As the Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), I am pleased to present this annual report highlighting the research efforts and programs supported by the Institute. The NIDDK has a broad research responsibility that includes some of the most common, debilitating, and costly conditions affecting Americans. These conditions include diabetes and other endocrine and metabolic diseases; liver disease and other digestive diseases and conditions, such as inflammatory bowel disease and irritable bowel syndrome; nutritional disorders; obesity; kidney diseases, such as polycystic kidney disease and glomerular disease; urologic diseases and conditions, such as interstitial cystitis/painful bladder syndrome, prostatitis, and urinary tract infection; and blood diseases.

In view of the profound effects that COVID-19 (Coronavirus Disease 2019) has had on our Nation and the world, and the ways in which the disease has exacerbated some of the existing health disparities in the NIDDK’s mission diseases, the “Cross-Cutting Science” chapter of the 21st edition of this report highlights our Institute’s multi-pronged efforts toward the goal of health equity. In addition, the report describes recent NIDDK-supported scientific advances on topics such as:

- An innovative approach from NIDDK intramural researchers shows the potential importance of speech in transmitting the virus responsible for COVID-19;
- Lab-generated cell clusters that can produce insulin in mice while avoiding destruction by the immune system, a step toward a possible long-term treatment for type 1 diabetes;
- A dramatic increase in knowledge of type 2 diabetes genetics from combining analyses of studies in people of East Asian descent;
- Finding that community barbershops are promising venues for screening Black men for type 2 diabetes;
- Demonstration of health benefits in people from a treatment that converts energy-storing fat cells into an energy-burning form of fat;
- Testing of medications that now make it possible to partly restore the function of the protein missing in 90 percent of people with cystic fibrosis;
- The weight-loss and metabolic effects of bariatric surgery compared to non-surgical weight-loss approaches;
- The physiological effects of exercise;
- The role of the microbiome, including its regulation of circadian rhythms and its effects on nutrient absorption;
- Development of a new mouse model that mimics the immune system features and gluten-dependent intestinal damage seen in people with celiac disease;
- Insights into the way high fructose consumption may promote nonalcoholic fatty liver disease;
- Kidney development and function, as novel insights bring us closer to new strategies to address kidney diseases;
- Development of a noninvasive technique with potential application to treat urinary stones; and
• Identification of a compound that may one day lead to improved treatment for dyskeratosis congenita, a rare blood disease.

In addition to reporting on recent advances, this publication traces the multi-step path to research achievements through several "Stories of Discovery." These essays illustrate how major new discoveries that have greatly advanced biomedical science and are benefitting human health often emerge from incremental insights gained from research investments spanning many years and even multiple research disciplines.

This report also includes personal perspectives of those who have given time and effort to participate in NIDDK-sponsored clinical research. A woman describes how an artificial pancreas device she tested as part of a clinical trial helped her manage her type 1 diabetes and improved her mental well-being during some challenging personal times. Parents share their experience raising a daughter born with a life-threatening liver disease called biliary atresia and their participation in clinical research to find better ways to detect and manage the disease. A woman tells of her decades-long participation in a landmark study demonstrating that type 2 diabetes can be prevented with lifestyle modifications. A retired chemist describes how her participation in clinical research revealed that she has a rare type of kidney disease—a diagnosis that for years had eluded her physicians.

The NIDDK continues efforts to ensure that knowledge gained from its research is disseminated to health care providers, patients, and the public. We develop science-based information on diseases and disorders within the NIDDK mission and distribute it through our information and outreach programs and our website. I invite you to visit us at www.niddk.nih.gov. Health information, news, and scientific advances related to NIDDK research are also available on our Twitter feed: @NIDDKgov.

This report reflects only a fraction of the immense body of NIDDK-funded research across the country, performed by basic scientists, clinical investigators, and patient volunteers. Moving forward, we remain committed to supporting these important areas of research and translating scientific discoveries into improvements in the health and quality of life of all people.

The efforts featured in this publication reflect the core mission of the NIDDK, including the Director's guiding principles:

• Maintain a vigorous investigator-initiated research portfolio
• Support pivotal clinical studies and trials
• Promote a steady and diverse pool of talented new investigators
• Foster exceptional research training and mentoring opportunities
• Ensure knowledge dissemination through outreach and communications

More information on how the NIDDK’s activities support these guiding principles can be found in the "NIDDK Extramural Funding Trends and Support of Guiding Principles" section at the end of this report and on our website at: www.niddk.nih.gov.

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