Participant Information Sheet

Title	***Proteins of the Immune System in Psychosis***
Short Title	PIP
Protocol Number	HREC/51194/MH-2019
HREC ID number	2019.067
Principal Researchers	Dr Vanessa Cropley, A/Prof Andrew Zalesky, Prof. Christos Pantelis, Prof. Dennis Velakoulis, A/Prof Cynthia Shannon Wiekert, Dr Franz-Markus Leweke,
Associate Researchers	Prof. Susan Rossell, Dr Wei Lin Toh, Dr Eleni Ganella, Dr Mahesh Jayaram, Dr Ajit Selvendra, Alicia Stevens
Students	Megan Thomas
Location	Melbourne Health, Melbourne Neuropsychiatry Centre, University of Melbourne, St. Vincent's Hospital

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Part 1 What does my participation in the project involve?

1. Introduction

You are invited to take part in this research project; the Proteins of the Immune System in Psychosis (PIPs) Sub-Study. This is because you are involved in the PIPs study. The research project is aiming to learn more about brain changes that may explain why a person develops psychosis.

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

Please read this information carefully. You may ask questions about anything you don't understand or want to know more about. Before deciding whether or not you want to take part, you might want to talk about it with a carer, relative, friend or healthcare worker.

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 participate in the research processes that are described;
- Consent to the use of your personal and health information as described.

You will be given a copy of the Participant Information and Consent Form to keep as a record.

2. What is the purpose of this research?

This sub-study is an extension of your other involvement in the PIPs study. Like your previous involvement this study aims to investigate if there are changes in the brain that may explain why a person develops schizophrenia. To do this, we will be investigating the role of the immune system in people with recently diagnosed schizophrenia, and people without schizophrenia, to see if the immune system affects how the brain develops. The immune system is made up of organs, cells and proteins and is the body's defense against infections which helps keep us healthy. Recent research has found that some components of the immune system are expressed in the brain and can affect how the brain develops. This sub-study wants to see if specific proteins of the immune system are increased in the brain in people who experience schizophrenia, and whether higher levels of these proteins might affect the structure and function of the brain.

In this sub-study, we will use a lumbar puncture to collect cerebrospinal fluid (CSF) to investigate proteins involved in schizophrenia and brain development. CSF is a fluid that flows in and around the hollow spaces of the brain and spinal cord and is collected from a gap between two vertebrae in the lower spine. We need CSF because it better reflects the biochemical contents of the brain than blood. This is because there is a barrier between the circulating blood system and the brain and spinal cord that prevents many molecules from entering the brain. In this study, we are interested in the level of certain immune factors in the brain. The CSF will therefore provide 'a window' into what is happening in the brain. The lumbar puncture will be done by a doctor trained in this procedure and involves lying still on your back.

This study has been initiated by Doctor Vanessa Cropley, The University of Melbourne. The study involves researchers from a number of organisations working together. The study has been funded by a National Health and Medical Research Council Project Grant.

The results of this research may be used by Megan Thomas to obtain a Doctor of Philosophy – Medicine, Dentistry and Health Sciences.

3. What does participation in this research involve?

Consenting to the main PIPs study does not mean you have consented to the sub-study. Separate consent will be signed prior to any involvement in the sub-study.

If you agree to take part in this research project, you will undergo a lumbar puncture at the Royal Melbourne Hospital. This will take about 1-2 hours.

You are asked to avoid taking alcohol or drugs prior to the session to ensure that these substances do not influence the study results.

i) Lumbar Puncture

In the previous PIPs session, you had a blood test and an MRI scan. These will be checked prior to the lumbar puncture to make sure your blood clots normally and you do not have an intracranial mass lesion, hydrocephalus (water on the brain) or any other structural conditions that mean you could not have a lumbar puncture.

The lumbar puncture will use a special needle to collect a small amount of fluid called CSF (approximately 10-15ml, less than 1 tablespoon) from a gap between two vertebrae in the lower spine called the spinal canal. CSF

is only found around the spinal cord and the brain, but nowhere else in the body. Like blood, CSF is completely replaced several times per day, so that it is constantly being produced.

The lumbar puncture will be performed at the Department of Radiology at the Royal Melbourne Hospital. The doctor, who is trained in doing lumbar punctures, will use an image guided machine to help in the procedure. Once at the clinic you will meet the research team carrying out the procedure, including a medical specialist called a radiologist. A radiologist is a medically trained specialist who is highly qualified and experienced in carrying out lumbar punctures.

The lumbar puncture will take place on a bed in a specially equipped room. You will be asked to lie down so that the doctor can give you a local anesthetic prior to the lumbar puncture. The local anesthetic involves small injections into the back so it will numb the area and make you feel more comfortable. Once the area is numbed, you will be asked to lie down on your side and tuck your knees up around your chest. The doctor will use an image guided machine, that helps with accuracy, to help position a special needle to collect CSF from the lower part of your spine. You will be encouraged to stand up and walk around 10-15 mins after the lumbar puncture.

There will be nurses available while you rest who will check on you and make sure you are comfortable both before, during and after the lumbar puncture. Once you are feeling ok, you will be able to leave the hospital and go home. A nurse will contact you via phone to check on how you are feeling after the lumbar puncture.

The total time for this session will be 1-2 hours. You are asked to wear loose and comfortable clothing for this visit and are encouraged to have someone you know come with you (e.g. a family member). If you cannot have someone collect you, we will organize transport for you to get home.

It is recommended that you avoid strenuous exercise or activity for the next couple of days after the lumbar puncture procedure. If you have any concerns, or do not feel well after the procedure, you should contact your local doctor and take this consent form with you to your appointment so that they are aware of your participation in this project.

4. Reimbursement

There are no costs associated with participating in this research project, nor will you be paid. You will be reimbursed $220 for completing the lumbar puncture. This is to cover costs that happen because of participating in this research project, including transportation to and from testing sessions and parking. You will be given this reimbursement in the form of an e-Gift card of your choosing.

5. Other relevant information about the research project

This project is a sub-study to the main PIPs study, which you have previously participated in. This sub-study will collect further information about a participant's immune system, specifically additional biological samples, that will help us further understand how the immune system is related to schizophrenia and the brain.

The main PIPs study aims to recruit 140 participants: 40 individuals with recently diagnosed schizophrenia (within the first 5 years) and 100 participants with no history of a psychotic disorder or current psychiatric condition. For the sub-study, we aim to recruit all interested and eligible participants from the main PIPs study. All individuals who have schizophrenia will be registered with a mental health service and all controls will be recruited from the general community.

You have been invited to participate in this sub-study because you are between the age of 18 and 40 years, from the general population, and are currently participating in the main PIPs study. You will need to meet certain eligibility criteria to participate in this study. The eligibility criteria will be discussed with you by a study doctor or other members of the research team.

6. 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.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

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 University of Melbourne.

7. What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research. Your involvement will help us improve our understanding of the onset of psychotic disorders and ways of providing treatment for young people at risk of psychosis.

8. What are the possible risks and disadvantages of taking part?

Lumbar puncture: Lumbar punctures are a routine procedure; therefore, the risks are very low. The lumbar puncture will be performed by a highly trained and experienced doctor.

The most common risks associated with having a lumbar puncture include:

- Discomfort when the needle is inserted and the CSF is taken. This is usually minor and short-lasting. There may be a bruise and some bleeding where the needle is put in. Some people experience leg pain at the time of the procedure.
- Headache after the CSF has been taken; this can last a few days. The risk of this headache is around 10% or 1 in 10. If the headache does not go away in 1 or 2 days, it may be due to a leak of CSF. This is extremely rare (about 1 in 1000 people) but if it does happen it can be treated with a blood “patch”. This is when your blood is injected into the area where the leak is happening. You will be able to take painkillers for the headache.
- Pain or tenderness in your lower back after the procedure.
- An allergic reaction to the local anesthetic.

There are also risks, which are very rare, such as bleeding into the spinal canal or an infection of the spinal fluid (known as meningitis). These very rare complications may be serious. They could require hospitalization for urgent care, such as antibiotic therapy, brain surgery, or a breathing machine (known as a ventilator).

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team.

9. What will happen to my CSF samples?

By consenting to take part in this research sub-study, you consent to the collection, storage and use of samples as specified below:

After your CSF is collected it will be stored in a freezer at the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) laboratory at the Mental Health Research Institute (MHRI) in Melbourne Victoria. This is a secure facility and only the key investigators in the study will have access to the use of your samples. A small amount of CSF (2ml) will also be sent to RMH Pathology for routine clinical screening. Your CSF samples and any paperwork accompanying the samples will be labelled with the same unique identifier used in the larger PIPs study. This means that we will remove your name and other identifying details. Only the researchers directly involved in the current project will have access to the information that links your personal data with your unique identification number, and only if it is necessary to do so. Consent forms containing your name and contact information will be stored in a locked cabinet at the Melbourne Neuropsychiatry Centre. Any electronic research data pertaining to this sub-study will be stored on password-protected computers at the Melbourne Neuropsychiatry Centre. The CSF samples will be stored until they are analyzed for specific markers at a later date. Any information obtained in connection with this research project that can identify you will remain confidential, stored securely, and will only be used for the purposes stated in this document. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

With your consent, some of the CSF collected will be stored for use in other research studies in the future. Only relevant investigators or scientific partners of this study will have access to these stored samples in the future. This is an **optional** part of the study. If you do not want your CSF samples stored for future studies, you don't have to and they will be disposed of. Furthermore, you can consent to the storage and use of your CSF samples for future studies, and later change your mind. If you consent to the long-term storage and use of your samples the samples will be kept indefinitely in the Melbourne Neuropsychiatry Centre Research Tissue Bank. Please see Section (16) below for further information about the registration of your samples into this Tissue Bank. As outlined above, these samples will be stored in locked freezers at the MHRI. The stored CSF samples may be used to examine particular molecules that are involved in neuropsychiatric disorders, inflammation or immune function. Future studies using your stored CSF samples will only take place following ethics approval from a relevant Human Research Ethics Committee. No identifiable information (i.e. name, address or date of birth) will be provided to researchers, ensuring the privacy and confidentiality of your data. You will be asked to indicate your choice for the collection, storage and use of your CSF samples for this future research in the consent section of this document.

The CSF samples collected for this specific research and future research are for research purposes only and not for any commercial gain. They will not produce the type of results that will have any useful meaning that would affect your health or treatment. The type of genetic testing that may be done on your stored CSF samples in future studies is not testing that would result in information about your future health or risk of having children with a genetic disorder, or information that may be relevant to the health of family members who are not a part of the project. Therefore, you will not be provided with the results of the tests or of any

genetic testing conducted in future studies. If the investigators become aware that any analyses have implications for you or your family members, you will be made aware of the information. In general, we will not give you any individual results from the study of the samples you give us

10. What if new information arises during the project?

Sometimes during the course of a research project, new information becomes available about the risks and benefits of the project may become known to the researchers. If this happens, the study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, the study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, the study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, they will explain the reasons and arrange for your regular health care to continue.

11. Can I have other treatments during this research project?

Yes, you can continue to receive any treatment you are presently having. However, it is important to tell the research staff about any treatments or medications you may be taking. This includes, over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also inform us about any changes to these during your participation in the research.

12. What if I withdraw from this research project?

If you decide to withdraw from the sub-study, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to inform you if there are any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant 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 and to comply with law. You should be aware that data collected by the researchers up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

13. What will happen when my participation in this research project ends?

In the future, we may follow-up participants in this study to see how specific functions (e.g. cognition or brain structure) have changed over time. A follow-up study will only take place following ethics approval from a relevant Human Research Ethics Committee. You will be asked to indicate whether you would like to be contacted about any follow-up studies in the future.

Upon request, a short summary of the results of the study will be sent out to you once the study is complete. To obtain this please contact one of the investigators listed in Section (18).

14. What happens if I am injured as a result of participating in this research project?

If you suffer any injury as a result of participating in this research project, hospital care and treatment will be provided by the public health service at no extra cost to you if you elect to be treated as a public patient.

Part 2 How is the research project being conducted?

15. What will happen to information about me?

By signing the consent form, you consent to the relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this sub-study that can identify you will remain confidential. Consent forms containing participants' names and any contact information will be stored in a locked cabinet at the Melbourne Neuropsychiatry Centre. The CSF collected from you will be coded with the same unique identifier used in the main PIPs study and stored at a secure facility as described above in Section (9). You may choose to have a support person, such as your carer, present during these discussions.

Information about you may be obtained from your health records held at this and other health services for this sub-study. By signing this consent form, you agree to the research team accessing health records if they are relevant to your participation in this sub-study. Your participation in this sub-study will be added to your medical record.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about you. You also have the right to request that any information, with which you disagree, be corrected. Please contact one of the researchers named in Section 18 if you would like to access your information.

i) Registration of data into the Melbourne Neuropsychiatry Centre Research Databank and Tissue Bank

The Melbourne Neuropsychiatry Centre (MNC) plans to assemble a database of over 5,000 brain scans and associated clinical research data and biological material (i.e. CSF) neurosciences since 1994 and have collected clinical research data and brain imaging data in over 3,000 research participants.

With your consent, we would like to keep the CSF samples from this sub-study indefinitely and store it in the MNC Research Databank and Tissue Bank. Please read the separate information sheet regarding the MNC Research Databank and Tissue Bank before consenting to your data being stored in a particular way. The MNC Research Databank and Tissue Bank has received Melbourne Health Human Research & Ethics Committee approval (MHREC: 2009.067, Melbourne Neuropsychiatry Centre (MNC) Research Databank and Tissue Bank, Professor Christos Pantelis). We would like to keep your information and CSF samples in this Databank/Tissue Bank indefinitely as there is a possibility that it may be re-used at a later stage to address future research questions. However, if you do not want your information to be stored indefinitely for this purpose then you have the option of your information being destroyed after the minimum of 7 years following completion of the study. You will be asked to indicate your choice for the registration of your biological samples into the MNC Research Databank/Tissue Bank in the consent section of this document.

ii) Registration of data for future use

Some scientific journals are now asking to provide de-identified data for future use by scientists around the world. As mentioned above, the de-identified data is data that does not include any information that could identify you (i.e. name or initials). Bio samples (e.g., CSF) may be coded and uploaded to secure servers. Please

indicate on the consent form whether you are happy for your de-identified data to be stored on secure servers and used in future research collaborations.

16. Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

For further information on who to contact please see Section (18) below.

17. 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 Melbourne Health HREC.

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.

18. Further information and who to contact.

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact any of the following people:

Contact persons:

Name	Dr Vanessa Cropley
Position	Principal Investigator
Telephone	(03) 8344 1876
Email	vcropley@unimelb.edu.au

Name	Professor Christos Pantelis
Position	Associate Investigator
Telephone	(03) 8395 8118
Email	cpant@unimelb.edu.au

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person:

Name	Dr Vanessa Cropley
Position	Principal Investigator
Telephone	(3) 8344 1876
Email	vcropley@unimelb.edu.au

The Melbourne Health Human Research Ethics Committee (HREC) has approved this study. If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details:

Reviewing HREC Name	Melbourne Health HREC
HREC Executive Officer	Manager HREC
Telephone	(03) 9342 8530
Email	Research@mh.org.au

Local HREC Office contact (Single Site – Research Governance Officer)

Name	Director Research Governance and Ethics
Position	Complaints Manager
Telephone	+61 3 9342 8530
Email	Research@mh.org.au

Consent Form – Sub-Study

Title	***Proteins of the Immune System in Psychosis***
Short Title	PIPs
Protocol Number	HREC/51194/MH-2019
HREC ID number	2019.067
Principal Researchers	Dr Vanessa Cropley, A/Prof Andrew Zalesky, Prof. Christos Pantelis, Prof. Dennis Velakoulis, A/Prof Cynthia Shannon Wiekert, Dr Franz-Markus Leweke,
Associate Researchers	Prof. Susan Rossell, Dr Wei Lin Toh, Dr Eleni Ganella, Dr Mahesh Jayaram, Dr Ajit Selvendra, Alicia Stevens
Students	Megan Thomas
Location	Melbourne Health, Melbourne Neuropsychiatry Centre, University of Melbourne, St. Vincent's Hospital

Declaration by Participant

- I have read the Participant Information Sheet, or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the project.
- I have had the opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.
- I understand that I will be given a signed copy of this document to keep.

Optional consent items:

I consent to researchers contacting me in the future to participate in a follow-up study related to this study. I understand I am under no obligation to participate in follow-up studies:

☐ Consent to contact for follow up studies Initial: _____ Date: _____ / _____ / _____

I consent to the researchers contacting me in the future regarding involvement in other research. I understand I am under no obligation to participate in future research:

☐ Consent to contact for future research studies Initial: _____ Date: _____ / _____ / _____

Registration of research data to the MNC Research Databank and Tissue Bank:

I consent to allow my CSF to be securely stored and included in the MNC Research Tissue Bank and future research as explained in this document:

☐ Consent to brain scans to go into MNC Research Databank Initial: _____ Date: _____ / _____ / _____

Declaration of Participant for access to de-identified data:

By signing this consent section, I acknowledge that anonymous CSF data (as outlined on Page 5) may be stored in secure servers accessible (on request) by scientists around the world to facilitate further research:

☐ Consent to facilitate future research Initial: _____ Date: _____ / _____ / _____

Name of Participant (please print) _____

Signature _____ Date: _____ / _____ / _____

Name of Witness to Participant's Signature[†] (please print) _____

Signature _____ Date: _____ / _____ / _____

[†] Witness required when participant cannot read this document for themselves except where an interpreter is used.

Declaration by Principal, Associate Investigator or Research Assistant:

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Principal, Associate Investigator

or Research Assistant (please print) _____

Signature _____ Date: _____ / _____ / _____

Time (00:00 format) of consent: _____

Note: All parties signing the consent section must date their own signature.

Form for Withdrawal of Participation – Sub-Study

Title	***Proteins of the Immune System in Psychosis***
Short Title	PIPs
Protocol Number	HREC/51194/MH-2019
HREC ID number	2019.067
Principal Researchers	Dr Vanessa Cropley, A/Prof Andrew Zalesky, Prof. Christos Pantelis, Prof. Dennis Velakoulis, A/Prof Cynthia Shannon Wiekert, Dr Franz-Markus Leweke,
Associate Researchers	Prof. Susan Rossell, Dr Wei Lin Toh, Dr Eleni Ganella, Dr Mahesh Jayaram, Dr Ajit Selvendra, Alicia Stevens
Students	Megan Thomas
Location	Melbourne Health, Melbourne Neuropsychiatry Centre, University of Melbourne, St. Vincent's Hospital

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my relationship with Melbourne Health, Melbourne Neuropsychiatry Centre/ University of Melbourne or St. Vincent's Hospital.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/

Senior Researcher[†] (please print) _____

Signature _____ Date _____

[†] A senior member of the research team must provide the explanation of, and information concerning withdrawal from the research project.

Time (00:00 format) of consent: _____

Note: All parties signing the consent section must date their own signature.