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You cannot claim that you understand the human genome without sequencing representatives of the whole human race

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Dr Said Ismail, geneticist and professor of genomics at Hamad Bin Khalifa University, reflects on his role as the founding director and one of the architects of the Qatar Genome Programme (QGP), one of the Middle East's most established and globally recognised population-level genomics initiatives. He describes the pivotal decisions required at a time when large-scale national genome projects were uncharted territory and highlights the expanding importance of multi-omics in precision health, particularly in pharmacogenomics and in guiding individuals toward preventive actions. He notes that Qatar is the first country to translate a population level genome programme into preventive medicine informed by predictive genomics. Ismail also emphasises the value of international collaboration and the growing role of artificial intelligence (AI) in clinical practice.

Can you tell us a bit about yourself and the QGP?

I am a geneticist and professor of genomics at Hamad Bin Khalifa University. I recently moved back to academia, after being the founding director of the globally recognised QGP for the past ten years, one of the most established large-scale population-level genome projects in the Middle East. We set up everything in Qatar, from sequencing to interpretation to implementation, working closely with Qatar Biobank (QBB). The two initiatives were later brought together under the Qatar

Precision Health Institute (QPHI), officially launched in 2024 to consolidate the country's national precision health and genomics efforts.

Her Highness Sheikha Moza bint Nasser was the visionary behind this initiative. She envisioned Qatar becoming a pioneer in the implementation of precision health and recognised early that this would require generating large-scale population data through the establishment of both a national biobank and a genome programme. With her support, we were able to bring that vision to life.

Once the data had been collected, made available to researchers, and shared into strong scientific publications, the focus shifted toward implementation in routine healthcare, which is now the central aim of QPHI.

How did you end up being part of the project, and what key decisions did you make early on in the journey of the QGP to be where you are today?

I was in Qatar as a conference speaker, where I met Dr Asmaa Ali Al-Thani. She had been tasked with assembling the team and believed I could be of help. I accepted the offer immediately.

It would have been easier to collect samples, send them abroad for sequencing, and receive the data back for analysis. However, the team wanted everything to take place in Qatar. Capacity building is one of the key deliverables of large-scale projects, both in terms of human capital and infrastructure. We therefore developed a strategy that tapped into the local ecosystem. We visited research centres, universities, hospitals, and laboratories to coordinate efforts and ensure we would not reinvent the wheel or reinvest in resources that already existed. The advantage of working in a small country was that we could bring all those stakeholders together and align them around a shared national effort.

One of the earliest strategic decisions was whether to focus on specific diseases or take a population-level approach. We chose the latter, because we were the first in the Middle East to undertake population-level whole genome sequencing (WGS). To do this properly, we first needed the background information, essentially a map of healthy genomes in the population. Another important decision was to localise everything.

We also decided to work closely with Qatar Biobank and prioritise deep phenotyping rather than light phenotyping. This approach allows the genomes to be analysed against hundreds of thousands of parameters linked to numerous phenotypes, which in turn opens the door to disease-focused genomics.

After sequencing a representative sample of Qataris, we expanded the effort to include long-term residents (LTRs), as we wanted the data to reflect the broader region. Around 20 percent of our sequences belong to Middle Eastern or Arab individuals, with samples from across the region. Altogether, our dataset is representative of more than 450 million individuals, making it the largest collection of whole genomes from the Middle East and North Africa (MENA) region. To date, around ten percent of the Qatari population has undergone WGS, which corresponds to approximately 35,000 individuals. Of these, around 10,000 to 15,000 are LTRs or Arabs.

Another important strategic direction was to expand into “other-omics.” With deep phenotypic data and a representative genetic sample, we were able to capture the most important variants associated with diseases prevalent in this population. The next step was to expand horizontally into additional layers of biology. Other-omics, including proteomics, transcriptomics, epigenetics, and microbiomics, can reveal insights that go beyond the genome itself. Currently, around 10 to 20 percent of participants have multi-omics data, which represents an extraordinary resource for discovery. Very few national genome projects have datasets of this depth.

What motivated the decision to extend the project outside of Qataris?

This was both a contribution to the region and to global scientific efforts. 90 percent of the genomes sequenced around the world belong to Western Europeans or North Americans. You cannot claim that you understand the human genome without sequencing representative samples of the whole human race. We therefore felt a responsibility to represent this region and to generate knowledge that could benefit countries across the Middle East that do not yet have access to such technologies, as well as the global scientific community. This is also why there is increasing discussion around diversity in human genome data: underrepresented populations must be included.

A paper from researchers at Harvard highlighted this imbalance, noting that 96 percent of genome-wide association studies involving Middle Eastern populations relied on data generated in Qatar.

Are there particular areas of multi-omics that have the most benefits or results?

Approximately 90 percent of the Qatari population carries an actionable pharmacogenomic mutation. We are now incorporating these data into the healthcare system. This clinical information can help determine whether a person should or should not take a particular drug, as their genome

may indicate a risk of serious side effects.

Another important reference point is the guidance from the American College of Medical Genetics and Genomics (ACMG). It identifies mutations that make individuals susceptible to disease, and this information is also actionable. Through our research, we published numerous papers showing that our population carries cancer-causing mutations, rare-disease variants, and pharmacogenomic mutations that increase susceptibility to severe drug side effects.

This raised an ethical question: what are we going to do with this information? Large-scale genome projects are not necessarily obligated to return data to participants. I therefore sought the advice of a bioethicist. He asked whether these mutations were life-threatening and whether actions could be taken to prevent loss of life. When I confirmed that they were and that preventive measures existed, he advised that we were ethically obligated to inform participants. I was pleased with that conclusion, because this is where the real impact lies.

However, my team and the clinicians were concerned about informing thousands of participants about thousands of mutations. We therefore began with a pilot programme, limiting the number of mutations and focusing on a single condition. We selected BRCA1 and BRCA2, mutations that increase susceptibility to breast cancer in women. We contacted dozens of women and informed them that they might be carrying one of these mutations. We asked whether they would be willing to provide another sample for confirmation and then be referred through the healthcare system if needed.

The response was overwhelmingly positive. The pilot demonstrated that most people are interested in knowing about their risks. While some prefer not to know, the vast majority want information and the opportunity to act on it. One participant from this pilot encouraged women in her extended family to be tested, and one of her sisters was found to have early-stage ovarian cancer. She was able to undergo a simple operation that ultimately saved her life.

Through this initiative, Qatar became the first country to translate a large-scale research-based national genome project into a screening and preventive medicine program based on predictive genomics.

Regarding the translation of genomic results into the clinical setting, how are you looking to collaborate with industry partners?

Any large-scale project rests on three pillars: research, clinical implementation, and industry engagement. Over the past year, we have generated a substantial dataset through strong research efforts. Clinical implementation is progressing well. QPHI is now focused on establishing a framework that will facilitate meaningful engagement with industry partners.

Can you tell us more about the pilots and clinical implementation?

In addition to the BRCA pilot, we have launched several pilots focused on pharmacogenomics. One targets heart patients to determine whether they should receive blood-thinning anticoagulants during and after surgery. These drugs are among those most strongly influenced by a patient's genetics. Typically, determining the correct dose relies on trial and error and can take weeks.

In this pilot, before a patient undergoes surgery, clinical staff take a blood sample. DNA is extracted and analysed using a nearby machine. Within 15–20 minutes, the results are provided to the physician or surgeon, allowing them to determine the appropriate drug dosage and avoid placing the patient at risk of developing clots or falling outside the therapeutic window. We have already observed results showing that hospitalisation time for these patients can be reduced from seven days to three.

Another pilot integrates genomic data directly into electronic health records (EHRs). When a patient visits a clinic and a drug is prescribed, the system can automatically flag the appropriate dose for that individual based on their genomic profile. These successful pilots demonstrate that genomic medicine can move into routine clinical practice, and the next step is to scale these approaches more broadly.

How did you foster international collaboration regarding sharing information?

The first wave of large-scale whole genome sequencing projects emerged around 2014–2015. At that time, sequencing was extremely expensive and the field was largely uncharted territory. Many of the decisions facing national genome programmes had never been addressed before.

During my first year, I visited other genome projects around the world and established relationships so that we could learn from one another. We quickly realised that we were facing very similar challenges, which led to regular discussions and legal consultations among the different initiatives. These projects represent enormous investments for any country, so it is essential to

build them correctly from the outset. Today, when countries approach us, we are able to share practical guidance on how to design and implement a national genome programme and adapt it to their specific context.

What is your vision for the future?

One-size-fits-all healthcare will be a practice of the past. We are heading toward a place where we will be able to know much more about individuals – both their current health and their future risks for many diseases and thus tailor their healthcare accordingly.

In addition to genomics, if we are successful in bringing multi-omics to the clinic, this will greatly leverage the ushering of the age of precision health. We will increasingly be targeting individuals before they get sick. In that sense, they will not yet be patients. That is why we call it precision health, not precision medicine. This is a paradigm shift in healthcare.

However, there are many challenges. If you look for a variant in a whole genome, it is like searching for a needle in a haystack. With multi-omics, you are effectively searching across several haystacks for that same needle.

With these huge amounts of data, another question is whether we can meaningfully interpret them in a clinical context. This is where AI can help. We must start training AI systems on these large datasets, which means the data must be made available rather than kept in silos. Training these models will help guide clinical decisions, both to treat existing diseases and to prevent future ones.

The future is bright, and it lies in the combination of multi-omics and AI.

Can you share your perspective on how Qatar is positioned today and what role it could play regionally and globally?

Qatar has developed a model that many countries can learn from. The country benefits from one of the most advanced healthcare systems in the region and has generated large-scale genomic and health data covering more than ten to 15 percent of the population. At the same time, it has built state-of-the-art infrastructure and invested in training both local and international talent.

Because Qatar is a relatively small country, these different components can be integrated efficiently. Implementing such a system in a larger country could be far more complex, particularly

where healthcare systems are fragmented or questions around data ownership arise.

In that sense, smaller countries such as Qatar, Iceland, and Estonia can play an important role in demonstrating how the promises of future healthcare can be translated into real clinical practice and ultimately improve people's lives.

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