ST.GALLEN SYMPOSIUM

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THOUGHT PROVOKING IDEAS OF THE GLOBAL ESSAY COMPETITION 2023

The Journey Towards Equitable Human Genetics Research

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The diversity of human genomes

Human genomes are 99.9% identical, but the 0.1% of variances make each of us unique. This could include things like eating preferences, hair colour, and even sleeping habits. Genome variations can be caused by things like human migratory patterns, our ancestry, who we choose to mate with, and frequently environmental variables which, in addition to genetics, can influence a trait like height and weight[1].

These variations frequently occur at various frequencies in various populations. Sometimes they are uncommon and only affect a few families, while sometimes they are widespread and can be found in different groups[1].

Brief introduction to genome wide association studies

To be able to answer questions relating to genetic disorders, scientists predominantly conduct genome wide association studies (GWAS). These studies examine the genomes of thousands of individuals to look for variations linked to disease features[2]. The GWAS catalogue[3] is the most thorough and easily available compilation of human genetic association studies.

Underrepresentation of non-Europeans in genetic studies

Although only 16% of the world's population is of European heritage, the GWAS catalogue indicates that 79% of all participants are of European ancestry. This disparity is particularly troubling because prior research has demonstrated that studies on African Americans and Hispanic/Latinos

generate disproportionately more associations than studies of comparable size on Europeans[4].
More worryingly, since late 2014, the percentage of GWAS participants who are not Europeans has stalled indicating that there is no trajectory in place to address this imbalance[5].

As a result of their predominance in populations with European ancestry, large-scale genetic studies of human disease have not adequately reflected the degree of variation that exists globally[6].

Why the biasness

The overrepresentation of European ancestry in GWAS could be a legacy from previous biases. The biasness could be due to several factors such as lack of trust, limited engagement with participants, limited access to resources, researchers' preference for data analysis from well-characterized, powerful cohorts with a predominance of European ancestry, relatively smaller sample sizes in diverse communities pose challenges for publication and funding, lack of diversity in the research workforce, and issues with existing genotyping technology that prevent it from accurately capturing variance among diverse persons[7].

Lack of trust and participation in research stems from the overrepresentations of populations from the European ancestry as well as historical injustices and lived experiences of underrepresented populations. Additionally, the understanding of advantages and usage of participants' personal data has been hampered by limited and unavailable communications.

Lack of diversity in the research workforce arises due to the underrepresentation of scientists from low-resource settings and diverse communities[8,9]. This may result in the loss of priorities and hypotheses brought to genomic research by specialists with various points of view.

Why we should care

To ensure that genomic medicine benefits everyone in the world and not just the privileged few, it is important to

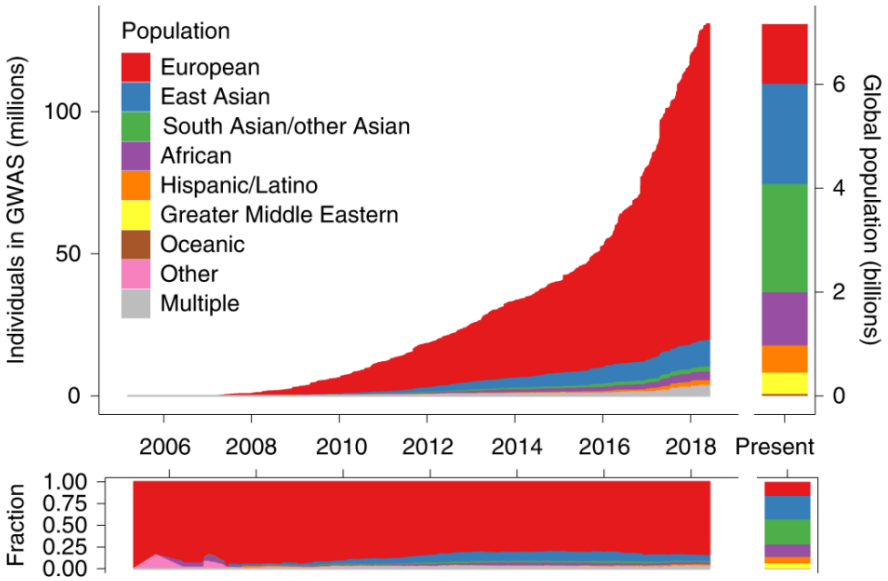

Figure 1: GWAS participants' ancestry across time in comparison to the world's population[5]

expand such studies to underrepresented populations. The African continent, for instance, is considered the most genetically diverse continent, made up of 54 countries and over 3000 ethnic groups[10] with the heaviest disease burden[11], yet we have very few GWAS studies occurring in the continent.

Also, GWAS results from European populations might not replicate in other ethnic groups, resulting in missingness of opportunities to find novel correlations between disease traits in other populations[2]. This lack of replications across populations is expected due to the history of evolution of populations across the world[6].

For example, in at least one out of every five populations of non-European ancestry, the strength of association varies for 25% of the variations in European Americans that GWAS have found as being associated with type 2 diabetes, lipid levels, and body mass index. The variation indicates that a mutation linked to diabetes may impart a different risk of disease on a person of European ancestry than, for example, a person of African ancestry[12].

Furthermore, including diverse populations is not only ethically correct, but also necessary for genomics research. Humanity's answers to problems faced by some or all populations can be found in great abundance in the genomes of diverse individuals. These problems range from the diets, infectious illnesses, and climate change[7].

On-going efforts

Several initiatives have been set up to advance genomics research in underrepresented communities worldwide. The US National Institute of Health and Wellcome Trust for instance founded the Human Heredity and Health in Africa (H3Africa) Consortium[13] in 2012 to support the development of infrastructure and genomics expertise throughout Africa, led by African investigators.

Although the H3Africa project came to a closure in 2021, it has left a tremendous impact of Genomics research in Africa. One key impact has been the development of a comprehensive genetic repository for African populations, encompassing DNA samples. This tool has been employed to research the genetics of numerous illnesses, such as cancer, cardiovascular disease, and infectious diseases like HIV and tuberculosis[14,15].
Furthermore, H3Africa has helped build capacity for Genomics research in Africa by training scientists in cutting-edge genetic research methodologies[16]. African scholars now have the chance to contribute to international efforts to study the genetics of diseases, helping to expand the representation of African perspectives in genetics.

A similar consortium known as the “Data Science Initiative in Africa (DSI-Africa)” has been set up to continue with the work started by H3Africa. The initiative seeks to utilise data science tools to transform biomedical and behavioural research and create solutions that will improve the health of people[17].

The existence of the Malaria Genomic Epidemiology Network[18] has helped to provide resources for genomics data to help combat and eradicate malaria in Africa. Additionally, Segun[19] has proposed the setup of the Nigerian 100K Genome Project consortium to serve as a template

for large scale genomics research in the African continent.

Other global programs have also joined the movement. They include Genomics England[1], set up to lower health disparities and enhance patient outcomes in genomics medicine for minority communities and All of Us research program[20], that seeks to increase representation of diverse participants in genomics studies.

Conclusion

Although there has been significant progress in including Afrocentric datasets in genomics research, substantial work is still needed to prevent genetic medicine from only benefiting "a privileged few."

To address this, Popejoy[2] suggests that financial incentives for the development of diverse cohorts of study participants should be developed by funding organisations. Prioritizing grant submissions that call for research in populations with non-European, particularly African ancestry would be one approach for them to achieve this.

Also, good medical facilities that offer genetic testing in neighbourhoods with a high concentration of Black or Hispanic residents could increase trust by engaging with people as stakeholders rather than study subjects. Another suggestion is to allow Biomedical research recruitment initiatives in under-represented groups to be carried out by researchers with similar racial or ethnic backgrounds in collaboration with organisations trusted by those populations[2]. Additionally, researchers should always work on getting participants' informed consent, safeguarding their privacy and confidentiality, and carrying out the research in a way that respects the participants culture and community's norms.

Amy[7] suggests encouraging diversity while discouraging a lack of it as an effort to increase diversity in genomics research. Their work also encourages responsible biospecimen and data sharing, the need for reviewers to understand the historical and contemporary context of performing genomics research in diverse populations, the call for initiatives aimed at advancing the careers of scholars from diverse backgrounds and increasing the size and quantity of diverse population cohorts that are well-characterized in large studies[7].

The African continent offers enormous opportunities for genomic discovery and personalized medicine. Genomics studies biasness should thus be addressed to pave way for translating genomics research in underrepresented populations into public health policies or clinical practice.

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