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MRC Human Genetics Unit

Case study

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Oragene™ saliva collection kits broaden participant reach for genomic research studies

Complex diseases such as heart disease, diabetes and cancer are affected by a combination of a person's genes and environmental factors. Genetic studies investigate complex diseases by looking at specific genes, their interactions with each other and the environment. Since genetic traits are written into our DNA and heritable in families, understanding the effect of genes and their interactions could lead to better ways of preventing and treating complex diseases.

While blood was traditionally considered the preferred sample type for genomic DNA, there are several disadvantages to consider when planning a study. Acquiring blood is invasive and inconvenient for the donor; the collection requires a trained medical professional, the samples must be refrigerated for transportation and storage, and blood can be difficult to transport across borders. All of these factors can add significant costs and complexities to any genetic study and impact compliance rates.

As a result of the COVID-19 pandemic, several industries, including genomics research, have shifted to remote-based models with the use of online tools. In research, the recruitment, participant consent forms, and questionnaires can all be organized virtually. Naturally, obtaining genetic samples from patients is still required, and this is where Oragene saliva collection kits come in.

From a researcher's perspective, key requirements for a genetic sample include quality and consistency, along with sample stability, as it will likely take time to collect and transport samples to the laboratory. Oragene saliva collection kits are a proven viable and beneficial alternative to blood samples[1,2] and offer a combined DNA collection and stabilization device[3,4] that enables efficient storage and transportation of high-quality biological samples at ambient temperature.[5]

A user comprehension study was conducted to assess the use of Oragene saliva collection devices for a typical direct-to-consumer at-home DNA sample collection application.[6] The study involved 212 naive, adult, general population donors who received an Oragene saliva collection kit, including instructions and a two-way mailing box for return shipping. Data obtained from this study demonstrated the Oragene collection kits were easy to use: over 95% of the participants comprehended the instructions for use and could successfully provide a saliva sample at home. Additionally, the study also described the technical performance of the collected DNA samples, which met all of the required acceptability criteria.

DNA Genotek Inc.
3000 - 500 Palladium Drive
Ottawa, ON, Canada K2V 1C2
Subsidiary of OraSure Technologies, Inc.

Toll-free (North America): 1.866.813.6354
Tel.: 613.723.5757 • Fax: 613.723.5057
www.dnagenotek.com
info@dnagenotek.com

In summary, Oragene saliva collection kits maintain the quality and consistency of DNA sampling at scale and are low-burden tasks for participants. Participants prefer a convenient, non-invasive sample collection option with easy-to-understand instructions. These benefits can increase participant compliance rates, making at-home studies a cost-effective and convenient way to conduct genomics research.

VIKING Genes — at-home collection case study

The Medical Research Council (MRC) Human Genetics Unit, based in the U.K. and part of the Institute of Genetics and Cancer at the University of Edinburgh, sought to understand how changes in DNA impact human health and disease, and how genes and the genome act in normal development and physiology.

VIKING Genes is one of the flagship projects from the MRC Human Genetics Unit. The project examines genomic information from isolated human populations in the Northern Isles of Scotland in four studies: VIKING Health Study — Shetland, the Orkney Complex Disease Study, VIKING II and VIKING III.

The Viking Genes research team. From left to right: Rachel Edwards (Communications Manager), David Buchanan (Database Manager), Dr. Shona M. Kerr (Project Manager), and Professor Jim Wilson (Chief Investigator)

The first two VIKING studies (VIKING Health Study — Shetland and the Orkney Complex Disease Study) included clinic-based recruitment that lasted for approximately a decade, ending in 2015. Roughly 4,000 participants were recruited from Orkney or Shetland. Consent from these cohorts was obtained for feedback on the phenotype that was collected in clinic visits but not for genetic results. Blood samples were collected in the clinics and converted into plasma serum, DNA and RNA, allowing for a multi-omic research approach. When volunteers could not provide a blood sample, they were asked to provide a saliva sample instead. Initially, DNA samples were genotyped; later, the researchers conducted whole genome sequencing, before finally conducting exome sequencing for all cohorts.[7]

For the 3rd and 4th studies (VIKING II and VIKING III), the researchers sought to recruit additional participants. For the VIKING II study, the researchers adopted a new approach, requesting that participants complete an online questionnaire and provide a saliva sample using Oragene•DNA collection kits.[8]

Why Oragene•DNA?

The VIKING II study chose to use Oragene•DNA saliva sample kits because of their "spit-and-post" collection method. These devices offer researchers and study participants several benefits, including ease of use and a non-invasive collection method that yields high-quality and high-quantity DNA. The reagent included in the saliva kits preserves DNA at ambient temperature for years, far longer than blood samples, which require cold-chain logistics and must be processed within days.

The research team reported that the "spit-and-post" collection method enabled access to a wide range of participants that previously could not be reached geographically. They also found increased participation from needle-phobic donors as a result of being able to offer them a non-invasive DNA collection method. Most importantly, the success of the project was not negatively impacted by the COVID-19 pandemic as the Oragene•DNA collection kits enabled at-home sample collection to continue throughout the peak of the pandemic and routine lock-downs.

Over 90% of the participants' compliance, as measured by the rate of sample returns in the VIKING II study, could be attributed to the ease of use of the Oragene•DNA saliva collection kits. Participants were able to use the kit by themselves, and could then send the collection device back to the laboratory via the standard postal system.[8]

Results — variant analysis of cohorts

In the Shetland cohort, the research team analyzed 5 actionable variant carriers and showed, by haplotype analysis, that all five had a distant relationship deriving from a common ancestor. However, in the modern era, these 5 volunteers fell into two families, A and B, that were not connected in the pedigree or in the genealogical records that are available in these populations. An index case of genetic-variant carrier pathogenic B carrier is used to cascade out into their family, because family B would not have been identifiable by cascade testing in the clinical setting.[9,10]

"We were particularly focused on making it easy for the participants to return the sample and chose to work with DNA Genotek as it has a long history with lots of data about yield, stability and ease-of-use" —

*Dr. Shona M. Kerr, project manager of the **VIKING Genes** study and member of the MRC Human Genetics Unit.*

The analysis of more than 4,000 exomes, derived by the Regeneron Genetics Center, identified an actionable BRCA1 variant — a founder mutation, as the participants were all descendants from the Isle of Westray in Orkney. This variant is known to increase the risk of breast and ovarian cancer, and while it was found in 20 instances in the Orkney cohort, only 4 instances were documented in the U.K. Biobank.[11] The researchers suspected that the higher frequency of incidence in the Orkney cohort was likely due to genetic drift.[11]

Thanks to record linkage through the National Health Service (NHS) electronic health records, the research team was able to link 1 of the 7 female carriers in Orkney as having been diagnosed with ovarian cancer. Similarly, of the 3 female carriers in the U.K. Biobank, 1 female was diagnosed with breast cancer.

The **VIKING Genes** studies demonstrate the value of genetic research in fully describing the burden of rare, clinically-actionable variants in isolated and non-isolated populations, ultimately supporting the improved planning and delivery of genetic services by the NHS.

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