Participant Information Sheet/Consent Form

Genetic Study - *Adult providing own consent*

Title	Investigating the genetic basis of undiagnosed inherited retinal diseases
Principal Investigators	Dr Alexis Ceecee Britten-Jones A/Prof Lauren Ayton
Study locations	• Department of Optometry and Vision Sciences, University of Melbourne • Centre for Eye Research Australia, Department of Surgery (Ophthalmology) Other recruitment sites: • Royal Victorian Eye and Ear Hospital, 32 Gisborne Street, VIC, 3002 • Royal Melbourne Hospital, 300 Grattan Street, Parkville, VIC 3010

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project because you have an inherited retinal disease. You will be asked to donate a blood sample (or in some cases, saliva may be accepted) for genetic research.

This Participant Information Sheet/Consent Form tells you about the research project and explains the tests involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
• Understand what you have read
• Consent to take part in the research project
• Consent to have the tests and treatments that are described
• Consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is genetic research?

Genes are made of DNA – the chemical structure carrying your genetic information that determines many human characteristics, such as the colour of your eyes or hair. Sometimes a gene contains a "spelling mistake" that upsets the gene's coded message. This type of mistake is sometimes called a "variant" or a "mutation". These types of variants can change the way the

gene works and cause different diseases. Many rare diseases are caused by a variant in one or more genes.

Researchers study genes in order to understand why some people have a certain condition (such as retinitis pigmentosa, macular dystrophy, and other inherited retinal diseases) and why some people do not. For some retinal diseases we already know the gene variant that causes the condition. For others, the exact variant that causes the condition is not known. If we cannot find the gene variant that explains the retinal disease in your family, we will look for new variants and new genes to try to find a diagnosis.

3 What is the purpose of this research?

The purpose of the research project is to investigate what genetic changes are associated with inherited retinal diseases. To achieve these aims, we would like to look at genetic changes of both individuals with inherited retinal diseases, and their closely related family members, to investigate how these genetic changes correlate with eye health.

A better understanding of the genetic changes in inherited retinal diseases and the effects of these changes can help improve disease diagnosis. This understanding can also fuel future research into developing new treatments for retinal diseases.

4 What does participation in this research involve?

History: You will be asked to answer some questions about your medical, eye and family history, and any risk factors for eye diseases.

Medical records: We will ask for access to copies of your previous health records (for example copies of eye test results and images of your eyes and genetic test results) to obtain information on your eye health. Records could be from the Eye and Ear Hospital, Royal Melbourne Hospital, eye doctors/ophthalmologists, optometrists, and from the Centre for Eye Research Australia (if you have participated in other research projects in the past).

Clinical examination: Depending on how recent your last eye test was, we may undertake a research eye examination to obtain information about your eye health. All the tests we may do are standard clinical tests that you may have done with your optometrist/ophthalmologist. However, participation in this research project is not a substitute for your regular eye examinations.

You may have all or some of these tests:

- **Vision assessments**: You will be asked to report the smallest letter that you can see on a vision chart.

- **Imaging:** We will take some photos and scans of your eyes, using instruments like a camera or an optical coherence tomography (OCT) system, to obtain a record of the appearance of your retina.

- **Visual function:** We may undertake tests to understand how well the retina (tissue inside the eye responsible for vision) is functioning, using methods such as perimetry, which is where we ask you to indicate if you see spots of light in various parts of your field of vision. In some cases, we may undertake electroretinography, which tests your eye's reactivity to light by showing you flashes of light, and measuring your eye's automatic response

using very thin wires placed over the front of your eye, directly above your bottom eyelid. The electrodes might feel strange, but shouldn't hurt or be uncomfortable.

- **Questionnaires**: We may ask you to complete a brief questionnaire about the significance of genetic testing to you.

Genomic sequencing: You will be asked to provide a blood sample for genomic sequencing. If donating blood is not possible, you may be able to provide some saliva (spit) instead if saliva can be used as an alternative. This will be discussed with the study researchers. Most of the techniques we use require blood rather than saliva. This sample will be sent to a laboratory for testing. These testing laboratories may be within Australia or at international testing sites. They may be an industry or a research collaborator, depending upon the expertise we need to try and understand the genetic cause of your (or your family member's) eye disease.

There are no additional costs associated with participating in this research project, nor will you be paid. You may be reimbursed for any reasonable travel and parking expenses associated with attending the research visit, up to a maximum of $50 in the form of gift cards.

5 Do I have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with the researchers at the University Melbourne or Centre for Eye Research Australia.

6 What are the possible benefits of taking part?

This genetic test is for research purposes. Therefore, the reliability of testing results is unknown, and you will not be contacted to receive your results. This is because any genetic changes we find are likely to be new to scientists, and will require significant time to be fully tested to understand how they affect eye health.

This means that it is likely that there will be no direct benefit to you in the short term, in performing this test. Information learned from the test results will help improve our understanding of genetic changes associated with inherited retinal diseases. You will not receive any treatment as part of this research.

However, if we find that the results show important information about you, which could be relevant for your medical management, you may be contacted to see if you wish to be referred local ocular genetic testing services, who will explain what the results mean for you and to support you as necessary. It will be necessary to refer you for re-testing by genetic services outside this research project.

7 What are the possible risks and disadvantages of taking part?

Blood test: There are no major health risks associated with providing a saliva or blood sample for genetic tests. Possible adverse effects from the act of drawing blood include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection. If you feel faint, tell the study staff right away.

Pupil dilation: As part of a routine assessment of your eyes and vision, your pupils may be dilated. The risks and discomfort of eye examinations in the study are similar to those of standard eye examinations by eye care providers, such as some degree of light sensitivity and glare for a few hours after the eye drops to dilate your pupil (it is advisable not to drive during this period and sunglasses may help alleviate the glare).

Genetic Findings: As mentioned above, you will not be given your genetic testing results if the effect of these DNA changes on eye health is not yet well understood or does not change your medical management. If we discover new information that is important for your health care, we may contact you to see if you wish to be referred to local ocular genetic testing services, who will explain what your results mean and to support you as necessary. Any results from this study are likely to relate only to your known eye condition.

If you wish to be referred, it's important for you to consider how discussion of genetic results might impact you, as receiving genetic results can be an emotional process for some people and their families. If you have any concerns, we encourage you to discuss this with your healthcare provider and family before deciding whether you wish to be referred to ocular genetics services and to receive the results. You can also choose not to be referred and to not know your results if you wish. You can make the decision not to be notified at the start of the process, if you prefer, or make the decision if we contact you in the future.

8 What will happen to my test samples?

Your biological samples (i.e., blood or saliva) will only be used for the purpose of this research project. The samples will be destroyed at the completion of this research project.

Prior to analysis, your biological sample(s) will be deidentified and stored at the University of Melbourne in a locked laboratory. Analysis will occur in a research laboratory either in Australia or overseas. The results of the analysis will be provided to researchers involved in this study. The laboratory will not be provided with any information that would allow anyone to identify you.

No identifying information will be shared with anyone outside our research team. If you withdraw from this study, you can request to have your test sample(s) destroyed.

9 What is the potential impact on my family if I take part?

You may be asked to give us health information about your relatives. Any information you give us will be kept confidential. We may discuss with you the possibility of including your relatives in the research project in the future, as information about them could help us understand the genetic changes associated with your inherited retinal diseases.

If it is desirable that your family members are recruited to the study, we will ask either yourself or someone else you choose to make initial contact with them. We will provide you with the relevant study information you can pass on to your family members. We will not ask for your relatives' contact information and we will not contact your relatives without your permission.

If the research discloses that one of your family members may be at risk of a life-threatening or serious illness for which treatment is available or pending, this information may, with the prior approval of a Human Research Ethics Committee, be offered by the study investigators to the family member, even if you as the participant do not consent to this.

10 Will I be given the results of the research project?

You will not be given your genetic test results, because the research is still in an early phase and the reliability of the results is unknown. Many of the analyses are done in a research setting will have little individual meaning as the effect of these DNA changes on eye health is not well understood, and they can often take a long time to obtain (in some cases several years).

In the future, if during the course of this research project we discover new information that is important for your health care, you will be asked whether you wish to receive the results. If you agree, we may contact you if such a situation arises. Should you wish to know your results, you will be referred local ocular genetic testing services to explain what the results mean for you and to support you as necessary.

Any research results that could be of significance to you or your family will need to have the tests repeated and the results verified. This will involve having a blood sample taken and having it retested in an accredited laboratory. This is standard practice for all patients receiving the results of genetic testing and would be provided free of charge to you. Genetic counselling may also be provided free of charge if it is appropriate. Before a test is repeated to verify a research finding, you will be informed about the possible risks involved for you.

Because genetic information is complex and sensitive, the results should be discussed with a clinical geneticist and genetic counsellor who can give you details that are relevant to you, answer your questions and discuss your concerns.

It can sometimes take a long time for research results to be finished. The research team may or may not update you when all results have been finalised. If you have not heard anything once the study has finished, this usually means that no result was found. This would not necessarily mean that you do not have genetic risk factors, just that the study did not find any results that were thought to be important to return.

Part 2 How is the research project being conducted?

11 What will happen to information about me?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential.

Your sample will have all identifiers (e.g. name and personal details) removed and replaced with a code. It will be possible to re-identify the sample as yours using the code. This can only be done by researchers on this project. Your personal information will only be used for this research project and it will only be disclosed with your permission, except as required by law.

Data collected as part of this research study will be stored in secure, controlled-access storage systems and databases at the that meet national and international data standards. Your data will be handled in accordance with the local data protection regulation/law. Stringent security measures will help prevent unauthorised access to or misuse of the data.

Your health records and any information collected and stored by the study investigators during the research project may be reviewed for the purpose of verifying the procedures and the data. This review may be done by the ethics committee which approved this research project, regulatory authorities, Centre for Eye Research Australia, or as required by law. In these circumstances, your personal information (such as name, date of birth, etc) will not be collected nor shared. By signing the consent form, you authorise release of, or access to, this confidential information as noted above.

You have the right to request access to the information collected and stored by the research team about you. You also have the right to request that any information with which you disagree be corrected. Please contact the research team if you would like to access your information. Data from this project will be kept for a minimum of 7 years, at which time, deidentified digital data will be archived and hard copies will be destroyed. If you withdraw, no new data will be collected, and you may ask for any remaining samples to be destroyed.

We may share your de-identified genetic results and some health data (e.g., images of the eye, results of vision tests) with collaborators (research and industry partners) both nationally and internationally to help us further examine them if this is thought to be useful as part of the search for a genetic cause of inherited retinal diseases. We may also use this data for education or teaching. We may also use this data for future projects that in the same general area (i.e., to investigate other eye diseases or conditions closely associated with IRDs, for example, hearing loss), or could make valuable use of this data.

Before any data that is released to laboratories or collaborators, either in Australia or overseas, the data will be coded, any identifiable data (e.g. name and personal details) will be removed and replaced with a study code. Only researchers named on this project will be able to re-identify the sample as yours using the code. Your samples and data will not be released for any use without your prior consent, unless required by law. Data will only be shared for projects that have received appropriate approvals from a Human Research Ethics committee.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified.

Using your data to further advance knowledge
In addition to the above uses of your data, you can also consent for your anonymised genetic and health data obtained through the research study to be shared with national or international genetic databases. This improves understanding of human genetics by comparing your results to those from other people around the world. The types of data that may be shared include information about your eye health or information about specific genetic changes, like where they are located without necessarily knowing how those changes relate to certain diseases.

This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access the information, and they will agree not to attempt to identify you. The information is made available to approved clinicians to access so it can be used to 'match' genetic changes and clinical features that are the same or similar as your family with their families to help with identifying the genetic cause of another family's condition. Information will be stored on these databases for an unlimited period of time.

This data sharing is what advances our understanding of DNA changes associated with different rare diseases, including retinal diseases. In such cases, your data will be 'anonymised'. This means that there will be no personal information or study code attached to the data and it cannot be linked back to you. Therefore, there is no direct benefit to you, but your data can help researchers collaborate and understand diseases better, and support health advances.

The sharing of this data more broadly, in this manner, is optional. You can withdraw from the sharing of clinical or research data at any time, but that if data have already been shared it may be impossible to retrieve and/or destroy that data.

12 Who is organising and funding the research?

This research has been initiated by researchers at the University of Melbourne and has been funded by the University of Melbourne and Illumina, as a part of a grant by The Advanced Genomics Collaboration.

By consenting to taking part in this research project, you agree that samples of your blood or saliva (or data generated from analysis of these materials) may be provided to the research team at the University of Melbourne. You will not benefit financially from your involvement in this research project even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to the University of Melbourne, the study researchers, or their institutions. No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

13 What if I withdraw from this research project?

If you decide to withdraw from this research project, please notify a member of the research team. If you withdraw your consent during the study, the research team study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly as they will form part of the results of this study. If you do not wish for this to happen, you must tell the research team before you join the research project. If you wish to have any of your remaining samples destroyed, we will destroy them upon receiving this request from you.

14 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of University of Melbourne.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

15 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you would like more information about the project, please contact:

Name:	Dr Alexis Ceecee Britten-Jones (Principal Investigator)
Telephone:	(03) 8344 5980
Email:	ac.brittenjones@unimelb.edu.au

Who can I contact if I have any concerns about the project?
This project has human research ethics approval from The University of Melbourne [ID: 27246]. If you have any concerns or complaints about the conduct of this research project, which you do not wish to discuss with the research team, you should contact the Research Integrity Administrator, Office of Research Ethics and Integrity, University of Melbourne, VIC 3010. Tel: +61 8344 1376 or Email: research-integrity@unimelb.edu.au. All complaints will be treated confidentially. In any correspondence, please provide the name of the research team and/or the name or ethics ID number of the research project.