The CNN Summer 2016 issue introduced you to HESI THRIVE, a new program that seeks to provide seed funding for research to improve quality of life for cancer survivors. HESI sought research proposals in July 2016 and we are pleased to share that the first grants have been awarded! The ultimate goals of these and future research initiatives are to help cancer patients stay safely on therapy, select optimal treatments, reduce long term adverse effects and improve long term quality of life.

The 2017 awardees include:

- Irina Budunova, MD, PhD and Leo Gordon, MD FACP, Northwestern University Feinberg School of Medicine. Research focus on evaluating co-therapies that may reduce atrophic and metabolic side effects of glucocorticoids in patients with blood cancers.
- Maria Suarez-Almazo, MD, PhD, MD Anderson Cancer Center. Research focus on defining the genetic profiles of patients that experience adverse responses to immunotherapy to help inform future treatment selection.
- Barbara Ehrlich, PhD, Yale University. Research focus on developing a nerve function test that can characterize breast cancer patients mostly likely to experience serious nerve injury from breast cancer treatment.
- Jennifer Jordan, PhD, Wake Forest University School of Medicine. Research focus on evaluating novel mechanisms of chronic heart damage with cardiac MRI in patients who have received anthracyclines.

HESI is actively working with THRIVE partners to identify additional sources of funding so this important new program may continue. THRIVE is seeking new partners and funders to support the 2018 funding call. If you have interest in becoming a THRIVE supporter please contact: research@hesithrive.org

For more information about THRIVE, visit the website: http://hesithrive.org/.

Welcome to new members for 2017: Abcam and Coyne Scientific!

HESI 2017 ANNUAL MEETING: SCIENCE FORWARD

The HESI 2017 Annual Meeting is scheduled for June 13-15, 2017 in Dublin, Ireland at the Radisson Blue Royal Hotel.

Don’t miss this opportunity to hear innovative keynote speakers and learn more about HESI’s new Scientific Foresight efforts, our ongoing scientific programs (and where they are headed), and new emerging issues proposals!

Visit the meeting website for the full agenda, registration and hotel information: hesiglobal.org/nesianualmeetings.
New Transitions
As many of you heard, Melissa Gilden, Scientific Program Associate, left HESI in January 2017. Melissa supported the Program Managers, Jennifer Pierson and Stan Parish, with administrative tasks for the committee. We are happy to announce we have filled this position and Alexandra (Alex) Feitel is our newest Scientific Program Associate! Alex received her bachelor’s degree in environmental health from the University of Michigan. Her interests include toxicology, epidemiology and global health. Welcome to Alex!

**INTegrative Strategies Working Group**

The Integrative Strategies Working Group has been working on a few projects in various phases of work. The Contractility Subgroup has nearly completed two additional manuscripts, in addition to their two previously published manuscripts. One manuscript took a statistics-based approach, while the other detailed the correlation of endpoints collected by either echocardiograph or telemetry. In addition to wrapping up the planned contractility manuscripts, HESI has harvested the data for a second time for use in other publications and data driven solutions by outside organizations. Currently, there are ongoing discussions that would bring in the expertise of the working group with outside collaborators, including in the area of mathematics.

Finally, a new work stream has recently launched in the area of cellular systems, with the objective of constructing and ultimately testing a framework on the use of non-animal methods to assess contractility. While these discussions are still in early stages, the group is working towards the goal of setting a series of criteria across various contexts to ultimately use in a position paper. This could possibly be followed by a series of proof of concept studies to “stress test” the criteria outlined.

**ProA Working Group**

The ProA Working Group members are developing manuscripts to detail results from the Phase 1 and 2 efforts to understand predictivity of nonclinical to clinical proarrhythmic models. The Phase I author team received reviews back on the submitted paper and plans to review and resubmit to the *British Journal of Pharmacology* by the end of June 2017. The acceptance of this paper will mark the end of Phase I and over 8 years worth of work. Everyone involved is commend- ed for their contributions to this project! The Phase 2 Subteam has worked throughout the past year to identify the discordant compounds in the Phase 1 database, retrieve additional data that may lead to an explanation for discordance, and publish the results. Despite challenges in obtaining some of this data, much of which is proprietary and internal to sponsors, the Subteam has several case studies and a promising manuscript to provide context and details on the discordance in the database. This paper is expected to be delivered by the end of 2017.

At the same time, CiPA has been progressing and the ProA Working Group has been contributing their expertise to this initiative through several mechanisms. One mechanism is the High-Throughput Systems (HTS) Subteam, which is working to characterize automated patch clamps using the CiPA 7 ion channel protocols and providing this data to the FDA for the in silico model. The study is progressing and data is anticipated by 3Q 2017.

Lastly, the JT Peak Subteam was established just a few short months ago to explore the usage of JT peak as a predictive biomarker in nonclinical species. This effort will complement the ongoing effort at the FDA that is looking at JT peak as a clinical biomarker. More details will be available on this project soon. Contact HESI staff for more details.
CARDIAC BIOMARKERS WORKING GROUP

The Cardiac Biomarkers Working Group has been making progress on their Proof of Concept #2 (POC2) study. With the completion of the in-life portion of the study last year, the group has been analyzing and presenting on selected biomarkers as outlined in their study design. Those potential biomarkers look across various technologies that include microRNA, microparticles and extracellular vesicles, flow cytometry, histology, and more. The goal is to complete this analysis within the next few months and to begin drafting up a manuscript. This has not only provided a rich dataset on the selected biomarkers tested, but also on the ability to further characterize the model (Zucker Diabetic Fatty Rat) beyond what was previously described in the literature. A series of abstracts are also being drafted with the goal of presenting some of these initial findings before a more comprehensive manuscript is published.

Finally, the working group has begun discussions surrounding a 3rd POC. While no final decisions have been made, the goal over the next few months is to determine if there is a specific model and class of compounds that would be of interest to test.

STEM CELL WORKING GROUP/MYOCYTE SUBTEAM

The Stem Cell Working Group and Myocyte Subteam have been focusing their efforts on the CiPA Phase II Validation Study. With more than 35 participating sites, 10 cell lines, and 14 different platforms, the study will produce robust data for the CiPA initiative to complete its mission.

The Myocyte Subteam met on April 5, 2017 with core sites to finalize the data analysis plan. Noncore sites were requested to submit data by the end of May with the goal of unblinding compounds to all participants. HESI is developing a strategy for handling and analyzing all data and remains focused on the core data and planned publications.

As the Validation Study winds down, the group looks to the horizon for the next project. As it happens, the Integrative Strategies Working Group recently launched the new Cellular Systems Subteam to explore and evaluate in vitro technologies to measure contractility. The steering group members are working to thoroughly frame the problem and how HESI can help address it through data generation and sharing. The Stem Cell Working Group will be an integral part of this new Subteam once a plan is finalized. Stay tuned for more details soon!

The latest CiPA Update Meeting was held on December 6, 2016 in Rockville, MD. Each of the CiPA work streams provided an update on progress and shared recent data. The presentations from this meeting are available online.

CiPA is based on a deep understanding of the mechanisms of TdP and is not a biomarker validation project. The proposed nonclinical testing schema includes evaluation of ionic currents via high-throughput automated patch clamps to produce an in silico reconstruction and proarrhythmia score/rank. Human stem cell cardiomyocytes will be used to confirm current effects. Human Phase 1 ECGs will also be included to confirm nonclinical results. A draft CiPA package is anticipated by late 2017.

In addition to the December CiPA Update meeting, the FDA held an Advisory Committee meeting on March 15, 2017 and dedicated the afternoon to learning and discussing CiPA. Overall, the Advisory Committee was very positive about CiPA and the resulting vote around the assay and validation process received a majority of votes in favor. The full meeting information including slides and transcript are available online.

Visit the new CiPA website, www.cipaproject.org, and find more information in the FAQs, related meetings and webinars and publications!
Since 1989, the ILSI Health and Environmental Sciences Institute (HESI), a non-profit 501c charitable organization, has provided the framework for scientists from the public and private sectors to meaningfully collaborate in developing science for a safer, more sustainable world.

The Cardiac Safety Committee is committed to improving public health through modeling and early detection of adverse cardiovascular risks. The committee brings together scientists and technical disciplines within the international community of public, private and government sectors to develop best practices for translation of in vitro and non-clinical cardiovascular data.

**PUBLICATIONS OF NOTE**


Don’t miss the latest publications from the CiPA initiative: [http://cipaproject.org/publications/](http://cipaproject.org/publications/)

**UPCOMING MEETINGS**

**Related Meetings:**  
- JSOT 2017, July 10-12, Yokohama, Japan  
- ASCP 2017, September 6-8, Chicago, IL  
- EUROTOX 2017, September 10-13, Bratislava, Slovakia  
- SPS 2017, September 24-27, Berlin, Germany


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Have a publication or article you think your colleagues would find interesting? Contact HESI staff to include it in the next issue of CNN!

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