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## ASN Proposal for Future Common Fund Initiatives

**Title:** Enhancement of Clinical and Translational Research Infrastructure

**Problems and Opportunities:** While academic institutions and NIH invigorate their clinical research enterprises, the rarity of many diseases and the interrelationship among disorders limits the number of patients available for each unique clinical trial. No single research center has sufficient prevalent study subjects or sustainable research infrastructure to recruit enough subjects for meaningful research. Single centers that house patient information may limit inquiries to one disease without tracking appropriate data on other associated diseases, limiting the ability to assess interrelationships of disease. Opportunities for genetic research, in particular, are missed because of a lack of common clinical databases or genetic material for analysis. These deficiencies are amplified in the study of pediatric disease because of the greater rarity of disease and an exacerbated concern about patient protection in clinical trials.

As an example of current deficiencies, chronic kidney disease (CKD) is recognized as a burgeoning public health threat due to increasing prevalence; high associated morbidity and mortality; significant correlation with disorders such as acute kidney injury, diabetes, and hypertension; and enormous health care costs. Yet CKD research has been limited due to a lack of effective infrastructure, resulting in many small, underpowered studies, but limited introduction of novel treatments. During the past 20 years, there has been no successful implementation of a therapeutic agent specifically designed for the treatment of glomerular diseases, even though they account for more than 50% of cases of CKD and end-stage renal disease (ESRD) in the US. The etiology of CKD is varied, ranging from developmental or hereditary disorders to acquired systemic, auto-immune, or metabolic disorders. For many of these diseases, the only connection among them is the final pathway of nephron destruction. By storing and coordinating patient data, opportunities increase for large-scale studies and disease-related analyses that can uncover the etiologies and appropriate therapy for the disease.

**Approaches to Address the Problem:** There are examples of infrastructure that are similar to what is proposed that have helped support single disease databases and networks; however, to assess the increasingly complex interrelationship between diseases, these small-scale examples must be enhanced on a broader level. The Pediatric Oncology Group has been responsible for the development and testing of novel treatment protocols as well as basic cancer research. The Immune Tolerance Network unites several NIH Institutes and pharmaceutical companies to investigate long-term organ transplantation treatment as well as treatments for auto-immune diseases. In this network, the relationship of clinical trials and mechanistic studies is carefully maintained.

The starting point for many of these investigations is a common disease-oriented registry that maintains long-term clinical information that would otherwise be unattainable. While some individual disease registries exist (e.g. The United States Renal Data System, which, however, is largely restricted to ESRD), ASN proposes that NIH fund necessary infrastructure support for these and additional registries as well as multi-center clinical trials networks linked to human tissue sample repositories. ASN encourages NIH to develop the infrastructure to allow data-consolidation among the specialized databases which would require common data dictionaries and algorithms. The merged databases would also require similar standardization and cataloging of human specimens (blood, urine, biopsies, DNA, RNA) obtained from various mechanistic studies that could be shared with other studies, such as genetics. The data-connected networks would assure timeliness in protocol development, maintain Health Insurance Portability and Accountability Act compliance, and could include a common IRB for increased expertise and facilitation of institution interaction with the repositored materials. The proposed infrastructure is critical for storing and archiving biological samples obtained for future analysis, as well as tracking of patients for evaluation of outcomes and recruitment into a variety of studies including epidemiologic assessments and clinical trials.

Terms: Clinical Trials, Registries, Biological Specimens, Repositories