Dear Members of TTCF,

We are delighted to launch the TTCF Progress Report. We hope you find it educational and enjoyable.

In this issue, you will learn about important dates on the TTCF calendar and upcoming membership salons, read updates from our award recipients, and meet a new member of the Mattel Children’s Hospital UCLA development team.

This year’s goal is to increase our membership from 63 to 80. With an amazing group of like-minded individuals such as you, we are confident that we will succeed. Thank you for your commitment to Mattel Children’s Hospital UCLA, where every day, faculty members are discovering a better future for today’s and tomorrow’s children. We look forward to your continued active participation in 2012!

With heartfelt gratitude,

Amanda Brown Chang
Co-Chair
Beth Friedman
Co-Chair
Ellen Sandler
Co-Chair

In This Issue...

Member News
You’re Invited: 2012 Membership Salons
2012 Renewal Process
Rumor Has It...
Award-Recipient Updates
Progress Reports from 2011 Winners
Catching Up with Dr. Noah Federman
Stay Connected
New Staff / Staff Roster
Come See Us!
**Member News**

**Rumor Has It...**

What our members are saying about the annual faculty presentation and awards day:

“I thought it was a great day; I especially appreciated when last year’s winners spoke about the impact our contributions have had on their work. I am excited to be a part of the group and look forward to continuing to support TTCF.”

- Sabina Nathanson

“I can’t tell you enough how excited I am to be a part of this fantastic organization! It was extremely meaningful and worthwhile for me.”

- Stacie Shaheen

“I loved the recap from previous recipients – made it feel so worthwhile!”

- Malinda Krantz

**You’re Invited!**

We are delighted to announce two membership salons in January 2012. Thanks go to our hosting members Lorna Auerbach, Allison Berg, and Nicole Nathanson.

These salons are wonderful opportunities to showcase TTCF. We encourage you to invite new guests, who might share our vision in making a philanthropic investment.

**Monday, January 23 • 10 a.m. - Noon**
Hosted by Allison Berg & Nicole Nathanson
Beverly Hills

**Tuesday, January 24 • 10 a.m. - Noon**
Hosted by Lorna Auerbach
Pacific Palisades

RSVP today! Call (310) 267-1836 or send an email to lpescatore@support.ucla.edu. A formal invitation will follow.

**Send Us Your Invitation Lists!**

Gather the names, addresses, and emails of those you would like to invite to the salons, and send your guest lists to Laura Pescatore at lpescatore@support.ucla.edu by December 9.

(Please indicate preference for January 23 or 24 date.)

**It’s Renewal Time**

Remember to make your 2012 gift online at www.uclahealth.org/ttcf or by phone at (310) 267-1836.

If you prefer to mail your contribution, please make your check payable to The UCLA Foundation (indicating TTCF in the memo section), and send it to the following address:

Attn: Laura Pescatore
UCLA Medical Sciences Development
10945 Le Conte Avenue, Suite 3132
Los Angeles, California 90095-1784

Thank you for your continued support of today’s and tomorrow’s children!
2011 Award Winners

A Mid-Year Progress Report

First Place Winner: Kuk-Wha Lee, M.D., Ph.D.
Project: Humanin, a Potential Therapy for Type 1 Diabetes

Dear TTCF Members,

I am delighted to provide a mid-year progress report for my research entitled “Humanin, a Potential Therapy for Type 1 Diabetes.” Thanks to support from TTCF, this project will generate much-needed pre-clinical information to prepare Humanin as a therapy/diagnostic tool in children with Type 1 diabetes.

Progress-to-date:

1. We “cloned” the Humanin gene into an expression vector and are able to detect increased protein expression in our unique assay. This difficult task was undertaken unsuccessfully by several groups worldwide. We achieved success because we included special regulatory areas that had not been incorporated. Now, large amounts of the Humanin protein can be made for use in animal studies.

2. We obtained special vectors that will allow the production of Humanin from the liver, which makes the largest amount of protein in the body. Using these tools, we will produce high concentrations of Humanin circulating in the blood of mice. We will then mate them with others that spontaneously develop Type 1 diabetes to see if we can prevent the onset of the disease.

3. We determined that the published “neuronal Humanin receptors” are made in human insulin-producing cells.

4. We initiated a collaboration with Dr. Isabel Hernandez (pediatric endocrinologist and former trainee at UCLA) in Chile, and we wrote a protocol and began the Institutional Review Board (IRB) approval process to measure plasma Humanin levels in children with Type 1 diabetes mellitus and age- and sex-matched controls. We also will measure levels in diabetic ketoacidosis, in which fat, not glucose, is used as a fuel source.

Additional Funding Opportunity:

I am happy to report that an additional funding opportunity has been made available. TrialNet has banked samples from thousands of children who developed Type 1 diabetes and their genetically prone siblings who haven’t yet developed the disease. We will use the preliminary data derived from point four above to apply for this large and prestigious National Institutes of Health grant that also will give access to this valuable repository of blood samples from the youngsters with Type 1 diabetes.

TTCF Fund Impact:

The TTCF Award has allowed me to move forward with preliminary results, thus being able to attract additional grants to continue my investigations. Thank you, again, for investing in this project, as my colleagues and I generate data so important to promoting children’s health.
Second Place Winner: Paul Krogstad, M.D.

Project: Identification and Initial Testing of Therapeutic Agents for Enterovirus Infections

Dear TTCF Members,

I am pleased to report that my colleagues and I have made deep progress with the research project presented at the 6th Annual TTCF Faculty and Award Presentation in May 2011. Thanks in large part to funding from TTCF, we have been able to pursue our general goal of finding ways to effectively treat enterovirus infections, ranging from the common cold to hepatitis and infections of the heart, for which there are no current medications.

In August 2011, we infected mice with an enterovirus strain (CVB3-H3) that produces heart-muscle infection and injury (myocarditis) and administered either placebo injections or anisomycin. On the fourth day after infection, the animals were humanely euthanized and tissues were collected for measurements of the amount of virus present. We were surprised to find that anisomycin produced a measurable increase in the concentration of CVB3-H3 in the liver, heart, and pancreas of these mice. We speculate that antibiotics that work like anisomycin may interfere with immune system responses that help control enterovirus infection. At present, we do not plan to examine anisomycin any further.

After the disappointing results obtained with anisomycin, we moved to the most important aspect of our research, a systematic search for additional chemical inhibitors of enterovirus replication. Enteroviruses rapidly kill cells growing in the laboratory, and we devised an assay to identify compounds that block this effect of CVB3-H3 on HeLa-RW cells (HeLa cells were the first human cells to be continuously grown in culture). By mid-September 2011, we managed to screen all 85,500 chemical compounds present in seven chemical libraries in the Molecular Screening Shared Resource (MSSR) at UCLA's California Nanosystems Institute. From them, we tentatively identified 276 chemicals as possible inhibitors, and subsequent retesting dropped many, as expected, but 76 chemicals and known drugs emerged for additional testing. We are just beginning more labor-intensive assays, but we are pleased to note that we have identified several unique classes of chemicals and drugs and filed an Invention Report through UCLA's Office of Intellectual Property. In addition, we already submitted two grant proposals to the National Institutes of Health based on these data.

Our final objective is to determine if recent increases in enterovirus disease activity reported at UCLA and elsewhere in the community reflect a change in the viruses, reporting methods, or both. We completed a re-evaluation of a laboratory test that has been used for two years at UCLA to identify viruses causing respiratory tract symptoms in children and adults. We found that this test is inaccurate and often falsely indicates that an enterovirus infection is present when other viruses are at fault. A reassessment of UCLA's testing methods is underway. We also have developed a system to further study the genetic differences among viruses isolated from patients and to determine if changes in a specific part of the virus (called the IRES – internal ribosome entry site) explain why the coxsackievirus B1 (CVB1) has become the leading enterovirus identified in the United States since 2006.

In conclusion, I am very pleased to report rapid progress in all the objectives set forth in my TTCF proposal aimed at reducing deaths and severe illnesses caused by enteroviruses. We are particularly proud to note our advances toward identifying novel inhibitors of enterovirus replication. In September, I presented our work at Grand Rounds, where TTCF’s generous support was recognized. My team and I are deeply appreciative of TTCF’s backing over these past six months and look forward to continuing our investigations.
Dear TTCF Members,

This year, TTCF awarded our research team a grant to support the study to evaluate the role of iron supplementation in promoting bacterial and viral infections. Over the past six months, in large part thanks to this funding, we were able to establish the preclinical models of infection that are directly relevant to common children's infections. We used Streptococcus pneumoniae bacterium and influenza virus to cause respiratory infection in an animal model. Using wild-type mice, we determined the range of infectious-agent doses that cause no to moderate mortality on a standard diet, and we also determined the critical time-points for the analysis of infection. These data are essential for the comparison of mortality rates between wild-type and mutant mice on different iron diets.

In the meantime, we also bred a large number of hepcidin knockout mice. Hepcidin is the key iron-regulatory hormone, which is thought to have an important role in host defense against infection by sequestering iron away from microbes. Currently, we are conducting a large infection study comparing mortality of wild-type mice on low- and high-iron diets, and hepcidin knockout mice also on these diets. The data will answer if iron increases the severity of infection and mortality and if hepcidin has a role in protection against bacterial or viral infections.

If our experiments indicate that hepcidin has a protective effect against infections, using our mouse models, we will initiate a new study that has direct relevance to improving infection treatments. Our lab has developed mini-hepcidins, small peptides that act as hepcidin agonists in mice. We will administer mini-hepcidins before and during infection to examine the course and severity of both bacterial and viral infections in mice.

In parallel with mouse studies, we have been analyzing hepcidin regulation by microbes in human and mouse hepatocytes (main source of hepcidin in vivo). Human hepatocytes are a precious resource, as they are generated from fresh livers not used for transplantation. Hepcidin regulation in infection is of great importance to understand if both bacteria and viruses trigger hepcidin-mediated iron sequestration as a host defense response, and to provide information on the pathways that can be manipulated to improve host-defense responses. Our results suggest that both bacteria and viruses induce hepcidin via the interleukin-6 pathway, although bacterial molecules can directly stimulate hepatocytes to produce hepcidin, whereas viruses require an intermediary cell type for this effect.

Recently, we presented our findings at the 2011 International BioIron Congress in Vancouver, Canada. Our study titled “Hepcidin Regulation by Microbes” was selected for oral presentation in a plenary session. In the coming months, we anticipate completing mouse studies in wild-type and hepcidin-deficient mice and delineating the effect of an iron diet on the severity of infection. We also will prepare two manuscripts describing our findings (one related to infection in mouse models, the other to hepcidin regulation by microbes). Moreover, we intend to apply for additional funding, including submitting a National Institutes of Health R01 proposal. We are deeply appreciative of the support of TTCF, which allowed us to obtain critical preliminary data to lay the framework for human studies and the submission of grant proposals.

2011 Award Winners

A Mid-Year Progress Report (continued)

Third Place Winner: Yonca Bulut, M.D.

Project: Do No Harm: Is Iron Supplementation Worsening Infections in Children?
How much funding did you receive from TTCF, and how did it impact your research?
I received $130,000, and it was invaluable in allowing my research project to get off the ground. I was able to leverage the gift to generate valuable data that allowed me to apply for other grants. The research started under TTCF was seminal to being awarded the St. Baldrick's Career Development Award ($330,000 over three years), the Hyundai Hope on Wheels Research Award ($100,000), and the STOP Cancer Research Award ($150,000 over three years). Overall, the TTCF gift has been vital to pursuing this revolutionary technology, as we continue to make important progress.

Can you share the current status of your research?
There have been challenges along the way, but that’s part of research. Fortunately, funding from TTCF and others has made it possible for the project to be where it is today. We still have a long way to go, but I am excited to report that it is now ready for a pre-clinical trial using mouse models of a rare bone cancer, osteosarcoma, to test a targeted nanoparticle to this aggressive cancer in children, adolescents, and young adults. This is an important step before it can be ready for human trials.

Anything you would like to say to our members?
Of course. I want to thank TTCF members for seeing the value in my project and investing in it two years ago. I hope they realize how incredibly valuable their pooled support has been, not only to me, but also to all other winners, especially in this economic climate. TTCF's mission is as innovative as our research projects!

“I want to thank TTCF members for seeing the value in my project and investing in it two years ago.”
– Dr. Noah Federman

What research project did TTCF fund in 2009?
My project was titled Fighting Cancer in Children Using Nanotechnology. It is about delivering targeted therapy to destroy tumor cells.
Childhood cancer patients often suffer severe side effects with chemotherapy treatment. Strategies that would improve the delivery of anti-cancer agents specifically to tumor cells would not only increase the effectiveness of chemotherapy, but also reduce its systemic toxicity. A molecular vehicle is needed that could target tumor cells—nanoparticles provide such a potential vehicle. I wanted to develop and test targeted nanoparticles to treat pediatric sarcomas (bone and soft tissue cancers), in which the survival rate for patients is less than 20 percent, despite incredibly aggressive chemotherapy, surgery, and radiation treatments. This completely novel project would be a breakthrough in our current treatment of pediatric cancers, leading to the development of powerful new therapeutic strategies in aggressive childhood malignancies.
Meet the New Development Staff

Welcome Laura Pescatore, Associate Director of Development! Working alongside Jennifer Jung, Director of Development, Laura will play a key role in TTCF and in working with its members.

Laura earned a Bachelor of Science in Art and Psychology from the University of Wisconsin-Madison, and she has more than 10 years of professional experience in university programming, marketing, and development. After relocating to Los Angeles in 2007, she joined the UCLA School of Dentistry development team and became its Associate Director in January 2010. Working for the dental school gave Laura an appreciation for the complexities of campus health sciences programs—including their connections to the broader university and commitments to the community. She looks forward to applying this knowledge to advance the philanthropic initiatives of Mattel Children’s Hospital UCLA and the Department of Pediatrics.

Come See Us!

If you’ve never been to Mattel Children’s Hospital UCLA, our staff members would love to give you an insider’s view. Contact Laura Pescatore at lpescatore@support.ucla.edu or (310) 267-1836 to schedule a tour.

Thank you to our 2011 TTCF members! Leslie J. Aronzon • Lorna Auerbach and the Ernest and Lisa Auerbach Family Foundation • Allison Berg • Lynn R. Bider • Glenn Bozarth • Stephanie Bronson • Amanda Brown Chang • Suzanne J. Brown • Gail Buchalter • Andrea P. Burroughs • Tim Campbell • Andrea Cayton • Victoria Chapus • Joyce Chernick • Jill E. Chozen • Lisa Cohen • Cynthia Sprague Connolly • Beth L. Cutler • Mikelyn Dooley • Marianna Fisher • Angela Pennington Folk • Marcelle Frey • Beth C. Friedman • Darriel S. Gerson • Janice Gipson • Nancy Glaser • Beverly Gruber • Gina Hagopian • Mary Ann Hagopian • Marissa Hamilton • Victoria Hornstein • Joleen Julis • Jean Moran Kaplan • Suzanne Kayne • Laurie Konheim • Malinda Marks Krantz • Wendi Doyle Lohmar • Sarah Madison • Nicole Maloney • Tina J. McFarlin • Anne McGrail • Linda Medvene • EJ Milken • Hillary Milken • Lori Milken • Sarah Moritz • Nicole Nathanson • Sabina Nathanson • Mieke E. Neumann • Harriet Nichols • Melissa C. Pennington • Jeanne S. Reynolds • Kathleen Rosenbloom • Maxine Rosenfeld • Karen Richards Sachs • Ellen H. Sandler • Karen S. Sandler • Dena Schechter • Stacie Shaheen • Jennifer Simchowitz • Anne Sisteron • Karen Sraberg • Janis Susskind • Alicia Tranen • Bruce Willock