The **Genetic Resources** of Finland

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Finland is a homogeneous population of about 5.5 million people, geographically isolated from the rest of the world. Although the country keeps no official records based on ethnic diversity, official statistics report that more than 35 different languages are spoken. However, outside of the largest language groups speaking Finnish and Swedish, who account for over 90% of the population, only about 300,000 people speak those other 30+ languages. So not surprisingly, the vast majority of Finns share a common heritage, and they also seem largely willing to participate in clinical health studies. Three out of four Finns will agree to be a research subject, and thankfully, access to their clinical records is relatively easy, for both domestic researchers and foreign scientific collaborators.

After thousands of years of isolation, Finns have become a relatively uniform population, genetically speaking. Additionally, the genealogies of Finns trace back numerous generations and hundreds of years, providing plenty of correlated genetic information and an excellent source of scientific data to study. An unfortunate side effect of a limited number of ancestors is a sizable array of hereditary disorders. Dozens of genetic diseases have been identified from Finland's genetic resources—and are collectively known as Finnish heritage diseases.

Finnish heritage diseases are thankfully rare, but they do not afflict only Finns. Conversely, some other genetic disorders such as cystic fibrosis and phenylketonuria are disproportionately uncommon in Finland. The molecular details of Finnish genetics have provided lessons for all of humanity, elucidating the connections of genes to a wide variety of health conditions. Ultimately, Finland's contributions to genetics and science will be far out of proportion to the country's modestly-sized population, and what researchers learn from the Finns may prove invaluable to global health.

IMPACT

The Finnish population has been the target of extensive genetic studies over many decades. A list of about 40 genetic disorders (also known as Finnish heritage diseases) has been compiled and traced to ancestors using records kept by the government and Lutheran church documents dating back over 400 years. Single-gene disorders—that are unusu-

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ally prevalent in Finland, such as diastrophic dysplasia—have been identified, and an estimated one in five Finns possesses a gene defect associated with at least one Finnish heritage disease. As the genetic causes of these disorders are known, genetic testing and counseling methods are being developed and improved, and an estimated one in 500 babies born in Finland could be affected by a Finnish heritage disease.

More complex diseases have also been studied since Finns provide a natural control group for human DNA. Researchers are studying the genetic component of asthma, type 2 diabetes, lactose intolerance, dyslexia, arthritis, heart disease, Parkinson's and many more health conditions in Finland—based on Finland's genetic data and its modern, accessible medical records. Moreover, common diets, easily obtained socio-economic data and the cultural environment also make Finland a unique population for studying and controlling for non-genetic factors for many health-related issues.

Lactose intolerance is hardly a life-threatening condition, but it occurs all over the world—though only in 18% of the population of Finland. In Asia and Africa, the occurrence can be nearly 80%. Lactose intolerance was apparently the normal condition in the human genome until about 100,000 years ago, when a mutation in a gene now found in many Europeans allowed for lactose tolerance into adulthood. This gene mutation was identified by Finnish researchers in 2002, based on an analysis of lactose intolerance in Finnish families, as well as other samples from Germans, Italians and South Koreans. This common intolerance now has a straightforward genetic test for diagnosis, and the genetic cause of this condition is better understood and explains some ancient dietary differences related to dairy products.

Asthma is a more complicated condition compared to lactose intolerance, but its genetic roots have been traced to at least one gene held in common to certain Finnish families and, coincidentally, to patients living in Quebec. Unfortunately, asthma hasn't been conquered, and its symptoms can arise from several other pathways. Over 30 genes have been associated with asthma symptoms, and environmental factors are a significant contributor as well. There may not be a single treatment, but the genetic findings may help identify risk factors and help manage this disease.

Researchers are drawn to Finland, not simply because the gene pool is relatively small.

Researchers are drawn to Finland, not simply because the gene pool is relatively small and lifestyle variables are manageable. Genetic scientists say, "Finland is a good place for medical research because people feel positive about it." The cultural environment is favorable for sharing family history information, dating back centuries, and this openness fosters a place where connections to the past using cutting-edge technologies can be made.

Beyond acute medical conditions, human evolution spans millennia, and studies of Finland's population have provided insight into how ancient humans migrated around the world. Analyses of hundreds of thousands of genetic markers may be one of the very few ways to gain access to prehistoric information on humans—which archaeologists estimate is over 99% of

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humankind's experience. And while fossils and Paleolithic remnants decay with time, the DNA evidence of distant ancestors preserved in living descendants is still fresh. Research on thousands of Finns suggests a population bottleneck event occurring 10,000-20,000 years ago in Finland. The cause of this bottleneck may never be known, but its existence might not have been detected without access to the genetic resources of Finland.

POLICY IMPLICATIONS

The study of human genetics isn't limited to Finland—and anything learned about the human genome could have significant impact on our species. Increasingly, how this information is collected and treated will be critical in determining the pace of progress in medicine and the broader biotech industry. International genetics studies will undoubtedly be subject to a growing number of restrictions, for a variety of justifiable reasons such as privacy and ethical considerations. The funding and ownership of projects to increase the scientific body of knowledge, however, could also be held up by other non-technological or non-scientific issues.

The Human Genome Project was conceived in the mid-1980s, started sequencing in 1990 and completed its goal about a decade later, formally in 2003. This publicly-funded DNA sequencing effort cost about $3 billion and required intellectual contributions from over 200 scientists from around the world. Just five years after the Human Genome Project published its final results, a complete genome for an individual was sequenced in four months with far less effort for about $1 million. By 2013, an XPrize challenge offering $10 million to any team that could sequence entire human genomes for less than $1,000 each was canceled because technology had outpaced the challenge, and commercial genome sequencing technology was already targeting a cost of $100 per genome.

With sequencing costs falling dramatically and thousands of people getting their DNA decoded, the concerns for obtaining this extremely personal information—and making it publicly known— are reasonable. Potential for discrimination, discovery of various health problems and the unknown possibilities raise serious questions. Some of these concerns have been addressed in a piecemeal fashion, varying by country and culture. In general, regulations agree that no one should face discrimination—and that no one should be required to undergo genetic tests as a condition of obtaining insurance or employment. Also, there is a general consensus that personal genetic data should not be shared without informed consent.

Beyond those basic views, legislation and policy split into a few different camps. Some countries ban the use of personal genetic information with total prohibitions for insurance coverage in an attempt to protect privacy. Other nations try a middle ground approach where usage is prohibited with certain limits. Still others invoke a moratorium as a wait-and-see strategy or have no regulations, allowing practices to be established with uncertain regulations for the future.

With a national goal to advance science and become an international partner in genome research, Finland has proposed its own genome strategy to promote its citizen's health and to secure the rights of individual privacy. Finland's genome goals focus on improving health and establishing economic benefits by 2020, but it doesn't address concerns outside of medicine—such as finding genes linked to violent crime or other non-health-related issues. Additionally, the issues of genes as intellectual property haven't been fundamentally concluded.

Without agreements on genetic information as intellectual property, disputes over information that exist freely in nature could hinder the development of useful applications and life-saving treatments. Thousands of patents on human genes have been granted, though various courts have only recently started to overturn the validity of patents on human DNA. Shortly after the first human genome was available, the company which competed with the Human Genome Project, Celera, tried to own and sell the genomic information. That business faced public criticism and withdrew, putting Celera's genomic data into the public domain—and potentially setting a precedent for how genetic data should be published. Still, the questions of ownership and the appropriate use of genetic data remain unresolved.

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