

Genetic Diversity and Selection: A Double Edged Sword

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Ancestral background and geography have long been associated with varied disease presentations, prevalence and outcomes. While some of these differences are clearly related to distinct environmental factors, a significant portion can be explained by specific population level genetic selection. For example striking differences in the prevalence and/or progression of IgA nephropathy, HIV associated nephropathy, diabetic nephropathy and chronic kidney disease (CKD) progression rate have been noted to be, at least in part, based on ancestral background.

Bearing in mind that allelic variability is greater among individual within a single population than between distinct populations, the question as to why any alleles associated with a poor outcomes such as CKD remains specifically enriched in a given population becomes central. One such, of several reasons, is that the same allele is also causal for a positive trait, which at some point in time outweighed the negative consequences.

We will review recent seminal discoveries related to the identification of a strong positive selection for distinct *APOLI* and *HBB* alleles in certain regions of Africa, resulting in great immunological and survival advantages, but at the high cost of increased renal injury and end stage renal disease. These examples can help illustrate the evolutionary double edged sword used in our continuous battle to keep pace with our changing environment. Moreover, they can remind us of the need to focus on both edges, as we seek a better understanding our evolutionary path towards health and disease.