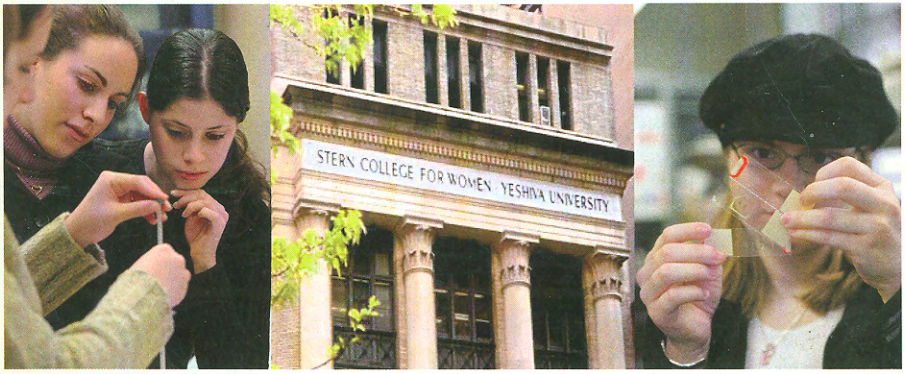
Stern College for Women
Yeshiva University

2004-2005
2003-2004
2002-2003

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 to 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 are 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 involving them 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. The faculty actively encourages science majors to apply for competitive undergraduate research internships, both nationally and in Israel. In the summer of 2005, at least 40 SCW students were involved in research, either at SCW, AECOM (see "Roth Scholars"), or at external research facilities, including the Mount Sinai School of Medicine, the University of California (San Francisco), Washington University School of Medicine (St. Louis, MO), The Children's Hospital (Boston), Brookhaven National Laboratory, and Vitra Bioscience Inc. (Mountain View, CA), as well as in Israel through internships sponsored by Yavneh Olami. (See the "Abstract Booklets of Student Research" section for a descriptive analysis of the various projects 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 Pre-Med 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 data 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.

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 2005, Malka Krupka, Helen Nissim, Reina Roth, and Sarah Nemzer attended the 229th National Meeting of the ACS, held in San Diego, CA. (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. (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 the *Derech HaTeva* section for a listing of articles that have appeared in volumes 1 through 9).

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

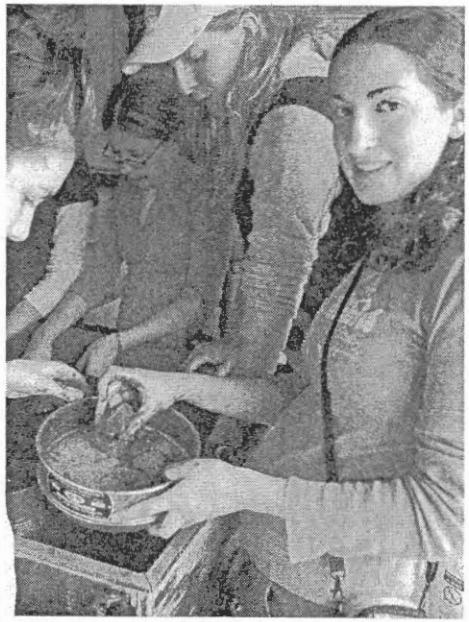
Faculty: Harvey Babich, Ph.D.; Bill Bassman, M.S.; Joseph DeSantis, Ph.D.; Emil Gernert, Ph.D.; Brenda Loewy, Ph.D.; Jeffrey Mollin, M.S.; Esther Prero M.S.; Nicole Schreiber-Agus, Ph.D.; Jeffrey Weisburg, Ph.D.; Richard Weiss, Ph.D.; Harriet Zuckerbraun, Ph.D.

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. Thus for example, the offerings span the gamut from Ecology, Genetics, Immunology, Microbiology and Physiology, to courses in Neuroendocrinolgy, Forensics and the Epidemiology of Bioterrorism.

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 and the Albert Einstein College of Medicine), have included the following semester-long topics: Stem Cell Research; Cancer Research; Apoptosis; and Mouse Models of Cancer. The analytical proficiency fostered by these journal clubs promotes success on those aptitude tests required for entrance into professional and graduate schools.

During early June of 2004, eleven 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 from boats, mud flats, and rocky shores and original behavioral research within a modern wet-lab facility. Students spend Shabbat in nearby Portland as guests of the Jewish community. This unique course will be offered again during the Summer of 2006.

Students look through mud flats for specimens.



Sarah Weinerman sifts through the debris for specimens.

The group on the boat.

Various members of the Department provide openings for students to participate in their research activities. For example, Dr. Weisburg, who studies cancer cells that are resistant to chemotherapeutics, and Drs. Babich and Zuckerbraun, who study the differential sensitivities between malignant and normal cells to green and black teas, have all had students as part of their research teams. Opportunities for off-campus research abound including the Roth Scholars Program at AECOM during the summer. See "Abstract Booklets of Student Research" and "Student Publications" for additional details.

The Department hosts a spectrum of interesting seminars. Past programs have included a panel discussion on hereditary breast cancer in the Jewish community featuring Dr. Kenneth Offit, Director of Clinical Genetics at the Memorial Sloan-Kettering Cancer Center, Dr. Jessica Israel, a carrier of the BRCA2 breast cancer gene, and Rabbi Dr. Richard Weiss, who discussed the ethical and halachic issues involved in such personal dilemmas; presentations by Rabbi Nosson Slifkin (affectionately known as the "Zoo Rabbi" of the Biblical Zoo in Jerusalem) on, "Zoo Torah - Jewish Perspectives on the Animal Kingdom" and "Untangling Evolution;" and Dr. Natan Aviezer, Department of Physics, Bar-Ilan University, lecturing on "Evolution, Darwin, Dinosaurs, and the Torah." Dr. Aviezer is scheduled to speak again in December, 2005 on the topic, "Contradictions between Torah and Science: the Creation of the Universe."

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. Past programs have included a discussion of balancing a medical career with family obligations; a seminar hosted by SCW doctoral candidates in graduate programs in the biomedical sciences; a presentation by the Associate Provost of the SUNY School of Public Health describing the variety of career options in the field of public health; and a seminar by Dr. Robert Shorr, Director of the Business Development Center for Biotechnology at Stonybrook, advising how an Orthodox Jewish scientist can successfully climb the ladder of corporate success.

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 inaugural year, the Biology Department provided a hands-on laboratory course in genetics and molecular biology. The students worked with bacteria, bacteriophage, yeast, fruit flies, and plants and human cells and employed a variety of sophisticated techniques including DNA extraction, digestion of DNA by restriction endonucleases, DNA agarose gel electrophoresis, and polymerase chain reaction (PCR). 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.

Department of Chemistry

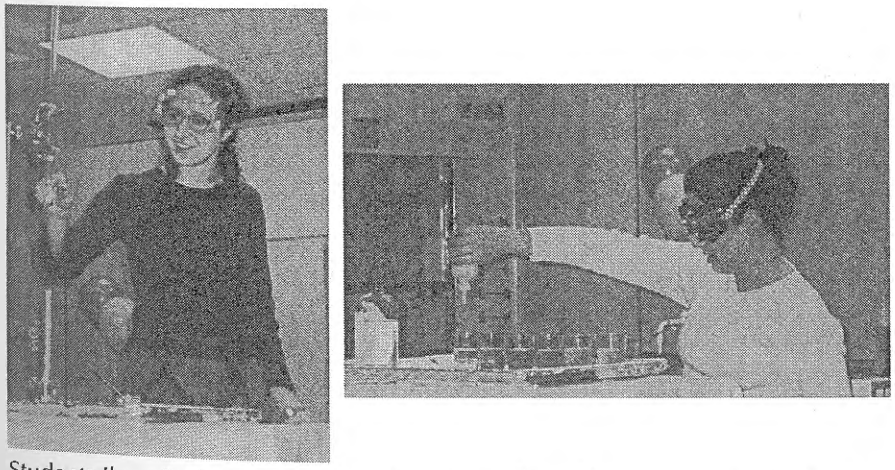
Faculty: Lea Blau, Ph.D.; Cecily Dobin, M.S.; Donald Estes, Ph.D.; Chaya Rapp, Ph.D.; Lance Silverman, Ph.D.

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.

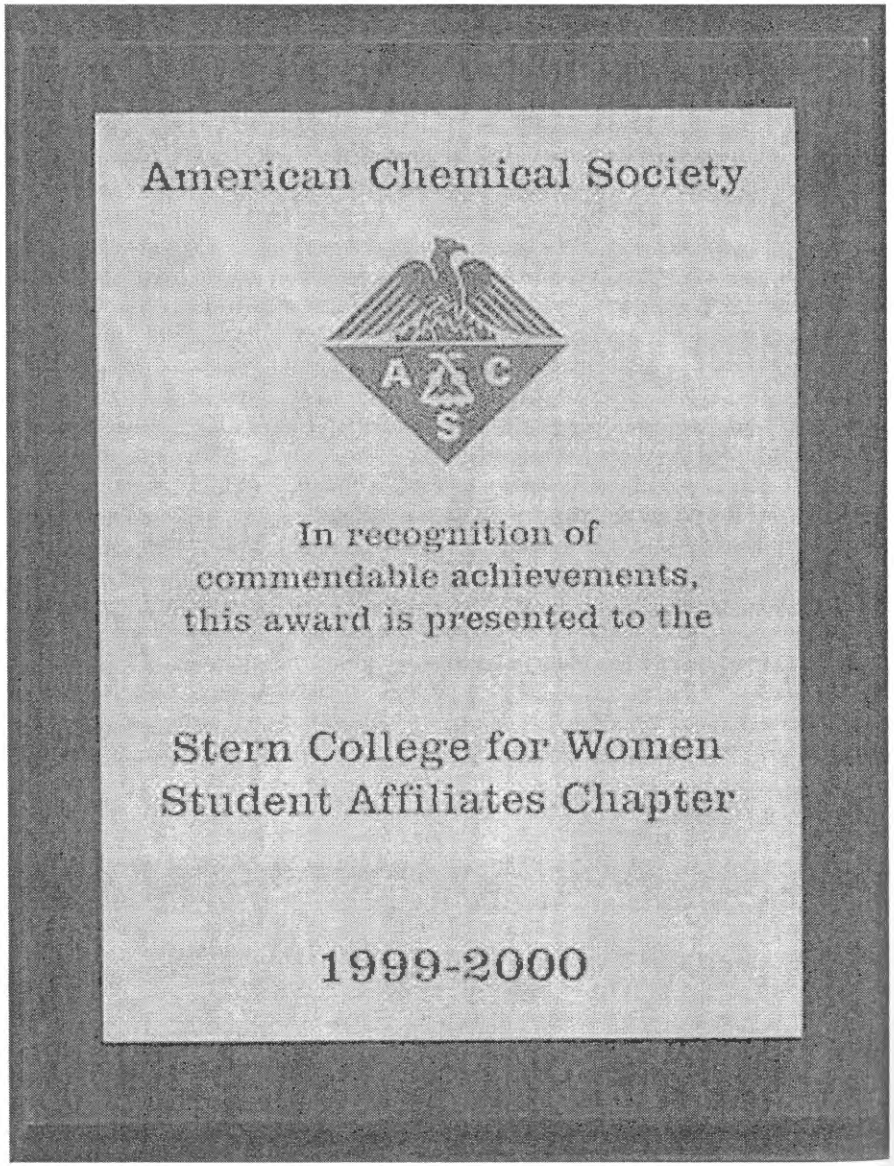
Off campus, summer research student (2005) Elisheva Levine has contributed to a manuscript on implicit solvent treatment of electrostatic forces, being prepared in collaboration with researchers at the University of California, San Francisco. Dinah Zaghi spent summer 2005 at the University of California's Department of Pharmaceutical Chemistry as part of an ongoing joint project between Dr. Matt Jacobson (of UCSF) and Dr. Chaya Rapp. Pesia Solovetchik has begun working with Dr. Shelly Rackovsky at the Department of Pharmacology and Biological Chemistry of the Mount Sinai School of Medicine, as part of a recently initiated collaboration.

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 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.



Students Ilana Sedletscaia (L) and Rebecca Eisenberg (R) perform in the magic show.

Recently, students have expressed greater interest in chemistry as it pertains to the life sciences. To meet the needs of these students, the Biology and Chemistry Departments collaborated on the initiation of the Biochemistry major. Since its inception interest in this area has grown impressively, with one major graduating in 2001, two in 2002, and seven in 2004. Graduates have gone on to medical and optometry school as well as graduate programs.



An award presented to Stern College from the American Chemical Society.

Department of Physics

Faculty: Dennis Engel, Ph.D.; Anatoly Frenkel, Ph.D.

The Physics Department at Stern College for Women has been steadily gaining interest among incoming freshmen due to its emphasis on a "Research and discovery approach" to education. During fall 2005 over 40 students were enrolled in the two introductory courses in the department. Although most physics students continued to be interested in careers in medicine and allied health fields, a growing number of talented women aspire towards physics professions, as well. The department has stimulated much of this interest by providing students with access to state of the art experimental facilities in the Brookhaven National Laboratories and other major research centers. Starting with the academic year 2005-2006, a new B.A. physics program is being offered to incoming freshmen.

One of the unique aspects of the department is its strong ties with the Materials Research Science and Engineering Center (MRSEC) at SUNY (Stony Brook) funded by National Science Foundation. NSF MRSEC is a regional center that, led by its director, Professor Miriam Rafailovich, attracts undergraduate students and high school students from the tri-state area and beyond. The Center offers summer programs where students, guided by faculty mentors and visiting scientists, work on individual research projects of their choice. In Summer 2003, the NSF MRSEC was a location for part of a new honors course created by Yeshiva College and SCW physics professors Frenkel, Cwilich and Zypman, where students studied modern physics at Brookhaven National Laboratory on Long Island.

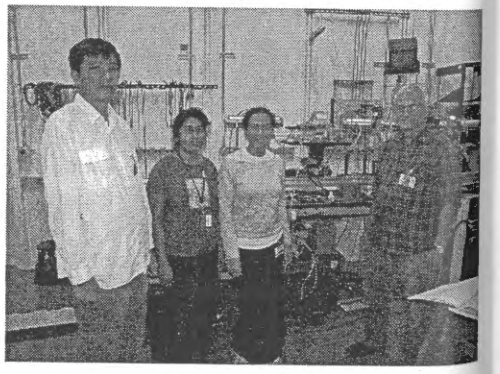
Stern's Nanoscience Research Group at MRSEC in Summer 2004. From left to right: Prof. M. Rafailovich (SUNY), Prof. A. Frenkel, I. Pister, L. Soussan, S. Nemzer, T. Harris (SCW).

After two years of collaboration in science and education, Yeshiva University and Stony Brook University signed an Articulation Agreement for a new program that the two departments, the SCW Physics Department and SUNY's Materials Science and Engineering Department, jointly developed. This program is a Joint Program in Engineering that will allow YU undergraduates to spend three years at YU and two years at SUNY and graduate with two degrees: a B.A. from YU and a B.E. from SUNY.

After visiting SUNY labs and studying the state-of-the-art nanoparticle synthesis methods, SCW students and Dr. Frenkel started their own Nanoparticle Factory at Stern College, where they synthesize ligand-protected, gold and palladium nanoparticles to study their unique properties. More information about our group research is on the Stern Physics Department web: www.yu.edu/stern/physics (follow the link to Student Research).

Frenkel Research Group at Stern College's chemistry lab. From left to right: S. Nemzer, L.Soussan, D. Glasner, Dr. Frenkel and I. Pister.

Faculty and students at Stern College for Women perform multiple trips to Brookhaven National Laboratory's National Synchrotron Light Source throughout the year. For some projects, competitive research can be done at the world's best synchrotron sources, such as Argonne National Laboratory's Advanced Photon Source. Faculty trips are supported by research grants. Student trips are generously supported by the office of the Vice President for Academic Affairs. New research grants that have been recently awarded to Dr. Frenkel by the Department of Energy allow him to hire up to six students for summer internships to do cutting-edge research in the fields of condensed matter physics, nanoscience, catalysis, biophysics, and in the cross-disciplinary fields. Dr. Frenkel and his students and associates conduct research in the fields of nanoparticle synthesis and characterization by synchrotron techniques (Funded by Department of Energy), and Studies of Metal-to-Insulator Transition in Chromium-Doped Vanadium Oxides (Department of Energy).



SCW Students at National Laboratories. Left: S. Nemzer and L. Soussan at Brookhaven's National Laboratory's National Synchrotron Light Source. Right: N. Abitbol (second from right) at Argonne National Laboratory's Advanced Photon Source.

SCW physics students were active in research in summers and throughout the year. They presented their results at highly visible national and international meetings and gave seminar talks. Many students gave oral presentations at the regular sessions of the science societies. (See "Student Publications.")

Stern College for Women Combined Degree Program

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 two combined plans in Engineering with Columbia University. Under the 3-2 Plan, the student attends SCW for 3 years, takes the prescribed coursework and, with recommendation of the Pre-Engineering advisor, may be admitted to Columbia University School of Engineering and Applied Science. After successful completion of the 2-year program at Columbia, SCW awards the B.A. and Columbia awards the B.S.

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

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, 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 University
2	November 4, 1992	Jerold Meinwald	The Chemistry of Everyday Insect Life	Cornell University
3	December 7, 1993	Elias J. Corey*	Molecular Robots, Small Molecules az Enzyme-Like Catalysts	Harvard University
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 University
8	October 28, 1998	Dudley Herschbach*	The Impossible Takes a Little Longer	Harvard University
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	University of Arkansas
12	October 29, 2002	Mario Molina*	The Antarctic Ozone Hole	MIT
13	November 12, 2003	Ronald Breslow	The Chemistry-Biology Interface	Columbia University
14	October 11, 2004	Jacqueline K. Barton	DNA Charge Transport: Chemistry and Biology	California Institute of Technology
15	December 13, 2005	Martha Greenblatt	The Beauty and Fascination of Solids	Rutgers University

* Nobel Laureates

Mary Good, the 2001 Kukin lecturer, talks to students before her seminar.

Ronald Breslow, the 2003 Kukin lecturer, with students during the reception.

Ronald Breslow, the 2003 Kukin lecturer, with students during the reception.

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. As our students learn and develop state-of-the-art laboratory skills and techniques in our college's science courses, the SCW track record for placing students in prestigious external research laboratory facilities is most impressive.

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:

(a) 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)

(b) 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

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

Academic Year, 2002-2003; Summer, 2003
Graduating Seniors

Discipline	Number of students entered	Professional/Graduate Schools
Medicine	10	AECOM; NYU Sackler; SUNY Downstate; NYU; Univ. of Laval
Dentistry	6	UMDNJ; NYU
Optometry	1	SUNY
Podiatry	1	NY College of Podiatry
Ph.D. Programs	5	Sue Golding, AECOM; Univ. of Miami
M.S. programs	4	NYU (Computers in Biol. Res.); Columbia Univ. (Biotechnology); Weizmann Inst.
Genetic Counseling	2	Mt. Sinai College of Medicine; Univ. of Maryland
Occupational Therapy	12	Columbia Univ.; SUNY Downstate; Univ, of Chicago
Physical Therapy	3	Columbia Univ.; Hunter College; Touro College
Nursing	8	Columbia Univ.; NYU; Fairleigh Dickinson Univ.

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:

Tamar Belsh: Howard Hughes Honors Summer Institute at NYU

Diana Benmurgui: Department of Chemistry, SCW

Nomi Ben-Zvi: Roth Scholar, AECOM

Arielle Berger: Rusk Institute of Rehabilitation Medicine; Neurosurgery

Gizela Braun: Rusk Institute of Rehabilitation Medicine; Rehabilitation Medicine

Elisheva Douglas: Roth Scholar; AECOM
Tamar Epstein: Children's Hospital of Philadelphia; Autism Center

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

Tova Fischer: University Summer Undergraduate Research Scholar; AECOM

Rena Frankel: Sloan-Kettering

Shira Frankel: Washington Group International (in conjunction with: NYC Office of Management and Budget); Shira is a student in our 3+2 engineering program with Columbia University

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

Nelli Fromer: SUNY Downstate

Tova Gavrilova: Montefiore Hospital

Dana Glasner: Department of Physics, SCW

Negin Gohari: Howard Hughes Honors Summer Institute at NYU

Rebecca Goldstein: Rusk Institute of Rehabilitation Medicine; Preschool

Chaya Gopin: Roth Scholar, AECOM

Miriam Kirschenbaum: Rusk Institute of Rehabilitation Medicine; Occupational Therapy

Avital Merl: Department of Physics; SCW

Michelle Neuman: Rusk Institute of Rehabilitation Medicine; Occupational Therapy

Ilanit Newton: Arizona State University Photosynthesis Center; Tempe, AZ

Dina Ohevshalom: Roth Scholar; AECOM

Pegah Rabizadeh: AECOM

Ilana Reinman: Department of Chemistry, SCW

Rachel Rothenberg: Children's Hospital of Philadelphia; Laboratory of Metabolic Diseases, head - Dr. Paige Kaplan.

Aviva Schuman: St. Louis University

Tannaz Sedaghat: Laboratory of *In Vitro* Toxicology, Department of Biology, SCW

Shoshana Simpson: Cornell University

Pesia Soloveichik: Department of Physics; SCW

Deena Weissman: Laboratory of *In Vitro* Toxicology, Department of Biology, SCW

Dikla Wexler: Rusk Institute of Rehabilitation Medicine; Nursing

Lori Zellner: Rusk Institute of Rehabilitation Medicine; Nursing

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 - 2005

Stern College for Women
Yeshiva University

Department of Biology
Department of Chemistry
Department of Physics

Table of Contents

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]

[1]Physics Department, Stern College for Women, Yeshiva University, New York, NY 10016;
[2]Physics Department, University of Connecticut, Storrs, CT 06269

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.

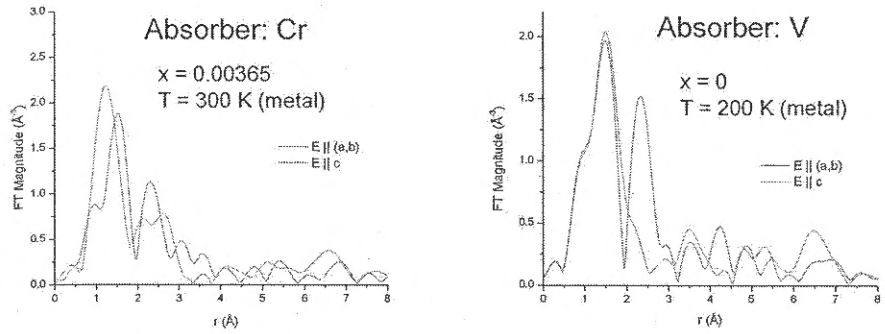


Figure 1: Comparison between the Cr data and V data in metallic phases of single crystals $(Cr_xV_{1-x})_2O_3$ and pure V_2O_3, respectively.

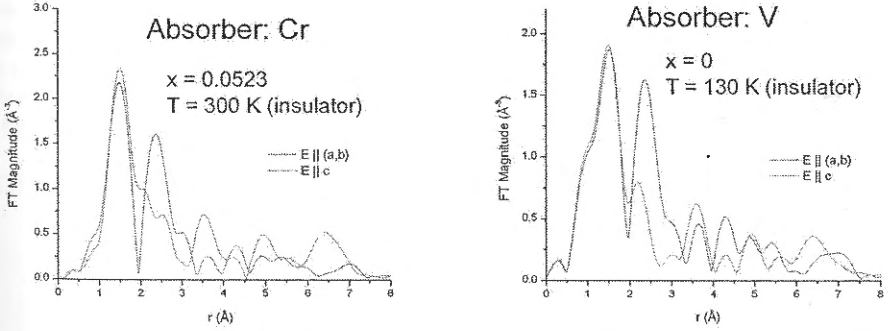


Figure 2: Comparison between the Cr data and V data in the insulating phases of single crystals $(Cr_xV_{1-x})_2O_3$ and pure V_2O_3, respectively.

The DNA Melt: Composition, Sequence, and Thermodynamics

by

Nomi Ben-Zvi, D. Estes, and L. Blau

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

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

Jessica Feig[1], S. Ha[2], R. Ruoff[2], and S. Logan[2]

[1]Stern College for Women, Yeshiva University, New York, NY, 10016;
[2]Department of Urology and Pharmacology, New York University School of Medicine,
New York, NY, 10016

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 overexpressing 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.

NOTE: For consistency in format, when listing the sequence of names on any given abstract, the liberty was taken of citing the SCW undergraduate as first author.

Investigation of Potential Inhibitors for Human Purine Nucleoside Phosphorylase, Bovine Xanthine Oxidase and *E. coli* Thymidine Phosphorylase

by

Frida M. Fridman[1], E.A.T. Ringia[2], and V.L. Schramm[2]

[1]Stern College for Women, Yeshiva University, New York, NY 10016;
[2]Department of Biochemistry, Albert Einstein College of Medicine, Bronx, New York, NY 10461

Characterization of the transition-state structures of enzymes involved in important biochemical pathways allows for the development of powerful inhibitors that may have medical applications. Three medicinally important enzymes involved in nucleoside metabolism: purine nucleoside phosphorylase (PNP), xanthine oxidase (XO) and thymidine phosphorylase (TP) have been interrogated with both transition-state analogue inhibitors and inhibitors based upon other design methods. PNP is recognized to be essential for proliferation of T-cells, thus it is a target for autoimmune disorders and T-cell malignancies. XO is involved in a metabolic pathway whose end product is uric acid, excess of which causes gout, and TP has recently been identified as an important factor in angiogenesis of many solid tumors. Identification of a potent inhibitor for these enzymes may lead to development of effective pharmaceuticals. Inhibitors designed by modeling the active site at the Institute of Molecular and Cellular Biology (France) were assayed against PNP and XO. Transition state analogue inhibitors synthesized by the National Institute of Health and Industrial Research Limited (New Zealand) were assayed against TP. Compounds found to have greater then 20% inhibition at a concentration of 10 mM were further analyzed and enzyme inhibition constants were calculated. Comparison of the inhibition specificity of these compounds leads to a greater comprehension of the mechanism, as well as leading to design and development of more specific inhibitors for the use as therapeutic agents.

NOTE: For consistency in format, when listing the sequence of names on any given abstract, the liberty was taken of citing the SCW undergraduate as first author.

Sequence Analysis of Inversion and Deletion Breakpoints in the Igh Locus of a Plasmacytoma Cell Line: Evidence for Physical Interaction Between the Variable Region and the 3' Regulatory Region

by

Tamar Gold[1], S.A. Volpi[2], R. Hassan[2], and B.K. Birshtein[2]

[1]Stern College for Women, Yeshiva University, New York, NY 10016;
[2]Department of Cell Biology, Albert Einstein College of Medicine, Bronx, NY 10461

The B cell is the only cell to produce antibodies and therefore is an essential part of the immune system. My studies focused on the IgH locus, which codes for the heavy chain of the antibody. This gene includes ~200 variable (Vh) genes, 16 diversity (Dh) genes, and 4 joining (Jh) genes. In addition, there are eight constant region genes, i.e., μ, δ, γ3, γ1, γ2b, γ2a, ε and α.

The Igh locus is unique because it undergoes various DNA rearrangements and modifications that contribute to antibody diversity. These processes, i.e. V-D-J recombination, somatic hypermutation, and class switching, are controlled by cis regulatory sequences. In addition to the intronic enhancer, there is a 3' regulatory region (3'RR), an ~30 kb region lying immediately downstream of the antibody heavy chain gene cluster. The 3'RR contains several enhancers, hs3A, hs1,2, hs3B, and hs4. The 3'RR has been shown to influence class switching and is predicted to regulate heavy chain expression in plasma cells. Hence, the 3' RR must be able to influence promoters, located ~40-200 kb away. The mechanism by which this occurs is unclear and of great interest.

Previous analysis of DNA rearrangements in a mouse myeloma cell line, F5.5, showed physical association between the 3'RR and the VH gene, accompanied by a rearrangement of sequences downstream of Cε. Two sets of primers were designed to PCR the region of the breakpoints. Sequences were analyzed via Blast. The data confirmed our prediction that there was an inversion of the entire IgH gene from the VH region to the 3'RR, accompanied by a deletion of the Cα gene. These results provide a model by which the 3'RR can influence distally located Igh target sequences.

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

by

Michaella S. Goldberg[1], J.P. Gerke[2], and B.A. Cohen[2]

[1]Department of Biology, Stern College for Women, Yeshiva University, New York, NY;
[2]Department of Genetics, Washington University School of Medicine, St. Louis, MO

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

Yonit Gross[1], M. Klotman[2], N. Teleshova[2]

[1]Department of Biology, Stern College for Women, Yeshiva University, New York, NY,
[2]Department of Infectious Disease, Mount Sinai School of Medicine, New York, NY

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

Sarah Guigui, Louisette Soussan, and C. Rapp

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

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

Yelena (Leah) Kozirovsky[1], T. Oren[2], I. Torregroza[2], and T. Evans[2]

[1]Stern College for Women, Yeshiva University, New York, NY 10016;
[2]Department of Developmental and Molecular Biology, Albert Einstein College of Medicine, Bronx, NY 10461

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

Elisheva Levine and C. Rapp

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

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

Eliana T. Muskin[1], N. Pernodent[2], A. Frenkel[1], and M. Rafailovich[2]

[1]Department of Physics, Stern College for Women, Yeshiva University, New York, NY 10016; [2]Department of Material Science, State University of New York, Stony Brook, NY

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.

An Implicit Solvent Study of Phosphorylation in Protein Molecules

by

Elisheva Levine and C. Rapp

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by

Eliana T. Muskin[1], N. Pernodent[2], A. Frenkel[1], and M. Rafailovich[2]

[1]Department of Physics, Stern College for Women, Yeshiva University, New York, NY 10016; [2]Department of Material Science, State University of New York, Stony Brook, NY

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Regulation of Mts1 Binding by Myosin-IIA Heavy Chain Phosphorylation

by

Helen A. Nissim[1], N.G. Dulyaninova[2], and A.R. Bresnick[2]

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Mts1, which is a member of the Ca^{2+}-regulated S100 family of proteins, has been charac terized as a metastasis factor and is thought to regulate the motility and invasiveness of can cer cells. In previous studies, we demonstrated that mts1 specifically binds to nonmuscl 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 no affected by PKC phosphorylation. Rather, phosphorylation on Ser1944 by CK2, which located 20 residues downstream of the mts1 binding site, inhibits mts1 binding and protect against mts1-induced destabilization of myosin-IIA filaments. To examine the regulation o mts1 binding by heavy chain phosphorylation in vivo, we created A, D or E substitutions a 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 hov 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 phospho rylated 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 func tion 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 interfer ing 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 identi fy 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.

NOTE: For consistency in format, when listing the sequence of names on any given abstract, the liberty was taken of citing the SCW undergraduate as first author.

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.

NOTE: For consistency in format, when listing the sequence of names on any given abstract, the liberty was taken of citing the SCW undergraduate as first author.

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

by

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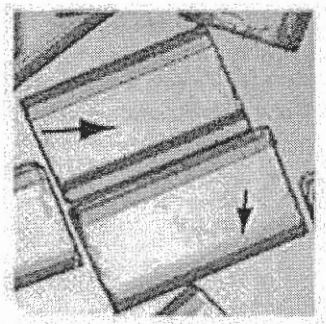
A cell analysis platform, based on encoded microcarriers, enables multiplexed analysis of a diverse range of cellular assays. At the core of this technology are classes of microcarriers that have unique, identifiable codes that are deciphered using CCD-based imaging and subsequent image analysis.



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.

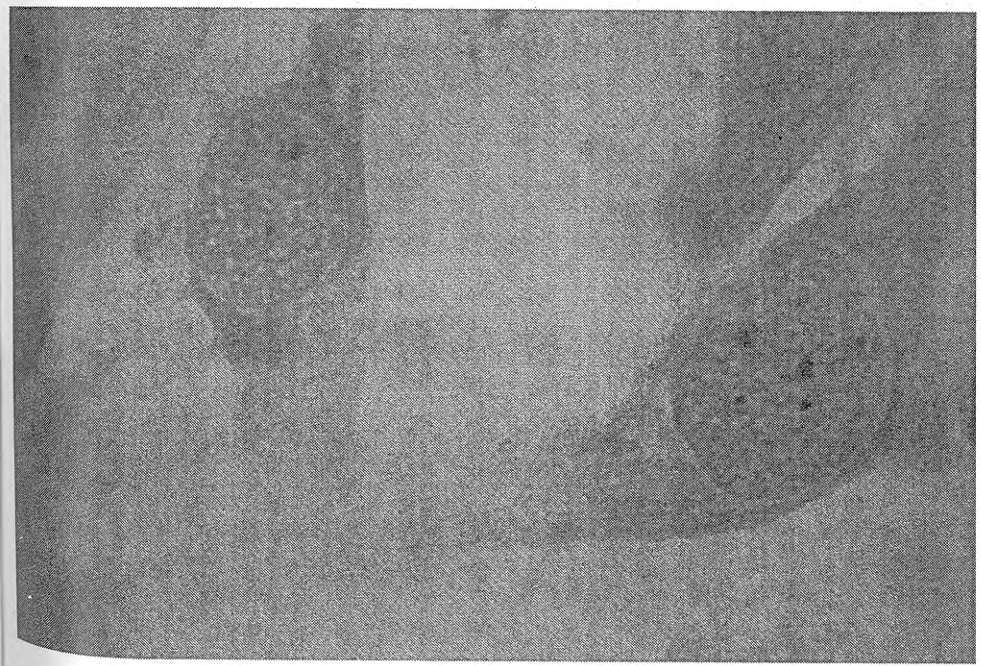

Figure 1. GT1 fibroblasts exposed for 24 hrs to 2.25 μM sanguinarine chloride. Original magnification, 1,000X; Giemsa stain

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.

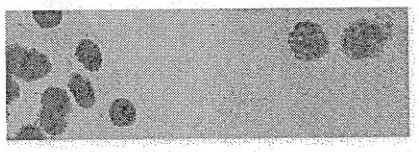


Fig. 1. Hypercondensed nuclei (left) and normal nuclei (right)

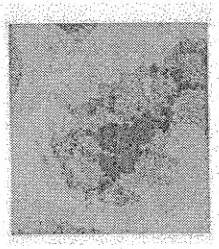


Fig. 2. Sticky chromosomes

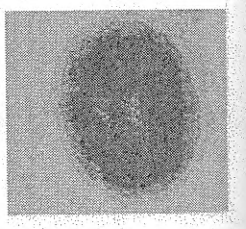
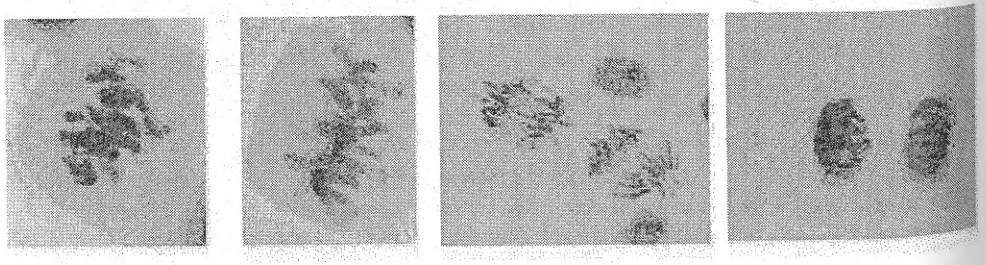


Fig. 3. Enlarged nucleus

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 ctronic, structural and catalytic properties which makes it important for applications such catalysis or hydrogen storage. We investigated the possibility to control the size of the thiol- bilized palladium nanoparticles by just one parameter: the palladium/thiol ratio. We also died the effect of hydrogenation on the thin Pd nanoparticle films made by the Langmuir dgett (LB) technique. While hydrogen incorporation in Pd lattice has been heavily studied, ng nanoparticles for hydrogenation is a relatively new research field. Since nanoparticles ve much more surface and subsurface sites than bulk metals, one expects unique absorp- n properties may be revealed due to the change in absorption caused by the surface-spe- ic and nano-scale effects.

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

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

We then used the Langmuir-Blodgett technique to deposited nanoparticles on Kapton film bstrate. It consists of a trough that needs to be filled with distilled water, and two barriers at compress the film spread over the water. We spread nanoparticles in the trough and per- rmed the pressure-area curve measurement to find the pressure at which the films were lift- d. About 750 layers were stacked together in order to have a sample thick enough for EXAFS. Ve found that the Kapton-supported nanoparticles retained their structure. EXAFS measure- ents were performed on the 1:1 and 3:1 samples before and after their exposure to hydro- en. We obtained that the structure of the hydrogenated samples had enhanced disorder hich 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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[1]Department of Biology, Stern College for Women, Yeshiva University, New York, NY 10016; [2]Department of Cell Biology, Albert Einstein College of Medicine, Bronx, NY 10461

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.

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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

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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 bridgès 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.

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Unfolding and Refolding of the Mini-Protein TC5b in a Confined, Cell-like Environment

by

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The primary structure of a protein and the interaction of its residues with the solvent environment are sufficient for consistent folding of proteins into their native and stable state. However, the folding 'code' that is implicit in the primary structure is not well understood. If the 'code' could be unlocked then it would be possible to design proteins that function in ways that one could control. Protein unfolding and refolding experiments were designed as steps to achieve this goal. The encapsulation of the mini-protein, TC5b, in a silica sol-gel was the system used in these experiments. This mini-protein contains one tryptophan residue, a spectroscopic marker, and is only 20 amino acids long. The tryptophan residue, attached to a single alpha helix, is environmentally sensitive and it is surrounded by a proline helix. Thus, TC5b is an ideal peptide model for protein unfolding studies. As the helices unfold, the spectroscopic signal of tryptophan changes, which allows us to follow the unfolding process. The sol-gel allows for a closer approximation to cellular conditions than solution conditions because it mimics the spatially confined environment within the cell. The sol-gel also slows down the refolding process, allowing the use of conventional spectroscopic techniques to study the process.

Fcγ Receptor Expression on Peripheral Blood Mononuclear Cells in SLE

by

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Fc gamma receptors are widely expressed cell surface receptors that recognize the constant region of IgG. The Fc_R family includes a number of activating receptors and one inhibitory receptor. One of the primary causes of mortality in systemic lupus erythematosus (SLE) is glomerulonephritis caused by the deposition of immune complexes in the kidney. Fcγ receptors have been shown to play a role in the modulation of SLE disease activity, presumably through their role in the removal of immune complexes from the blood. The importance of the Fc_R in murine models has been well established. In NZBxNZW mice, which spontaneously develop lupus-like autoimmune disease, the susceptibility locus *Sle1* has been shown to be syntenic with human chromosome 1q23, which contains the genes encoding Fcγ receptors; the murine FcγR genes are also found within this region. C57BL/6 mice with a deletion of Fc_RIIB spontaneously develop antinuclear antibodies and fatal glomerulonephritis . NZBxNZW lupus-prone mice with a deletion of the FcR γ chain do not develop the severe lupus nephritis associated with the strain, though it has recently been shown that lupus-prone MRL/lpr mice with an FcR _ chain deletion continue to develop glomerulonephritis. In humans, a number of studies have associated polymorphisms in Fc_RIIa, IIb, IIIa, and IIIb with SLE susceptibility or severity.

In the current study we characterized by flow cytometry the expression of Fc_R on peripheral blood mononuclear cells in both SLE patients and in normals. We found that SLE patients differed from normal individuals with respect to both activating and inhibitory receptors. There was a trend to decreased Fc_RIIb on B cells of SLE patients. There was a significant decrease in expression of Fc_RIIa and IIIa on dendritic cells from SLE patients, although there was an increase in the percent of dendritic cells expressing Fc_RIIIa. These changes may reflect important differences in signaling capacity and may be future targets for SLE therapy.

Diallyl Disulfide Upregulates Glutathione S-Transferase and Tumor Suppressor Genes

by

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Diallyl disulfide (DADS), a compound found in garlic, has been reported to have anti-cancer benefits. The disulfide moiety of DADS probably undergoes sulfhydryl exchange reactions with glutathione and cysteine residues of certain proteins, processes that are thought to be important for the induction of glutathione S-transferases (GSTs). GSTs are a class of enzymes that function in xenobiotic metabolism and detoxification of noxious substances in the cell. Previous studies in our laboratory showed that treatment of C57BL/6 mice with DADS for 48 hours significantly increased the levels of GSTs in the gastrointestinal tract, primarily the duodenum of the small intestine, stomach, liver and colon, but not in other organs. To determine the mechanism of action of DADS in protecting the cell, and in particular, the consequences of GST elevation on other important processes in the cell, a genomic microarray analysis was performed using mRNA from mouse duodenum. Certain metabolically relevant genes, transcription factors and signal transduction pathway genes have altered gene expression by DADS treatment. In this study, quantitative RT-PCR and northern blot analyses were used to analyze selected genes that were affected by DADS treatment. As expected, the GSTs, primarily the Mu and Alpha classes, were significantly elevated in duodenum and liver by DADS treatment. A down-regulation of the cell signaling gene *LIM-SH3* and of the apoptosis inducing gene *LKB1-STK11* determined by the intestinal microarray is consistent with results obtained by quantitative RT-PCR and northern blots. The up-regulation of the Mu class of GSTs (that was shown in the duodenal microarray and protein analysis) was confirmed by both RT-PCR and northern blot analysis in both liver and duodenum. RT-PCR and northern blots analyses also showed evidence of a previously unknown up-regulation of the *LIM-SH3* transcript in the liver after administration of the DADS. Analysis of the expression profile of relevant signal transduction genes, and pathological and histological studies of the effects of DADS treatment on the GI tract, can further clarify the mechanism by which DADS may act as an anti-cancer agent. Such studies could demonstrate the potential use of DADS and other similar organosulfur compounds in the prevention of cancer.

Recognition of *Ureaplasma urealyticum and Mycoplasma hominis* in Tracts of Postmenopausal Women with Gynecologic Cancers and Benign Tumors

by

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At the present time, the cause of gynecological cancer or benign tumors is mostly unknown. However, recently it has been recognized that certain infectious agents may contribute to carcinogen sis or abnormal growth formations by inducing a state of persistent inflammation. The female upper genital tract is a frequent site of infection. Thus, the relationship between detection of *Ureaplasma urealyticum* and *Mycoplasma hominis* in tracts of postmenopausal women with gynecologic cancers and benign tumors was investigated.

PCR-ELISA analysis was performed on specimens from 96 women: 67 women were over the age of 65 with gynecological malignancies and 29 women were over the age of 55 with benign growths.

U. urealyticum and *M. hominis* were identified in 6 (9.0%) and 4 (6.0%) of subjects respectively with gynecological cancers and, in 3 (10.3%) and 2 (6.9%) of subjects respectively with benign tumors. *U. urealyticum* was detected in 1 patient with ovarian cancer, 5 patients with endometrial cancer, and in 3 patients with benign growth formations. *M. hominis* was detected in 1 patient with ovarian cancer, in 1 patient with uterine cancer, in 2 patients with endometrial carcinoma, and in 2 patients with nonmalignant conditions; one with human papillomavirus and the other with adenexal mass.

During the study presence of these microorganisms did not show a strong correlation with occurrence of ovarian, endometrial and uterine cancers or with the presence of benign growth. However, further study using more samples might be necessary in order to diminish sampling error, demonstrate greater significance and to suggest that persistent infection with *U. urealyticum* and *M. hominis* may be a risk factor for gynecologic cancer and tumor growth.

Geometrical Properties of Metal Nanoparticles

by

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The purpose of this project was to determine the geometric properties of gold nanoparticles. Results from Extended X-Ray Absorption Fine-Structure (EXAFS) experiments gave the average coordination numbers of the first through the fifth nearest neighbors in the samples containing thiol-stabilized gold nanocluters. To determine the size and shape of the clusters of different sizes, the following modeling strategy to fit the experimental data was developed. Namely, the three theoretically most probable shapes for metal nanoparticles are the cuboctahedron, icosahedron, and the truncated octahedron. Programs were written to generate 3D cluster coordinates of these three shapes for any cluster order. These coordinates were then processed by another program that calculated the radial distribution function (RDF) for all the clusters, that is, the average change in the number of atoms per radial distance from the absorbing atom. The area under each RDF peak determined the average number of the first through the n^{th} nearest neighbors. The structural model that matched the EXAFS data would thus provide both the correct size and shape of the cluster.

Another way to establish the shape of the cluster is to determine which cluster geometry is characterized by the least cohesive energy for a given size cluster. Out of several models that were compared, the configuration of atoms that has the least cohesive energy, must best approximate the actual cluster. A program was written using Equivalent Crystal Theory (ECT) to calculate the cohesive energy of any cluster. The cohesive energies of the cuboctahedron, icosahedron, and truncated octahedron were compared for various sizes, and the structures that are characterized by the least cohesive energy were obtained for each cluster size. The conclusion of this study is that the combination of ECT and EXAFS methods allows to reproduce many geometric features in small gold clusters that are predicted by ab initio theories.

Animating the Conformational Changes of DNA Polymerase β

by

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Genomic DNA present in every cell of the human body is constantly being damaged by various physical and chemical agents. DNA Polymerase β (pol β) plays a central role in filling short DNA gaps during repair synthesis of the base excision repair pathway. The increased efficiency and fidelity of pol _ is thought to be a result of an induced fit mechanism; as polymerase binds to correct deoxynucleoside triphosphate it undergoes a conformational change from open structure to closed ternary substrate complex. The basic architecture of pol β consists of two domains, the 8-kDa N-terminal domain is responsible for the lyase activity and the 31-kDa C-terminal domain performs the phosphoryl transfer. The 31-kDa domain consists of three subdomains, including the fingers, thumb, and palm. The fingers of the polymerase control the interactions between the base entering to fill in the gap and the base on the template strand; the palm plays a role in catalysis. The thumb is responsible for most of the motion closing motion. Langevin dynamics simulations and targeted molecular dynamics (TMD) simulation have revealed key residues during conformational transitions between open and closed states. Transition path sampling (TPS) was used to determine the complex sequence of events in the overall catalytic mechanism of DNA polymerase β. Free energy profiles were computed and five transition state regions were identified: partial thumb closing, Asp192 Flip, Arg258 rotation, Phe272 Flip, and rearrangement of catalytic region. The combined data on the conformational changes, allowed us to smoothly interpolate between the open and closed crystal structures of pol β and visualize the complete process. We used the graphics program Visual Molecular Dynamics (VMD) to animate the trajectory and display the sequence of events as a movie. The movie, containing 1575 frames, was assembled using bitmap (BMP). The animation sequence provides an overall picture of the local motions during nucleotidyl transfer reaction that steer the system to the reaction-completed state.

Cycling in a "Backward" System

by

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Previous research has shown that the endocytosis and exocytosis of AMPA-type glutamate receptors into and out of the synaptic membranes of neurons in the hippocampus is an important mechanism underlying synaptic plasticity. There is a continuous internalization and reinsertion of AMPAR, which maintains a constant level of these receptors at the cell surface. GRIP, PICK, and several other PDZ-domain-containing proteins, which bind to GluR2 AMPAR subunits seem to be involved in regulating this AMPAR transport. GRIP is thought to stabilize the receptors that are at the cell surface, while PICK removes receptors from the surface. When the cell is inundated with an excess of glutamate, however, additional receptors are internalized, thereby disrupting this delicate balance and reducing surface AMPAR.

Unlike the cells in the hippocampus, neurons in the retina are continuously exposed to glutamate in the absence of external stimuli. In fact, the presence of light causes the cells to hyperpolarize and release less glutamate. As a result, we hypothesize that the receptors in the retina will not down regulate in response to excess glutamate, as the neurons of the hippocampus do. We tested this theory in dissociated P-2 rat retinal cells. Immunofluorescence was used to ascertain that PICK and GRIP, proteins that are involved in the maintenance of regular receptor cycling, are indeed present on the surface of the cells in the retina. We further used electrophysiological techniques to test whether AMPAR cycle in retinal cells. After disrupting AMPAR endocytosis, we observed a run-up in the current that passed through the cells since the receptors that were not being endocytosed would build up along the cell surface. These results indicate that there is AMPAR cycling in the retina, but the receptors do not down regulate in response to excess levels of glutamate.

X-ray Absorption Fine Structure Analysis of Gold Nanoclusters

by

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Gold catalysis has sprung interest in the last years due to its catalytic activity with a number of important reactions. One key factor which influences its catalytic activity is the size of the gold particles, which must be in the nanometer range. This presentation describes the use of the technique of Extended X-ray Absorption Fine-Structure spectroscopy (EXAFS) to study the local structure of thiol-stabilized gold nanoparticles. Three nanocluster samples of different average particle sizes were synthesized for this experiment by adding $LiB(C_2H_5)_3H$ to a THF solution of $H[AuCl4]\cdot 3H_20$ to reduce the ions of $[AuCl4]^{-1}$ to gold nanoparticles stabilized by thiol chains. Then this mixture was poured into a large amount of ethanol to precipitate the nanoparticles. X-ray absorption coefficient was measured as a function of photon energy for each sample by using beamline X16C at the National Synchrotron Light Source at Brookhaven National Laboratory. Afterwards, several computer programs used the experimental data to best fit the theoretical EXAFS equation and obtain the unknown structural variables. Among the unknown variables were the coordination numbers of the gold atoms in the particle. Different scattering paths (including multiple scatterings) of the electrons away from the central atom were chosen for the fit. Finally, through the use of a new computer program generating 3D coordinates of the cuboctahedron, truncated octahedron, and icosahedron clusters, the first five nearest neighbor coordination numbers were generated for any given cluster order for a given cluster geometry and kept fixed in the fits of theory to the data. The fits were performed repeatedly until the lowest chi squared was obtained. This procedure allowed us to obtain the best geometrical model of the gold nanocluster as a function of its size. We obtained that for the smallest size (38 atoms), the structure is truncated octahedral, for the intermediate size (55 atoms): icosahedral, and for the largest size (147 atoms): icosahedral, in a qualitative agreement with theoretical predictions.

Theoretical Investigation of Ligand Stablization in Fatty Acid Binding Proteins

by

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The Fatty Acid Binding Proteins (FABP) are a family of small cytosolic proteins which are involved in the transport and metabolism of fatty acids. Subtle molecular differences within the family produce distinct ligand binding properties and diverse functional roles. Using a physical chemistry based energy function to calculate enthalpies of interaction, we investigate the source of ligand stabilization in FABPs from two tissue types. Our calculations support the following description of stabilization in the two proteins: In Intestinal-FABP, electrostatic stabilization of the fatty acid carboxylate is achieved by a single salt bridge with Arg-106 while in Muscle-FABP, stabilization is achieved by hydrogen bonds with the following components of the binding cavity: Arg-126, Tyr-128 and a structured water molecule, Wat-152. In both FABP types, stabilization of the hydrocarbon tail is achieved by Lennard Jones interactions with several residues lining the binding cavity: Val-49, Val-60, Tyr-70, Trp-82 and Tyr-117 in Intestinal-FABP; and Phe-16, Pro-38, Ala-75 and Asp-76 in Muscle-FABP. The ability to identify the effect of a particular set of residues on binding affinity enhances a general understanding of protein-lipid interactions and can ultimately contribute to the rational design of drug compounds which bind particular fatty acids.

Time-Resolved X-Ray Absorption Spectroscopy Study of CuO Reduction with Carbon Monoxide

by

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This study investigated the existence, nucleation, and activation energies of reaction intermediates and products in the reduction of CuO to Cu at high temperatures via the use of carbon monoxide. The technique of Extended X-ray Absorption Fine Structure (EXAFS) was used, and many EXAFS scans were taken as the CuO reduced to copper. This procedure was repeated at 250, 270, and 280° C. The EXAFS scans of the reduction contained no isosbestic points (points where the graphs overlap), suggesting the presence of a reaction intermediate. The technique of principle component analysis formally confirmed the existence of an intermediary stage and identified it as Cu_2O, and this technique also produced graphs of the mixing fractions of all three stages - CuO, Cu_2O, and Cu - as functions of time. These graphs served as the data for the Kolmogorov-Johnson-Mehl-Avrami (KJMA) Equation, the equation that uses mixing fractions and reaction rates to determine the nucleation of a reaction's product. The KJMA Equation produced consistent nucleation numbers at different temperatures for the formation of Cu_2O, and these nucleation numbers indicate that Cu_2O undergoes two-dimensional surface nucleation, as opposed to three-dimensional volume nucleation. This equation, however, produced consistently high, nonsensical values of the nucleation number for the formation of Cu, demonstrating that the equation's approximations are too crude to use for Cu nucleation studies.

The rate of the reactions increased as temperature increased, in accordance with the Arrhenius Rate Law. This law was used to determine the activation energy of the second half of the reaction - the Cu_2O transformation to Cu.

The Effect of the Inflammatory Cytokine (IL)-1≤on Osteoclast Formation and Function in Human Umbilical Cord Blood Cells

by

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Osteoclasts are specialized cells formed by fusion of monocytes. The function of osteoclasts is to resorb bone in order to facilitate the continuous process of bone remodeling. Human osteoclasts are not easily available. The purpose of this study is to further characterize human umbilical cord blood cells (HUCBC) as a possible source of osteoclasts. More specifically, the response to the inflammatory cytokine interleukin IL-1β on osteoclast formation from HUCBC was studied. The IL-1 family of cytokines is expressed by many different cells and has multiple functions. IL-1β has been shown to stimulate the formation and function of osteoclasts in various sources of osteoclast precursors including murine bone marrow and spleen and human bone marrow. Our results showed that HUCBC are capable of forming cells that are multi-nucleated, tartrate resistant acid phosphatase (TRAP) positive and have the ability to resorb mineral when cells are cultured in alpha MEM with 20% FCS and 100 ng/ml RANKL. The addition of 50 ng/ml IL-1β to cultured HUCBC caused an increase in osteoclast-like cell formation, as revealed by TRAP positive staining. Anti- IL-1β was added to cells, in an effort to block the endogenous IL-1β≤ that was shown to be around 10ng/ml. TRAP positive staining revealed an inverse relationship between the concentration of anti- IL-1β , and the number of osteoclasts formed and this was shown to be dose dependent. The decrease in the number of apparent osteoclasts confirmed that IL-1β regulates formation of osteoclasts. These preliminary findings indicate that IL-1β≤ operates on HUCBC in a manner similar to how it works on other osteoclast precursors. Further research needs to be conducted to determine the mechanism of action of IL-1β on osteoclast formation from HUCBC. This work was funded by the CIHR of Canada.

In vitro Cytotoxicity of Epigallocatechin Gallate (EGCG) and Tea Extracts to Cancerous and Normal Cells from the Human Oral Cavity

by

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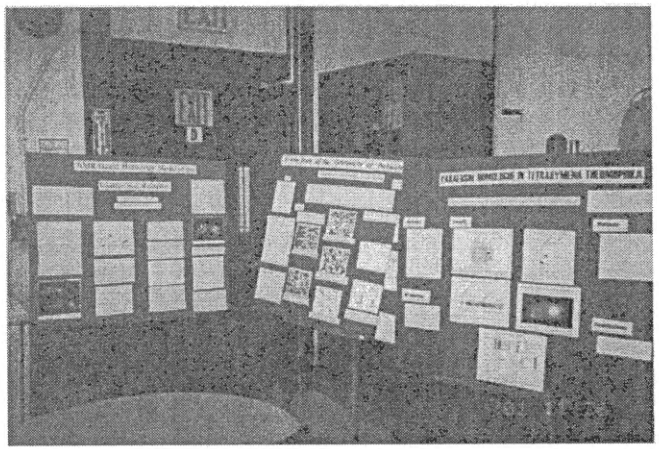
The chemopreventive properties of green tea has been shown in many cancerous cell culture systems, laboratory animal-model tumor bioassays, and epidemiological studies. The chemopreventive efficacy of green tea is thought to be mediated by its main polyphenolic component, (-)-epiepigallocatechin gallate (EGCG). Few studies have compared the *in vitro* responses of malignant and normal cells to tea extracts and to EGCG. The initial portion of this research evaluated the relative sensitivities of six cell lines derived from malignant and normal tissues to tea extracts and to EGCG. The antiproliferative effects of green tea extract, black tea extract, and EGCG were more pronounced towards the immortalized, tumorigenic (CAL27, HSC-2, and HSG$_1$) and nontumorigenic (S-G) cells than towards the normal (GN56 and HGF-1) cells and green tea was more growth inhibitory than black tea. An inverse correlation was noted between cellular sensitivity to EGCG and cellular doubling time. Having observed that the addition of green tea extract, black tea extract, or EGCG to cell culture medium led to the formation of hydrogen peroxide (H_2O_2), the next portion of the research focused on EGCG as an inducer of oxidative stress. These studies used three of the above cell lines: CAL27 cells (the cancerous cells most sensitive to EGCG), HSG1 cells (the cancerous cells least sensitive to EGCG), and GN56 cells (normal fibroblasts). It was reported that upon addition to cell culture medium, EGCG reduced Fe(III) to Fe(II), which then initiated the Fenton reaction to generate H_2O_2, an inducer of oxidative stress. To confirm this mode of toxicity, we showed that dual exposure of the cells to EGCG and catalase, an enzyme that degrades H202, or deferoxamine, a chelator of Fe(III), decreased the toxicity of EGCG. Conversely, pretreatment of the cells with the glutathione depleters, 1-chloro-2,4-dinitrobenzene and 1,3-bis(2-chloroethyl)-N-nitrosourea, potentiated the toxicity of EGCG. Furthermore, a 4 hr exposure to EGCG lessened the intracellular level of reduced glutathione in the CAL27 and, to a lesser extent, in the HSG1cells, but not in the GN56 fibroblasts. In all cell types, cytotoxic concentrations of EGCG induced significant cytoplasmic vacuolization. The results presented herein are consistent with EGCG acting as a prooxidant, with the cancerous cells more sensitive to oxidative stress than the normal cells.

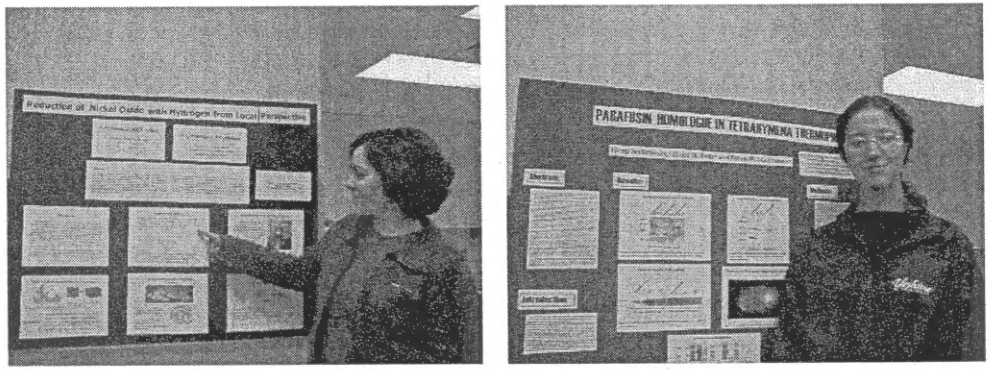
Student Publications

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.



The poster competition.



Students Shira Frenkel (L) and Anna Sedletcaia (R) present posters at the poster competition.

Stern College for Women

Scientific Publications

Scientific Journals

(Undergraduate names are in **bold** type)

Frenkel, A.I., **Nemzer, S., Pister, I., Soussan, L., Harris, T.**, Sun, Y., and Rafailovich, M., 2005, Size-controlled Synthesis and Characterization of Thiol-stabilized Gold Nanoparticles, J. Chem. Phys. (accepted).

Liu, W.C., Feldman, S.C., Schulder, M., Kalnin, A.J., Zimmerman, A., **Sinensky, R.**, 2005, The effect of tumour type and distance on activation in the motor cortex, Neuroradiology, in press (Epub ahead of print; September 2nd).

Ponnusamy R., **Nissim H.A.**, and M. Barad, 2005, Systemic blockade of D2-like dopamine receptors facilitates extinction of conditioned fear in mice, .Learn Mem. 12::399-406.

Jiang, T., Wang, Z., Proctor, G., **Moskowitz, S.**, Liebman, S.E., Rogers, T., Lucia, M.S., Li, J., and M. Levi, 2005, Diet induced obesity in C57BL/6J mice causes increased renal lipid accumulation and glomerulosclerosis via a sterol regulatory element binding protein-1C dependent pathway, J. Biol. Chem. in press (Epub ahead of print; October).

Yu, Z., Jacobson, M.P., **Josovitz, J.**, Rapp, C.S., and R.A. Friesner, 2005, First shell solvation of ion pairs: Correction of systematic errors in implicit solvent models, J. Phys. Chem., part B, 108: 6643-6654.

Frenkel, A.I., **Frankel, S.C.**, and T. Liu, 2005, Structural stability of giant polyoxomolybdate molecules as probed by EXAFS, Physica Scripta, T115: 721-725.

Rapp, C.S. and **R.M. Pollack** (R. Frankel), 2005, Crystal packing effects on protein loops, Proteins: Structure, Function, & Bioinformatics 60:103-109.

Babich, H., **Gold, T.**, and **R. Gold**, 2005, Mediation of the *in vitro* cytotoxicity of green and black tea polyphenols by cobalt chloride, Toxicol. Lett., 155:195-205.

Jiang, F., Zhang, Z.G., Katakowski, M., Robin, A.M., **Faber, M.**, Zhang, F., and M. Chopp, 2004, Angiogenesis induced by photodynamic therapy in normal rat brain, Photochem. Photobiol, 79:494-498.

Weisburg, J.H., **Weissman, D.B.**, **Sedaghat, T.** and H. Babich, 2004, *In vitro* cytotoxicity of epigallocatechin gallate (EGCG) and tea extracts to cancerous and normal cells from the human oral cavity, Basic Clin. Pharmacol. Toxicol., 95:191-200.

Babich, H., **Krupka, M.E.**, **Nissim, H.A.**, and H.L. Zuckerbraun, 2004, Differential *in vitro* cytotoxicity of (-)-epicatechin gallate (ECG) to cancer and normal cells from the human oral cavity, Toxicol. In Vitro 19:231-242.

Nehler, M.R., Coll, J.R., Hiatt, W.R., Regensteiner, J.G., Schnickel, G.T., Klenke, W.A., Strecker, P.K., Anderson, M.W., Jones, D.N., Whitehill, T.A., **Moskowitz, S.**, and W.C. Krupski, 2003, Functional outcome in a contemporary series of major lower extremity amputations, J Vasc Surg. 38:7-14.

Babich, H., **Sedletcaia, A.**, and **B. Kenigsberg**, 2002, In vitro cytotoxicity of protocatechuic acid to cultured human cells from oral tissue: involvement in oxidative stress, Pharmacol. Toxicol., 91:145-253.

Babich, H., **Reisbaum, A.G.** and H.L. Zuckerbraun, 2000, *In vitro* response of human gingival epithelial S-G cells to resveratrol, Toxicol. Lett., 114:143-153.

Babich, H., Zuckerbraun, H.L., **Hirsch, S.T.** and L. Blau, 1999, *In vitro* cytotoxicity of the nitric oxide donor, S-nitroso-N-acetyl-penicillamine, towards cells from human oral tissue, Pharmacol. Toxicol., 84:218-225.

Zuckerbraun, H.L., Babich, H., **May, R.J.** and M.C. Sinensky, 1998, Triclosan: cytotoxicity, mode of action, and induction of apoptosis in human gingival cells *in vitro*, Eur. J. Oral Sci., 106:628-636.

Babich, H., Zuckerbraun, H.L., **Ricklis, A.S.** and L. Blau, 1998, *In vitro* toxicity of sodium nitroprusside to human endothelial ECV304 cells, Environ. Toxicol. Pharmacol., 5:135-144.

Davis, D.L., Gottlieb, M.B. and **J.R. Stampnitzky**, 1998, Reduced ratio of male to female births in several industrial countries: a sentinel health indicator? JAMA 279:1018-1023.

Babich, H., **Segall, M.A.** and K.D. Fox, 1997, The *Allium* test - a simple eucaryote genotoxicity assay, Amer. Biol. Teach., 59:580-583.

Babich, H., Zuckerbraun, H.L., **Wurzburger, B.J., Rubin, Y.L.**, Borenfreund, E. and L. Blau, 1996, Benzoyl peroxide cytotoxicity evaluated *in vitro* with the human keratinocyte cell line, RHEK-1, Toxicology, 106:187-196.

Babich, H., Zuckerbraun, H.L., **Barber, I.B.**, Babich, S.B. and E. Borenfreund, 1996, Cytotoxicity of sanguinarine chloride to cultured human cells from oral tissue, Pharmacol. Toxicol., 78:397-403.

Sinensky, M.C., **Leiser, A.L.** and H. Babich, 1995, Oxidative stress aspects of the cytotoxicity of carbamide peroxide: *in vitro* studies, Toxicol. Lett., 75:101-109.

Babich, H., **Wurzburger, B.J., Rubin, Y.L.**, Sinensky, M.C., Borenfreund, E. and L. Blau, 1995, An *in vitro* study on the cytotoxicity of chlorhexidine digluconate to human gingival cells, Cell Biol. Toxicol., 11:79-88.

Babich, H., **Palace, M.R.**, Borenfreund, E. and A. Stern, 1994, Naphthoquinone cytotoxicity to bluegill sunfish BF-2 cells, Arch. Environ. Contam. Toxicol., 27:8-13.

Babich, H., **Markenson, D.F.**, Blau, L. and A. Stern, 1994, *In vitro* cytotoxicity of the chlorinated naphthoquinone, dichlone, to human endothelial ECV304 cells, Toxicol. In Vitro, 8:1075-1081.

Babich, H., **Palace, M.R.** and A. Stern, 1993, Oxidative stress in fish cells: *in vitro* studies, Arch. Environ. Contam. Toxicol., 24:173-178.

Babich, H., Martin-Alguacil, N., **Raul, C.**, Rosenberg, D.W. and E. Borenfreund, 1991, Response of human cell cultures to cytotoxicants requiring metabolic activation, In Alternative Methods in Toxicology, vol. 8, Goldberg , A.M.(ed.), Mary Ann Liebert, Inc., NY, NY, pp. 263-276.

Babich, H., **Goldstein, S.H.** and E. Borenfreund, 1990, *In vitro* cyto- and genotoxicity of organomercurials to cells in culture, Toxicol. Lett., 50:143-149.

Goldstein, S.H. and H. Babich, 1989, Differential effects of arsenite and arsenate to *Drosophila melanogaster* in a combined adult/developmental toxicity assay, Bull. Environ. Contam. Toxicol., 44:456-460.

Blau, L., **Stern, R.B.**, and R. Bittman, 1984, The stoichiometry of A23187- and X537A-mediated calcium ion transport across lipid bilayers, Biochim. Biophys. Acta 778:219- 223.

Minor Publications (Abstracts - Professional Societies)

Estes, D.W., **Ben-Zvi, N.**, and L. Blau, 2005, The DNA melt: Composition, sequence, and thermodynamics, Gordon Research Conference on Chemistry Education Research and Practice, Connecticut College, New London, CT, June.

Nissim, H.A., Krupka, M.E., Zuckerbraun, H.L., and H. Babich, 2005, Differential *in vitro* cytotoxicity of (-)-epicatechin gallate to cancer and normal cells from the human oral cavity, 229th National Meeting of the American Chemical Society, San Diego, CA.

Roth, R., Ozelius, L., and L. Liu, 2005, Explanation of alternative splicing in SGCE gene, 229th National Meeting of the American Chemical Society, San Diego, CA.

Nemzer, S., Harris, T., Pister, I., Soussan, L., Sun, Y., Rafailovich, M., and A. Frenkel, 2005, Characterizing nanoparticle size using EXAFS and TEM, 229th National Meeting of the American Chemical Society, San Diego, CA.

Nemzer, S., Harris, T., Pister, I., Soussan, L., Sun, Y., Rafailovich, M., and A. Frenkel, 2005, Size control of thiol-stabilized gold nanoparticles: combined EXAFS and TEM characterization, 229th National Meeting of the American Chemical Society, San Diego, CA.

Pister, I., Soussan, L., Nemzer, S., Harris, T., A. I. Frenkel, Y. Sun, and M. Rafailovich, 2005, Size dependent changes of the local structure in dodecanethiol-stabilized gold nanoparticles, Annual Meeting of the American Physical Society, Los Angeles, March (oral presentation).

Ben-Zvi, N., Juszczak, L. and J. Friedman, 2004, Unfolding and refolding of the mini-protein TC5b in a confined, cell-like environment, 227th National Meeting of the American Chemical Society, Anaheim, CA.

Douglas, E., Ravetch, J.V. and B. Diamond, 2004, Fcγ receptor expression on peripheral blood mononuclear cells in SLE, 227th National Meeting of the American Chemical Society, Anaheim, CA.

Glasner, D., Frenkel, A.I, and F.R. Zypman, 2004, Geometrical properties of metal nanoparticles, 227th National Meeting of the American Chemical Society, Anaheim, CA.

Suttner, S., Sukhu, B., and H.C. Tenenbaum, 2004, Effect of the inflammatory cytokine (IL)-1β on osteoclast formation and function in human umbilical cord blood cells, 228th National Meeting of the American Chemical Society, Philadelphia, PA

Reinman, I., **Benmergui, D.**, and C.S. Rapp, 2004, Theoretical investigation of ligand stabilization in fatty acid binding proteins, 228th National Meeting of the American Chemical Society, Philadelphia, PA

Glasner, D., Zypman, F., and Frenkel, A.I., 2004, Geometric properties of metal Nanoparticles, Annual 2004 NSLS Users Meeting, Brookhaven National Laboratory, May.

Frenkel, A.I., **Glasner, D.**, Zypman, F., Nuzzo, R., and L. Menard, 2004, 3D-Structure of thiol-capped gold nanoparticles, Annual Meeting of the American Physical Society, Montreal, Canada, March.

Reingold, S.O., Gu, J., Fernandez, R. and R.L. Katz, 2003, Interphase fluorescence *in situ* hybridization (FISH) to demonstrate translocation of cyclin D1 (CCD1) gene to chromosome 14 immunoglobulin heavy chain locus (IGH) with resultant overexpression of cyclin D1 protein in a mantle cell lymphoma cell line, 225th National Meeting of the American Chemical Society, New Orleans, LA Spring.

Sedletcaia, A. and P. Cohen, 2003, Localization of PMS2 in meiotic cells, 225th National Meeting of the American Chemical Society, New Orleans, LA., Spring.

Josovitz, J., Verdier-Pinanrd, P. and S. B. Horwitz, 2003, Analysis of stathmin and MAP- 4 content in taxol resistant cell lines, 225th National Meeting of the American Chemical Society, New Orleans, LA., Spring.

Gamss, C.A., Ting, L.-M., and K. Kim, 2003, Inhibition of the purine salvage pathway in *Plasmodium falciparum*, 226th National Meeting of the American Chemical Society, New York City, NY.

Frankel, R., **Fischer, T.** and C.S. Rapp, 2003, The effects of crystal packing on protein loop structures, 36th Middle Atlantic Regional Meeting of the American Chemical Society, Princeton, NJ

Frenkel,A.I., **Frankel, S.C.**, and T. Liu, 2003, Structural stability of giant polyoxomolybdate molecules as probed by EXAFS XAFS XII conference, Malmo, Sweden, June.

Frankel, S.C., and A. Frenkel, 2002, Reduction of nickel oxide with hydrogen from local perspective, 223rd National Meeting of the American Chemical Society, Orlando, FL, Spring

Kenigsberg, B., Kaufman, H. and R. Glover, 2002, Immune responses to recombinant BCG expressing carcinoembryonic antigen, 223rd National Meeting of the American Chemical Society, Orlando, FL, Spring

Kenigsberg, B., **Sedletcaia, A.**, Estes, D. and L. Blau, 2002, Twenty years of bonding; the Chemistry club and the ACS, 223rd National Meeting of the American Chemical Society, Orlando, FL, Spring

Nivasch, R., Chill, J. and J. Anglister, 2002, NMR-based homology model of the interferon ± receptor, 2002, 223rd National Meeting of the American Chemical Society, Orlando, FL, Spring

Sedletcaia, A., **Kenigsberg, B.** and H. Babich, 2002, *In vitro* cytotoxicity of protocatechuic acid, an inducer of oxidative stress, 223rd National Meeting of the American Chemical Society, Orlando, FL, Spring

Sedletcaia, E., Matthiesen, S.H. and B.H. Sator, 2002, Parafusion homologue in *Tetyrahymena thermophila*, 223rd National Meeting of the American Chemical Society, Orlando, FL, Spring

Frankel, S.L. and D.R. Maglot, 2001, LOCUSLINK and REFSEQ: Developing tools for genomic annotation and analysis, 221st National Meeting of the American Chemical Society, SanDiego, CA., Spring.

Rivkin, S.Y., Oh, S. and T.A. Bargiello, 2001, Determinants of Vj gating polarity in connexin 32 hemichannels, 221st National Meeting of the American Chemical Society, San Diego, CA., Spring.

Goldfischer, R.E., Wencker, D., and R. Kitsis, 2000, Myocyte apoptosis.is sufficient to cause cardiomyopathy, 219th National Meeting of the American Chemical Society, San Francisco, CA., Spring

Marton, D., Kang, Y.H., and F. Berthiaume, 2000, Chronic exposure to cytokines suppresses liver-specific function of cultured hepatocytes, 219th National Meeting of the American Chemical Society, San Francisco, CA., Spring.

Badrian, C.C., Haspel, J., Friedlander, D., and M. Grumet, 1999, Promotion of neurite outgrowth by regions in human L1, 217th National Meeting of the American Chemical Society, Anaheim, CA., Spring.

Blau, L., Babich, H., Zuckerbraun, H.L. and **S.T. Hirsch**, 1999, In vitro cytotoxicity of the nitric oxide donor, S-nitroso-N-acetyl-penicillamine, towards cells from human oral tissue, 217th National Meeting of the American Chemical Society, Anaheim, CA., Spring.

Feig, J.S., Cleary, J., and B. Diamond, 1999, Detection of estrogen receptor α mRNA in B and T cell lines by reverse transcriptase chain reaction, 217th National Meeting of the American Chemical Society, Anaheim, CA., Spring.

Babich, H. and **S.H. Goldstein**, 1988, Bioassays for monitoring the environment: study with arsenics, 9th Annual Meeting, Society of Environmental Toxicology and Chemistry, Arlington, VA, November.

Ambalu, M. and L. Blau, 1986, The study of ion fluxes across lipid bilayers, 191st National Meeting of the American Chemical Society - 7th Student Affiliates Research Symposium, NY, NY, April.

Gutman, E.A. and L. Blau, 1985, X537A-mediated transport of calcium across phosphatidylcholine bilayers, 189th National Meeting of the American Chemical Society - 6th student Affiliates Research Symposium, Miami Beach, FL [E.A. Gutman was awarded 1st prize, Biochemistry Section].

Blau, L., **Stern R.B.**, Wun, T.C., and R. Bittman, 1984, Calcium transport across phosphatidylcholine vesicles, 8th International Biphysics Congress, Bristol. United Kingdom, August.

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

ROTH SCHOLARS

Every year, several of Stern College for Women's most talented sophomores and juniors apply for the Roth Scholars Program. This prestigious internship, hosted by YU's Albert Einstein College of Medicine (AECOM), provides students with exposure to nine weeks of intensive biomedical research each summer. For the summer of 2005, eight Stern College women (of a total of 10 recipients) were selected for this undergraduate research experience, having successfully passed the rigorous application and interview process. Under the guidance of AECOM's top scientists, these women participated in research projects, many of which were at the cutting edge of medicine.

Summer, 2005

Roth Scholars

Yael Barak
Helen Nissim
Frida Fridman
Ilana Pister
Sarah Weinerman
Tamar Gold
Tehilla Stepansky

University Undergraduate Summer Research Scholar

Suzanne Snyder

Summer, 2004

Roth Scholars

Esther Flaschner
Debbie Rybak
Eydie (Pesi) Porat
Reina Roth
Malkie Krupka

Summer, 2003

Roth Scholars

Nomi Ben-Zvi
Dina Ohevshalom
Elisheva Douglas
Chaya Gopin

University Undergraduate Summer Research Scholar

Tova Fischer

Summer, 2002

Roth Scholars

Caryn Gamss
Meryl Sava
Julia (Tobi) Josovitz
Anna Sedletcaia

Summer, 2001

Roth Scholars
Shayna Aster — Elena Sedletscaia — Yehudit Weinberger

University Undergraduate Summer Research Scholars
Bracha Kenigsberg — Hadassa Rutman — Meredith Weiss

Summer, 2000

Roth Scholars
Shira Rivkin — Shiry Wagner

Summer, 1999

Roth Scholars
Olga Dynina — Rochelle Goldfisher

Summer, 1998

Roth Scholars
Jeniffer Feig — Sivah Shifteh — Malka Skiba

Summer, 1997

Roth Scholar
Sarah Friedman

Summer, 1996

None

Summer, 1995

Roth Scholars
Caren Gottlieb — Lauren Insel — Azita Simoni

Summer, 1994

Roth Scholars
Judy Ehrenberg — Stacey Renee Rubel — Brenda Wurzburger

Summer, 1993

Roth Scholars
Yaffa Cheslow — Rashel Monhian — Stacey Tuckman

Summer, 1992

Roth Scholars
Nava Goldman — Marcia R. Palace — Randi Kay Sasnowitz

Summer, 1991

Roth Scholars
Monica Kriger — Aviva Rosenstein

Summer, 1990

Roth Scholars
Sandra Benchimol — Cindy Tuckman

Summer, 1989

Roth Scholar
Heather Rush

Summer, 1988

Roth Scholars
Bat Sheva Levine — Tamar Silverstein

Summer, 1987

Roth Scholars
Miriam Berger — Aviva Kahane

Summer, 1986

Roth Scholar
Deborah Bernstein

Summer, 1985

Roth Scholars
Shoshana Kah — Francine Anne Ziv — Elana Unger

Summer, 1984

Roth Scholars
Michelle Small — Susan Mandelbaum

The Anne Scheiber Fellowship

The Anne Scheiber Fellowship Program provides scholarship support to Stern College undergraduates as well as graduates pursing 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 College of Medicine may apply for awards up to full tuition for their four years of medical training. We proudly salute the current Anne Scheiber Fellows at the Albert Einstein College of Medicine who are fulfilling Ms. Scheiber's dream:

Tamar Belsh

Deena Blanchard

Yael Boyarsky

Aliza Charlop

Esti Charlop

Tova Fischer

Rena Frankel

Caryn Gamss

Ariella Glueck

Julia Josowitz

Chava Kahn

Yael Raymon

Necahma Mina Shoshani

Yehudit Weinberger

Meredith Weiss

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Derech HaTeva is an undergraduate publication of Stern College for Women. Articles are authored primarily by our 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.

Volume 9: 2005

Volume 8: 2004

Volume 7: 2003

Volume 6: 2002

Volume 5: 2001

Old Age - an Age Old Aspiration

by

Yael Grunseid

This Article has been reprinted from Derech HaTeva Volume 9, pages 23-27, 2005

Deep down inside, each and every one of us desperately yearns for the chance to live a long life. Personally, even as a little kid, I distinctly remember the enthusiastic applause my family gave to the television image of a woman vigorously running on the treadmill as Good Morning America wished her a happy centennial. If longevity is such a blessing, and clearly it is regarded as such, then why is it that we pluck out the gray hairs, avoid birthdays like the plague, and smear on the wrinkle cream like there's no tomorrow? It's a paradox of life that goes beyond semantics- everyone wants to eventually *be* old, but no one wants to *get* old. Perhaps if the human lifespan would increase several fold, then mankind could make peace with process of aging. Interestingly, in early Biblical times, extreme longevity was a fact of life. At the dawn of civilization, the Bible's longest recorded life was that of Methuselah at 969 years... just slightly different from today's average lifespan of 70-80 years! Surprisingly though, the magnitude of the early Biblical numbers differs even from those recorded in later Biblical times, as Abraham's recorded date of expiration is at age 175, while Moses, who lived circa four hundred years later, lived only to the age of 120. These pieces of information raise a series of questions whose answers may hold exciting implications for the world of science today. They are as follows: What are the possible causes of the remarkable longevity found in early Biblical times, and what brought about its sudden and dramatic decrease? Why is it that, until today, people have been left to seek out the elixir of life to no avail? Most significantly, can humanity hope to achieve its lost longevity once again? This issue warrants both Biblical and scientific examination.

The exploration of this topic begins in Genesis 2:17, at the very first moments of human life. There, G-d commands Adam and Eve to refrain from eating of the Tree of Knowledge, as the verse states, "On the day you will eat from it, you will surely die." The text seems to imply that obeying this command will bring immortal life. Ramban on the spot comments on the words, "you will surely die," by saying that this death is not one of an instantaneous nature, for as is clear from later verses, Adam lived a full life of 930 years. Rather, the words "surely die," decree the inevitable process of death and the fallibility of every living creature. This idea recurs with the sin of Adam and Eve in Chapter three of Genesis. There, G-d reiterates the concept of mortality by saying, "for you are made of dust, and to the dust you will return." Following these words, verse 22 contains a very ambiguous statement, "And G-d said, man will become one of us [let us chase him from the Garden of Eden] lest he should stretch out his hand and eat of the Tree of Life and live forever." Ramban continues with his previous idea that the Tree of Life had not been of value before Adam's sin because he already had been created an immortal being, but, with the advent of death to the world, the Tree would override G-d's decree, and thus Adam was banished from the Garden of Eden. These two sources in Genesis highlight the beginning of man's mortality.

Going forward in time, the ten generations succeeding Adam had a collective life span average of 857.5 years [1]. Along with their increased life spans, there is another unusual link between the people of these generations; namely, many of them were able to sire children at advanced ages. Noah is the most extreme example, fathering Shem at the age of five hundred, but, in general, the average age of fatherhood was 117 years [1]. The life spans during the ten generations between Noah and Abraham spiral downward from Shem's six hundred years to

Terah's 205. Post-Terah, the life span seems to somewhat stabilize, gradually decreasing with each generation until the days of Moses. As the final figure appearing in the Bible, Moses's age of expiration pretty much sets the maximum age of mortality for humankind thus realizing G-d's declaration to the sinful Flood generation in Genesis 6:3, "My spirit shall not abide in man forever, for that he also is flesh, therefore shall his days be a hundred and twenty years." Subsequent cases of extreme longevity that appear in later Biblical books (e.g., Ruth and Daniel) are based in Aggadic sources rather than in the texts themselves and are viewed as exceptions from the norm. King David, as a representative of the pre-Temple period, expresses the average mortality age of his generation in Psalm 90; "The days of our years among them are seventy years, and if with strength, eighty years."

Assuming that the time count and length of the years mentioned in the Bible correspond to the system that is currently used (this is explained by the Abarbanel on Genesis 5), the longevity phenomenon begs explanation and is addressed by commentators throughout Jewish history. Josephus, in his book of *Antiquities,* seems to be the first commentator to attempt an explanation. He launched into his theory of longevity by stating that the early Biblical generations possessed the special status of being "beloved by G-d" because they were the first of His human creations. As such, they were granted lengthy years. These people also adhered to a diet capable of sustaining longevity. Furthermore, Josephus believed that G-d granted extreme longevity so that humanity could live to observe and learn the laws of astronomy [2]. The Rambam was of the opinion that that not all the people of that time lived extended years; instead, long life was limited only to those individuals enumerated in the text. Like Josephus, Rambam attributed this exclusive longevity to diet and a general healthy lifestyle. Though Rambam looked first to natural causes, both he and the Ralbag leave open the possibility that the elongated life spans of these generations can be ascribed to outright miracle [3]. The Ramban, on the other hand, came out strongly against Rambam's idea that longevity was limited to only a few individuals and stated that Adam's "biological perfection" was the reason for his longevity and that of all his early descendents. It took climatic changes caused by the Flood in Noah's time to disrupt the inborn human perfection and bring a gradual end to the longevity [4]. Lastly, the Abarbanel was of the opinion that restraints in sexual activity, as well as in diet were the root causes of the longevity. He highlighted the unusually late average age of paternity for these early generations and attributed it to delays in their adolescent development. He speculated that the delays came as a result of an altered biological clock, which in turn affected the age of mortality [5]. The ideas and opinions of the above-mentioned Jewish scholars were limited by the scientific knowledge of their eras. Remarkably, these ancient and medieval scholars have not fallen far a field from the current possible causes of the longevity offered by modern scientific technology.

R. Schontal, of the University of London, believed that the culprits causing the drastic decrease of longevity in early Biblical times were pathogenic fungi, colloquially termed as "mold." Extensive research in the field of mycology during the last quarter century has shown that the fungal metabolites, called mycotoxins, are "involved in the etiology of many disorders," including fetal and neonatal abnormalities, as well as tumors. Such disorders could result in the decrease of the human lifespan. Microfungi and their mycotoxins are almost as old as the earth itself. Since pre-historic times, the fungi flourished in dampness, such as after a rainfall and in high humidity. After the Great Flood, which lasted for forty days and nights, fungi thrived and proliferated. Schontal theorized that the lifespan decrease of four hundred years that elapsed between the pre-and post-flood generations was due to "deleterious agents" (possibly, mycotoxins) that adversely affected parents before and during their reproductive years and caused malfunctions to occur in their offspring. He further claimed that the advanced age of paternity indicated that "sexual maturity took longer to attain during the pre-

flood period." Sex hormones, perhaps, were damaged by the mycotoxin zearalenone, which is known "to have estrogenic action, and to affect the sex organs...and the functioning of the steroidal structure itself [6]. "The research of Schontal is reminiscent of both Ramban's opinion that climatic changes caused by the flood were the reason for the lifespan reduction and Abarbanel's claim that the human biological clock had somehow been altered.

In a completely different approach to the issue, Nathan Aviezer, of Bar Ilan University, asserted that the current scientific consensus is that "the cause of all aging processes is genetic [7]. "The progression of aging and death is determined by individual genetic defects, running the gamut from those that trigger the production of chemicals to destroy tissues by oxidation reactions, to others that alter proteins resulting in the rigidity of heart muscle, lungs, ligaments and tendons, and to genes that predispose individuals to Parkinson's disease and diabetes. In the absence of these defective genes, humans could live as long as 1300 years! Referring back to Adam and Eve, Aviezer proposed that the ancient couple had genes free of genetic defects and hence were theoretically immortal beings. Living in the Garden of Eden, they avoided non-genetic causes of death such as accidents or disease. Once they sinned and were expelled from the Garden, although their perfect genes remained intact, they were now in danger of environmental elements. As they did not succumb to the deleterious effects of aging, their extreme longevity is understandable, as is their ability to reproduce at advanced ages. Apparently, their deaths and those of their early descendents were attributed to the lack of medical technology, such as antibiotics and immunizations, that could protect them from deadly microbial and viral illnesses. Aviezer additionally called upon William's concept known as *antagonistic pleiotropy,* and explained that, "the same gene necessary for one important bodily function early in life may sometimes be harmful to the body later in life [8]. "Employing this term, Aviezer modified his gene defect-free theory to include genes, albeit in a small number, that would cause aging and eventual death for all humanity- even for Adam and Eve. He proposed that the moment of G-d's decree (Genesis 6:3) dooming man to the limit of 120 years was the point in time that aging/defective genes were instituted into the gene pool. Life span did not immediately diminish to this decreed number because it took time for these genes to establish in humanity. In fact, no aging seems to appear at all in Jewish Biblical literature until the time of Abraham. In Bereishis Rabbah 65:9, the Sages explain that Abraham and Isaac, with almost a century between them, so resembled each other that people would generally mistake them for one another. The lack of physical aging masked the difference of their years. Abraham, seeing that such confusion was robbing all the elder generation of their due respect, applied to G-d to institute the physical symptoms of aging. G-d readily agreed and said, "You request a good thing. I will grant it; and since you asked, I will begin with you. "Accordingly, the Bible precedes Abraham's death with a description of old age, as stated in Genesis 24:1, "Abraham became old; he was along in years." Thus, from Adam to Abraham, Aviezer's proposal seems to be plausible as it covers all Biblical bases.

Presently, it remains only to discuss the probability that humans may recover their lost longevity. At this point, it is worthy to mention the recent scientific discoveries that have lead Aviezer and others to believe that they have unlocked both the mystery of the early Biblical generations, and more significantly, the secret of longevity today.

M. Azbel of Tel Aviv University researched the idea of a genetic basis to aging and death and suggested that "there exists a genetically programmed ability to die at a given age...that age may be manipulated [9]." Indeed, experimental research does seem to substantiate his proposal. Tom Johnson of the University of Colorado discovered that changing of the gene called *Age-1* in nematode worms (*Caenorhabditis elegans*) doubled their lifespan [10]. In 1992, Michael Rose of the University of California succeeded in establishing a genetic strain

of *Drosophila* fruit flies that lived about twice as long as flies raised in a neighboring laboratory. At every stage of life, these new and improved flies were stronger than the average fly. A third study by Michal Jazwinski identified genes that strengthen and extend the life of brewer's yeast [11].

As exciting and fascinating as the concept of genetic manipulation may be, it can hardly be proven that this is the single reason for human aging, not to mention the considerable bridge to be crossed to extrapolate conclusions from studies with insects to the human beings. So what defines aging and what causes mankind to age? Studies, in the past decade by the researchers Ricklef, Finch, and Hayflick provide a few probable theories [12,13].

One theory proposes that genetic mutations at the DNA level set in motion the events of aging. Mutations are changes in the DNA of a cell that are passed on to daughter cells during the process of mitosis, or cell division. Changes in DNA, in turn, cause the genes, to encode for defective proteins. A genetic mutation in a significant location can wreak havoc on enzymes, transcription factors, and regulatory proteins that mediate DNA and regulate the individual activities of genes. Notably, the mutations of the tumor suppressant genes, p16 and p35, which slow cell proliferation also accelerate during the process of aging. These mutations raise the risks for an individual to develop cancer [12]. Gene mutations may damage mitochondria, the powerhouses of cells, as they contain their own DNA with which they replicate and encode for enzymes that aid in the production and storage of ATP molecules, the body's form of stored energy. Damage to mitochondrial DNA may cause the loss of functioning of the mitochondria and a reduction in energy production. The storage of ATP molecules may adversely affect brain and muscle function. Thus, for example, at the end of the lifespan, some areas of the brain possess a whopping 3% of abnormal mitochondrial DNA. Mutations are thus a significant factor of the aging process [12].

Not all aging can be explained by genetic mutation. A second theory, called the Free Radical Theory, involves the deleterious effects of free radicals, molecules or atoms that contain unpaired electrons. This instability creates an uneven electric charge and, to regain stability, these free radicals attract other electrons by detaching them from nearby DNA in a process called oxidation. Theorists propose that such oxidations are directly involved in the wrinkling of skin, the loss of flexibility, and rigor mortis [14]. Oxidized lipids may cause arteries to abnormally thicken. Furthermore, the tremors seen in Parkinson's disease, the slowness of motion apparent in old age, and Type II diabetes are also associated with free radical induced oxidative damage [12].

It is generally agreed that to some degree, a biological clock gene is involved in human aging. For example, the death of brain cells is "due to regular, programmed cellular destruction. "Combining these two facts, the clock gene is theorized to work as follows. As cells divide, the gene monitors the number of divisions. After the cells reach their maximum number of divisions, the gene encodes proteins for cell destruction [15]. In 1961, Leonard Hayflick presented the idea that normal diploid cells, like those of the skin, lungs, and bone marrow, which were at first thought to continually replace themselves throughout life, only divide a limited number of times [16]. Subsequent research showed that as the age of a cell increases, the number of potential cell divisions decreases. The point at which the cells cease to divide is called the Hayflick limit. This concept was furthered by the telomere theory [12]. Telomeres are highly repetitive sequences of nucleic acid bases located at the tips of chromosomes that protect the chromosome from unraveling. In DNA replication, the telomeres of daughter cells become shorter than those in the parent cell. At the Hayflick limit, the telomeres are extremely small and cell division ceases. As protective telomeres are no longer effective, genes produce proteins that cause the destruction of the tissues, a known characteristic of the aging process. In substantiation of this theory, research has found that infinitely dividing cells, such as spermatogonia and cancer cells, also maintain their telomeres indefinitely [17]. These cells synthesize the enzyme telomerase, which maintains the telomeres. If this theory held true, then perhaps a boost of telomerase in cells, if somehow separated from their counterpart cancerous mutations, could be a possible key to human longevity.

Though the above theories point to genes as only the perpetrators of disease and aging, a groundbreaking study published in August 2001 by geriatrician Dr. Thomas Perls and geneticist Lou Kunkel arrived at the opposite conclusion. Encouraged by previous research maintaining that the alteration of just a few genes in fruit flies caused noticeable increases in lifespan, and Dr. Lithgow's discovery of a longevity gene in worms in 1994, Perl and Kunkel set out to find such parallels in the human genome as well. They conducted a study comparing 137 pairs of siblings who had each respectively reached beyond the ages of 98 and 91. Remarkably, they found that in a significant number of these cases, the elderly sibling-pairs shared uncanny commonalities of DNA in small genetic regions located on specific areas of Chromosome 4 that could not be credited to chance [19]. Additionally, many of the participants in the study enjoyed decent physical condition despite lifelong tendencies toward unhealthy eating and smoking. Thus, the researchers posited that a handful of genes -yet to be determined- found on chromosome 4 might well be responsible both for human longevity as well as for deterring the degenerative diseases associated with aging. As thrilling and novel as this discovery is though, it is presently only in its beginning stages. Researchers will have long roads to pave before they can pinpoint the exact genes that are the key to longevity. In Dr. Perls' own words, "If we were looking all over the world for a clue to exceptional longevity, we might say we have now found the city. But to find the clue itself, we have to find not only the apartment, but the kitchen sink in that apartment where that clue is actually located [20]."

In another vein, an article in the Washington Post on September 4, 2001 reported yet a different theory on aging. Stephen Spindler of the University of California proposed that drastic calorie reduction could reverse the process of aging. In his study, Spindler put elderly mice on a four-week low calorie diet. The diet reversed the activities of many genes that normally function in the aging process. Spindler said, "My work shows that calorie restriction not only prevents (age-related) changes, but quickly reverses the majority of changes that take place with age [18]. "Though his theory is proven in mice, Spindler's low calorie diet remains unproven in humans.

As theories and research on aging abound, there are no definitive answers to date. However, with the fast pace of current research and scientific technology it remains only a matter of time before mankind reaches longevity once again. The possibility of a world without aging seems fascinating, yet scary, as it would change the face of the humanity as we know it. Yet, such a world is not novel; it did exist for Adam and Eve many thousands of years ago. With the right touch of telomerase and with an appropriate diet, humankind may find itself marching to an older tune...and, who knows, knee-length gray beards may be the height of fashion again sooner than we think!

Acknowledgements: To my parents: Long life would be worthless without you! Thanks for being there twenty-five hours, eight days a week!

References

[1] Genesis 5, as cited in: Kaplan, A. (1993). Immortality, Resurrection and the Age of the Universe: A Kabbalistic View. Ktav Publishing House, Inc.: Hoboken, New Jersey, p. 20.

[2] Josephus. *Antiquities* 1:3:9. As cited in: Kaplan, A. (1993).

[3] *Moreh Nevuhim* 2:47

[4] *Ramban* on Genesis 5:4. As cited in: Kaplan, A. (1993).

[5] *Abarbanel* on Genesis 5. As cited in: Kaplan, A. (1993).

[6] Schontal, R. (1987). Mycotoxins, the Flood, and Human Lifespan in the Bible. Korot. 9:5-6: 503-506.

[7] Aviezer, A. (1998). The Extreme Longevity of the Early Generations in Genesis. Bekhol Derakhekha Daehu. 7:5-14.

[8] Williams, G.C. (1957).Evolution. 11:398-411. As cited in: Aviezer, A. (1998).

[9] Azbel, M. (1997). Physics Reports. 288:545. As cited in: Aviezer, A. (1998).

[10] Johnson, T.E. (1988).Genetics. 118:75-86. As cited in: Aviezer, A. (1998).

[11] Rusting, R.L. (1992). Scientific American. December 1992: 87. As cited in: Aviezer, A. (1998).

[12] Ricklefs, R.E. & Finch, C.E. (1995). Aging. Scientific American Library: New York.

[13] Hayflick, L. (1994). How and Why We Age. Ballantine Books: New York. As cited in: Aviezer, A. (1998).

[14] Kronhausen, E. et al. (1989). Formula for Life. William Morrow and Company, Inc.: New York, NY.

[15] Keeton, K. (1992). Longevity: The Science of staying Young. Penguin Books: New York, New York.

[16] Hayflick, L. and Moorehead,P. (1961) The serial cultivation of human diploid strains. Exp. Cell Res. 25: 585-621.

[17] Lafferty, E. et al. (1996). Can We Stay Young? Time Magazine. 25/11/96:53-62.

[18] Okie, S. (2001). Low Calorie Diet Slows Aging in Mice Study. The Washington Post. 9/4/04: A10.

[19] Infoaging. http://www.infoaging.org/feat10.html. (retrieved January 27, 2005)

[20] PNAS. http://www.grg.org/TPerls1.htm.(retrieved January 27, 2005)