

THE NUCLEUS

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Project SEED

An article by Mindy Levine

Professor Samuel Kounaves

*On the Phoenix Mission to Mars and Beyond
By Sonia Taktak*

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Patrick Gordon Selected Chair-Elect for 2010

Summer Scholar Report

Chromatin Regulation of Pancreatic Endocrine Identity and Function

By Alexander D. Gütlin, Stefan Kubicek, Bridget K. Wagner and Stuart L. Schreiber



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Cover: *Pictured is the winning entry in the Chemists Celebrate Earth Day Haiku Contest. The winning illustrated haiku was submitted by Jay Hatchett, Grade 10, Norwood High School.*

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Project SEED

By Mindy Levine

Mei Wang could have gone the route of other local high school students, spending her summer working as a camp counselor or a lifeguard. Instead, Ms. Wang spent the summer of 2008 studying the inhibition of sugar-processing enzymes. Ms. Wang was a participant in Project SEED (Summer Experience for the Economically Disadvantaged), a chemistry research internship program for economically disadvantaged high school students. Through the program, she found an internship working in the laboratory of Professor Louis Liotta at Stonehill College. "My favorite part of the program is the surprise," said Ms. Wang. "Unlike experiments I've done previously in school, these experiments did not have guaranteed results. Each assay is a surprise."

Project SEED has existed for forty years, and is organized and coordinated by the National Project SEED Office, a division of the American Chemical Society. Project SEED allows high school students from low-

income families to perform paid scientific research at local colleges and universities. The program has branches in 34 states, Washington DC, and Puerto Rico, with approximately 400 students, 200 mentors, and 100 coordinators planning to participate in the program this summer. Each mentor supervises 1 to 2 high school students in a chemistry research project.

One of the key goals of Project SEED is to ensure that the students are actively involved in substantive research projects. "It is important to see that the students are doing chemistry, and not just washing glassware," said Ms. Cecilia Hernandez, director of the National Office of Project SEED. For example, Hao Trieu worked with Professor Cheryl Schnitzer of Stonehill College in the summer of 2008 on the synthesis and purification of biodiesel from waste vegetable oil in the cafeteria. "I love this project because it is about improving our environment, and in the future I believe that this project

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will expand and become very successful," said Ms. Trieu. "My future plan is to promote environmentally-friendly actions within my town of Randolph."

Professor Schnitzer, an associate professor of physical chemistry, has been the coordinator of Project SEED at Stonehill College since 2001. Stonehill College is one of the few local colleges that are involved in Project SEED. Professor Schnitzer explained that the chemistry department decided to start a Project SEED program as part of the strategic goals of the department to introduce under-represented groups to the sciences. "It has been a very successful program," said Professor Schnitzer, with between 2 and 5 students participating each summer since 2001. "These economically disadvantaged students are also extremely academically talented as they must go through a rigorous application and interview process." As part of the Project SEED program at Stonehill College, the students are involved in

continued on page 12

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| Trustee | |
| <u>Peter C. Meltzer</u> | 232 |
| Joseph A. Lima | 193 |
| Councilor/Alternate | |
| <u>Amy E. Tapper**</u> | 359 |
| <u>Catherine E. Costello**</u> | 359 |
| <u>Patricia A. Mabrouk**</u> | 322 |
| <u>Dorothy J. Phillips**</u> | 320 |
| <u>Ruth Tanner**</u> | 317 |
| <u>Michaeline F. Chen*</u> | 278 |
| <u>Jerry P. Jasinski*</u> | 259 |
| <u>Gary R. Weisman*</u> | 253 |
| <u>Marietta Schwartz*</u> | 253 |
| <u>Norton P. Peet*</u> | 244 |
| Edward J. Brush | 237 |
| Mick Hurrey | 235 |
| Raj (SB) Rajur | 227 |
| Ira S. Krull | 153 |
| Director-at-Large | |
| <u>Alfred Viola</u> | 272 |
| <u>James E. Phillips</u> | 190 |
| Nominating Committee | |
| <u>Michael Filosa</u> | 332 |
| <u>Ralph T. Scannell</u> | 271 |
| Richard C. Moreton | 225 |
| Esselen Award Committee | |
| <u>Howard R. Mayne</u> | 317 |
| <u>Anna W. Sromek</u> | 301 |
| Shainaz M. Landge | 201 |
| Richards Medal Committee | |
| <u>Patricia A. Mabrouk</u> | 356 |
| <u>Jeffrey I. Steinfeld</u> | 332 |
| Ira S. Krull | 162 |

Winners are underlined. Councilors** and Alternate Councilors* are elected for a three year term beginning 1/1/2010. ◇

ALMA National Conference

The Association of Laboratory Managers (ALMA) is pleased to announce that it will be holding its 30th annual conference on October 27-30, 2009 at the Georgia Tech Global Learning Center in Atlanta, Georgia. This year's conference features workshops, presentations, roundtable discussions and networking opportunities focused on helping managers build leadership skills in employees, utilizing diversity and managing your career. These are skills that are becoming even more important in an era of cost-cutting, downsizing and the continued need to do more with less. Also featured in the conference are supplier exhibits, a tour of the Georgia Tech laboratories and presentation on green chemistry by Professor Charles Liotta of Georgia Tech.

Conference information and registration can be obtained at www.labmanagers.org. ◇

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**Saturday, November 14, 2009
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Leadership Without Authority

By Jackie O'Neil ([oneil,ja\(at\)neu.edu](mailto:oneil,ja(at)neu.edu))



At first glance, the phrase "leadership without authority" may seem like an oxymoron to many; however, it would seem that this concept is something that everyone should think about and apply. Consider this:

have you ever known anyone who has demonstrated himself or herself as a leader without having any formal authority? Whether it's a fellow colleague who is able to bring people together to work on a task or whether it's a volunteer coordinator who is helping a project, chances are you will find or have found yourself in one of these situations. Thus, it can be said that the ability to demonstrate leadership skills without having formal authority is an ability that not only helps others around you; it also helps you become a more effective member of your team.

The ACS offers leadership development courses both online and in-person—one of which I had the opportunity to take at the most recent national meeting in Salt Lake City. The title of the course that I took was named *Leadership Without Authority*. This course outlined the fact that everyone, at some point in his or her life, will be called upon for a leadership position. How you handle this responsibility will reflect on you to both your peers and your superiors. For some, an innate sense of leadership is something that comes very easily, while it takes others many years of practice to gain this same attribute. Personally, I feel that my leadership skills are in the making. As a vice president for North-

continued on page 12

Professor Kounaves: on the Phoenix mission to Mars and beyond

by Sonia Taktak, PhD



On May 25, 2008, the Phoenix Lander arrived on Mars after a 10-month space flight, carrying on board the first wet chemistry laboratory to perform extra-terrestrial chemical analysis. Tufts University chemistry professor and adjunct geology professor Samuel Kounaves was a co-investigator for the 2007 Phoenix mission to Mars and lead scientist for the wet chemistry laboratory. *The Nucleus* had the chance to interview Professor Kounaves in his laboratory at Tufts University and to learn a little more about his journey as a scientist whose dream, of doing chemistry on another planet to answer fundamental questions about our solar system, had come true.

The concept of sending a wet chemistry laboratory to perform on-site analysis of Martian soil took form back in 1997, when an international group of scientists, including Professor Kounaves, launched a project with NASA for a 2001 mission to Mars. Although the initial mission was canceled unexpectedly by NASA after the loss of the Mars Orbiter in 1999, a new team was put together for a proposal and subsequently funded in 2003 for a 2007 Mars Scout Mission.

When asked about his experience working with NASA and the Phoenix team, Kounaves said he was most impressed to see how NASA managed the project, an assemblage of literally

millions of parts from countless sources that ultimately had to survive the rigors of space travel to function properly after arriving on the surface of Mars. The wet chemistry laboratory was part of a larger instrument package, the Microscopy, Electrochemistry, and Conductivity Analyzer (MECA). MECA also included an optical and atomic force microscope, and a thermal and electrical conductivity probe. The solar-powered robot also carried a meteorological station, a thermal and evolved gas analyzer (basically a scanning calorimeter and mass spec) and, of course, several cameras.

The wet chemistry group at Tufts started work in 2003 under Kounaves' supervision, initially developing several of the sensors and analytical procedures and later characterizing and testing the final sensor assembly. They were also responsible for loading the final reagents into the 5 crucibles for each of the 4 chemistry cells that were sent to Mars. Specially developed Ion Selective Electrodes (ISEs) were used for the detection system, including sensors for sodium, potassium, chloride, magnesium, calcium, sulfate, and perchlorate ions, and for measuring pH. One of the main challenges that the group had to overcome was to design the ISEs to survive and perform under the extreme temperatures and vibrations that they would be subjected to on the way to Mars and during launch and landing, and on the surface during its operation. The device had to survive exposure to temperatures from -80 °C to + 60 °C for a month prior to analyzing the Martian soil.

When results came back from the mission, the team was very excited to have uncovered how "friendly" Martian soil really is to potentially support life. First, the pH of Martian soil was found to be slightly basic and very well buffered, around pH 8, rather than very acidic, as previously hypothesized. Further soil tests confirmed the

presence of sodium, potassium, chloride, magnesium and calcium carbonate in quantities similar to what one finds in Earth's soil. By digging 10 cm underground, the robot further revealed the presence of a solid white material, which the on-board mass spectrometer definitively confirmed to be pure water (ice). Interestingly, unexpectedly high levels of perchlorate, on the order of 1%, were also found in the soil. Although naturally high levels of perchlorates are rare on earth, they are found in arid places such as the Atacama desert in Chile. When asked about the possibility of life on Mars, Kounaves said "We did not find anything that would preclude the soil from being habitable by a variety of organisms, but because of the high levels of UV radiation on the surface, if life as we know it on Earth exists on Mars, it is most likely subterranean."

As a child Kounaves was always curious about science. He was greatly influenced by his father and by science teachers in middle school and high school. "I was born during the days of Sputnik and was brought up with Star Trek," he said, "I always had an interest in science and a curiosity about how the world and the universe work." When talking about his experience working with NASA and being on the Phoenix mission, Kounaves said what he enjoyed the most was working at the cutting edge of science, close to science fiction, to answer fundamental questions about chemistry and life on Mars. "In the lab it is easy to test the pH of solutions, but on another planet it is a real challenge because the environment is so extreme," Kounaves explained. With the success of the Phoenix mission, Kounaves's group has deservedly earned the reputation of being the "extreme analytical chemistry" group. The group is now applying its ability and expertise in developing ISE sensors for extreme

Continued on page 12

Notable New England Chemists

We continue to present here biographies of New England chemists written by Lyman G. Newell of BU and Tenney L. Davis of M.I.T. for the guidebook for the 76th ACS Meeting held in September 1928 in Swampscott, Massachusetts. Transcribed for the Nucleus by M. S. Simon.

James Mason Crafts 1839-1917

James Mason Crafts, best known as the co-discoverer of the Friedel-Crafts reaction, was born in Boston, Mass. He attended Boston Latin School and the Lawrence Scientific School, receiving the Bachelor of Science degree in 1858. He studied with Plattner at Freiberg, with Bunsen at Heidelberg, and then for four years with Wurtz at Paris. Returning to America in 1865, he traveled for a year as inspector of mines in Mexico. He was the first Professor of Chemistry, 1867-1870, at the newly established Cornell University, and in 1870 succeeded Storer as Professor of General and Analytical Chemistry at the Massachusetts Institute of Technology. He returned to Paris in 1874 and remained there for seventeen years, doing most of his research with Friedel, but some of it independently or with other co-workers. The first three papers on the Friedel-Crafts reaction appeared in 1877, and covered nearly the entire field of the process, yet the experimentation on which the papers were based had been carried out in five or six weeks. Crafts also published papers on the densities of the halogens at high temperatures and on the organic compounds of silicon. His work on thermometry won him the Jecker prize of the French Academy and the Rumford medal of the American Academy of Arts and Sciences. In 1891 Crafts returned to Boston. He was Professor of Organic Chemistry at the Massachusetts Institute of Technology from 1892

William Polik Named 2009 James Flack Norris Awardee



Dr. William F. Polik, the Edward and Elizabeth Hofma Professor of Chemistry at Hope College in Holland, Michigan, has been named by the Northeastern Section of the American Chemical Society (NESACS) the win-

ner of the 2009 James Flack Norris Award for Outstanding Achievement in the Teaching of Chemistry. This annual award was established in 1950 by NESACS to honor the memory of James Flack Norris (1871-1940), professor of chemistry at Simmons College and the Massachusetts Institute of Technology, chair of NESACS in 1904, and ACS President in 1925-26.

Professor Polik, who received a B.A. in chemistry and mathematics (Phi Beta Kappa) from Dartmouth College in 1982, joined the faculty of Hope College in 1988 after receiving his Ph.D. in physical chemistry from the University of California at Berkeley. A molecular spectroscopist, he is a member of the American Chemical Society, American Physical Society, American Association for the Advancement of Science, and the Council for Undergraduate Research. He works very closely with undergraduate students in his research laboratory and is active in the development of web-based materials for the teaching of physical chemistry. He has been recognized for his achievements in the past through receipt of an NSF Presidential Young Investigator Award, Camille and Henry Dreyfus Foundation Fellowship, the Hope College Provost's Award for Teaching Excellence, and election as a Fellow of the American Association for the Advancement of Science.

The Norris Award, which consists of a plaque and \$3,000, will be presented to Professor Polik at the NESACS monthly meeting on November 12, 2009, at Boston University in recognition of his outstanding work as a teacher and mentor, and for his leadership as member and chair of the ACS Committee on Professional Training in developing the new guidelines for undergraduate chemistry programs and bringing them toward implementation.

◇

Josiah Willard Gibbs 1839-1903

Josiah Willard Gibbs was born in New Haven, Conn. He entered Yale College in 1854, graduated in 1858, continued his studies in New Haven, and received his Ph.D. in 1863. During the next three years, he was a tutor at Yale. From 1866 to 1869, he studied in Europe, especially at Heidelberg with Kirchoff and Helmholtz. Upon his return to New Haven, he continued to teach, and in 1871 was appointed Professor of Mathematical Physics, a position which he held until his death. Within the first ten years after his

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A Report on NESACS – GDCh German Exchange 2009

By Deniz Yüksel (Immediate Past Vice Chair, NSYCC 2008-2009)
and Raeanne Napoleon (Incoming Chair, NSYCC 2009-2010)

The ninth annual exchange between the German Chemical Society's (Gesellschaft Deutscher Chemiker) Younger Chemists Forum (Jung Chemiker Forum) and the NESACS Younger Chemists Committee (YCC) took place in March. Prof. Ruth Tanner (U.Mass. Lowell), Prof. Mort Hoffman (Boston University), and Dr. Mike Strem (Strem Chemicals) accompanied the American delegation during their weeklong stay in Essen, Germany. The American delegation was comprised of Boston area graduate and undergraduate students.

The group was well received by the Organizing Committee of Frühjahrssymposium Essen at the Düsseldorf airport on March 8th. The German hosts then provided a walking tour of Essen that concluded at the restaurant Der Löwe, where everyone had the chance to sample authentic Bavarian food and get acquainted. Chemical research in Germany has a long and storied history and during the first few days of the stay the American delegates saw some of it first-hand. On Monday, two Max Planck Institutes in Mülheim an der Ruhr were visited – Max Planck Institute for Coal Research and Max Planck Institute for Bioinorganic Chemistry. The following day, our group toured the facilities of a chemical industry giant Bayer AG in Leverkusen. During the tour, different product groups were introduced, job and career opportunities were explained at Bayer, and then concluded with a trip in the Chempark Leverkusen with an explanation of the modern chemical park concept and the waste management plant. That afternoon, the city of Cologne was visited. On Wednesday, a local Essen company – Evonik Goldschmidt was toured.

The American delegation agrees that the highlight of the trip was that afternoon: most geared up as miners and went 1000 meters below the ground to take “a trip into a pit” and see coal mining. That evening was the welcome reception for the 11th JCF-Frühjahrssymposium at the University of Essen-Duisburg.

During the three-day conference, Andrew Kleinke (Boston University), Courtney Pfluger (Northeastern University), and Daniel Turner (MIT) delivered oral presentations and the rest of the group presented posters at the symposium. In addition to presenting research, everyone was engaged in extensive networking and scientific discussions with German and European students participating at the conference. At the end of the conference two members from the delegation, Erin Iski (Tufts University) and Brian Steinberg (Boston College), were recognized for their poster presentations skills. Erin, who is a 4th year graduate student in Prof. Charlie Sykes lab, presented her work entitled, “AgCl Monolayers on Au(111): Novel, Ultra-stable and Atomically-flat Surfaces.” Brian, who anticipates graduating this year, presented his thesis work entitled “Target Oriented



American delegation at Evonik before (top) and after (bottom) the trip into a pit – Legend for the top picture: Front row (l-r) Daniel Turner, Courtney Pfluger, Christina Li, Deniz Yüksel, Olga Makhlynets, Rachel Tsui, Mariam Ismail, Marina Pellon Consunji. Back Row (l-r) Evonik Representative, Carol Bischof (JCF), Brian Steinberg, Tamara Halkina, Erin Iski, Raeanne Napoleon, Andrew Kleinke, Igor Schapiro(JCF).

Total Synthesis Leads to a New Class of Unnatural Products” which he carried out in Prof. Lawrence Scott's lab.

At the end of the week, American students were invited to a farewell dinner hosted by Dr. Kurt Begitt, Deputy Executive Director and Director of Education and Professional Affairs of the GDCh and members of the JCF. The American and German delegations exchanged gifts to say thank you for such an eventful week during the meal. Lifelong relationships were forged during the week, and neither group will forget the fun that was had during the ninth annual German Exchange. ◇

Announcements

The James Flack Norris and Theodore William Richards Undergraduate Summer Research Scholarships, 2009

The Northeastern Section of the American Chemical Society (NESACS) established the James Flack Norris and Theodore William Richards Undergraduate Summer Scholarships to honor the memories of Professors Norris and Richards by promoting research interactions between undergraduate students and faculty. Research awards of \$3500 have been given for the summer of 2009. The student stipend is \$3000 for a minimum commitment of ten weeks of full-time research work. The remaining \$500 of the award goes to the research advisor to use on supplies, travel, and other items relevant to the student project. The 2009 scholarships have been awarded to:

Danelle Raad, Brown University, Professor Theodore Betley, Advisor, Department of Chemistry and Chemical Biology, Harvard University

Elizabeth Neuhardt, Keene State College, *The Synthesis and Characterization of New N-Heterocyclic Germylene Complexes of the Early Transition Metals*, Dr. Colin Abernethy, Advisor

Rita Ciambra, University of New Hampshire, *Redox Reactivity, Ligand Substitution, and Conformational Changes in a Geobacter Heme Protein GSU093*, Ekaterina Pletneva, at Dartmouth College, Advisor

John Sirois, University of Massachusetts Dartmouth, *Nucleophilic Displacement Reactions in Hindered Allylic Systems*, Dr. Donald Boerth, Advisor

Award winners are required to submit a report of their summer projects by November 2009 for publication in *The Nucleus*. They are also required to participate in the Northeast Student Chemistry Research Conference (NSCRC) in April 2010. ◇

The Phyllis Brauner Memorial Book Award

The Book Award is a memorial to an outstanding member of the Northeastern Section, Dr. Phyllis Brauner. She served in many offices of the Section, in 1974 became the first woman Chair of the Section, and contributed to the activities of the Section with her bold, innovative ideas and practical ways of carrying them out. She taught at Simmons College and Framingham State College and was an inspiring teacher. Her research and education interests are mirrored in the prize, which is given to a student who excels in the undergraduate oral presentation at the Northeast Student Chemistry Research Conference (NSCRC), as judged by a com-

mittee of the conference judges that includes the Education chair. The book is chosen by the student. A presentation bookplate inside the cover honors both Dr. Brauner and the awardee. The book is presented to the awardee at the May meeting of the Section.

This year's awardee is **Samuel Beal** from Wheaton College for his poster presentation at the 2009 Northeast Student Chemistry Research Conference (NSCRC) entitled *Chemical Weathering Along the Greenland Ice Sheet Margin*. His research advisor is Professor Matthew Evans. The book he has chosen is "Earth: Portrait of a Planet" by Stephen Marshak. ◇

Summerthing 2009

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Summer Scholar Report

Chromatin Regulation of Pancreatic Endocrine Identity and Function

Alexander D. Gitlin*, Stefan Kubicek, Bridget K. Wagner, Stuart L. Schreiber

Abstract

At the heart of Type-I Diabetes is a deficiency of pancreatic beta cells. Many questions remain about the relationship between chromatin, the native state of DNA within the nucleus, and beta cell identity. The role of enzymes that modify chromatin's structure, and their potential role as small molecule drug targets remain unexplored. Here, we report chromatin immunoprecipitation analysis of activating and repressive chromatin states in mouse pancreatic cell lines and human pancreatic islets that sheds light on chromatin's regulatory contributions to pancreatic cellular identity and function.

Introduction

In Type-I Diabetes, a patient's immune system destroys his or her pancreatic beta cells, causing complete dependence on exogenously administered insulin or pancreatic islet transplantation. Yet both of these therapeutic strategies remain inadequate. Exogenous insulin cannot provide the precise regulation of blood glucose afforded by unimpaired pancreatic beta cells, and efficacy and practicality greatly limit islet transplantations.¹ To address this critical and unmet medical need, our project seeks to discover small molecules that promote the regeneration of beta cell function and amplification of beta cell number.

Our approach to this small molecule discovery seeks to strategically modulate chromatin-modifying enzymes. Chromatin modifying enzymes, in particular, those that deposit or remove post-translational modifications on histone proteins, contain catalytic pockets that can be targeted by small molecules. These enzymes also play a role in regulating cell type specific gene expression programs and functions. As a result, we believe this family of enzymes represents a crucial group of targets for our purposes.² Here we report studies that begin elucidating the relevant chromatin factors to be targeted by small molecules for regeneration of beta cell functionality.

Results

To begin identifying how chromatin and the enzymes that modify its structure regulate pancreatic endocrine function and cellular identity, chromatin immunoprecipitation (ChIP) experiments were performed to map the genomic locations of histone modifications known to be either activating (H3K4me3 and H3K36me3) or repressive (H3K27me3).^{3,4} We first investigated these modifications in murine alpha and beta cell lines, and found the expected regulatory differences at the developmental transcription factors known to specify alpha and beta cell identity, as well as at the hormone genes insulin and glucagon (Figure 1).⁵ In particular, Pdx1, a key developmental and glucose-responsive transcription factor present mainly in adult beta cells, was marked by H3K4me3 at the promoter of beta cells

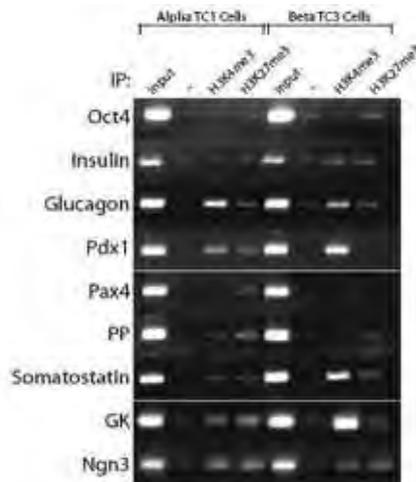


Figure 1. ChIP was performed in mouse alpha TC1 and beta TC3 cell lines using either no antibody (-), H3K4me3 or H3K27me3 specific antibodies. Immunoprecipitated genomic DNA was amplified in the linear range using primers for promoters of various genes (indicated on left) and analyzed by agarose gel electrophoresis.

exclusively. The glucagon and insulin promoters' H3K4me3 levels similarly correlated with their exclusive expression patterns in alpha and beta cells, respectively, though to a lesser extent.

Having observed this preliminary difference in the chromatin-based regulation of these endocrine lineages, we next investigated histone modification localizations in primary human pancreatic islets prepared from cadavers. These islets are known to contain a majority of beta cells, but also contain a variety of pancreatic endocrine lineages. Thus, instead of analyzing chromatin-based differences in specific cell types, we analyzed chromatin's regulation of pancreatic glucose-responsive functionality.

Because human islets were received in limited quantities, our ChIP protocol was first optimized to function robustly with few cells (Figure 2). Utilizing this protocol, we determined the presence of H3K4, K36 and K27me3 at targeted genomic regions in islets from two donors subjected to high or low glucose for 24 hours. Surprisingly, regulation of one gene, thioredoxin interacting protein (TXNIP), which is known to be upregulated by high glucose, was regulated in a distinct manner by the two donors.⁶ In the first donor, H3K4me3, a mark that correlates with transcription initiation at the 5' end of genes, remained at constant levels at the TXNIP promoter regardless of glucose levels (Figure 3). In contrast, H3K36me3, a mark that correlates with transcription elongation and is found throughout the body of genes, was significantly upregulated under high glucose. This suggested a mechanism whereby transcription of glucose-responsive genes may be controlled by enhanc-

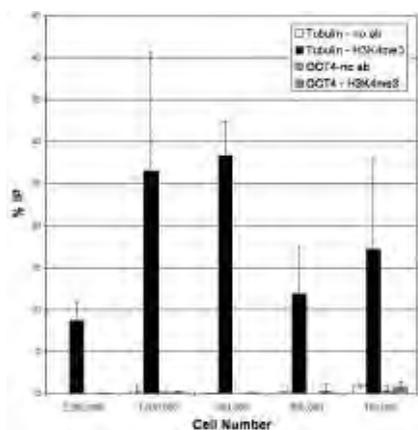


Figure 2. ChIP protocol was optimized for robust and specific detection of histone marks (H3K4me3) at expected enriched loci (Tubulin) versus non-enriched loci (OCT4) using various HeLa cell numbers. ChIP genomic DNA was quantified by real-time PCR using SYBR green probes (Applied BioSystems).

ing elongation and/or the elongation-associated histone mark, H3K36me3.

Surprisingly, when we performed the same experiments in islets from a second donor, we observed different results. Under high versus low glucose, neither changes in H3K4me3 or H3K36me3 levels were observed at the TXNIP promoter nor open reading frame, respectively. Instead, we observed a significant decrease in repressive H3K27me3 levels in the open reading frame of TXNIP under high glucose (Figure 4). As in the first donor, this result suggested that glucose-responsive genes like TXNIP may be upregulated under high glucose by promoting a chromatin state permissive to transcriptional elongation. However, the mechanism in the second donor appears to be de-repression rather than activation of the chromatin in the glucose-responsive gene body under high glucose.

Discussion

Because of its role in regulating gene expression programs, chromatin and its indexing histone modifications are believed to play significant roles in regulating physiological cellular identities and functions. Here, we report ChIP of murine pancreatic alpha and beta cell lines, as well as of primary human pancreatic endocrine cells, which detects the genomic locations of key histone modifications. In particular, we find that activating histone modifications differentially regulate alpha and beta cell genomes in an expected manner. Further, histone modifications appear to regulate glucose-responsiveness in part by facilitating chromatin states permissive to or facilitating gene elongation rather than initiation of TXNIP. Surprisingly, the two donors accomplished this regulation differently; while the first donor upregulated activating H3K36me3 in the TXNIP gene body, the second donor downregulated repressive H3K27me3 in the TXNIP gene body.

Our current efforts are two-fold. First, to pinpoint novel regulatory regions or pathways and to determine which chromatin mechanisms facilitate glucose-responsive gene control globally, we are extending these ChIP studies genome-wide via Solexa Sequencing. Second, we are investigating the potential of small molecules that antagonize enzymes that remove the H3K36me3 or deposit the H3K27me3 marks as amplifiers of glucose-responsive islet

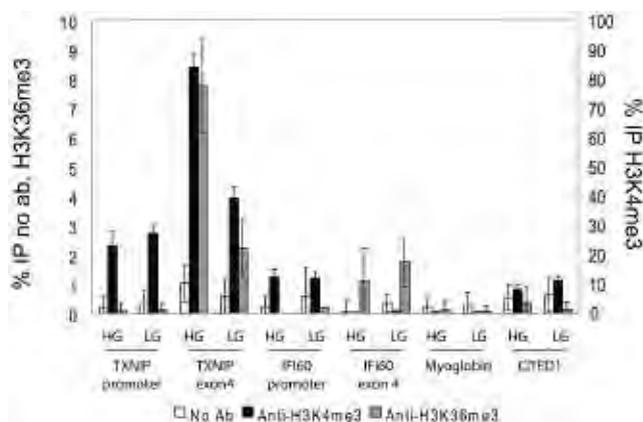


Figure 3. ChIP was performed in human islets from first donor subjected to high (11 mM, HG) or low (1.1 mM, LG) glucose for 24 hours using either no antibody (no ab), H3K4me3 or H3K36me3-specific antibodies. Indicated genomic regions were quantified by real-time PCR using SYBR green probes (Applied BioSystems).

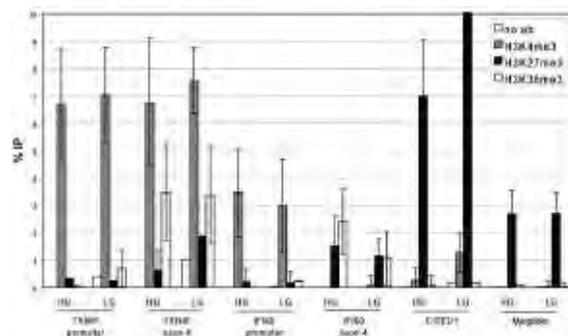


Figure 4. ChIP was performed in human islets from second donor subjected to high (11 mM, HG) or low (1.1 mM, LG) glucose for 24 hours using either no antibody (no ab), H3K4me3, H3K27me3 or H3K36me3-specific antibodies. Indicated genomic regions were quantified by real-time PCR using SYBR green probes (Applied BioSystems).

behavior. It will be important to continue characterizing the extent and mechanisms by which chromatin contributes to regulating pancreatic cellular identity and function, as well as the therapeutic potential of small molecules targeting enzymes that modify chromatin structure.

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Acknowledgments

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Project SEED

Continued from page 4

several auxiliary activities. There are college-wide weekly luncheons, for example, that the SEED students attend. Joel Anifowose, another Project SEED student at Stonehill College, said, “My favorite part of the program was all the meetings we did with all the college students...including the weekly lunches.”

Another aspect of Project SEED provides substantial assistance to students navigating the college application process. For example, at Stonehill College, the students meet with the Dean of Admissions and a representative from the Financial Aid Office. “I got a chance to meet great people and learned steps and tips for college applications” from these meetings, said Ms. Wang.

Mr. Marc McKithen participated in Project SEED in 1991, and is now an attorney in the intellectual property group of Milbank, Tweed, Hadley & McCloy LLP. He also received advice in navigating the college application process while he was a student in Project SEED at Rider University, working for Professor John Sheats. This advice ultimately helped Mr. McKithen obtain a full academic scholarship to Rider University.

For many students, simply being exposed to college life is novel and exciting, as they are often the first members of their family to attend college. “My summer research experience as a high school student was my first encounter with college life,” said Dr. David Blauch, a project SEED alumnus (1979) and professor of chemistry at Davidson College. Dr. Imelda Udo, an obstetrician-gynecologist (Project SEED 1990), agreed that a significant benefit of Project SEED was that it allowed her to be on a campus, and “see what campus life was like.”

One of the goals of Project SEED is to “encourage students to go into science,” said Mr. McKithen, and approximately half of the students decide on science-related careers. However, even if the alumni decide not to pursue a career in science, Mr. McKithen said, “I have never met someone for whom

Leadership Report

Continued from page 5

eastern University’s Student Affiliate Chapter, I have found that the techniques in leadership I learned in this course will help me become a much better vice president next year, and in return, help our chapter and student affiliates.

One of the best things about these courses that I have found is that this program helps you develop your leadership skills with others who want to do the same. And while not even the best course can teach you everything that there is to appreciate about being an effective leader, this course, with its great students and instructors, without a doubt helped me lay a foundation for understanding how everyday interactions build relationships that reflect the course’s mantra. ◇

the program was not beneficial.”

According to Professor Schnitzer, the main goal of Project SEED is to “introduce great high school students to research in a laboratory setting.” Dr. Udo agreed that one of the goals of Project SEED is to “get under-privileged students...into a science-oriented environment, and allow them to be exposed to science in general.” Additionally, Dr. Udo added that many inner-city high students are unaware of the variety of career options available to them. Project SEED teaches them about the breadth of career options.

Overall, participants had very few negative things to say about the program. Mr. Anifowose said, “I really can’t find an improvement for the program...it is in great shape.” Some of the SEED alumni expressed an interest in more follow-up and contact with the national SEED office. Dr. Udo suggested that the national office should call the alumni once each year to check whether they need academic or career assistance.

Ms. Hernandez spoke about the tremendous job gratification that she receives from Project SEED. “We are transforming many lives,” she said, “Not only the lives of the students, but

Professor Kounaves

Continued from page 6

terrestrial applications, where “the only way to analyze correctly is to measure *in situ*,” as in deep sea vents or the Antarctic Dry Valleys.

“To understand Earth’s climate and be able to produce good models, it is important to understand our two neighboring planets Venus and Mars. Mars is colder than it should be, and Venus is warmer than it should be if you only account for their position in the solar system. So why and how did Mars become so cold? If we build a climate model for Mars that works, we can then apply it to predict climate change on Earth by adding complexity to it. Mars is a simpler system to build a model for because it doesn’t have an ocean, for example. There is some evidence that Mars was warmer before, but the planet still holds a lot of mysteries on how the environment changed. The history of a planet is recorded in the chemistry of the soil, so to answer a lot of these questions, we need to taste the chemistry and not just look at it.” Kounaves said.

When asked what advice he could give to younger scientists, students, or faculty, who have a dream to participate in complex multi-disciplinary and visionary projects such as in planetary science, Kounaves said that for him the most important thing for success is to first have a solid foundation and expertise in one area of science that can be applied to broader areas such as planetary science, for example. Second, you should choose some area you are passionate about, because “you’ll never work a day if you do what you love to do.” Finally, you should not have any hesitation about interdisciplinary collaboration, because exploring the unknown in science often requires a wide variety of specializations and expertise. ◇

also the lives of their families.” Ms. Tahirat Nasiru, who participated in Project SEED in the summer of 2008, added, “The SEED program blessed me with a mentor and friend.” ◇

BUSINESS DIRECTORY

Historical Notes

Continued from page 7

appointment as professor, Gibbs published three long papers. In 1873, he published in the Transactions of the Connecticut Academy of Sciences, "Graphical Methods in the Thermodynamics of Fluids," and "A Method of Geometrical Representation of the Thermodynamic Properties of Substances by Means of Surfaces." In 1876 and 1878, he published the two parts of his famous paper "On the Equilibrium of Heterogeneous Substances." These papers are now highly regarded by many chemists, but they were overlooked for several years, partly from their inaccessibility to investigators and partly from their difficulty. When Ostwald and Arrhenius were arranging for the publication of the *Zeitschrift für physikalische Chemie*, Ostwald expressed a desire to translate the equilibrium paper, and later (1892) the German translation appeared. Subsequently (1899), Le Chatelier made a French translation. As soon as the paper was accessible, chemists throughout the world, especially in Holland and Great Britain, interpreted it to readers who were unwilling, or unable to follow the original.

Theodore William Richards 1868-1928

Theodore William Richards, Nobel laureate and one of the most distinguished of American chemists, was born in Germantown, Pennsylvania, and received the S.B. degree from Haverford in 1885. He studied at Harvard with Professor Josiah Parsons Cooke, Jr. and was awarded the A.B. degree in 1886, the A.M. and Ph.D. in 1888. During the year 1888-1889 he studied at Gottingen and visited in England, after which he returned to Harvard, where he was Assistant in chemistry 1889-91, Instructor 1891-94, Assistant Professor 1894-1901, Professor from 1901, Chairman of the Chemistry Department from 1903, and Director of the Gibbs Memorial Laboratory from 1912. In 1894 he went to Leipzig for one semester of study, and

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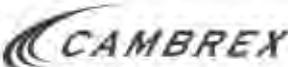


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in 1907 to the University of Berlin for a short period as Exchange Professor. He was the recipient of many honorary degrees, medals, awards and memberships in learned societies. His determinations of the atomic weights of

oxygen, copper, barium, strontium, calcium, zinc, magnesium, iron, cobalt, silver, carbon, nitrogen, and lead, etc. were everywhere accepted as more accurate than those of earlier workers. His announcement in 1914 that lead from radioactive minerals has a lower atomic weight than ordinary lead paved the way for an understanding of

isotopes. He invented the nephelometer and made many other improvements in apparatus and method. His studies and speculations on compressibility, on atomic volume, and on the forces within and between molecules have opened new and still-to-be-explored fields in our knowledge of the constitution of matter. ◇



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