Viking Genes Newsletter Spring 2025

Welcome to your Spring newsletter!

Happy Spring from the Viking Genes team!

In this edition, we have a summary of our latest research paper: our most important to date, footage from Jim's talk on genomic medicine at the OISF24, a brilliant interview with a researcher using Viking Genes data, another powerful volunteer story – but our first from a male, and a Viking Genes fundraising update!

Read on to find out more.

Researchers identify 10 genetic variants of concern to highlight the need for population screening in Scottish islands!

Pioneering genetics study outlines practical and ethical pathway to return actionable results to volunteers and discovers harmful genetic variants

The benefits of returning clinically 'actionable' genetic results to participants in research studies are many, but it is a challenging process and has rarely been attempted, particularly in the UK. From the outset of recruitment to VIKING II/II in 2019, the opportunity was taken to implement this process, working closely with NHS geneticists. This option of consent to return of selected clinically actionable results was chosen by an overwhelming majority (98%), of the participants who consented and completed the study questionnaire online. Between 2005 and 2015, Viking Genes recruited >4,000 adults with grandparents from Orkney and Shetland into the ORCADES study and Viking Health Study – Shetland (VIKING I), respectively.

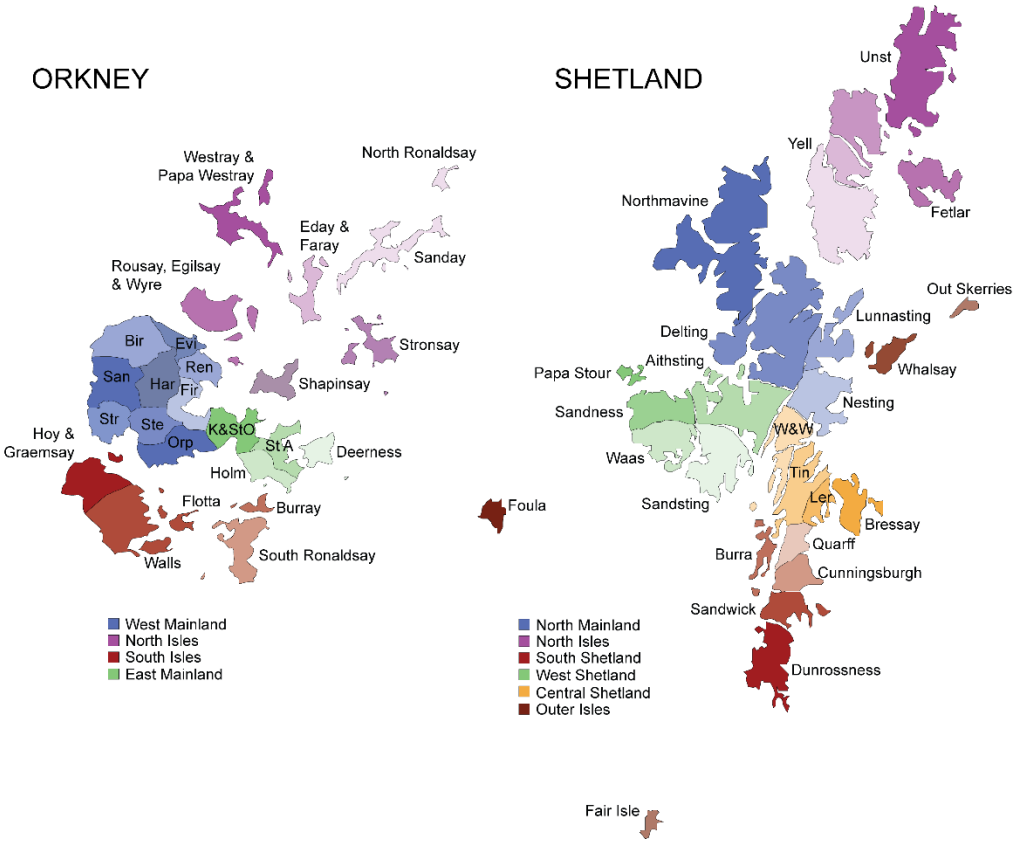
In 2023, invitations were sent out for consent to return of actionable genetic findings to these participants. This meant that UK-based participants in all four studies within the Viking Genes project had the same opportunity to receive actionable genetic findings, if discovered. Professor Jim Flett Wilson explained in 2023 why consent was being sought: *"It's the most important thing we, as researchers, can do for the volunteers, and is a foretaste of the future of medicine, as more and more people get the chance to take part in screening like this."*

Through the partnership of Viking Genes with the Regeneron Genetics Centre in the USA, DNA "exome" sequence data from 4,198 participants in ORCADES and VIKING I was generated. Viking Genes then analysed 81 genes containing actionable variants that are on a list compiled by the American College of Medical Genetics and Genomics. These genes are related to serious conditions, which can be prevented or improved by treatment. Early knowledge could enhance how well the preventative measure or cure works – these are beneficial to know about.

104 individuals were identified in the two studies, carrying actionable findings in 23 genes from the list. Data quality checks were done and each result was validated using a second method of DNA sequence analysis, at the University of Edinburgh. Working closely with the NHS Clinical Genetics Service in Aberdeen, and after expert clinical review, Viking Genes notified 64 consenting participants (or their next of kin) of their actionable results. The letter from Viking Genes included contact details for the NHS clinical genetics team who supported and advised participants and their families, allowing them to take up the pathway of care appropriate to their genetic findings (e.g. mammogram, heart echo, blood tests).

10 genetic variants which have become common enough to warrant population screening found in Orkney and Shetland

The most extraordinary finding was a number of variants that were between 50 and over 3000 times more common in Orkney or Shetland than elsewhere. For example, a deletion in the titin (*TTN*) gene, that increases the risk of a heart condition called cardiomyopathy, which can lead to heart failure, was 3700 times more common in Shetland than in the general UK population. A variety of medical and surgical treatments are available for this condition. In total, ten actionable variants across seven genes (*BRCA1, BRCA2, ATP7B, TTN, KCNH2, MUTYH, GAA*) had become significantly more common in Orkney or Shetland.



When someone carries actionable variants in both their copies of the *ATP7B* gene (one from their mother and one from their father), this causes the normally rare condition Wilson disease. Copper levels build up in the organs of people with this condition, particularly the liver, brain and eyes, leading to liver problems and neurological or psychiatric symptoms. The disease is very treatable, if caught in time. In Shetland, two different variants in the *ATP7B* gene have become much more common, such that 1/45 Shetlanders is a carrier and thus at risk of having a child with Wilson disease.

All ten of these variants show clear ancestral links to one or more isles or parishes within Orkney or Shetland. For example, all carriers of the titin deletion linked back to Yell in Shetland, whereas one of the *ATP7B* Wilson disease variants originated in Burra Isle. Our previous work established the connection of the *BRCA1* variant to Westray in Orkney and the *BRCA2* variant to Whalsay in Shetland, while the *KCNH2* Long QT Syndrome variant links to Aithsting and Unst in Shetland. We call these variants founder variants, for they originally occurred in one of the founders of the population.

Professor Wilson said: *"The discovery that a relatively large number of disease-causing genetic variants are hundreds of times more common in Orkney and Shetland than in the rest of the UK presents an opportunity for low-cost genetic screening of the population. This would capture a significant portion of the inherited risk for a number of diseases, as we move away from treating people who are already ill to a preventative approach, that should deliver better outcomes."*

Read our research summary with link to the paper here.

Jim's talk on genomic medicine at last year's Orkney International Science Festival ties in perfectly with our latest research summary, and you can now watch it on YouTube by clicking here or via the arrow above. You can also watch Viking Genes Project Manager Dr Shona Kerr's talk 'Getting Your Genetic Results Back' here.

Volunteer story: John Arthur

John Arthur is a volunteer in VIKING I.

His powerful story started with a Viking Genes return of results letter from Professor Jim Flett Wilson, telling John Arthur he is a carrier of the Whalsay BRCA2 variant, which can cause breast and prostate cancer in men.

Here are excerpts from his diagnosis and treatment diary, told through his correspondence with Jim. John Arthur has kindly allowed us to reproduce this for the Viking Genes website and newsletter.

We have translated from the original Shetlandic to allow more people to read it.

Date: Fri, 21 Jun 2024
Hi Jim, just thought I would give you a message to bring you up to speed with what happened after your trip up to Whalsay. I really enjoyed your talk as did most folk I spoke with after the night at the hall. It was quite amazing to see the huge difference in the gene pool even here in Shetland.
I actually went up to the doctor's surgery the next day to see about other tests I might get done. After a blood test was done a couple of days later, the doctor phoned me the day before I came to Spain to say there was indeed a slight increase in my blood count to do with the prostate. He asked me a few questions about the water works and I said that I had seen a difference over the last year or so but I knew that could be expected with my age. I had intended to get an appointment to discuss the water works before, but after your meeting that gave me the push, I needed to do that.

Date: Fri, 25 Oct 2024
I just thought I would update you on what's happened since I last messaged.
I ended up getting an MRI scan done after the raised blood tests showed some abnormal signs. There was no certainty with that test so I ended up getting a prostate biopsy. I waited nearly 5 weeks for the results and now they tell me that there are signs of cancer in the prostate. So, I'll need to have a good chat with the doctor and the surgeon to see how we might go from here.

On Sat, 10 Feb 2025, John Arthur's had surgery to remove his prostate.

Date: Mon, 10 Feb 2025
I got the catheter out on Friday and so far, so good with passing water. Bladder seems to be doing his thing. I had my last meeting online with the surgeon tonight, he was very happy with how I was coming on with my recovery, and so am I. I would never have expected to be coming on as well as I am at this stage. The results from the lab were as good as I could have wished for, there was no cancer outside the prostate and the lymph nodes they took out to test were clear of any signs of cancer.
There would be no further treatment required at this time. A great relief as you can well imagine. It's been a rollercoaster this last few months that's for sure, hopefully never to be repeated. And it's all thanks to your study that this has all been done as fast as it has, or I would probably never have gone to the doctor about it until it was too late for anything to be done.

Viking Genes Fund update!

In January, Jim was on Shetland to attend Up Helly Aa in Lerwick. It also gave him the opportunity to meet some of our amazing Viking Genes fundraisers whose efforts are vital to our work continuing.
Jim received two magnificent donations in Aith, Shetland, for the Viking Genes Fund. £5000 from the Aith Charity Shop: Elizabeth Nicolson pictured left, handing Jim the cheque. And Sharon Deyell rounded-up her "swapshop" total to a brilliant £3,500! Sharon is pictured with her husband right, handing Jim the cheque. We simply can't thank our volunteers and supporters enough!

We are looking for other supporter partners across Orkney, Shetland and the Hebrides to help raise funds for Viking Genes through community support and events. If you can help, let's get talking, we are grateful for all the community help. Email **viking@ed.ac.uk**.

Researcher spotlight: Jurgis Kuliešius

What is your research focus?

My research is centred on proteomics, which involves studying the levels of proteins circulating in the human body. Proteins are the building blocks and messengers of our cells, and they play a vital role in keeping our bodies functioning properly. When the levels of these proteins are out of balance, it can lead to a range of health issues, from common illnesses to more serious diseases a vital role in keeping our bodies functioning properly. When the levels of these proteins are out of balance, it can lead to a range of health issues, from common illnesses to more serious diseases.
However, many of these links between protein levels and specific diseases are still not fully understood. My work is dedicated to uncovering these connections. By studying how genetic variations, which are determined at birth, influence protein levels, we can begin to understand the root causes of these imbalances.

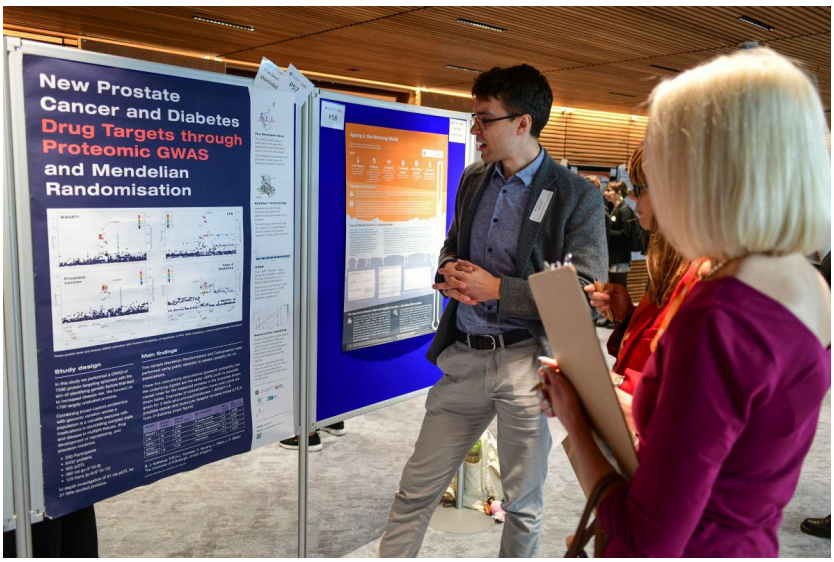
The ultimate goal of my research is to identify these causal links between proteins and diseases. If we can pinpoint exactly how certain protein disturbances lead to specific health conditions, we could open up new possibilities for medicine. Imagine being able to prevent a disease before it even starts by targeting the underlying protein imbalance. This could revolutionize how we approach healthcare, shifting the focus from treatment after the fact to prevention before the disease has a chance to take hold.

What made you interested in pursuing a career in health research?

I suppose I've always been drawn to answering life's most challenging questions. Whether it was philosophy, biology, or art, every aspect of human nature fascinated me from a young age. My curiosity knew (and still knows) no bounds, and I was eager to explore these different disciplines. The decision to focus on biochemistry, however, solidified just before high school, largely thanks to three exceptional mentors in an after-school chemistry club. They ignited my passion for science, and within a few years, I was already working on real scientific projects in a university lab—while still in high school!

The next major turning point in my career came more recently while working on the Viking Genes project in Edinburgh. After spending a decade in a wet lab environment, where I manually gathered data to test various scientific hypotheses, I realized how transformative modern high-throughput methods can be. These methods generate an incredible amount of data, far more than any researcher could ever collect manually. The key to harnessing this data lies in programming. I've come to believe that coding is now an essential skill for any modern scientist. It's crucial for conducting fit-for-purpose, in-depth data analysis, as well as for statistics and visualization.

Now, I'm excited about combining proteomics and genetics to create a vast resource for exploring human health-related questions. This interdisciplinary approach not only allows us to delve deeper into understanding diseases but also opens up new avenues for preventive medicine. The potential to make a real difference in people's lives by answering these complex questions is what drives me every day.



How has Viking Genes volunteer data supported your research?

The Viking Genes cohort is truly a unique and invaluable resource for my research. The genetic makeup of this population is distinct from the rest of the world, and this uniqueness has drawn significant interest even at scientific conferences, where colleagues are eager to discuss the insights that can be gleaned from such a special group.

This is why Viking Genes allows us to conduct research that would typically require much larger study populations. This distinctiveness also makes it highly relevant to identifying new drug targets for diseases that affect people worldwide. For instance, I'm currently working on a paper where we've identified potential new treatment opportunities for type 2 diabetes, among other diseases. These discoveries were only possible by utilizing the Viking Genes dataset in combination with other cohorts across Europe, allowing us to draw more powerful and meaningful conclusions.

Additionally, the few opportunities I've had to interact with the people from the Isles have left a lasting impression. They are incredibly warm, and their enthusiasm for participating in research is evident. Their support and engagement make all the difference, enabling us to push the boundaries of what we know about genetics and its impact on health. The Viking Genes volunteers are not just subjects in a study; they are active partners in advancing science.

Tell us about the most interesting Viking Genes research you've worked on.

The most interesting research I've worked on with the Viking Genes project revolves around the sheer volume and complexity of the data we're able to generate using cutting-edge high-throughput methods. We're dealing with terabytes of data and thousands of analyses, which is both exciting and challenging. One of the most intriguing problems we had to solve was figuring out how to standardize the different protein measurements. With so many variables, ensuring that the same analysis method could be applied consistently across the field was a significant but rewarding challenge.

Another fascinating aspect of this work is remembering that behind every data point is a person—a person with their own unique experiences and the environment they grew up in. In population genetics, we often focus on large groups, which can sometimes lead to losing sight of the individual. However, working closely with a smaller cohort like the Viking Genes volunteers allowed me to dig deeper into the outliers. It was an eye-opening experience to see how well—or sometimes how poorly—the population averages reflected the reality for individual people. This approach added a layer of depth and humanity to the research that is often missing in larger studies.

Perhaps the most exciting part for me has been the ability to take a data-driven approach without focusing on a single disease. By leveraging the vast number of proteins and associated genetic signals, we've been able to explore therapeutic targets across a wide spectrum of conditions. I'm particularly passionate about the fact that, with these rich datasets, we can now go hypothesis-free and let the data guide us. Instead of being confined by preconceived ideas of what we're looking for, we can explore new and unexpected connections, opening up possibilities for discovering treatments for a range of diseases. This freedom to let the data speak for itself is one of the things I find most thrilling about this research.

Viking Genes continues to grow on social media.
We now have 4,000 followers on Facebook. Thank you!

To find us on Facebook, click on the button here.

You can also follow us on:
Instagram

Contact Us

Our research team is based at the University of Edinburgh, in the Usher Institute.
If you ever have any questions, you can email us at viking@ed.ac.uk

Your Data Privacy

We want to make sure you're aware of how we protect your data when conducting our research. For more information about how we use your data and keep it safe, please see our Privacy Policy at www.viking.ed.ac.uk/privacy-notice, or let us know if you'd like to have a copy posted to you.

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