EDITORIAL

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Precision medicine in nephrology

Insights into the heterogeneity of processes underlying kidney diseases and their relationship with disease phenotype could redefine classifications of disease and improve patient outcomes.

The field of nephrology suffers from a lack of therapies that target specific disease aetiologies. This dearth of specific therapies is, in part, a consequence of the use of classification systems that categorize kidney diseases according to their chronicity and severity based on non-specific markers. This Focus issue explores how the adoption of a precision medicine approach in nephrology could more closely align disease classification to pathophysiologic processes, aid the identification of therapeutic targets and potentially improve the success of clinical translation.

The ultimate goal of precision medicine is to tailor medical treatment to specific disease processes and thereby optimize patient outcomes. This aim is in principle achieved by combining knowledge of disease mechanisms to define subgroups of patients who may benefit from specific therapeutic strategies. The potential of precision medicine is best exemplified by advances in the field of oncology, in which the use of classification systems that focus on molecular disease processes has enabled the development of specific therapeutics that have improved outcomes for various tumour types.

A body of evidence suggests that nephrology could also benefit from a precision medicine approach. Sequencing analyses have identified vast numbers of genetic variants associated with kidney-specific traits. Some of these variants can be readily linked to specific kidney diseases — usually those that manifest early in life and are caused by single gene mutations[1]. However, most kidney diseases are genetically and phenotypically complex, and the contribution of individual genetic variants to disease aetiology is often unclear. Improved understanding of how the complex genetic architecture of different kidney diseases interacts with environmental exposures provides an opportunity to re-classify chronic kidney disease (CKD) into molecularly defined subgroups that reflect the underlying disease mechanisms and might benefit from specific therapeutic interventions.

The transition to disease classification based on molecular classifiers will require numerous technological developments. Integration of data from multiple domains, including high-dimensional omics, pathology and longitudinal clinical data will be needed, for which computational advances for high-throughput analysis of genetic and omics data will be essential. In addition, developments in digital pathology and computational image analysis, including machine-learning approaches, will facilitate understanding of the relationships between structural changes and molecular phenotypes. Central to these efforts will be the development of new ontologies — such as those being developed by the Kidney Precision Medicine Project — which will improve definitions of kidney molecular and histopathological phenotypes and support the development of new disease classifications.

Multinational initiatives are also needed to ensure that our understanding of disease pathways is as comprehensive as possible and that new recommendations for the classification and treatment of kidney diseases have global support. The support and long-term participation of patients is also key to the success of current and future initiatives in precision medicine. Thus, processes need to be ethical and transparent, patients should have an active voice throughout the research process and their priorities must be embedded into the design and implementation of research efforts.

Importantly, the cost of precision medicine approaches warrants consideration. Massive inequities exist in access to therapies for kidney disease, with millions of people dying each year owing to a lack of access to kidney replacement therapy. Targeted interventions that prevent progression to kidney failure will circumvent the need for costly dialysis, but the introduction of precision medicine approaches cannot risk further increasing inequities in access to care. Measures must be put in place to ensure that diagnostic technologies and therapeutic strategies are not only available to patients in high-income regions but also to those in low-to-middle income regions to stem the expected growth of CKD in these areas.

The benefits of precision medicine in oncology are the result of a long-term spotlight on the field and decades of investment. A similar spotlight on nephrology and higher levels of investment are needed — and are long overdue — as evidenced by the global burden of kidney disease, which remains unacceptably high. Realization of the promise of precision medicine to identify the best treatment approaches for individual patients based on knowledge of pathophysiologic pathways or predictive biomarkers is a worthwhile goal.

> “patients should have an active voice throughout the research process”

1. Vivante, A. & Hildebrandt, F. Exploring the genetic basis of early-onset chronic kidney disease. *Nat. Rev. Nephrol.* **12**, 136–146 (2016).