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The National Center for Advancing Translational Sciences (NCATS) is dedicated to understanding and transforming *translation*, defined as the process of turning scientific, medical, and public health observations in the laboratory, clinic, and community into interventions that improve the health of individuals and the public. At a time of unprecedented fundamental science discoveries, our collective ability to translate research findings into health benefits often is too slow and ineffective. Developing a new drug requires on average 10 to 15 years and more than \$2 billion given the high prevalence of failure along the translational pipeline. We must deliver the promise of science to patients and the public in an accelerated and more efficient manner. NCATS studies and supports translation on a system-wide level as a scientific and operational problem, addressing roadblocks that impede or preclude promising research advances.

Hastening Clinical Translation

The largest portion of NCATS' budget is dedicated to its Clinical and Translational Science Awards (CTSA) Program, which supports a national network of medical research centers, called hubs. The hubs collaborate locally, regionally, and nationally to foster innovation in clinical researcher training, patient involvement, and new research tools and processes. There are multiple initiatives within this program, including the Trial Innovation Network that is composed of Trial Innovation Centers, a Recruitment Innovation Center, and the CTSA Program hubs. Through this network, researchers are identifying and implementing ways to improve the clinical trial process, including participant recruitment and other aspects of clinical trial conduct.

The process of obtaining ethics approval for multisite clinical research by multiple institutional review boards (IRBs) is a longstanding challenge that can lead to significant delays in study activation. To address this problem, NCATS supported the development of a single IRB reliance platform for multisite clinical studies, enabling study sites to rely on a single IRB of record. The platform, known as the Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB, includes resources such as umbrella agreements, guidance documents, and technical assistance that institutions nationwide can access to streamline IRB review for multisite studies. SMART IRB is serving as a roadmap to help implement the NIH policy released in June 2016 that generally expects all sites participating in multi-site studies, which involve non-exempt human subjects research funded by the NIH to use a single IRB to conduct the ethical review required for the protection of human subjects.

Providing the resources to train, cultivate, and sustain future leaders of the biomedical research workforce is another key CTSA Program goal. The program supports a coordinated, national effort to help ensure a pipeline of trained translational

investigators who can move basic research findings into applications for improving health as novel therapies, diagnostics, and preventives. Program grantees have developed clinical and translational sciences training resources, including educational core competencies, best practices for training mentors, and curriculum materials. These tools are freely available and many institutions nationwide are using them.

Engaging patients at all stages of translation is crucial: Their perspectives as members of the research team provide insights, focus, urgency and connectivity that can be instrumental in making the development, testing and deployment of new interventions more effective. NCATS supports the Rare Diseases Clinical Research Network (RDCRN) which emphasizes including patient groups as full partners on the consortium research teams, an approach that helps achieve greater success. The RDCRN Coalition of Patient Advocacy Groups develops and shares best practices, and the RDCRN website includes a contact registry for patients who may be interested in participating in RDCRN clinical studies. Rare diseases, which cumulatively affect approximately one in 10 people in the U.S., are in crucial need of innovative translational technologies, so are a particular focus for NCATS.

Measurable outcomes can help determine whether a new translational process is actually an improvement. NCATS' Discovering New Therapeutic Uses for Existing Molecules program matches academic investigators with pharmaceutical companies that have compounds that were found to be ineffective in treating specific targeted diseases. Repurposing these compounds for potentially treating other diseases saves time in the drug development process because significant foundational work already has been completed. NCATS helps to further accelerate this process by providing collaboration agreement templates that now are being used broadly in the research community and by supporting researchers with new ideas for how existing compounds can be repurposed.

Finding New Therapies for Clinical Study

NCATS also is dedicated to removing pre-clinical translational science roadblocks. Through its Therapeutics for Rare and Neglected Diseases (TRND) program, the Center works to “de-risk” potential therapeutics so that private sector companies can feel more confident about acquiring them to finish their development.

Through its Tissue Chip for Drug Screening program, NCATS is working on new methods for predicting both safety and efficacy of experimental drugs using engineered “chips” that contain human cells and model human organs. Current methods such as animal and cell models are not always reliably predictive and can result in wasted time and effort. In addition to developing these chips for testing potential drugs, NCATS sent tissue chips to the International Space Station (ISS) to conduct research on the effect of microgravity on these model organs. Microgravity has been observed to accelerate aging and have other effects relevant to diseases on earth, making the ISS a unique yet significant research environment.

New drug development for currently untreatable diseases has been greatly limited because known chemical structures affect only 10 percent of potential drug targets within the human body. To help move past this impediment, NCATS launched its Automated Synthesis Platform for Innovative Research and Execution (ASPIRE) program to bring together chemistry, robotic engineering, biological activity testing, and artificial intelligence. Tools developed through ASPIRE will minimize the amount of time chemists spend on tedious and repetitive tasks, freeing them up for more complicated pursuits such as designing, synthesizing, and testing compounds for diseases that currently have no FDA-approved treatment.

Adaptability to Tackle Emerging Public Health Needs

With its unique collection of programs, initiatives and resources, NCATS has the capacity and capability to address public health crises. For example, a team of researchers from NCATS and the Icahn School of Medicine at Mount Sinai developed a miniaturized assay for high-throughput screening to find compounds that block the ability of Ebola virus-like particles (VLPs) to enter and infect cells. A screen using 2,816 compounds identified 53 drugs with entry-blocking activity against Ebola VLPs.

In another example, investigators from Johns Hopkins University and Florida State University collaborated with NCATS experts on drug repurposing and high throughput screening to identify rapidly two classes of existing compounds that potentially can be used to fight Zika. These compounds were effective either in inhibiting the replication of Zika virus or in preventing the virus from killing brain cells. All data has been made available to public databases, allowing these compounds to be further studied by the broader research community to help combat the Zika health crisis.

NCATS also is combatting the current national epidemic of opioid abuse. Approaches can include using the Center's high-throughput screening facility to test potential opioid abuse therapeutics and requiring CTSA Program-supported researchers to help identify opioid patients and rapidly enroll them in newly initiated multisite clinical trials.

Conclusion

Through its programs and initiatives described above, and others, NCATS is improving health through smarter science in unprecedented ways, with the ultimate goal of getting more treatments to more patients — and to the public at large — more quickly.

Christopher P. Austin, M.D.
Director, National Center for Advancing Translational Sciences

Dr. Austin leads NCATS' work to improve the translation of observations in the laboratory, clinic and community into interventions that reach and benefit patients—from diagnostics and therapeutics to medical procedures and behavioral changes. Under his direction, NCATS researchers and collaborators are developing new technologies, resources and collaborative research models; demonstrating their usefulness; and disseminating the data, analysis and methodologies for use by the worldwide research community.

Austin's career has spanned the spectrum of translational research, in the public and private sectors. Austin joined NIH in 2002 as the senior advisor to the director for translational research at the National Human Genome Research Institute, where he was responsible for conceptualizing and implementing research programs to derive scientific insights and therapeutic benefit from the newly completed Human Genome Project. While at NHGRI, he founded and directed the NIH Chemical Genomics Center, Therapeutics for Rare and Neglected Diseases program, Toxicology in the 21st Century initiative, and NIH Center for Translational Therapeutics. Upon creation of NCATS in 2011, he became the inaugural director of the NCATS Division of Pre-Clinical Innovation, and was appointed NCATS director in 2012. In 2016, Dr. Austin was elected chair of the International Rare Disease Research Consortium (IRDiRC). Prior to joining NIH, Austin worked at the pharmaceutical company Merck, where he directed programs on genome-based discovery of novel targets and drugs, with a particular focus on schizophrenia and Alzheimer's disease.

Austin is trained as a clinician and geneticist. He trained in internal medicine and neurology at the Massachusetts General Hospital in Boston, and practiced medicine in academic and community hospital settings as well as in urban primary care and in rural Alaska and Africa. He completed a research fellowship in developmental neurogenetics at Harvard, studying genetic and environmental influences on stem cell fate determination. Austin earned an M.D. from Harvard Medical School and A.B. summa cum laude in biology from Princeton University.