Australian IMmunity (AIM) Trial

Participant Information Sheet and Consent Form

Principal Investigators

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You are invited to participate in a research study about how the type of protein in cow's milk could impact immunity. This research is being conducted independently by Nutrition Research Australia (NRAUS).

Knowing more about this study will help you decide if you want to take part. Please read this information carefully and ask questions about anything that you don't understand or want to know more about. You can view this Participant Information any time by following the same link previously used to access this form. We encourage you to save a copy for your own records.

To ensure we are confident in our findings, we are aiming to recruit 100 participants to this study. Before deciding whether or not to take part, you might want to talk about this study with a relative, friend, or a health professional. If you decide you want to take part in the research project, you will be asked to indicate your consent by completing an electronic consent form.

Purpose of the study

We know that what we eat can affect the way our immune system works. There is some evidence which suggests that certain types of proteins in cow's milk could affect our immune system, and other aspects of health related to immunity such as gut health and brain health.

This study will be used to compare two different types of cow's milk, each with a different type of cow's milk protein, on biomarkers of immune function.

Why have I been invited to participate?

You have been invited because you are a young and healthy adult living in Queensland or Northern New South Wales who can read and speak English and can tolerate drinking cow's milk products daily. If you are allergic to cow's milk protein, are lactose intolerant, diagnosed with functional gut disorders (e.g., inflammatory bowel disease or irritable bowel syndrome), or you are currently pregnant or breastfeeding, you should not participate in this study.

All aspects of this study are voluntary, and you do not have to participate if you don't want to. If you agree to participate, you can change your mind at any time without any negative consequences. If you decide to withdraw from the study, researchers will not collect any more data from you. However, any data collected up until the point of your withdrawal from the study will be retained and may be used to inform study results. If you do not want your data to be included, you must tell the researchers when you withdraw from the research project. The meals provided to you during the study will also end when you withdraw from the study.

What will I be asked to do?

This is a double-blind, cross-over, randomised controlled trial. This means that over the course of the study, you will receive two separate interventions, in a random order, and neither yourself nor the researchers will know which intervention you are taking until after the study is complete.

If you agree to participate, you will be asked to consume the study diet for a period of 8 weeks, including a 2-week run-in period, 2-week intervention period, 2-week washout period, and another 2-week intervention period.

During each intervention period, you will be asked to have a cow's milk drink each day for 14 days, which will contain either A1/A2 beta-casein proteins, or A2/A2 beta-casein proteins, with or without lactoferrin. Both A1/A2 and A2/A2 beta-casein proteins naturally occur in cow's milk. Lactoferrin is another naturally occurring compound, which has been isolated and concentrated and added to the cow's milk.

You will be asked to follow a special diet for the 8 weeks you are participating in the study. You will be required to purchase Weet-bix or bread for your breakfast each day. Lunches and dinners will be provided for you, with meals ordered from a study menu, and delivered to you weekly. The meals will be provided by Lite and Easy and will contain a choice of dairy-free fresh and frozen meals for lunch and dinner daily, selected from Lite and Easy's seasonal menu. One of our study dietitians will calculate your energy requirements at the start of the study, and the portion sizes and calories provided will be designed to stop you from gaining or losing any weight across the course of the study.

You will be able to choose meals to suit a variety of dietary patterns, with vegetarian and gluten-free options available. A menu will be available from our study co-ordinator on request. Meals are designed to be consistent with the Australian Guide to Healthy Eating.

Any additional foods and snacks can be selected from an approved list which will be provided for you. During that time, you will be asked to limit some foods and drinks, including caffeine to no more than two caffeinated beverages per day, alcohol to no more than two standard drinks per day, avoiding taking prebiotic and/or probiotic supplements, and limiting artificial sweeteners, herbs, and spices in the diet. You will also be asked to avoid all animal-based milk drinks not provided by the study.

You will also be asked to:

- Complete 1-hour of online surveys on 5 different days (each 1-2 weeks apart)
- Have four fasting blood tests performed at your local QML pathology collection centre
- Provide your own transport to attend your local QML pathology collection centre
- Take four stool (poo) swabs using kits that will be provided for you, and give them to QML pathology staff when you have your blood tests.

What are the potential benefits of participating in this study?

The results of this study will be used to contribute to product design and potentially contribute to dietary recommendations aimed towards improving the health of Australian adults. Results may also help to inform future research to help adults who have poor immunity. By participating in this study,

you will have meals provided for you for 8 weeks. We cannot guarantee participation in this study will provide other direct benefits for you.

Are there any risks?

Sometimes changing what you eat can result in short-term and mild gut upset. There are also the usual risks associated with having blood taken, such as infection or bruising. There are no other risks to the study, however, some participants may find changing their diet or some questions in the surveys distressing.

Due to the nature of the study, the research team cannot offer support if you feel distressed or need health or medical assistance. If participation raises negative emotions, it is recommended that you contact Lifeline on 13 11 14, Beyond Blue on 1300 22 4636, infoline@beyondblue.org.au.

Your GP/local doctor will be notified that you are participating in this study and of any clinically relevant information noted in the conduct of the study. If you need medical assistance, it is recommended that you speak to your GP, or contact 000 in an emergency.

Reimbursement

The study will provide you with your lunch and dinner daily for 8 weeks, as well as provide the milk products for each intervention period. You will be reimbursed for the Weet-Bix or bread purchases you make for breakfast by a $45- Visa gift e-card, which will be provided for you at the end of the 2-week run-in period.

Compensation for injury

If you have any illness or injury as a direct result of participation in this study, you may be entitled to compensation. Each week that you are enrolled, you will be asked to report any adverse events in a short survey. If you become ill or injured, please let our study co-ordinator know as soon as possible. For any moderate or severe adverse events, you should seek attention from your usual GP for non-urgent matters, or from emergency care (hospital or ambulance) for urgent matters. If you are unsure of the seriousness or urgency of the adverse event, you should contact Health Direct on 1800 022 222.

You may also be able to seek compensation through the courts. It is the recommendation of the independent ethics committee responsible for the review of this trial that you should seek independent legal advice before taking any steps towards compensation for injury.

How will your privacy be protected?

The study will gather certain personal information about you. This information will be held by NRAUS and its authorised representatives, and your personal data will be strictly confidential. Your data will be collected online by the Qualtrics platform and by blood and faecal samples. Qualtrics hosts data in Australia and is secure; subscribers own the data collected. Qualtrics does not keep data after the survey account has been closed. All blood and faecal data will be deidentified and stored in password protected accounts. Your data will be saved and stored in Dropbox Business which uses Advanced Encryption Standard to protect data in a secure storage server. Storage servers are located in data centres across the United States. Data will be kept for a minimum of 5 years as recommended by the National Statement on Ethical Conduct in Human Research.

NRAUS researchers will use online project management software (Trello.com) to co-ordinate the study. This information will be accessible only to researchers working on the study, and no survey data or identifiable information will be stored, shared, available on Trello. Lite and Easy will be provided with your name and contact details for the purposes of ordering and delivering your meals. Lite and Easy will also be provided with limited de-identified data collected in the study, for the purpose of business feedback and quality control. Lite and Easy will not have access to other data or records collected by the study.

You should note that some data derived from your participation in this study will be sent overseas (e.g., blood samples may be shipped overseas for analysis); the regulatory regimes governing data access and use in other countries may not be the same as those that are in place in Australia. Your privacy will be protected by ensuring that information that may identify you will be stored in Australia only, and any samples will be de-identified immediately after collection. In the case of data that identifies you, or from which your identity may be ascertained, an entity subject to Australian privacy laws that has collected your information must take reasonable steps to ensure that an overseas recipient handles the information in accordance with any relevant Australian privacy principle (unless an exemption applies). If you have any questions about this, you can contact Dr Flavia Fayet-Moore (Principal Investigator).

How is this study funded?

NRAUS has received a research grant from The a2 Milk Company to conduct this study. The a2 Milk Company is not directly involved in the data collection, data analysis, or the publication of results in a peer-reviewed scientific journal.

Who will see the results of the study?

Results of the study's findings will be shared with The a2 Milk Company, the study funder. Study findings will also be published in a peer-reviewed scientific journal and may be presented at national and international conferences.

You can request a summary of the study findings to be sent to you by indicating this on your consent form.

Can I become pregnant?

No. The intervention is safe to consume if you are pregnant; however, becoming pregnant will change the results of the study. You should not participate if you wish to become pregnant during the study period. Therefore, you must use one of the following highly effective methods of birth control from now until the study is finished:

- Bilateral tubal occlusion/ligation,
- Vasectomised partner/s, provided the vasectomised partner has received medical confirmation of the surgical success and is your only sexual partner,
- Non-hormonal Intrauterine device (IUD),
- True abstinence (refraining from heterosexual intercourse, when this is in line with the preferred and usual lifestyle of the participant (Note: Periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable),

- If required, male or female condom or cap, diaphragm, or sponge.

Please note, if you are using oral contraception, injection contraception, Intrauterine hormone-releasing system (IUS), or Implanon or other hormonal implants, you are eligible to participate in this study provided you have been taking the same medication for at least 6 months, with no changes to medication planned during the study period.

What happens if I get COVID-19 during the study?

If you become infected with COVID-19 during the study period, you will not need to withdraw from the study. You will be asked to notify the study co-ordinators as soon as practical when you have a suspected or confirmed case of COVID-19. During your illness you will be asked to follow the study protocol as much as its possible to do so, record any medications you take, and record any times you cannot complete the study requirements (e.g. if you cannot eat or drink due to illness). If you cannot attend the pathology clinic for your sample collection due to isolation requirements, then let one of our team know as soon as you are able to. If it's feasible to move your appointment we will do so, otherwise you will not be required to provide a sample at that time.

Has this study received ethical approval?

The Bellberry Human Research Ethics Committee has reviewed and approved this study (2022-02-161) in accordance with the National Statement on Ethical Conduct in Human Research (2007) – incorporating all updates. Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the Operations Manager, Bellberry Limited on 08 8361 3222.

Further information

If you would like further information, please don't hesitate to contact the study co-ordinator on **0476 985 977** or email aimtrial@nraus.com.

Thank you for considering this invitation to participate in this research study by Nutrition Research Australia.

Dr Flavia Fayet-Moore, CEO
Nutrition Research Australia Pty Ltd.
Level 10, 20 Martin Pl, Sydney, NSW

Informed consent form

The informed consent form is completed electronically providing participants are eligible for the AIM Trial after completing the screening survey.

Declaration by participant:

By ticking the box below, I declare that:

- I agree to participate in this research project and give my consent freely.
- I am 18 years of age or over.
- I have read and understood the Participant Information Form about the project.
- I understand that my participation is entirely voluntary.
- I understand that I am free to withdraw my participation at any time, without the need for explanation.
- I understand that if I withdraw my consent after completing part of or all of the study, my data will not be destroyed and data collected up until my withdrawal may be used to inform the study results
- I understand that I can request my data be removed from the study at any time.
- I consent to my GP/local doctor being notified that I am participating in this study.
- I consent for any clinically relevant information noted in the conduct of the study to be shared with my GP/local doctor.
- I have had the opportunity to have any questions I had about the project answered to my satisfaction.

☐ I give my voluntary consent to participate in this study.
☐ I agree to follow the dietary parameters required for this study.
☐ I wish to receive a copy of my blood pathology reports via email once the study has finished.
☐ I wish to receive a summary of the study findings via email once the study has finished.