**PLAIN LANGUAGE STATEMENT AND CONSENT FORM**

TO: Participant

**Plain Language Statement**

Date: 17th May 2017

Full Project Title: The effects of hypoxia on muscle growth and inflammatory responses to resistance training.

**Principal Researcher:** Dr Craig Wright

**Student Researcher:** Mrs Giselle Keefe, Mr Andrew McColl and Mr Jackson Barnard.

**Associate Researcher(s):** Prof Aaron Russell, Mrs Samantha Hoffmann and Prof Julie Pasco,

This Plain Language Statement and Consent Form is13 pages long. Please make sure you have all the pages.

1. Your Consent

You are invited to take part in this research project.

This Plain Language Statement contains detailed information about the research project. Its purpose is to explain to you as openly and clearly as possible all the procedures involved in this project before you decide whether or not to take part in it.

Please read this Plain Language Statement carefully. Feel free to ask questions about any information in the document. You may also wish to discuss the project with a relative or friend or your local health worker. Feel free to do this.

Once you understand what the project is about and if you agree to take part in it, you will be asked to sign the Consent Form. By signing the Consent Form, you indicate that you understand the information and that you give your consent to participate in the research project.

You will be given a copy of the Plain Language Statement and Consent Form to keep as a record.

2. Purpose and Background

The purpose of this project is to gain a greater understanding of how healthy adults respond to resistance exercise, particularly how these responses may be modified with ageing. Little is known about how the human body recovers from resistance exercise. Understanding how our body responds to exercise and optimising the process is important in preventing muscle wasting associated with ageing. Exercise triggers responses within the body which initially cause muscle inflammation and soreness, but then stimulates muscle growth and adaptation. There is a widespread belief that manipulating the body’s inflammatory response to exercise can enhance this process of muscle re-building. Exposure to acute hypoxia or low oxygen concentrations such as those observed at high altitudes has long been known to impact biological processes common to exercise in young healthy men. Recent research has indicated that short-term exposure to hypoxia may influence muscle growth and adaptation. This study aims to characterise what affect hypoxia has on the ageing body immediately following resistance exercise, and the downstream effect on the muscle and inflammatory response to training.

We would like to invite 60 healthy adults aged 18-35 and 60 healthy adults aged 60-80 to participate in an 8 week training program for research purposes. We will examine the effects of resistance exercise in hypoxia on post-exercise ‘muscle building’ and inflammatory responses, and the chronic effects of repeated training in these conditions. To do this we will randomly assign participants to one of four groups; 1) exercise in simulated altitude (called hypoxia), 2) exercise in sea level air (normoxia), 3) no-exercise in hypoxia or 4) no-exercise control. We will assess participant’s body composition, thigh muscle mass, muscle strength, endurance and physical fitness before and after the 8 week intervention. Blood and muscle samples will be taken before and after the training intervention to assess muscle growth and inflammatory responses to training. This study will allow us to determine whether resistance training in hypoxia improves muscle health and the inflammatory profile.

The researchers will measure:

1. Your aerobic fitness, muscular strength and muscular endurance.
2. Your body composition.
3. The expression of specific genes and proteins that regulate skeletal muscle growth and development following one resistance exercise session and subsequently following eight weeks of exercise training.
4. The regulation of specific genes and proteins involved in inflammation following one resistance exercise session and following eight weeks of resistance exercise training.

This study will provide detailed data on how each of the conditions affects muscle adaptation and inflammation. You are invited to participate in this research project as you are within the required age range and have no complicating medical issues that may affect your ability to participate.

3. Procedures

If you are interested, please read the following description of what is required to participate in this research study and what we plan to do with your blood and muscle samples. If you decide to take part in the study, you will be required to attend the laboratory on 29 occasions over an 11 week period.

**Pre-test Screening**

We will first ask you to complete a medical questionnaire to determine your current health risks and determine what medication you are currently taking. This will help inform the researchers of your current health status. If you are not suitable to participate in the study based on the information from your pre-test screening, your medical information will be returned to you. If you are suitable for the study, we will invite you to participate in the trial.

**Dietary record:** We will ask you to complete a dietary record before, during and after the completion of the study. This is to give us information on your typical dietary intake. It is important that you eat the food you normally consume during this time and record this on the form that we will give to you. This form will also ask you several questions about your current level of physical activity.

**Baseline assessment**

**Day 1: approximately 4 hours:** During this visit, information such as height, weight and blood pressure will be collected. You will also have a health screen to ensure that it is safe for you to participate in the study. On the same day you will be asked to complete a resistance exercise familiarisation session in our on-site gymnasium, where we will teach you how to safely perform the resistance training program. You may have completed these exercises before in a gymnasium. We will teach you how to perform the four exercises you will be performing during the eight week training program, and you will practice a submaximal strength assessment for each exercise. This is called a familiarisation session, where you will also be asked to complete an exercise test to become familiar with the equipment we will be using to test your health and fitness. You will be asked to sit in a chair where we will safely secure your leg to a metal lever that you can move up and down. We will ask you to extend your leg up and pull it back down again a maximum of 30 times. This exercise is called a ‘leg-extension’ exercise and the speed at which you can move will be controlled to minimise the risks of injury. This will allow us to estimate your maximal voluntary contraction (MVC) which is a measure of your leg strength and the rate at which you fatigue during the 30 contractions. We will also familiarise you with our bicycle ergometer, which will involve a brief session of pedalling on the bike at different levels of resistance. This is in preparation for assessment of your physical fitness which will occur during your next visit to Deakin University. You will then be given a referral to Barwon Health for two scans known as a Dual-energy X-ray absorptiometry (DXA) scan and a peripheral quantitative computed tomography (pQCT) scan. These scans are routinely used in clinical research and diagnostics, and are similar to an X-ray. These scans will provide information about your body composition such as fat mass and lean muscle mass, and more detailed information regarding the muscle, bone and fat mass of the of the lower leg. Please read the risk statement below which provides more information on the DXA and pQCT scans. You will be asked to refrain from vigorous exercise and from consumption of caffeine and alcohol in the 48 h prior to your first visit to the Deakin University Research Laboratory (Building DD, Waurn Ponds campus).

**Risk statement for ionising radiation:** This research study involves exposure to a very small amount of radiation from DXA and pQCT scans of your body. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose you will receive from these scans of your body will be approximately 0.09 mSv. At these dose levels, no harmful effects of radiation have been demonstrated, as any effect is too small to measure. The risk is believed to be minimal. If you have been involved in any other research studies that involve radiation, please inform us. Please keep this Patient Information and Consent Form that includes information about your exposure to radiation in this study for at least five years. You will be required to provide this information to researchers of any future research studies involving exposure to radiation.

**Day 2: approximately 3 hours**: During this visit you will be asked to complete a series of exercise tests to assess your muscular strength, endurance and aerobic fitness. The first test will involve performing leg press, leg extension, bench press and seated row exercises against increasing resistance, in order for us to measure the heaviest resistance you can perform 5 repetitions using correct technique. You will then have your MVC and rate of fatigue evaluated via a maximum 30 repeated contractions identical to the protocol completed in the familiarisation session the week prior. You will then complete an aerobic fitness test called a maximum oxygen consumption (VO₂max) test. This is completed on a on a bicycle. This test involves continuous, incremental cycling until volitional fatigue and usually lasts up to 15 minutes depending on your fitness levels. This test may be terminated earlier if you wish. This

exercise is performed with a mask over your nose and mouth that allows you to breathe freely while allowing the researchers to collect and analyse the gas composition in you breathing. This allows the researchers to assess your aerobic fitness. You will again be asked to refrain from vigorous exercise and from consumption of caffeine and alcohol in the 48 h prior to your second visit to the Deakin University Research Laboratory (Building DD, Waurn Ponds campus). You will be asked to fast on the day of this testing, which means you refrain from eating after 10pm the night prior. You are free to consume water on the day of testing. After the assessment is completed, we will provide you with a small meal to consume before you leave.

**Resistance training regime**

Following baseline assessment, you will be randomly divided into one of four groups to complete 24 training sessions over 8 weeks. These sessions will last approximately 60-90 minutes each.

* Group 1 will complete the eight week exercise regime whilst breathing normal air.
* Group 2 will complete the eight week exercise regime whilst breathing hypoxic air.
* Group 3 will complete eight weeks of resting exposure to hypoxic air.
* Group 4 will complete eight weeks of resting exposure to normal air.

You will be invited to attend 16 sessions at Deakin University over an 8 week period (2 days per week). These sessions will be delivered by Deakin staff and research students and will be at mutually agreed upon times. You will spend each session in an altitude tent in which the level of oxygen available to you will simulate sea level or 3,000 m above sea level. You will not know whether you are breathing normal or altitude simulated air. Importantly, oxygen availability associated with this altitude has been shown not to influence the intensity of resistance exercise and this should not affect your training sessions. Those assigned to an exercise training group will perform 4 sets of 10 repetitions of upper and lower body exercises at 70% of your pre-determined one-repetition maximum. Your one-repetition maximum will be estimated from the 5 repetition maximum you perform in the baseline assessment. This intensity is relative to your fitness and strength, and therefore it is expected that everyone will be at different levels. At two, four, and six weeks of your eight week program, your 5 repetition maximum will be re-evaluated, and 70% one-repetition maximum will be adjusted for training improvements as necessary. This ensures you are always working at the correct intensity to maximise the benefits of the exercise. Those assigned to the non-exercise groups will be able to watch TV during the session(s).

**Muscle and blood sample collection:**

During the 1st training session, three small muscle samples will be collected from your thigh and blood samples will be drawn from the vein in your arm. You will be asked to arrive in an overnight fasting state, meaning that you refrain from eating after 10pm the night prior. You are free to drink water on the day of testing. The blood sampling and muscle biopsy procedures are detailed below.

**Blood sampling:** You will be asked to lie on a bed and rest for 15 minutes. An experienced and trained staff member (phlebotomist) will then place a small needle into the vein in your arm and a small sample of blood (15 mL) will be drawn prior to your training session. Following your training session a small plastic tube known as a cannula will be placed into the vein in your arm, and a 15 mL sample of blood will be taken immediately after the training and at 30 minute intervals for 3 hours. You will be asked to return to Deakin University 24 and 48 hours later for two final blood samples. This means a total of 9 blood samples (135 mL) will be drawn to assess your response to the first training session. During a routine blood donation around 400 mL of blood is taken. The blood sampling procedure is painless, except the introduction of the needle and cannula into the arm, which will cause slight discomfort. The cannula reduces the need to repeatedly introduce a new needle into your arm.

**Biopsy procedure:** The licensed medical practitioner will then give you an injection of local anaesthetic into the middle of the thigh. This local anaesthetic may sting slightly for a few seconds. After 10 minutes, when the local anaesthetic has numbed the area, the licensed medical practitioner will make a small cut for each of the three biopsies through the skin above your thigh muscle. Each of these cuts will be 5mm long and there will be one for each biopsy. Using a needle, he will then take a small piece of muscle (about the size of a single “rice bubble”). This procedure is called a needle biopsy. **There are no pain sensors in the muscle; however pressure receptors will detect pressure as the needle is pushed in and may cause some localised pain and discomfort; similar to hitting your thigh on the corner of a table or a deep tissue massage**. The whole process of taking the sample lasts about 10 seconds. As soon as the small sample is collected, special sterile closures and a pressure bandage will be applied. We will ask you to donate 3 muscle biopsies during the first training session. These will be taken prior to the session, 3 hours after and 24 hours after the training session. The area will be stiff for a day or so but you will be able to continue with your normal physical activity. A researcher will contact you in the evening to check on your wellbeing.

It is common to experience local soreness for 24-48 hours after the procedure, but this should not limit normal activity levels. Occasionally bruising, swelling or a small area of numbness may occur. The numbness may last for several weeks, although it should recover fully, and has no impact on muscle function. If there is slight swelling or tenderness, apply an ice pack for 10 minutes over a damp cloth. There is a risk of infection with the needle biopsy sampling procedure and blood sampling, however, this risk is minimised by having all procedures performed using sterile techniques. Over the last 15 years we have not had a single case of infection. We have performed over 5000 muscle biopsies in the last 15 years without major complication.

**Follow up assessment**

On the 23rd (second last) session of your training program we will reassess your responses to the training session, through a series of small blood samples from a vein in your arm. We will ask you to arrive in a fasted state on the day of this session. We will request one small sample prior to the training session, then after the completion of training, a cannula will be inserted into a vein in your arm, and we will collect small blood samples at 30 minute intervals for three hours after the session. Two final blood samples will be requested 24 and 48 hours later. This means a total of 9 blood samples (135 mL) will be drawn to assess your response to the 23rd training session.

On the 24th (last) session of your training program you will complete a reassessment of your muscle strength, endurance and aerobic fitness, using identical assessments to the initial testing methods.

Approximately 4 days after the completion of your training program you will be invited return to the laboratory for follow up health assessment. During this session you will be given another referral to Barwon Health to undergo a Dual-energy X-ray absorptiometry (DXA) scan and a peripheral quantitative computed tomography (pQCT). Finally a small blood sample will be collected from a vein in your forearm (15 mL) and a trained licensed medical practitioner will perform a muscle biopsy from your thigh. These procedures are outlined above.

4. Collection of Tissue Samples for Research Purposes

By consenting to take part in this study, you also consent to the collection, storage and use of tissue samples as specified below.

Samples of blood will be taken from your arm vein. These blood samples will be spun in a centrifuge to separate out the plasma and blood cells. The plasma will be used to measure levels of hormones and proteins. A second potion of your blood will be used to analyse cell components of immune function such as white blood cells. Your plasma samples will be stored in a freezer. The muscle samples will be broken down and used to examine the expression of particular genes that regulate inflammation and muscle growth. Your muscle samples will also be stored in a freezer.

All your samples will be assigned a code that is known only to the researcher. This code will be written on the small plastic containers to store your samples. All analyses will only use your code. All samples will be stored and analysed over the duration of the study. Residual sample may be securely stored in a freezer, for use in future research projects which are closely aligned with this study. If at any stage you withdraw from participation in this study, you may ask that all blood and muscle samples to be destroyed.

5. Possible Benefits

Participation in eight weeks of resistance exercise training has significant implications for improving your overall health, particularly by increasing your strength and muscle mass. Improving your muscle mass and strength has been shown to reduce your risk of chronic diseases associated with being overweight and obese, such as cardiovascular disease. Resting exposure to simulated high altitude has been shown to improve various aspects of immune health and fitness.

Secondly, understanding how muscle growth, exercise performance and immune function is regulated has implications for the general population, and may have beneficial effects for disease populations leading to an improved quality of life.

6. Possible Risks

Possible risks, side effects and discomforts include having blood sampled. Taking blood from an arm vein involves the discomfort of having a needle and then a small flexible catheter in the arm vein. This is uncomfortable and may result in localised bruising. The muscle biopsy procedure may also cause localised discomfort, though this normally passes quickly. It is common to experience local soreness for 24-48 hours after the procedure, but this should not limit normal activity levels. As is the nature with any surgical procedure there is a small risk of infection and may result in localised bruising. If there is slight swelling or tenderness, apply an ice pack for 10 minutes over a damp cloth. As with any skin incision, there is the possibility of temporary alteration in sensation in the area, which may last for several weeks, but should recover fully and has no impact on muscle function. Possible, but very uncommon side effects are persistent bleeding and infection. All precautions are taken to avoid these risks, and all procedures are performed using sterile techniques.

***In the event of any ill-effects from the blood samples or muscle biopsy procedure (uncontrolled bleeding, severe pain, and signs of infection) you should contact Craig Wright as soon as possible, who will contact the attending physician at any time if required.***

Possible risks and side effects are also possible following exposure to hypoxia. Altitude sickness is a pathological effect of exposure to high altitudes and presents as a collection of non-specific symptoms including; headache, fatigue or weakness, shortness of breath, drowsiness and diarrhoea. To minimise these risks your heart rate and the oxygen levels in your blood will be monitored during all sessions.

***In the event of any ill-effects from exposure to high altitude you should inform the attending physician and you will be removed from high altitude conditions immediately.***

These symptoms typically subside when returned to sea level.

***In the event of any continuing ill-effect from exposure to high altitude you should consult your local doctor and inform the researchers as soon as possible.***

Importantly, your risk will be assessed by an attending physician prior to participation in this study.

7. Other Treatments Whilst on Study

It is important to tell your doctor and the research staff about any treatments or medications you may be taking, including non-prescription medications, vitamins or herbal remedies and any changes to these during your participation in the study.

8. Privacy, Confidentiality and Disclosure of Information

Any information obtained in connection with this research project that can identify you will remain confidential and will only be used for the purpose of this research project. It will only be disclosed with your permission, except as required by law. If you give us your permission by signing the Consent Form, we plan to share the results of your medical questionnaire with the medical doctor. All other results from the study will be grouped and your individual results will not be identifiable. The results of this research will be shared by the researchers as reports. Parts of these reports will also be prepared and published for scientific conferences and medical journals.

9. New Information Arising During the Project

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information. This new information may mean that you can no longer participate in this research. If this occurs, the person(s) supervising the research will stop your participation. In all cases, you will be offered all available care to suit your needs and medical condition. If the medical assessment by the medical doctor reveals any medical conditions not previously known, then medical doctor will advise you, and encourage you to contact your regular medical doctor for further assessment.

The genes that will be screened throughout the current project do not constitute risk to the individual. However, any genetic identification that could potentially impact the individual’s health profile will be strictly avoided by the researcher.

10. Results of Project

The results of the study will be forwarded to you on completion. This will be in the form of a report that will show your results compared to the group. The report will identify any findings that may be important for your health. This report can be shown to your Doctor if required.

**11. Project funding and research support**

Information about funding sources.

12. Further Information or Any Problems

If you require further information or if you have any problems concerning this project (for example, any side effects), you can contact Craig Wright. He can contact the Physician at any time of day if required. Dr Craig Wright will be available at any time on;

**Work telephone: 03 5247 9266**

**Mobile: 0400 110 247**

13. Other Issues

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about your rights as a research participant, then you may contact:

The Manager, Ethics and Biosafety, Deakin University, 221 Burwood Highway, Burwood Victoria 3125, Telephone: 9251 7129, research-ethics@deakin.edu.au

Please quote project number: 2016-308.

14. Participation is Voluntary

Participation in any research project is voluntary. If you do not wish to take part you are not obliged 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 School of Exercise and Nutrition Sciences, Deakin University.

If you have donated blood and/or samples, you have the right to ask for these samples to be destroyed and removed from all further analysis.

Before you make your decision, a member of the research team will be available so that you can ask any questions you have about the research project. You can ask for any information you want. Sign the Consent Form only after you have had a chance to ask your questions and have received satisfactory answers.

If you decide to withdraw from this project, 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.

15. Reimbursement for your costs

You will not be paid for your participation in this trial.

16. Ethical Guidelines

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

The ethical aspects of this research project have been approved by the Human Research Ethics Committee of Deakin University.

17. Injury

In the event that you suffer an 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 are eligible for Medicare.

18. Termination of the Study

This research project may be stopped for a variety of reasons. These may include reasons such as: unacceptable side effects of the tissue sampling protocol.

 **PLAIN LANGUAGE STATEMENT AND CONSENT FORM**

**TO:** Participant

**Consent Form**

**Date:** 9th February 2017

**Full Project Title:** The effects of hypoxia on muscle growth and inflammatory responses to resistance training.

**Reference Number: 2016-308**

I have read, or have had read and I understand the attached Plain Language Statement*.*

I freely agree to participate in this project according to the conditions in the Plain Language Statement.

I have been given a copy of the Plain Language Statement and Consent Form to keep.

The researcher has agreed not to reveal my identity and personal details, including where information about this project is published, or presented in any public form.

Participant’s Name (printed) …………………………………………………………………

Signature ……………………………………………………… Date ……………………

**TO: Participant**

**Consent Form for Tissue Sample Storage and Use**

Date: 9th February 2017

**Full Project Title:** The effects of hypoxia on muscle growth and inflammatory responses to resistance training.

* I consent to the storage and use of blood and tissue samples taken from me for use in further closely aligned research as described in this Plain Language Statement by Dr. Craig Wright.

Participant's name (Printed)…………………………………………..………..

Signature…………………………………………. Date……………….

Name of Witness to Participant’s signature (printed)………………………..

Signature......................................................... Date ………………

Researcher's name……………………………………………………………...

Signature………………………………………… Date……………….

Note: All parties signing the Consent Form must date their own signature.


## TO: Participants

**Withdrawal of Consent Form**

*(To be used for participants who wish to withdraw from the project)*

**Date:** 9th February 2017

**Full Project Title:** The effects of hypoxia on muscle growth and inflammatory responses to resistance training.

**Reference Number: 2016-308**

I hereby wish to WITHDRAW my consent to participate in the above research project and understand that such withdrawal WILL NOT jeopardise my relationship with Deakin University or Advance Healthcare.

Participant’s Name (printed)…………………………………… Signature ……………………………………… Date…………