

NCATS director inspires innovation in translation

By Shannon Whirkedge

During an Oct. 2 seminar, “Catalyzing Translational Innovation,” National Center for Advancing Translational Sciences (NCATS) Director Christopher Austin, M.D., explained that the establishment of the new center enables the National Institutes of Health (NIH) to move in exciting new directions.

While [Austin](#)

(<http://www.ncats.nih.gov/about/director/director-bio.html>)

is relatively new to his position at [NCATS](#)

(<http://www.ncats.nih.gov/>)

, NIEHS and National Toxicology Program (NTP) Director Linda Birnbaum, Ph.D., who hosted Austin’s talk, stressed Austin’s long and rich interaction with NIEHS and NTP, through his work with the Tox21 chemical toxicity screening project.

Austin described the [Tox21](#)

(<http://www.ncats.nih.gov/research/reengineering/tox21/tox21.html>)

project as the single best collaboration he has had in his career.

Linked Video

["Watch this NCATS video explaining the work NCATS is doing to find solutions to health challenges." \(5:15\)](#)

Discovering how to fix what is broken

According to Austin, though we now know more about ourselves and how our bodies work than ever before, the global public health community is not keeping up with these advances. “Understanding why something is broken and understanding how to fix it are fundamentally different,” he explained. For instance, because toxicity accounts for 30 percent of drug failure, predictive toxicology is at the top of the to-do list at NCATS.

The Tox21 collaborative effort by NTP, NCATS, the U.S. Environmental Protection Agency, and the U.S. Food and Drug Administration is making huge strides toward improving predictive toxicity assessment methods. Austin described it as the no compound left behind act, because scientists are testing more than 10,000 chemical compounds with a high-throughput robotic screening system.

Innovation through crowdsourcing

This large-scale system has generated roughly 50 million data points, and at a center where everything is a collaboration, this volume of data provides an opportunity for yet another type of collaboration. NCATS is crowdsourcing data analysis to develop computational models that can better predict toxicity. This type of data transparency represents one step toward overcoming obstacles to translational research.



“Everything at NCATS is an experiment. We are constantly evolving,” said Austin. (Photo courtesy of Steve McCaw)



In her introduction, Birnbaum revealed that, in addition to his rich history in science and medicine, Austin is an opera singer. (Photo courtesy of Steve McCaw)



Shepherd Schurman, M.D., acting medical director of the NIEHS Clinical Research Unit, and Serena Dudek, Ph.D., head of the NIEHS Synaptic and Developmental Plasticity Group, were among the full house for Austin’s talk. (Photo courtesy of Steve McCaw)

“If we want to comprehensively understand and predict toxicity, then we must know all the biological pathways in the human body,” said Austin, pointing out that it would be a significant challenge for individual scientists. In an effort to overcome the individualistic nature of research, the Tox21 researchers are designing an integrated pathway database, known as BioPlanet, to facilitate development and prioritization.

Tissue on a chip

In addition to predicting toxicity, the ability to predict effectiveness would drastically reduce time spent on candidate drugs that ultimately fail in human clinical trials. Meeting this challenge requires a unique pairing of biology and engineering.

Led by NCATS, NIH is supporting researchers across the country to develop [tissues on a chip](http://www.nih.gov/news/health/sep2014/ncats-23.htm) (<http://www.nih.gov/news/health/sep2014/ncats-23.htm>)

that can screen compounds for toxicity, effectiveness, and safety. These chips can mimic the complex functions of the human body, including major body organs, on individual chips, and may revolutionize preclinical testing of potential treatments.

Letting biology define the answer

Each year, around 15,000 people in the U.S. are diagnosed with chronic lymphocytic leukemia, the most common form of leukemia in adults. Unfortunately, it is generally considered incurable and prognosis varies. What these patients do have is an abundance of cells, and that is just what was needed to search for new drugs that selectively kill leukemia cells. Through a collaboration with the National Heart, Lung, and Blood Institute, NCATS was able to get patient samples onto the screening platform within one day, looking for drugs that will kill the leukemia cells, but not harm normal donor immune cells.

Unexpectedly, the arthritis drug auranofin was identified as just such a selective cytotoxic drug, demonstrating the ability of the NCATS process to discover that a drug approved for one use may be effective for an apparently unrelated condition. Within a year of this discovery, the collaborative team was able to complete all preclinical trials necessary to support clinical trials in patients, not to mention shedding new light on the basic biology of the disease.

(Shannon Whirledge, Ph.D., is a research fellow in the NIEHS Molecular Endocrinology Group.)



Austin spoke highly of Raymond Tice, Ph.D., in blue checked shirt, who will be retiring next year. “He is one of the best collaborators ever,” Austin said. (Photo courtesy of Steve McCaw)

A rapid-response innovation driver

NCATS is the most recently formed research center at the National Institutes of Health (NIH). At the helm, Austin hopes this center will become what he called a rate of change institute.

He defined translation as the process of turning observations in the lab and clinic into interventions that improve health of individuals and the public. “NCATS lets biology define what the answer is, rather than what preconceived notions say the answer should be,” said Austin.

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