COMMENT

# Overcoming barriers to equitable genomic healthcare

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*European Journal of Human Genetics*; https://doi.org/10.1038/s41431-024-01557-3

We all recognize the pivotal role of next-generation sequencing in the diagnosis and discovery of rare diseases that are majorly genetic in origin. While limited access might be the result of economic constraints in the three-fourths of the global population, it might also be due to infrastructure (genetic testing laboratories) or trained manpower (genome analysts) in other situations. In this issue, Cecilia Poli and colleagues address how limited genomic resources for rare disease diagnosis can be overcome [1]. Facility for high throughput next-generation sequencing and genome analysts were scarce in Chile. The local team (Universidad del Desarrollo [UDD]), collaborated with Baylor College of Medicine (BCM) for the analysis of exome data and established a rare disease program DEcoding Complex Inherited PHenotypes of Rare Diseases ('DECIPHERD') for Chile.

In the first phase (training), an international collaboration was initiated by the local team (UDD) with the Baylor College of Medicine in the USA, which imparted training to the UDD scientific team. In the second phase (local development), clinical evaluation and variant data analysis were performed locally. The sequencing was outsourced in both phases, however.

The first 103 probands had either congenital anomalies, neurological abnormalities or dysfunction of the immune system or a combination of these. The probands had no diagnosis from preliminary testing (but had not undergone exome sequencing). Trio exome sequencing was performed at BCM and the results were validated by Sanger sequencing at UDD. Parallelly, Mendeliomes (singleton) and whole exomes were sequenced (outsourced to laboratories in Switzerland and China respectively) and analyzed by the local team, integrating the in-house data of allele frequencies. The work resulted in a diagnosis for several participants, identifying several new disease-causing variants and confirming de novo origin in many of them. Thus, this study enriched the publicly listed variants and established a workflow for diagnosis of rare genetic diseases locally.

The study is limited by the small sample size, and clinical heterogeneity of the cohort (clinical features), and is not uniformly representative of the local population. It is too early to share potential new gene discoveries from this small effort and how the secondary findings are dealt with by the team. Without delving into what constitutes an 'undiagnosed disease' in this study, the efforts have clearly borne fruits in terms of establishing a local team for carrying this work forward and training more local talents. The results show that the team has a similar learning curve as other resource-sufficient teams in the world, trying to find out the best, yet cost-efficient approach (Mendeliome or whole exome, singleton or trio, in-house pipeline or a commercial analysis tool, etc.) for diagnosis of rare genetic disorders.

While Chile is a high-income country, the authors point out the lack of high throughput sequencers and trained manpower (due to lack of training programs) as the barriers for implementation of genomic medicine. These issues are limitations in other countries (Middle East) too who have 'high-income' but outsource their genetic testing to the laboratories in the developed nations. Such studies from underrepresented populations not only help the locals, but also those who have migrated from these countries.

How do we ensure no one is left behind [2] while we advance genomic medicine worldwide [3]? Here, I would appeal to all the stakeholders to consider the following steps to bridge the gap in access to genomic testing and diagnosis. First, develop programs to train molecular biologists, bioinformaticians and genetic counselors across the globe. Second, develop local dataset of variants and share them globally. Third, adapt international guidelines on genetic testing locally with suitable modifications to meet the demands of your own system. Fourth, develop a legal and ethical framework for delivering genomic health care. Fifth, build synergistic collaborations to overcome challenges and limited resources. While economic development is most desirable, prioritizing existing resources towards the above steps can speed up equitable access to genomic healthcare. Where there's a will there's a way!

## REFERENCES

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## AUTHOR CONTRIBUTIONS

KMG wrote this commentary to accompany an article in this issue.

## FUNDING

No financial assistance was received in support of the study.

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Received: 29 January 2024 Accepted: 30 January 2024
Published online: 13 February 2024

## COMPETING INTERESTS

The author declares no competing interests.

## ADDITIONAL INFORMATION

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