

PANEL SUMMARY: WHAT'S NOW AND WHAT'S NEW IN GENOMICS, EPIGENOMICS AND CARDIOVASCULAR DISEASE?

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SUMMARY

Panelists Kao, Reich and Hirschhorn described important health disparities that may have a genetic component, and presented key findings of genetic analyses involving the Jackson Heart Study and other cohorts. African Americans differ from European Americans in the incidence of several important diseases, including prostate cancer (1.6 fold higher in African Americans),¹ end-stage renal disease (ESRD; 3.7-fold higher),² uterine fibroids (2- to 3-fold higher),³ systemic lupus erythematosus (3- to 4-fold higher),⁴ and multiple sclerosis (1.5- to 2-fold lower in African Americans).^{5,6} Because most African Americans have both African and European ancestors, their chromosomes are a mosaic of African and European segments that can be identified by genetic analysis. By mapping the chromosomes of significant numbers of African Americans to determine the ancestral origin of each region of each chromosome, a process called “admixture mapping,” and comparing the maps to traits of interest, regions of the genome have been identified that contribute to prostate cancer,⁷ ESRD,⁸ and multiple sclerosis,⁹ as well as other traits like white blood cell counts.¹⁰ In particular, variation in a region on chromosome 22 that contains the *MYH9* and *APOL1* genes has been found to account for as much as 70% of non-diabetic ESRD in African Americans.⁸ Data that were presented in the session illustrated the importance of genetic studies in African-derived populations, which have significantly greater genetic diversity than other continental populations, as well as distinct patterns of association between different genetic variants, measured by linkage disequilibrium. These distinct patterns have allowed, for example, more accurate localization of variants in the *FTO* gene that are associated with variation in body mass index.¹¹

Questions that followed the formal presentations suggested important opportunities for future research. The question of whether a single genetic variant might influence multiple traits suggested testing variants that are associated with one trait for potential association with related traits, or even combinations of traits. The possible biological effects of copy number variation (CNV), wherein sequences from a few to several thousand nucleotides exist in varying numbers of copies in the genome, led to discussion of ongoing studies attempting to characterize CNVs more accurately and to analyze association between specific CNVs and traits of interest. The capacity of environmental factors to modify certain “epigenomic” features of DNA raised the question of whether environmental influences might have transgenerational effects, and of how such effects might best be studied. The need to work with clinicians to develop more discriminating phenotype definitions was emphasized, as a means of increasing capacity to make clinically important discoveries. Finally, the panelists and audience members discussed challenges and opportunities for the Jackson Heart Study over the next 10 years and beyond: the possible need for additional recruitment, the potential importance of additional family studies, and above all, the need to continue and expand genetic research among African Americans and other diverse populations, both for the sake of equity and for the best science.

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