

## **MYH9 gene, the high rate of FSGS in African Americans explained**

It has been well documented that African Americans have a higher risk for FSGS and end stage renal disease (ESRD) as well as other forms of kidney disease when compared to Americans of European descent<sup>1</sup>. In fact, the risk for developing idiopathic FSGS is five-fold higher and estimated to be up to 50-fold higher for HIV associated FSGS when compared to individuals of other racial backgrounds<sup>2</sup>. The reasons behind this health disparity cannot be fully explained by socio-economic differences or differences in the access to medical care<sup>3</sup>.

Physicians have known for some time that kidney disease can run in families and is more prevalent in certain ethnic groups. This appears to indicate that there likely is a genetic component. Recently, in a study conducted by the Kidney Disease Section of the National Institutes of Health, Dr. Kopp and colleagues performed a study to determine a genetic cause for this observed health disparity. The researchers identified a location on chromosome 22 found to be highly associated with FSGS, and other non-diabetic kidney diseases<sup>3</sup>. After mapping the area further, one gene on the chromosome was identified, MYH9, thought to increase the risk of developing FSGS<sup>3</sup>.

The results, published in the Journal *Nature Genetics*, have found that genetic variations found in the MYH9 gene, explain almost all of the increased risk of FSGS and HIV associated FSGS among African Americans<sup>3</sup>. In the same issue of *Nature Genetics*, Kao and colleagues independently identified MYH9 as a candidate gene for the increased risk<sup>4</sup>. An estimated sixty percent of African Americans carry the gene variants, a significant number when compared to four percent of European Americans<sup>3</sup>.

What is particularly striking about this research is that almost all of the genetic variance between African-Americans and European-Americans is explained by variations in a single gene. The risk of developing kidney disease is the strongest when an individual has two copies of the variant gene but even then kidney disease is not a certainty. While individuals may be genetically susceptible, other factors such as the individual's environment and possibly other genes are important in developing FSGS<sup>5</sup>.



The MYH9 gene is known to be expressed in the podocytes, specialized cells in the kidney that play a role in filtration<sup>6</sup>. Damage and dysfunction of the podocytes can lead to FSGS and without response to treatment this can lead to ESRD<sup>1</sup>.

While these studies indicate MYH9 as the candidate gene, they have not yet provided an explanation for the association of MYH9 with kidney disease. This discovery now allows researchers to learn more about the underlying molecular defects at this gene so that we can better understand how those defects result in kidney disease. Importantly, this research provides a basis for further work on the function and regulation of MYH9. Finally, this can ultimately lead to identification of patients that are at a higher risk of developing FSGS, can lead to improved patient care and we hope will lead to new therapies to fight the rise of ESRD in the US.

- 1) Fehally J, Floege J, Johnson R. Comprehensive Clinical Nephrology.3. Philadelphia: Mosby Elsevier, 2007. Print.
- 2) Kopp JB, Winkler C. HIV-associated nephropathy in African Americans. *Kidney Int Suppl* 2003;63:S43-S49.
- 3) Kopp J et al. MYH9 is a major-effect risk gene for focal segmental glomerulosclerosis. *Nat Genet* 2008, October; 40(10):1175-84.
- 4) Kao W et al. MYH9 is associated with non-diabetic end stage renal disease in African Americans. *Nat Genet* 2008, October; 40(10):1185-92.
- 5) Freedman B et al. Polymorphisms in the nonmuscle myosin heavy chain 9 gene (MYH9) are strongly associated with end stage renal disease historically attributed to hypertension in African Americans. *Kidney Int* 2009, April; 75(7):736-45.
- 6) Seller JR. Myosins: A diverse superfamily. *Biochim Biophys Acta* 2000:1496:3-22.
- 7) Pollack M, *Nat Genet* 2008, 40(10):1145-46.
- 8) Rao M, Balakrishnan V. The genetic basis of kidney disease risk in African Americans: MYH9 as a new candidate gene. *Am J Kid Disease* 2009, April; 53(4):579-583.

