A cute kidney injury (AKI) and chronic kidney disease (CKD) impose a significant global health burden; however, only a few drug therapies are available for AKI, and no effective drug therapies currently exist for CKD. Development of pharmacologic therapies for AKI and CKD has been hampered by non-predictive animal models, the inability to identify and prioritize human targets, and an underlying poor understanding of human AKI and CKD. A growing consensus suggests that CKD and AKI are not homogeneous diseases; rather, they are heterogeneous disorders that contain specific subgroups that are driven by different disease pathways. Thus, a better understanding of disease heterogeneity will likely inspire the development of more effective individualized treatment options.

One might envision a more individualized future for nephrology practice, where each person with kidney disease can find answers to important, patient-centered questions: What do I have? What will happen to me? What can I do about it? A nephrologist in this vision of the future might evaluate the person’s disease profile using blood and urine tests, image the kidney in real-time to identify and biopsy areas of kidney damage, then analyze the biopsy tissue using a kidney tissue atlas (a tool designed to classify the location and health of kidney tissue components), and select the appropriate drug to start individualized treatment. The kidney biopsy is essential to this vision of the future, as it will provide the information needed to answer the patient-centered questions. The analysis of kidney biopsy tissue will identify the specific subtype of AKI or CKD and the precise molecular pathway(s) driving the patient’s kidney disease. With this information, the nephrologist can select the appropriate therapy to enable individualized care for that patient.

How do we get to this future? We need to leverage novel technologies in multi-scale interrogation of single cells and biopsy tissue advanced primarily in oncology research. Such sophisticated technologies that have matured over the past few years can now be employed to analyze cellular and tissue heterogeneity (e.g., cell-, tissue-, and molecular pathway-specific markers; using two and three-dimensional imaging techniques) in exquisite detail, simultaneously using multiple markers at single-cell resolution to define specific kidney structures. Thus, researchers are now poised to initiate the construction of a complex kidney tissue atlas that can classify and locate different cell types, cell states (healthy, injured, dying, recovering, undergoing adaptive/maladaptive repair, etc.) and interstitial components (e.g., collagens, proteoglycans, signaling molecules, etc.). These breakthroughs will revolutionize renal pathology and give tremendous insight into the patient-centered questions.

But technological advances alone are likely insufficient for precision medicine to be applied to AKI and CKD. These advances must be accompanied by changes in the culture of three distinct but connected groups involved in the clinical care process. First, pathologists must utilize histologic markers from the kidney tissue atlas to improve their diagnosis, prognosis, and therapy recommendations. Second, nephrologists will need to recognize the benefits of biopsy to their patients, then use the biopsy information to stratify their patients into disease subgroups so they can more effectively develop personalized treatment plans with their patients. Finally, and perhaps most importantly, patients must be made aware of how a kidney biopsy may help determine the best therapeutic approach for their particular disease subtype. These three inter-related cultural shifts are undeniably challenging to achieve in the health care system. However, if patients more clearly understand the importance of a kidney biopsy to their own treatment and disease management, they will be much more likely to request them from nephrologists, thereby driving the entire process of cultural change.

Currently, kidney biopsies have limited benefit to an individual, but a large benefit to research efforts aimed at improving treatments. The kidney biopsy procedure is risky; there are well defined complications. Therefore, ethical and participant safety considerations must be a primary concern. Individuals who choose to participate in research studies must be provided with clear information about the risks associated with undergoing a kidney biopsy. The risks should be reasonable relative to expected benefits to that individual and to society, and biopsies must be safely collected by trained professionals. Specific, validated protocols for tissue handling and interrogation should be developed and implemented to ensure that when a participant donates his or her tissue, it yields the greatest possible benefit to that individual, the patient community, and society as a whole. Ensuring these ethical and safety practices will encourage participation and inform patients of the potential benefits of biopsy collection to their own health care.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is launching the Kidney Precision Medicine Program (KPMP) in summer 2017, with the goal of ethically and safely obtaining and evaluating human kidney biopsies from research participants with AKI or CKD; creating a kidney tissue atlas; defining disease subgroups; and identifying critical cells, interstitial components, and pathways that can be targeted for novel therapies. Human kidney biopsies will be analyzed to identify new markers that will characterize cells, cell states, and molecular disease pathways. In an iterative process, the biopsies will then be evaluated with this new information, and regions of the tissue that remained unlabeled (dark areas) will be further interrogated to obtain additional novel molecular data enabling identification of new cell types and signaling cascades. The array of molecular, cellular, and tissue markers will then be linked to important patient clinical outcomes. The emerging kidney tissue atlas will be used as a foundation to better understand renal disease heterogeneity and can inform decision-making by pathologists, nephrologists, and patients with AKI and CKD.

Tissue interrogation is a central component of the KPMP workflow. Researchers have already been collecting mRNA, protein, and even some epigenetic data on partially fractionated (glomerulus, tubule-intersitentium compartments) human kidney tissue; the KPMP will expand and extend these efforts to gain more depth of information at the single cell and single tissue compartment level. All resulting resources will be public, open, and transparent, and will be made available to everyone (e.g., patients, academic researchers, industry scientists). These findings and resources will help nephrologists better understand human kidney disease, and will invigorate kidney research, attract top talent from inside and outside nephrology, provide ample career development opportunities, and seed new investigator-initiated research. To achieve maximal success, the KPMP will foster partnerships among patients, academic researchers, private industry, advocacy organizations, and the NIDDK.

KPMP resources will undoubtedly be used by a variety of stakeholder groups. For example, a patient with diabetic nephropathy, or a family member of a patient with AKI, may request a kidney biopsy after learning about the benefits to his or her health and to the research enterprise; an academic researcher can use KPMP resources to evaluate whether a potential disease pathway or drug target is linked to a specific patient outcome; a pathologist who found a new object in a kidney biopsy could use the kidney tissue atlas for fine localization and correlate with a clinical outcome, further refining the disease scoring system; and a private industry scientist could utilize KPMP resources to identify and develop new human drug targets.

Our patient-centered, individualized vision for the future of nephrology drove us to keep the patient voice front and center in the design and implementation of the KPMP. Over time, we expect results and resources from the KPMP will drive the evolution of nephrology toward this future. An increased understanding of human kidney diseases is likely to catalyze the development of new therapies. Biopsy results will likely become more informative to clinical care as pathologists and nephrologists can better predict a drug’s effectiveness based on an individual’s specific renal pathophysiological profile. Ultimately, we predict that patients eager to better understand their disease subtype, specific prognosis, and individualized treatment will begin to demand a kidney biopsy.