain, in which the injured person has deep, steady pain in the area of his leg serviced by the injured nerve, which can be accompanied by numbness, tingling, and muscle weakness. This pain radiates from the thigh through the leg and is most commonly associated with pain radiating down the sciatic nerve, known as sciatica [12]. This pathology can be caused by a herniated, or a displaced, lumbar disc and meralgia paresthetica, numbness in the upper thigh area [13]. Meralgia paresthetica could have been evoked by the blow to Jacob's hip area, and the lumbar disc hernia would explain his temporary limp [2]. The Talmud in Chullin however seems to support a direct injury to the sciatic nerve, as opposed to meralgia paresthetica [2].

Hoenig also offers several possible soft tissue injuries which can be applied to explain the damage to Jacob's hip. According to Rav Hirsch's explanation, a muscle sprain or rupture would seem likely, though piriformis syndrome could explain Jacob's pain and limp [2]. Piriformis syndrome is the condition in which the piriformis muscle irritates the sciatic nerve, causing the injured person to suffer from sciatica [8].

As readers, we are constantly learning lessons and internalizing morals set out by the Bible. However it is through the biblical commentaries and their concurrence with modern science that we are able to better understand the experiences of our forefathers, allowing us to further relate those experiences to our own lives.

Acknowledgements:
I would like to extend my endless gratitude to my parents for giving me the opportunity to further my education at Stern College for Women and for encouraging and supporting me in all of my endeavors. I would also like to thank Dr. H. Babich for reviewing this article and for his constant guidance throughout my years in Stern.

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Science and Ethics: A Joint Perspective

The underlying theme of this journal is the integration of Torah, science, and bioethics. The goal is to demonstrate how Judaism effectively and eloquently addresses difficult ethical issues raised by the surging advances in the biomedical sciences. The articles, written and edited by the students of Stern College for Women, attempt to analyze these bioethical issues from both Torah and classical bioethics perspectives. At times, views of other major religions are presented as well. Comparisons and contrasts between the Torah's views and those of classical bioethics, and other religions, are essential components of the journal. Issues relating to genetics technology, organ donation, assisted reproductive technology, end-of-life care and other real life clinical challenges are discussed. The first volume was published in the Spring of 2006.

Volume 1 (Spring, 2006)

Gender Selection

Chava Fischer

While it may seem to be a recent technological development, the concept of choosing the sex of one's child, rather than leaving it purely up to chance, dates back to ancient times. The Talmud discusses various permissible methods that can increase the chances of having a child of one particular sex. These include timing of intercourse, practices during intercourse and special diets (Babylonian Talmud, Tactate *Niddah* 25b, 28a, 31a, 31b, Tractate Gittin 57a).

Modern science and technology have since come up with more scientific methods of gender selection. However, along with the introduction of new methods come new ethical dilemmas. This article will attempt to address the different forms of gender selection that are available, the reasons people seek to implement these procedures and the many ethical consequences, both from the secular and Jewish viewpoints, that arise in the process.

There are now a few scientific ways to perform sex selection. Firstly, an ultrasound or other forms of prenatal diagnosis may be performed on a fetus *in utero* to determine the baby's sex and subsequently, the fetus may be aborted if it is not of the desired gender. A second method of gender selection that is available is pre-implantation genetic diagnosis, more commonly known as PGD. This technique involves creating embryos in a laboratory setting through in-vitro fertilization (IVF) and selecting the embryos of a chosen sex to be implanted into the uterus. The third and newest means by which gender selection may be performed is by sperm selection.[1] While there are a number of ways to carry out sperm selection, one popular method is called "MicroSort." This technique was originally used for reproduction in livestock but a number of years ago the Genetics and IVF Institute, whose main offices and laboratories are located in Fairfax, Virginia, modified this process for humans. MicroSort relies on the fact that gymnosperm, or sperm bearing X chromosomes, contains 2.8 percent more DNA angiosperm, or sperm bearing Y chromosomes. The entire sample of sperm is treated with a fluorescent dye and a laser light is then shined onto the specimen. Since the DNA is what activates the dye and gymnosperm contains more DNA, scientists are then able to separate the two forms of sperm based on the amount of dye that they have activated. The sperm that produces the child of the desired sex can then be used to fertilize eggs and embryos can be implanted in the uterus.

It is universally agreed that performing sex selection through the employment of infanticide, or killing of babies who are not of a desired sex, is ethically wrong.[2] However much controversy exists regarding whether there are other stages of reproduction at which gender selection would be morally sound. Abortion has been a widely debated bioethical issue ever since Roe vs. Wade in 1973. In addition, while most can see a clear difference between aborting a fetus and discarding unwanted sperm, the distinction between preconception sperm sorting and post-conception PGD is more subtle and is surrounded by much debate.

Nevertheless, before the ethical grounds for gender selection technique can be evaluated, one must understand the various reasons a couple would decide to undergo this process and consider such reasons when deducing its ethical ramifications. One incentive for parents to resort to the methods of sex selection would

be in order to prevent the chances of having offspring with severe genetic disorders. There are hundreds of X-linked genetic diseases, such as hemophilia and a variety of forms of muscular dystrophy. The probability of a male fetus inheriting the disease is higher than that of a female fetus due to the fact that males only have one X chromosome. Sex selection enables modern society to assure that couples who are carriers of X linked genetic diseases have female children and eliminate the chances of giving birth to males with the genetic disorder.[3]

Aside from medical reasons such as the prevention of genetic diseases, other advantages of sex selection include religious, social and cultural considerations. In many countries, such as India and China, male children are preferred either for economic reasons or for the purpose of carrying on the family name. In addition, population growth in China is so explosive that in 1979 the country instituted a one-child policy.[4] Daughters are viewed as economic burdens because they cannot perform the same amount of physical labor as men and because they require dowries. Consequently, couples in these countries may look to sex selection to assure them the birth of a son. Studies show that due to widespread sex selection in these countries, major gender imbalances have occurred and between sixty and one hundred million women are "missing" from the world today.[3]

Family balancing is one more motivation for parents to rely on the techniques of sex selection. For instance, if a couple already has four sons and they would like a daughter, sex selection would seem like a good option to guarantee that their next child will in fact be a girl.[5]

Thus in debating the issue of sex selection, the various reasoning and techniques are important in deciding when and what sort of sex selection is ethical. While some ethicists may not see a difference in any of the cases, many do deem certain situations of sex selection permissible based on the motivations and method under which the procedure is performed.

There are a number of ethical arguments in favor of sex selection. Firstly, a child of the "correct" sex may benefit from a higher quality of life in a situation where parents prefer one gender over the other. In addition, mothers may also achieve superior quality of life due to sex selection since they will not have to undergo many pregnancies and births to bear the child or children of the sex they desire. Sex selection may even prevent husbands from abusing their wives for not conceiving children of a certain gender.[3] Tangentially, it is ludicrous for a man to criticize a woman for bearing the wrong gender child considering the fact that it is ultimately the father's genetic contribution that decides the baby's sex. Finally, many argue that a benefit of gender selection may be a lower population, an advantage for countries where high birth rates are causing economic and social distress. Thus assuming that people have preconceived wishes about the genders of their children, if people could program the genders of their children before they are born, they will not just reproduce by trial and error until they give birth to the children of the genders they desire.[3]

While there are many benefits that sex selection can potentially provide, these techniques also carry many dangers and disadvantages. Ethicists claim that sex selection only reinforces the idea of gender inequality by blatantly preferring one sex to the other. American society is constantly working to eradicate sex discrimination in all aspects of life and by allowing gender selection techniques to run rampant, we would be strengthening sexist mentalities. Secondly, many bioethicists criticize sex selection by claiming that it is wrong to use medical procedures that are meant to prevent the continuation of genetic diseases for purposes as mundane as the satisfaction of parents' gender preferences.[3] In addition, there is the fear that if parents feel that they can program the sex of their children, they may start manipulating other kinds of traits to their liking and reproduction will be a made-to-order concept.[5]

When faced with the question of whether or not one would support the idea of sex selection, many people indignantly answer that they feel it is their right to make decisions regarding their own procreation and family structure. At least, they claim, the option should be available.[1] However, this self-seeking mentality is not entirely an accurate representation of the issue at hand. Sex selection may in fact lead to gender imbalances, having negative effects on all of society. A higher percentage of males brings higher crime rates, increased prostitution, and numerous other negative externalities. Thus while parents may feel they have a right to make choices for their own family, the decision to undergo gender selection does affect others and societal benefit must be considered as well.[6]

In 1996, the American College of Obstetricians and Gynecology (ACOG) criticized the use of sex selection for non-medical purposes because it involves amoral actions including the killing of embryos, abortion, and prejudice. However, ACOG did agree that there may be room for exception in certain isolated cases.[6]

The American Society for Reproductive Medicine (ASMR) reached the conclusion that sex selection for medical purposes is ethical. However, the society raised many moral issues regarding PGD and sperm sorting as a means of gender selection for non-medical purposes such as gender biases and imbalances, as well as the misuse of medical procedures. Nevertheless, in 2001, the ASMR loosened its suspicions of sperm sorting and PGD even for purposes as mundane as family balancing. Since 2001, however, the ASMR has once again changed its mind stating that while sperm sorting may be an ethical way of performing sex selection, PGD involves discarding of embryos and thus presents more concern from an ethical perspective.[6]

The United Kingdom has banned sex selection for non-medically related purposes.[5] While no legislation has been passed in the United States, the President's Council on Bioethics has discussed the issue on a number of occasions. The committee has agreed that sex selection for the purpose of preventing genetic diseases is morally sound. However, in 1983 this group discussed choosing gender for preference and agreed that sex selection by amniocentesis is "morally suspect" as such techniques may encourage sex discrimination, conditional love of children by parents, and the desire to design other traits in descendants. Nevertheless, because there are cases that demand sex selection, the council decided against public policy restricting these techniques. This discussion recently resurfaced amongst the president's council and yet again the arguments for and against sex selection were merely discussed and no decisive legal action was taken.[6]

Thus it is apparent that as yet no clear or uniform policy exists among bioethicists as to what conditions and forms of sex selection are considered ethical. Similarly, there is much controversy about this concept in the field of Jewish bioethics as well. A range of rabbinic authorities present varying views regarding what practices may be acceptable in different cases when it comes to gender selection. However, these discussions merely revolve around the methods of PGD and sperm selection, since according to all *halachic* (Jewish legal) authorities, aborting a fetus merely because of gender preference is prohibited without a doubt.[7]

A number of issues arise within Judaism when the question is posed about the ethical ramifications of choosing gender. Firstly, the first commandment in the Bible is that of *p'ru ur'vu* (be fruitful and multiply). The Mishnah in Yevamot (6:6) cites a dispute between Hillel and Shammai regarding what this commandment constitutes. Hillel explains that the requirement is to bear one male child and one female child, while Shammai argues that the obligation is to bear two males. Practically the opinion of Hillel is followed, as is the general rule. Consequently, would it be permissible for couples to seek the aid of sex selection in order to fulfill the commandment of *p'ru ur'vu*? Furthermore, would it be required for Jewish couples to actively pursue and exhaust all possible methods in order to discharge this obligation?

Rabbi Moshe Feinstein clarifies that the commandment of *p'ru ur'vu* is not goal oriented but rather process oriented. A man is required to do his part and attempt to have children by getting married and having intercourse. The obligation of having one boy and one girl is merely the point at which a man has dispelled his biblical requirement. In this case, it is the effort that counts. The final results, whether a couple actually gives birth to a child of each sex, is up to G-d and is not within the realm of man's control. Consequently there would be no reason to employ PGD or MicroSort to fulfill the requirement of *p'ru ur'vu*.[8]

However, other rabbinic authorities hold that *p'ru ur'vu* is only fulfilled by obtaining results, by having a boy and a girl. Nevertheless, Rabbi Shlomo Zalman Auerbach explains that one does not have to go out of his way financially or cause himself physical pain in order to fulfill this commandment, as would be the case with methods such as gender selection.[8]

Rabbi Moshe Tendler, a well-known rabbinic authority, author and bioethicist, explains that sex selection done for the sake of *p'ru ur'vu* may in fact be counterproductive. People may utilize gender selection to produce one boy and one girl and subsequently cease to procreate because they feel that they have fulfilled their religious obligation. Yet, we must keep in mind that two children of different sexes is the minimum amount to fulfill the commandment. A drop in birthrate seems to be the opposite of what G-d had in mind when He commanded us to "be fruitful and multiply."[9]

Another *halachic* question in reference to sex selection is the issue of *hashchatat zerah*, the destruction or waste of sperm. Rabbi J. David Bleich states that many forms of fertility treatment potentially utilize all sperm, either in actuality or as backups, and therefore this does not constitute *hashchatat zerah*.[10] However, when performing sex selection, half the sperm is useless from the start. Thus it would seem that the prohibition of destroying reproductive material applies in this case.[8]

In his commentary *Nishmat Avraham* on the *Shulchan Aruch* (Code of Jewish Law), Dr. Abraham S. Abraham quotes the opinion of Rabbi Shlomo Zalman Aurbach, a foremost rabbinic authority. Rabbi Aurbach discussed a case where a couple that has already fulfilled its obligation of procreation but wants to continue to have children either to fulfill the commandment of *shevet* (to populate the earth) or because the wife is psychologically troubled by the fact that they do not have more children. In this case, the couple would be allowed to submit sperm counts to aid in their continued procreation. Although sperm counts result in the physical wasting of reproductive material, Rabbi Aurbach explains that since it is for an honorable cause it is not under the category of *hashchatat zerah*. Dr. Abraham

then asked Rabbi Aurbach whether sex selection would be in the same category as sperm counts and artificial insemination since all of them involve discarding of sperm? Rabbi Aurbach answered that the problem with sex selection is not *hashchatat zerah*. Rather, he quotes a passage from the Babylonian Talmud, Tractate *Berachot* (10) that cites a conversation between King Hezekiah and the prophet Isaiah. Hezekiah proclaims that he does not want to have any children because he saw in the future that the evil Manasseh will come from him. Isaiah answers that man cannot get involved in G-d's plans and he must still fulfill the commandment of procreation. Thus, Rabbi Shlomo Zalman Auerbach concludes that the problem with sperm selection is that man is not supposed to "play G-d" and get involved in aspects such as the gender of a child. However, Rabbi Auerbach states, there is room for exception when a couple is a carrier for a sex-linked genetic disease and through gender selection they may prevent the birth an affected child.[11]

There is also a *halachic* concept of not causing oneself undue pain or risk. Rabbi Moshe Feinstein holds that unlikle fertility treatment where the pain is for a medical purpose and therefore allowed, undergoing sex selection to serve one's personal preferences may not be permitted halachically. In addition, Rabbi Feinstein writes in *Iggerot Moshe (Orach Chaim* 3:90) that while intervening with the reproductive process for medical reasons is acceptable, it may be *halachically* problematic to use medical procedures for non-medical purposes.[8]

Thus, Rabbi Joshua Flug concludes in his comprehensive article on the topic of gender selection that since each case is different, there cannot be an overriding *halachic* ruling. Judaism maintains the advantage of reliance on halachic authorities and thus allows for each case to be evaluated individually and for appropriate action to follow.[8]

In 1902, John Beard of the University of Jena proclaimed, "Any interference with or alteration of the determination of sex is absolutely beyond human power."[6] Modern science and technology has proven Beard wrong and these advances have greatly improved medicine and fertility treatment. However, misuse and perversion of science can sometimes have devastating effects on society's values and cause difficulties for future generations. Perhaps if society would once again view children as gifts rather than made-to-order objects, many of the negative externalities that accompany these miraculous treatments would cease to exist.

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