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Commentary

The opportunity in African genome resource for precision medicine

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There is a critical need to increase and diversify genomic study in the global efforts to achieving full implementation of precision medicine. Given this central importance of Africa to human origins, genetic diversity, and disease susceptibility, there is a clear scientific and public health need to develop large-scale efforts that examines disease susceptibility across diverse populations within Africa [1]. The marked genomic diversity and allelic differentiation among populations in Africa, in combination with the substantially lower linkage disequilibrium (correlation) among genetic variants, will provide excellent opportunities to gain new insights into disease etiology and genetic fine mapping that have relevance for African populations and globally [2,3]. Importantly, given varying environments and adaptation, the spectrum and distribution of risk factors for a broad range of non-infectious and infectious diseases, and their individual contribution, may differ in African populations compared with European populations or those of African descent in Europe, North America and elsewhere [1]. However, despite the value of conducting such studies in Africa, there have been relatively few investigations of population diversity and the genetic determinants of non-infectious or infectious traits and diseases across the continent.

Analysis of genomic data is a key component of precision medicine and has significant potential to inform clinical care [4]. However, one potential limitation of genomic medicine is the underrepresentation of African and other populations in genomics research. Popejoy and Fullerton 2016 [5] warned that to reduce the risk of genomic medicine benefitting only the "privilege few, investigations into a much broader range of populations is required". This is especially problematic, as previous studies have shown that studies on Africans contribute an outsized number of associations relative to studies of similar sizes in Europeans [6]. To demonstrate the potential of genomics on Africans as a great resource for genomic medicine, we collected and analysed genome-wide data from 6407 individuals from a rural community in Uganda [2,3]. Data from other parts of Africa, including individuals from South Africa, Kenya and Nigeria were incorporated, making a total of 14,126 individuals across Africa. A range of health indices such as lipids, Liver function (LFT), full blood counts (FBC), Body Mass index (BMI) and Glycated hemoglobin (HbA1c) level – an indicator commonly used to diagnose diabetes – were measured. This study represents one of the largest ever genome studies in Africa. In this modestly sized study, we discovered ten novel genetic variants associated with several traits/diseases of which nine of them are specific to Africa population [3], thus reiterating the importance of conducting such work in African populations.

Our discoveries include a genetic variant that causes alpha thalassemia to be associated with HbA1c [3]. This variant is present in 22% of Africans and almost absent in European populations. The variant is understood to have become more common among African populations because it can prevent severe malaria. Our findings suggest that, as HbA1c levels are often used to diagnose diabetes globally, it is possible that diabetes may be misdiagnosed in some Africans because of their genetic composition. Notably, we also found that height is less genetically determined in Uganda relative to previous studies in European cohorts [3]. One reason for this might be environmental factors such as nutrition. Unsurprisingly, we found a higher level of genetic diversity in the Uganda population than previously observed in similar studies of European populations. 25% of the genetic variation we identified in our Uganda population had not been discovered before [3]. Our findings highlight the importance and usefulness of examining genetically diverse population within Africa.

While there is an urgent need to perform large-scale genomic research in Africa, several ongoing initiatives such as H3Africa [7,8] and the Nigerian 100K Non-Communicable Diseases – Genetic Heritage Study (NCD-GHS) [9,10] could provide the data to improve the evidence base and make genome medicine useful to diverse populations. These large-scale population-based African-ancestry cohorts could provide opportunities to: (1) discover novel disease susceptibility loci; (2) refine association signals at new and existing loci; (3) develop research capacity for genomics in Africa; and (4) enhance African participation in the global genomics research arena. I anticipate that these efforts will contribute to making genomic studies in Africa more comparable with European and Asian initiatives. The findings from such large-scale efforts may foster the development of new treatments that will benefit

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people living in Africa as well as people of African descent around the world.

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