The Genomic Portrait of a Nation

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The largest studies of whole-genome data ever published reveal the power of the sequencing revolution for understanding the roots of disease, diversity and evolution:

- *The most comprehensive population-wide tally to date of sequence variation*
- *A nationwide collection of human knockouts*
- *A new estimate for the most recent common patrilineal ancestor of all men alive today*
- *Variants contributing to risk of Alzheimer's, atrial fibrillation, and liver and thyroid disease*
- *New opportunities for using the genome to improve diagnostics and therapeutics*

REYKJAVIK, Iceland, 25 March 2015 – deCODE genetics, a global leader in analyzing and understanding the human genome, today published four landmark papers built on whole-genome sequence data from more than 100,000 people from across Iceland. The studies, written by a team of deCODE scientists and which appear in the online edition of *Nature Genetics*, together present the most detailed portrait of a population yet assembled using the latest technology for reading DNA.

"This work is a demonstration of the unique power sequencing gives us for learning more about the history of our species and for contributing to new means of diagnosing, treating and preventing disease," said Kari Stefansson, founder and CEO of deCODE and lead author on the papers.

"It also shows how a small population such as ours, with the generous participation of the majority of its citizens, can advance science and medicine worldwide. In that sense this is very much more than a molecular national selfie. We're contributing to important tools for making more accurate diagnostics for rare diseases; finding new risk factors and potential drug targets for diseases like Alzheimer's; and even showing how the Y chromosome, a loner in the paired world of our genome, repairs itself as it passes from father to son. Other countries are now preparing to undertake their own large-scale sequencing projects, and I would tell them the rewards are great," Dr Stefansson concluded.

The papers and their highlights:

"Large-scale whole-genome sequencing of the Icelandic population" demonstrates how deCODE is able to use comprehensive national genealogies to accurately impute even increasingly rare sequence data throughout the population, yielding new discoveries and key data for improving diagnostics.

"Identification of a large set of rare complete human knockouts." For decades, genes have been knocked out or switched off in mice, as a model system for studying what genes do and how they might affect human health. But what if we could find people in whom genes had been switched off due to rare mutations? The scale and detail of deCODE's data was used to identify more than a thousand knocked out genes, with nearly 8% of the 104,000 people studied having at least one gene knocked out in this way. The examination of health and other traits in these individuals should provide a unique way to study directly the effect of specific genes on human biology and potentially contribute to the development of new drugs and diagnostics.

"The Y-chromosome point mutation rate in humans" uses more than 50,000 years of male lineage to provide a much more detailed and accurate estimate of the mutation rate in the male sex chromosome. This rate can be used as a kind of evolutionary clock for dating events in the history and evolution of our species and its civilizations. It places the most recent common ancestor of all Y chromosomes in the world today as living some 239,000 years ago – nearly 100,000 years more recent than other estimates and much closer to that of the most recent common ancestor for all mitochondrial DNA, which is passed from mothers to offspring.

"Loss-of-function variants in ABCA7 confer risk of Alzheimer's disease" presents a rare but powerful new risk factor that is also replicated in several European countries and the US.

Based in Reykjavik, Iceland, deCODE is a global leader in analyzing and understanding the human genome. Using its unique expertise and population resources, deCODE has discovered genetic risk factors for dozens of common diseases. The purpose of understanding the genetics of disease is to use that information to create new means of diagnosing, treating and preventing disease. deCODE is a wholly-owned subsidiary of Amgen.

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