Changing patient management with Renasight kidney gene panel

Renasight™ is a comprehensive kidney gene panel for patients with chronic kidney disease (CKD), electrolyte disorders, or nephrolithiasis.

A New England Journal of Medicine publication assessing the utility of DNA testing for kidney disease found that a genetic diagnosis had implications for clinical management in 89% of patients.1 Highlighted are Renasight case studies that demonstrate how patient management and/or use of targeted therapies changed based on the genetic test results.
### Meet Jacob

**Late 20s**

Presents for evaluation for nephrotic range proteinuria

**History**
- No family history of CKD
- Proteinuria since childhood
- Biopsy showed FSGS
- No response to Prednisone or ACTH gel
- Given atypical FSGS course and steroid resistance, additional immunosuppression deferred

**Rationale for genetic test**
- Clarify etiology of FSGS
- Understand benefit of additional immunosuppression
- Counsel on likelihood of future progression

**Renasight Result**
- Positive for COL4A4-related Alport Syndrome

### Key Takeaway: Clinical Implications
- **No additional immunosuppression required**
- **Remains at high risk for long-term renal disease progression**
- **Very low risk for recurrence if patient requires transplantation**
- **Known genetic etiology allows for informed family planning, identification of at-risk relatives**
- **Identifies risk for hearing and vision deficits**

### Meet Angela

**Late 50s**

Referred for CKD stage 4T

**History**
- 2 kidney transplants
- Difficult to treat anemia
- Brother with kidney stones

**Rationale for genetic test**
- Evaluate for possible etiology of pancytopenia immediately after second transplant

**Renasight Result**
- Positive for CFI-related Atypical HUS

### Key Takeaway: Clinical Implications
- **Patient could have avoided second kidney transplant altogether if the genetic diagnosis was known**
- **Effective treatment with Eculizumab after second transplant**
Meet Martin

**Early 20s**
End stage renal disease with no family history

**History**
- Unknown family history
- C3 deposition on kidney biopsy

**Rationale for genetic test**
- To gain all possible prognostic information prior to a transplant in patient with ESRD of unknown etiology

**Renasight Result**
- Positive for NPHS2-related Autosomal Recessive Nephrotic Syndrome Type 2

**Key Takeaway: Clinical Implications**
- Transplant candidate as FSGS is unlikely to reoccur
- Known genetic etiology allows for identification of at-risk relatives

Meet Sarah

**Early 60s**
Elevated creatinine

**History**
- No history of kidney disease or autoimmune disease
- Generalized weakness
- Rheumatoid arthritis and sleep apnea
- Biopsy results: Focal necrotizing/crescentic and sclerosing pauci-immune (ANCA-associated) GN. Focal, mild tubular atrophy and interstitial fibrosis

**Rationale for genetic test**
- Unknown etiology of CKD

**Renasight Result**
- Positive for NR3C2-related Autosomal dominant pseudohypoaldosteronism

**Key Takeaway: Clinical Implications**
- Associated with mild salt wasting and hyperkalemia – improves with aging
- Patient’s electrolyte imbalances improved with steroids
- Known genetic etiology allows for identification of at-risk relatives
Genetic testing results can provide information to tailor therapeutic strategies or workups. Below are examples of how genetic testing results can inform patient management and treatment.

<table>
<thead>
<tr>
<th>Disease Name</th>
<th>Gene</th>
<th>Therapeutic Application</th>
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| Autosomal Dominant Tubulo-interstitial Kidney Disease (ADTKD)² | UMOD, REN, HNF1B     | • ADTKD-UMOD | Gout: Prevention with allopurinol, febuxostat, or probenecid can be considered. Treatment with prednisone, short-term NSAIDs, or colchicine.  
  • Allopurinol may slow the progression of kidney disease  
  • Kidney transplantation cures ADTKD-UMOD, REN, HNF1B.  
  • ADTKD-REN | Anemia: May be reversed by erythropoietin. Acute gout typically responds well to prednisone or colchicine. |
| CoQ10 Deficiency³                                      | COQ2, COQ6, PDSS1, PDSS2 | • Individuals with primary CoQ10 deficiency may respond well to high-dose oral CoQ10 supplementation (ranging from 5 to 50 mg/kg/day). |
| Fabry Disease⁴                                         | GLA                   | • Enzyme replacement therapy (ERT)  
  • Pathogenic missense variants can be treated with chaperone migalastat instead of ERT  
  • Diphenylhydantoin, carbamazepine, or gabapentin to reduce pain  
  • ACE inhibitors or angiotensin receptor blockers to reduce proteinuria |
| Primary Hyperoxaluria, Type 1⁶ (PH1)                  | AGXT                  | • Avoid related heterozygotes for patients with combined kidney and liver transplant⁵  
  • To reduce calcium oxalate supersaturation in the urine: maintenance of high fluid intake; inhibition of calcium oxalate crystal formation with potassium or sodium citrate, pyrophosphate-containing solutions.  
  • To reduce oxalate biosynthesis: pyridoxine supplements for those who are pyridoxine responsive |
| Renal Cysts and Diabetes Syndrome⁷                     | HNF1B                 | • Maturity onset diabetes of the young (MODY): A minority respond to sulfonylureas.  
  • Insulin is commonly needed. Anti-proteinuric agents and pancreatic enzyme supplements based on clinical presentation |

References:
3. PMID: 29071180, 11386930, 17483124, 19473999, 26937390, 17493038, 11493963, 17179302, 25769794, 17654478, 24889109.

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