TTCF Progress Report
for Members of the Today’s and Tomorrow’s Children Fund
Issue 5  December 2012

Message from the Co-Chairs

Dear Members of TTCF,

Welcome to the 5th edition of the TTCF Progress Report. In this issue, you will find faculty research updates from the most recent TTCF award recipients, catch up with past winner Dr. Paul Krogstad, and find an abbreviated profile of members Jill and Alison Chozen, who were featured in the most recent Women & Philanthropy at UCLA newsletter.

We are looking forward to another great year. If you have not already done so, please take the time to renew your membership and continue to recommend others to join. Thank you for your visionary support and dedication to Mattel Children’s Hospital UCLA!

With heartfelt gratitude,

Amanda Brown Chang
Co-Chair

Beth Friedman
Co-Chair

Ellen Sandler
Co-Chair

At a Glance: 2013 TTCF Calendar

January
- Faculty nominations by Dr. Devaskar

March
- Voting ballots sent to members with nominee projects
- Top three candidates selected

May
- Last chance to renew and vote!
- 8th Annual Faculty Presentation & Awards Day at UCLA

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Announcing the UCLA Children’s Discovery and Innovation Institute & Gala

The faculty and staff at Mattel Children’s Hospital UCLA and the Department of Pediatrics, David Geffen School of Medicine at UCLA, excel in pioneering research, compassionate patient care, and unparalleled education. Now the UCLA Children’s Discovery and Innovation Institute, founded to save lives and advance children’s healthcare around the globe, is poised to build on these accomplishments and make an even bigger impact. By driving innovative collaboration among its exceptionally talented and renowned faculty, the Institute will more rapidly deliver transformative research.

Dr. Sherin Devaskar is thrilled to announce an inaugural gala to be held on April 17, 2013. The gala, co-chaired by Shari Glazer, Beth Friedman and Amanda Brown Chang will benefit the Institute and celebrate its launch. Honorees include Steven Mnuchin, Chairman and CEO of OneWest Bank Group LLC, and his wife Heather Mnuchin, who has had an extensive career in retail and entertainment marketing.

The gala auction will feature ten custom-built and designed dollhouses. Each dollhouse, designed by Richard Manion and Robert Meiklejohn of Richard Manion Architecture, Inc., is a unique scaled down version of a designer showcase home. Interiors are created by some of Los Angeles’s most feted interior designers, led by Tim Campbell and Studio Tim Campbell.

All proceeds from the sale of these one-of-a-kind dollhouses benefit the UCLA Children’s Discovery and Innovation Institute. TTCF invites all members to attend this exciting and truly unique event.

It’s Renewal Season!

It’s time to renew your 2013 membership, and to consider increasing your support! Since its inception, TTCF has raised more than $1.5 million for lifesaving pediatric research.

You may give online at [www.uclahealth.org/ttcf](http://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, and send it to:

UCLA Health Sciences Development
ATTN: Laura Pescatore
10945 Le Conte Avenue, Suite 3132
Los Angeles, California 90095-1784
Dear TTCF Members,

Thanks to the support received from TTCF, I am successfully transforming my research project from a small local clinical trial into a large multi-institutional prospective clinical trial, and I am delighted to present this mid-year progress report.

Progress-to-date

Due in large part to TTCF funding, my colleagues and I established collaborative relationships with seven other large university hospitals over the past six months, and we are planning an extensive multi-institutional prospective phase II clinical trial in children with high-grade gliomas. It will be the first-ever pediatric high-grade glioma study that incorporates vaccine therapy in children newly diagnosed with the cancer. Expanding the trial to numerous institutions allows for many more patients to have access to this novel therapeutic approach.

Enrolled children will receive standard back-bone therapy with the addition of dendritic-cell vaccination. We hypothesize that this personalized method of immunotherapy will result in better outcomes than current standard therapies, which rely on chemotherapeutics and radiation alone.

In collaboration with Robert Prins, Ph.D., Associate Professor of Neurosurgery at UCLA, we are developing the biological correlate studies for the trial. We will obtain peripheral blood samples from all participating patients and measure anti-tumor immune responses after dendritic-cell vaccination. To establish induced T-cell activity, peripheral blood samples will be exposed to each young patient’s own tumor sample before and after vaccination and will run through a proliferation assay. Changes in cell-mediated toxicity also will be monitored by measuring tumor-cell kill by the patient’s immune system cells pre- and post-vaccination. Data generated will help us understand how dendritic-cell vaccine therapy affects the immune system.

Additionally, we have submitted a manuscript to a pediatric hematology-oncology journal detailing the data obtained from the initial feasibility study funded by TTCF in 2007. Moreover, I have given a number of didactic lectures at UCLA on dendritic-cell vaccination.

Additional Funding Opportunities and TTCF Impact

We have obtained additional funding from the Joseph Drown Foundation and Miles for Hope Foundation to help launch our clinical trial. We will use the derived data to apply for a large and prestigious National Institutes of Health grant that will allow us to further investigate the use of immunotherapy in the treatment of pediatric brain cancers.

Thanks to TTCF, I have been able to develop a large clinical trial that will reach many patients and further the development of new treatments, which will not only improve survival rates, but also decrease the difficult long-term side effects of traditional chemotherapy and radiation therapy. My team and I deeply appreciate your support!
Prize Recipient
Joyce Y. Wu, M.D.
High-Frequency Oscillations: A Potential Noninvasive Biomarker of Pediatric Epilepsy

Dear TTCF Members,

I am excited to provide a mid-year progress report on my research. Thanks to TTCF’s support, my project will generate much-needed clinical information to establish high-frequency oscillations (HFOs) as a noninvasive spatially localizing and temporally predictive biomarker among three pre-epileptic high-risk subgroups of children: newborns with hypoxic ischemic encephalopathy (HIE), infants with tuberous sclerosis complex (TSC), and young patients with traumatic brain injury (TBI).

Progress to Date

Establishing HFO as a spatially localizing biomarker:
• We are progressing from the previously published retrospective study to a prospective study, as well as to “live” interpretations of intraoperative electrocorticographies to record electrical activity in children undergoing epilepsy surgery. A manuscript has been submitted to the journal Neurology.
• Preliminary data have been generated from noninvasive scalp video-EEGs; this work has been incorporated in a recent National Institutes of Health (NIH) grant submission.

Establishing HFO as a temporally predictive biomarker:
• Infants with TSC are enrolled in a study funded by the Department of Defense/Congressionally Directed Medical Research Program (DOD/CDMRP). Additional funded research projects are forthcoming.
• Newborns with HIE and children of all ages with TBI are actively followed in their respective specialty clinics, along with clinical EEGs whenever possible, including HFO identification.

An NIH R01 proposal was submitted in June, encompassing specific aims and preliminary data, and has just received a high score that is slated to receive funding. Additionally, I have presented my research at numerous venues, including the Paul Crandall Symposium at UCLA, Grand Rounds, and the Tuberous Sclerosis Alliance Regional Conference, of which I am also Conference Chair.

Additional Funding Opportunities and TTCF Impact

I am happy to report that additional funding opportunities have been approved and will become available in the coming months through various federal grant mechanisms, including three from the NIH (tentative start, December 2012, January 2013, and February 2013 for the R01 proposal), one from DOD/CDMRP (tentative start, January 2013), and two pharmaceutical-sponsored clinical trials for epilepsy (expected start, January 2013).

I am grateful for TTCF’s visionary investment in my research, which has enabled me to generate preliminary results and apply for additional grant funding. Thank you for your dedication to advancing children’s health!
Prize Recipient
Julian A. Martinez-Agosto, M.D., Ph.D.

Genetic Risk Factors for Autism and Cancer Predisposition

Dear TTCF Members,

I was fortunate to receive support from the Today’s and Tomorrow’s Children Fund for studies on the genetic basis of conditions that affect growth and predispose children to cancer and autism, and I am pleased to report that the past six months have been very productive. My colleagues and I have recruited additional patients and extended our studies on the mechanism of how the genetic changes we identify cause disease. Additionally, we have completed whole-exome gene sequencing on a number of patients presenting with overgrowth and autism, allowing us to identify novel genes associated with these conditions; our findings encourage us to continue recruiting individuals for the study.

We now are testing the effects of mutations on the function of the proteins these genes encode and finalizing a study that compiles all the cases of growth disorders in which we have identified missing genes. By analyzing these genes’ functions, we have found that excessive insulin signaling is a cause of overgrowth. We also uncovered two additional unexpected findings. First, excessive activity of the Hedgehog signaling pathway, which gives cells information they need for proper embryonic development, also causes too much growth and can predispose to autism. Second, mutations in a gene part of the autophagy pathway, which allows cells to adapt to stress, can cause novel genetic conditions that predispose to kidney cancer and lung cysts – both common in patients with overgrowth. It is the first time the autophagy pathway has been affiliated with human disease, and we are collaborating with fellow researchers at UCLA to determine the function of this gene in lung development and how it predisposes to kidney tumors. We also will be screening for Food and Drug Administration-approved medications that, as potential treatments, can reduce the excessive signaling in these patients.

Results generated have enabled us to submit R21 and New Innovator Grants to the National Institutes of Health and to UCLA for its Oppenheimer Award. We also will be submitting additional grant requests to Autism Speaks and the Simons Foundation. Thus far, findings from our studies have been reported in two manuscripts accepted for publication, and we are submitting two book chapters on the topic, with several other drafts in the works.

Our research will be presented at the American College of Medical Genetics conference and the annual meeting of the Society for Pediatric Research. We will speak at the Tuberous Sclerosis Complex regional conference and have been invited to write an article for our Chapter of the American Academy of Pediatrics. In addition, we have presented portions of our work at Pediatrics Grand Rounds and have been invited to present at the annual UCLA Genomics Symposium and the Larry L. Hillblom Islet Research Center at UCLA.

We thank TTCF members for their vision and support, which have had an immediate impact on families who benefit from receiving diagnoses of their children’s genetic makeup. As our studies proceed, your impact will improve our understanding of the genetic basis of autism and cancer predisposition and eventually extend to cover the availability of potential treatments for these disorders.
TTCF Winner’s Update

2011 TTCF prize recipient, Paul Krogstad, M.D., is part of a team of UCLA researchers who have discovered that fluoxetine - commonly known as Prozac - shows promise as an antiviral agent and potent inhibitor of coxsackievirus replication. It is one of the viruses that include polio and echovirus. Exposure to this virus can cause other severe and potentially fatal infections and diseases.

Although traditionally used in the treatment of depression, anxiety, and some personality disorders, fluoxetine warrants additional study as a potential antiviral agent for enterovirus infections. Dr. Krogstad stated this work “will add to our understanding of enterovirus replication and lead to the assessment of its potential clinical utility for the future treatment of serious enterovirus infections.”

The study was published in the journal *Antimicrobial Agents and Chemotherapy* and supported through funds from TTCF and the UCLA Department of Pediatrics Nanopediatrics program.

Spotlight

The most recent Women & Philanthropy at UCLA newsletter celebrated TTCF’s own Jill and Alison Chozen and their inter-generational commitment to philanthropy. Jill Chozen discussed the excitement of passing down her desire to make a difference in the lives of children to her daughter, Alison, and the joyful experience of TTCF membership. Jill stated, “Sharing our experiences together in TTCF is a gift we give to each other and…it’s very special to me as a mother to share this dedication with Alison.” Read the whole story [here](#).

Thank you to all of our mother-daughter (and mother - daughter-in-law) pairs for your participation and support of today’s and tomorrow’s children!
Stay Connected

Coming Soon!

2013 TTCF Membership Salon

Watch your inbox for information on a 2013 TTCF salon, hosted at Mattel Children's Hospital UCLA. If you are interested in hosting a future salon, please contact Laura Pescatore at (310) 267-1836 or lpescatore@support.ucla.edu.

For more information on TTCF or Mattel Children's Hospital UCLA, contact us or visit www.uclahealth.org/ttcf

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2012 Holiday Card Collection

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December 2012