The Qatar genome project: translation of whole-genome sequencing into clinical practice

Qatar Genome Project was launched in 2013 with the intent to sequence the genome of each Qatari citizen in an effort to protect Qataris from the high rate of indigenous genetic diseases by allowing the mapping of disease-causing variants/rare variants and establishing a Qatari reference genome. Indeed, this project is expected to have numerous global benefits because the elevated homogeneity of the Qatari population, that will make Qatar an excellent genetic laboratory that will generate a wealth of data that will allow us to make sense of the genotype-phenotype correlations of many diseases, especially the complex multifactorial diseases, and will pave the way for changing the traditional medical practice of looking first at the phenotype rather than the genotype.

1 | INTRODUCTION

Qatar is a small peninsula on the Persian Gulf (Fig. 1) with a total population of approximately 300,000 Qatari citizens. Qatari have one of the highest rates of consanguineous marriages in the world,¹ which is still increasing,² and the rate of endogamous marriage in Qatar approaches ~100%. All these factors together with the large family size are the main reasons for the high rate of indigenous genetic diseases, which represent a financial burden on the Qatari budget. These factors triggered the Qatari government to seek a means to protect their own people from the threat of genetic diseases. Government officials decided to launch the Qatar genome project (QGP) in 2013 (http://www.gulf-times.com/story/374345/Qatar-launches-genome-project) with the intent to sequence all Qatari individuals and thereby to understand more about the structure of the Qatari genome.

2 | QATAR GENOME PROJECT

The QGP is a major initiative, involving the Qatar’s National Genome Committee, the National Blood Biobank, and genomic and bioinformatics scientists in Qatar, using the NextCode technology as theinformatics platform (www.genomeweb.com). The sample collections can be obtained from the Blood Biobank national repository (http://www.qatariobiobank.org.qa), where all the data from the blood donors are contained, including clinical, demographic, lifestyle and family history. Sample donors are requested to sign a generic consent form that allows their samples and data to be anonymously utilised for health-related research.³

The QGP started with a pilot phase of sequencing 3000 Qatari individuals, which will soon be concluded. The pilot programme will serve as a foundation for running the entire QGP, providing a practical demonstration of the feasibility of a large-scale sequencing endeavour that will target all willing Qatari individuals to be part of this national endeavour. The sequencing data are being deposited into a national repository and are available for researchers to make sense of this tremendous amount of complex data. Generous, postsequencing, competitive funding was established by a Qatar foundation, entitled Path towards Personalized Medicine (PPM) (http://www.qnrf.org), which aims to be used by scientists for applying cutting-edge genomics technologies to analyse and interpret these sequenced genomes, confirm genetic variants that are unique to Qatari, and initiate a genetic and epidemiological database for a Qatari reference genome as a path towards personalised medicine, with the goal of applying the information to clinical practice and allowing this approach to become a routine part of the Qatari healthcare system.

3 | QGP INTO CLINICAL PRACTICE

Whole-genome sequencing (WGS) is increasingly being utilised in clinical diagnostic practices, and as costs continue to decrease, there is a hope that WGS will soon be an integral part of a patient’s healthcare. WGS has shown promise in being a definitive diagnostic tool across a broad spectrum of genetic diseases for patients in whom previous screening had identified no pathogenic variants.⁴ It has also been proven to be a vital tool in solving diagnostic odysseys. With the continuous rising rates of genetic diseases that are threatening the Qatari healthcare system, the QGP could transform clinical practice in Qatar. The QGP will contribute to rapid diagnosis of genetic diseases, which will be steered more by a genetic assessment rather than the traditional phenotypic evaluation for known genetic diseases; even for unusual clinical scenarios, the ready access to genetic profiles and clinical family history that will be available in the Qatari national database will facilitate diagnostic scenarios that would normally require a much longer time. In addition, understanding the nuances of the structure of the Qatari genome carries great potential in mapping rare variants and novel disease-associated genes and in simplifying the mode
of inheritance of complex genetic diseases by the virtue of the high consanguinity and endogamy, which has led to the inbred and homogenous pockets of Qatari society that are considered to be very instructive genetic laboratories. Once this wealth of data is catalogued in a meaningful genetic scenario, additional genetic testing will not be required. The catalogued data will facilitate the genetic counselling of Qatari patients by providing direct benefits to the consanguineous Qatari families and families at high-risk of high rates of genetic diseases, enabling these persons to make informed decisions regarding marriage and reproduction and allowing for timely medical intervention. Although healthcare funding can provide a variety frameworks and tools to help guide the implementation of genome sequencing in clinical practice, the project requires a long time to achieve its goal and a significant amount of spending; however, the QGP is expected to save significantly in terms of the healthcare dollar in the long-term.

4 | CHALLENGES AND LIMITATIONS

To achieve the expected clinical application promise of the QGP, several serious challenges must be met, including the ethical and social implications (informed consent, privacy, and stigmatisation). It might be challenging to convince all Qatari citizens to enrol in this vital programme. However, intense awareness campaigns (which should be part of the QGP budget) that are tailored to both educated and non-educated sections of Qatari society and aim to ease the public’s doubts and educate them regarding the direct benefits of such a contribution to the public health in the state of Qatar would increase their participation and would fulfil the long-term objectives of the project. Other challenges are technical and are intrinsic to the sequencing technology, including production, variant-calling sensitivity and accuracy, analysis, and the interpretation of massive amounts of sequencing data; in addition, the massive number of novel variants that are expected to be generated will require a great deal of hard work to be confirmed and assessed for their degree of pathogenicity. The integration of the data with machine learning can aid in understanding the variable penetrance, and this type of clinical interpretation requires highly skilled and experienced scientists in the fields of genomics, bioinformatics, variant assessment, genetics and molecular biology. This analysis could also be facilitated by developing specialised apps for existing genes and variants, which could facilitate user-friendly usage of the database by clinicians and scientists. This could be achieved by recruiting skilful genomics scientists or partnering with reputable sequencing companies. Although, the former is the way forward for future progress in the genomics culture in Qatar, and a constructive way to apply WGS to clinical practice resources is limited.

The degree of unpreparedness of the medical workforce to address this complex genomics culture could represent a significant limitation to the adoption of clinical WGS sequencing; nonetheless, the routine use of a genetic database for personalised medicine can be achieved by inserting genetics into all medical specialities and providing focused training and workshops to nurses and physicians, which can be provided by clinical geneticists and genetics counsellors. This could also be linked to CME credits and be a prerequisite for annual medical licensing to ensure participation and learning. Therefore, concerted efforts among all disciplines are pivotal to drive the outcome of this project to a successful medical practice.

5 | CONCLUSION

With the completion of the QGP, the benefits will not only affect Qatari patients in terms of prognosis, diagnosis, treatment and medical advice but also generate a global impact, including the identification of novel disease-causing genes, the mapping of rare variants, and significant contributions to solving the mystery of genotype-phenotype correlations, especially for complex multifactorial genetic diseases, thereby leading to a transformation of the current medical practice for the good of human health, which will save lives now and in the future on a global scale.

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