Welcome to your spring newsletter!

Happy spring from the Viking Genes team!

As we welcome the spring and think about new beginnings, here at Viking Genes we also look back at everything we have achieved together. This includes one of our most important discoveries to date and is our breaking story!

In this edition, we also have a study update, a Return of Results consent reminder, and an exciting interview with a researcher using your data. We also look at a recent talk by Prof Jim Flett Wilson in South Africa.

Read on to find out more.

Breaking: Cancer risk gene variant discovered in Orkney

Orkney Complex Disease Study (ORCADES) volunteer data has helped to link a variant in the gene *BRCA1* to a historic origin in Westray, Orkney

Around one in 1000 women across the UK have a *BRCA1* variant that gives them an increased chance of developing breast cancer and ovarian cancer.

In contrast, one in 100 people who have grandparents from Orkney have a founder gene variant that causes a high lifetime risk of developing breast and ovarian cancer.

Most breast and ovarian cancers happen due to chance. However, some cases are caused in part by inherited gene alterations, which increase the chances that a woman will get one or both of these conditions. One of the most common of these predisposing genes is *BRCA1.*

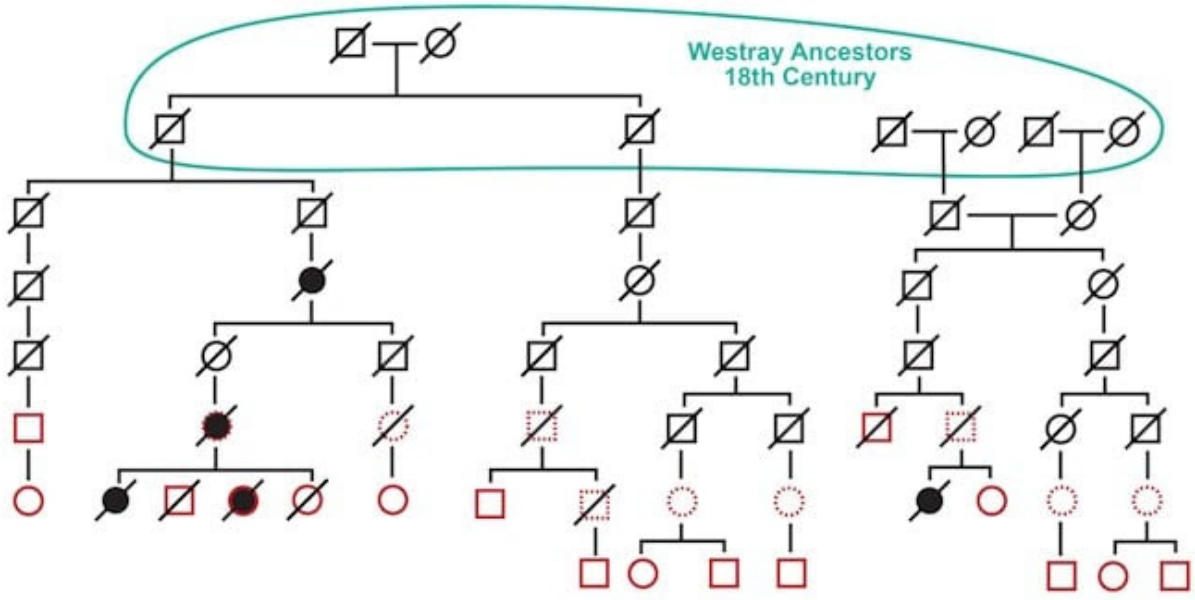
The Orkney Complex Disease Study (ORCADES), which is part of Viking Genes, is led by Professor Jim Flett Wilson.

Jim explains: “The fact that one in a hundred Orcadian women carry a high-risk variant for breast and ovarian cancer highlights the value of population studies such as Viking Genes, without which we would not know this. It is imperative that Scottish island populations are represented in research, to allow equitable delivery of genomic medicine across the country.”

Historic origin linked to Westray, Orkney

Over many years, the Orkney NHS genetics clinic team, led by the University of Aberdeen’s Professor Zosia Miedzybrodzka, found the same specific variant in the *BRCA1* gene repeatedly in women from Orkney with breast and / or ovarian cancer. The genetics team used clinical genealogy to show that the patients with the variant linked into one large family tree with an origin in the Orkney outer isle of Westray.

When the ORCADES (Viking Genes) team examined genetic data from more than 2000 volunteers, men and women with three or more Orkney grandparents, they found this *BRCA1 “V1736A”* variant present in the DNA of 1% of the volunteers. Many of the ORCADES participants with the variant are not closely related to branches of the family identified in the clinic, but all share historic Westray ancestors.



Professor Zosia Miedzybrodzka is director of the NHS Grampian Clinical Genetics service and Independent Genetic Advisor to the Viking Genes study; she has also run the Orkney genetic clinic for over 20 years.

She explains: “Developing cancer is not solely down to carrying the *BRCA1* mutation alone, there are many complex factors, and some people with gene alterations will not get cancer. However, we know that testing and the right follow-up can save lives."

The NHS Grampian genetic clinic is running a helpline for queries about breast and ovarian cancer in Orkney. The number to call is 01224 553940.

We can also provide more information if you have any questions or concerns.

To read more about the research, click on the link below.

Cancer risk gene variant discovered in Orkney

Viking Genes recruitment goes out in style!

Our recruitment closed at the beginning of February.

We had a great response to our final month of recruitment with over 750 people signing up for the study. This period also saw record engagement across our social media channels. A medium that has served us well in our recruitment drive since the launch of Viking II at the start of 2020.

10,186 people signed-up for Viking II and Viking III, and 7,704 consented to be part of the study. Out of the 6,169 people who completed their questionnaire, over 5,600 have returned a sample to us. That's a staggering 91% sample return!

Soon, we will start to send our DNA samples to the Regeneron Genetics Center for exome sequencing, so we are keen to have more samples.

ORCADES and Viking I RoR reminder

In the last newsletter, we were very pleased to let you know that we received approval for an important amendment to our ethics approvals. This meant we could now ask our Orkney Complex Disease Study (ORCADES) and Viking Health Study – Shetland (Viking I) volunteers for consent to receive ‘actionable’ genetic results, if they are discovered. This gives all our volunteers in the family of Viking Genes studies the same opportunity to chose to opt-in or opt-out of receiving 'actionable' genetic results.

Since then, we have been busy sending out emails and letters, asking for the Return of Results (RoR) consent. The response has been very good, but we would still like to receive all the forms back, whether or not you decide to consent to the return of results.

If you have lost the email we sent to you, we can resend the link. We can also provide more information if you have any concerns. Just send us an email at viking@ed.ac.uk or call us on **0131 651 8557.**

You can learn more about Return of Results by clicking on the link here.

One other thing, if you have recently changed address or have a new email, simply update us by clicking on the link below and completing our web form here.

Researcher Spotlight - Mihail Halachev

What's your research focus?

As a bioinformatician at the University of Edinburgh, I have the opportunity to work on a variety of projects related to human genomics and health.

My main research interests include exploring the DNA similarities and differences across individuals and human populations and more specifically when and how some of the DNA variants present in any of us may result in rare genetic conditions.

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

The rapid advances in genome sequencing technologies in the past decade provide unprecedented possibilities for augmenting our previous knowledge. My early academic career started in computer science and I consider it a privilege to have the opportunity to apply my research skills to questions in human biology, health and wellbeing, and in developing computational pipelines that have a direct clinical impact.

How has Viking Genes volunteer data supported your research?

Due to the unique history of the Northern and Western Isles, the Viking Genes volunteer data provide an unparalleled opportunity to explore fundamental biological questions. Examples include the impact of the population history on shaping DNA variability, and the roles of rare genetic variants in human conditions. Additionally, it can help in answering some practical questions such as how genetically similar/distinct are Shetland and Orkney individuals from each other and from the rest of the UK. Ultimately these findings may inform more targeted health care in the future.

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

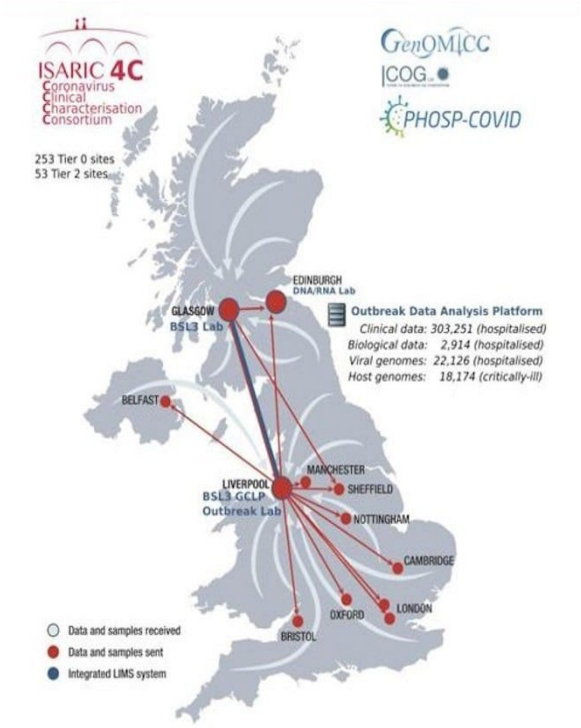
Using genome sequencing data from 500 Shetland individuals (where every letter in the DNA code is read) and comparing it to data from the mainland Scottish population revealed how geography and history influenced the Shetland genome - about one tenth of all variants discovered in the Shetland individuals are unique to the archipelago (“ultra-rare” variants) or are seen at frequencies at least ten times higher than in individuals from elsewhere. Furthermore, we showed for the first time that the Shetland genome is enriched for these “ultra-rare” variants not only in protein-coding genes, but also in the “promoter” regions, which are thought to act as an on/off switch for these genes.

The project which I am currently working on compares the genetic variation in exome sequencing data from about 2000 Shetlandic, 2000 Orcadian and 40,000 mainland British or Irish individuals. The preliminary results suggest that despite their geographical proximity, the populations from the Shetland and Orkney islands are genetically distinct from each other, as well as from rest of the UK – about as distinct as individuals with some Ashkenazi Jewish heritage. Future research into their population-specific genetic variants and their links with health conditions is thus warranted to assess the future potential of population-tailored health care. Take a look at Mihail’s work here.

Jim's talk in Cape Town

Jim was invited to the 14th International Congress of Human Genetics in Cape Town, South Africa in March, to give a talk on the genetic mechanisms of critical illness in COVID-19. His talk described work that he and his team were involved with during the pandemic, led by Prof Kenny Baillie, also from the University of Edinburgh.

The study focussed on the 1% of people who become critically ill with Covid and require admission to an intensive care unit. By recruiting thousands of these individuals with respiratory failure caused by COVID-19 from over 200 intensive care units across the UK and comparing their genetics to that of thousands of population controls, they were able to identify 49 gene variants which increase the risk of critical illness. Some of these genes highlighted innate antiviral systems of the body, such as interferon signalling.



More importantly, the study highlighted a number of genes which encoded targets for existing drugs, e.g. the *TYK2* gene which is one of four gene targets for a drug called baricitinib. Baricitinib is already used to treat rheumatoid arthritis. On the basis of this finding, the drug was added to the RECOVERY trial to evaluate whether it would help decrease mortality from COVID-19.

Patients randomised to baricitinib showed improved survival - this was the first ever proof-of-concept for drug target identification using genetics in critical illness and infectious disease. Many other different biological mechanisms were highlighted from the results of the study, giving insights into the pathophysiology of the disease.

To read more about the research, click on the link here.

Viking Genes team

The close of Viking Genes' recruitment window has seen some changes in the team. April sees the departure of our database manager, David, who developed and managed our IT systems on both our Viking II and Viking III studies.

After Rachel left in the autumn, Craig, who has supported the team since September 2020, stepped in to deliver communications to our volunteers and created our final recruitment campaigns. Early this year, we also saw additional help from Jim MacFarlane, who gave excellent support to the Study.

The good news is that Craig (pictured) will be staying on to deliver communications for the rest of the year, and Jim Flett Wilson and Shona will oversee the research phase. Team the Viking Genes Team here.

Contact Us

Our research team is based at the University of Edinburgh, in the MRC Human Genetics Unit and the Usher Institute. If you ever have any questions, you can email us at viking@ed.ac.uk or call us on **0131 651 8557**

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.ed.ac.uk/viking/privacy-notice, or let us know if you'd like to have a copy posted to you.

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