New era in diagnosis of kidney disorders via NGS.

Isa Abdi Rad*

Department of Medical Genetics, Motahari Teaching Hospital Urmia University of Medical Sciences Kashani Street, Urmia, West Azerbaijan, Iran

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Editorial

Next generation sequencing (NGS) or high-throughput DNA sequencing is a DNA sequencing technology which has revolutionized genomic survey. It has a remarkable impact on the clinical practice and diagnosis of genetic disorders through sequencing of entire human genome including all coding genes [1,2]. The speed and high-throughput of NGS enable clinicians to focus on the diagnosis of genetic disorders at a rate never before possible. However, currently, there are some challenges in application of this valuable technology such as the complexity of data analysis and interpretation.

Since genetic susceptibility plays an important role in the development of many different kidney disorders, application of genetic techniques including conventional cytogenetic analysis, PCR-based methods, Southern blot analysis, microarrays, and Sanger sequencing and NGS are an integrated part of diagnosis of renal disorders. Revealing the genetic basis of kidney disorders has impacts on the prevention of these prevalent disorders. Diagnosis of single-gene disorders such as autosomal-dominant polycystic kidney disease (ADPKD) or Autosomal-recessive polycystic kidney disease (ARPKD) can be carried on by conventional sequencing of known genes, that is, PKD1 and PKD2 genes in ADPKD or KHD1gene in ARPKD [3,4]. However, some kidney disorders are polygenic, that is many genes are involved in the pathogenesis of a single pathologic entity such as focal segmental glomerulosclerosis (FSGS) which can be caused by mutations in more than 20 podocyte-specific genes such as NPHS1, NPHS2, WT-1, LAMB2, CD2AP, TRPC6, ACTN4 and INF2 [5]. In these conditions conventional sequencing may be very time consuming and expensive, so, using NGS would be very helpful.

On the other hand, kidney disorders can be multi-factorial, that is, involvement of many gene accompanied by impact of environmental factors. And finally, renal disorder can be influenced by specific genetic polymorphisms such as a polymorphism in the CNDP1 gene, which encodes the enzyme carnosinase-1, determines susceptibility to develop diabetic nephropathy [6]. In these conditions, NGS can be a very valuable and time-saving method for the diagnosis of genetic mutations or variations.

Using NGS technology resulted in discovery of new genes involved in human diseases including renal disorders. For example; ARHGDIA was identified as a novel gene which implicated in nephrotic syndrome [7] or identification of MYO1E mutations in childhood familial focal segmental glomerulosclerosis [8] and Cubilin mutations in mono-gene proteinuria [9]. Of course, currently, confirmation with conventional Sanger sequencing is recommended or necessary.

Also, polymorphisms can be detected by NGS technology which will be helpful in prediction of susceptible individuals and more importantly by detection of mutations, prevention can be applied in the prenatal period. Revealing the genetic basis and predisposing factors of renal disorders have impacts on the prevention of these prevalent disorders which have a huge health burden.

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***Correspondence to:**

Isa Abdi Rad
MD, PhD
Professor of Neurogenetics
Department of Medical Genetics
Motahari Teaching Hospital
Urmia University of Medical Sciences
Kashani Street, Urmia
West Azerbaijan, P.O. 57146-15463
Iran
Tel: 98 4432240166; 0914 440 5829
E-mail: isaabdirad@yahoo.com