National Institute of Allergy and Infectious Diseases (NIAID)
Division of Allergy, Immunology and Transplantation (DAIT)
Group 3 Donor Consent Template

1. TITLE OF CLINICAL RESEARCH STUDY

Full Title: "**T**reg **A**doptive Therapy in **S**ubclinical Inflammation in **K**idney Transplantation" (TASK)
Protocol Number: CTOT-21
Short Title: Tregs in Subclinical Inflammation

2. YOUR PARTICIPATION IS VOLUNTARY

We will explain this research study to you. You may ask questions.
Research is different from regular medical care. When you receive standard medical care, your physician makes decisions based only on what is in your best interest. When you are in a research protocol, your physician is still bound to act in your best interest, but some medical decisions will be directed by the research study.

- Taking part in this study is your decision.
- You may change your mind about being in this study at any time.
- You will be given a copy of this consent form for your records

3. PRINCIPAL INVESTIGATOR

(Insert site Principal Investigator as well as other investigators if desired.)

4. KEY INFORMATION FOR THE STUDY

This document contains information that will help you decide whether to take part in a research study. We encourage you to read the entire document. All the information is important, but here are some key points to help you understand the study. Additional information is available in the document, in the sections noted in italics, below.

- This research study is for people who received a kidney transplant between 3 and 7 months after transplant, and who recently had a kidney biopsy showing inflammation. *See Section 5, Introduction and Background*
- The study will test whether a new product called donor-reactive T-regulatory cells (DRTregs), given one time through an intravenous line, is safe and will reduce inflammation in the kidney. *See Section 5, Introduction and Background; and Section 6, Purpose of the Study*
- The study asks kidney donors to make 1 to 2 office visits. However, kidney recipients can still be in the study if donors are not able to take part. *See Section 8B, Study Overview/Visit Schedule*
- Kidney donors who choose to be in this study will have:
    - Blood draw
    - Physical examination and interview. *See 7C, Study Procedures*
- The risks of receiving DRTregs are not known because they have only been given to a very small number of people (fewer than 10 people). The reason for giving them is that they might act on the immune system to prevent or decrease damage to the transplanted kidney. However, they might affect the immune system in other ways. For example, the immune system might be less able to fight off infection or cancer. There is also a risk for an immediate bad reaction such as rash, swelling, or breathing problems when the DRTregs product is given.
- There might be no direct medical benefit to you or your kidney recipient for being in this study. The information learned from this study might someday benefit future kidney transplant recipients. *See Section 8, Potential Benefits*

5. INTRODUCTION/BACKGROUND

You are being asked to take part in this study because you donated a kidney to a recipient who may qualify to be in this study. This research study is for people who received a kidney transplant about 3-7 months ago, and who recently had a kidney biopsy showing inflammation. One blood draw is needed from you, the kidney donor in order for the recipient to participate.

Inflammation occurs when the body's defense system recognizes a foreign object (such as a transplanted kidney), and responds by sending white blood cells to attack the foreign object. These cells and the substances they produce can damage the transplanted kidney. *Rejection* is a more severe form of inflammation and injury. Both inflammation and rejection are diagnosed by looking at a piece of kidney (a kidney biopsy) under a microscope. Kidneys that have inflammation and/or rejection do not work as well or last as long as kidneys without injury.

People who have a transplant take immunosuppressive drugs (IS) to prevent inflammation and rejection. Transplant researchers are interested in finding ways to prevent inflammation and rejection without IS, or with lower doses of IS in order to avoid side effects.

While some white blood cells cause inflammation, other types of white blood cells, called T regulatory cells (Tregs), can control inflammation. Tregs may have an important role in controlling or preventing inflammation and rejection. A person's Tregs can be grown in the laboratory to increase their number. These Tregs can be given back through a needle placed in a vein (IV). Researchers can expose a transplant recipient's Tregs to the donor's cells, which results in *Tregs that recognize the donor*. These are called donor reactive Tregs (DRTreg). Both Tregs and DRTreg, when given to the recipient, might reduce inflammation in the transplanted kidney. The DRTregs are thought to be more effective because they might be able to help the body specifically recognize and accept the donated kidney.

One of the IS drugs used in kidney transplant is everolimus. Everolimus has been shown to help Tregs survive better than other types of IS drugs.

6. PURPOSE OF THE STUDY

The purpose of this study is:

- To see if Tregs and/or "donor reactive" DRTregs can lower inflammation in the transplanted kidney.
- To find out what effects, good or bad, Tregs or DR Tregs will have in the kidney recipient.
- To find out what effects, good or bad, taking everolimus after Tregs or DRTregs will have in the kidney recipient.

Kidney transplant recipients who agree to participate in this study will be assigned to one of three groups. Group 1 will receive standard of care IS. This means that Group 1 will receive the same IS drugs that are given to kidney transplant recipients who are not in the study. Group 1 subjects will not receive Treg or DRTregs. Group 2 will receive Tregs, and Group 3 will receive DRTregs. Participants who are assigned to group 2 or 3 will have a kidney biopsy 2 weeks after receiving Tregs or DRTregs. If that biopsy shows inflammation is reduced, their IS drugs will be changed to include everolimus.

You, your recipient, and the study doctor cannot choose which group the recipient will be in. The assignment is made using a computer program and will be based on whether the donor is available and how many people are in the study already.

7. STUDY COMPONENTS

A. Number of Study Sites and Participants

This study is sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). The lead study doctor is Dr. Flavio Vincenti at the University of California, San Francisco. Dr. *<insert site principal investigator name>* is in charge of the study at *<insert institution>*. Up to <*insert expected number for your site*> subjects will be enrolled at <*insert institution*>. We plan to treat 45 kidney transplant recipients in this study at 6 transplant centers in the United States. For the recipients in Group 3 to participate, their kidney donors must be willing to give one blood sample so that we can grow up the recipient's Tregs that react to the kidney donor.

B. Study Procedures

Blood Draw

If the recipient is fully eligible for the study and is assigned to Group 3, you will be asked to have 100ml (just under 7 tablespoons) of blood drawn at the transplant center. Some of the cells in the blood will be removed from the blood specimen to make DRTregs for infusion in your recipient. Some of the cells will be stored for tests to determine if your recipient has a detectible reaction against you, as his / her kidney donor, and if this changes after receiving Treg cells.

At the same study visit, you will have additional blood (1.5 tablespoons, 23 ml) to test for infections that could be transmitted in the cells you donate. This testing is required by law since the cells from your blood will be used to make the Treg infusion to be given to the recipient. The tests will include human immunodeficiency virus, hepatitis B or C virus, syphilis, cytomegalovirus, Epstein Barr Virus, and human T-lymphotropic virus. This is the same type of screening tests that were done prior to the time of kidney donation. You will be informed of your test results. You will be referred back to your primary care giver if any of the tests are positive for infection and need investigation or treatment.

A study team member will review the information in this consent form with you at the transplant center. You will be asked to sign the consent form before your blood is drawn. You will not have blood drawn if the recipient is no longer eligible or willing to be in the study.

Physical Examination

A physical examination, including blood pressure and weight measurements, will be performed at the study visit.

Cell Therapy Donor Interview

Your medical records will be reviewed and you will be asked questions about your medical and social history to make sure you are eligible to donate cells for the manufacturing process. The study investigator or member of the study staff will ask you these questions at the study visit. The types of questions asked will be similar to those answered at the time of donation.

C. Risks and Discomforts

Blood Draw

The risks of blood draws are pain, bruising, infection, redness, and swelling at the sight of needle entry. There is a chance you may feel dizzy while your blood is being drawn.

Confidentiality

- *Infection Screening*

If any of the tests for infections turn out to be positive (not normal), there is a chance your recipient will know. The study team will not share personal information, including specific test results, without your permission. However, the recipient will be informed that he or she is no longer eligible to continue in the study.

- *Genetic Information*

Genetic information will be recorded from the specimen collected for this study. However, the specimen will be used in experiments planned for this study only. Your sample will not be looked at for other genetic conditions, genetic cloning, or paternity testing. However, basic genetic information about you will be known to researchers (e.g. sex, racial or ethnic group). We will keep all information recorded private as much as possible. However, because genetic information is unique to you, complete confidentiality cannot be guaranteed.

8. POTENTIAL BENEFITS

There is no direct medical benefit to you for being in this study. The information learned from this study might someday benefit future kidney transplant recipients.

9. ALTERNATIVES TO PARTICIPATION

Your doctor will talk with you about this study and other options available to you. Your decision to participate in this study will not affect the care the recipient would otherwise receive.

10. NEW FINDINGS

Your doctor will tell you about any new findings from this or other research that may affect your willingness to allow testing and use of your cells for this study. If new information is provided to you, we will ask for your consent to continue in the study.

11. VOLUNTARY WITHDRAWAL FROM STUDY

You will only have one study visit for the blood draw. However, you may decide to withdraw consent for testing and use of your cells at any time during this study. If you decide to withdraw, there is no penalty or loss of benefits in your routine medical care or any other benefit(s) that you or your recipient would otherwise be entitled to receive. Your doctor or research staff will destroy your samples at your request.

12. REASONS WHY YOU MAY BE TAKEN OFF STUDY WITHOUT YOUR CONSENT

You may be removed from the study without your consent at any time. Reasons why you may be removed from the study include, but are not limited to, the following:

- Your study doctor determines that it is in your best interest not to take part.
- You are unable to complete required study procedures.
- The study is stopped by the Institution, the Sponsor, or health authorities.

13. COSTS TO THE SUBJECT (YOU)

There will be no charge to you, your health insurance company, or your recipient's insurance company for any costs which are done specifically for this study.

14. PAYMENTS (REIMBURSEMENT)

You will receive no payment for taking part in this study.

(or)

You will receive $50 for coming into the hospital for a research visit if you travel within 100 miles for a study visit. If your travel distance is up to 300 miles, you will be reimbursed based on the current mileage reimbursement rate. If your travel distance is 300 miles or more, you will be reimbursed for reasonable travel expenses (e.g. hotel, airfare, ground transportation, etc.) based on current government allowances (per diem rates). You will need to give receipts and documentation of mileage to the study coordinator for reimbursement. Government mileage and per diem rates are publicaly available here: https://www.gsa.gov/travel/plan-book/transportation-airfare-rates-pov-rates-etc/privately-owned-vehicle-pov-mileage-reimbursement-rates

(*Payments are pro-rated and not held until completion of the study. If participant payments are tied to completion of specific study benchmarks, these stipulations should be noted in this section as well as other reimbursement specific to the study -i.e. parking, meal tickets, etc.*

15. RESEARCH-RELATED INJURY

<Insert your IRB required language.>

If are hurt or get sick from something that was done as part of this study, doctors at the clinic or hospital can arrange for emergency medical care. The Hospital does not offer financial compensation or payment for injuries due to participation in this research. No funds have been set aside to compensate you in the event of injury. Your insurance company will be billed for the costs of any care for injuries.

In case of injury resulting from this study, you will not lose any legal rights by signing this form.

16. CONFIDENTIALITY

Your medical and research records will be confidential to the extent permitted by law. Efforts will be made to keep personal information private. However, we cannot guarantee complete confidentiality.

As an NIH funded study, you are further protected through a policy that prevents the investigator from disclosing sensitive study information that would lead to your identity. This does not prevent you or a family member from voluntarily releasing information about yourself or your involvement in this research.

Your personal identifiers (for example, name and medical record number) will be used during the manufacturing process for the Treg infusion at the transplant center and at the UCSF laboratory (UCSF Human Islet and Cellular Transplantation Facility) where the Treg infusion is made. Use of the identifiers is required to ensure the cells are tracked accurately through the manufacturing process.

In all other parts of the study, you will be identified by a code, and personal information from your records will not be released without your written permission. You will not be identified in any publication or in the sharing of your data about this study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Organizations that may look at and/or copy your medical records for research, quality assurance and data analysis include:

- the National Institute of Allergy and Infectious Diseases, (NIAID) sponsor of the research
- NIAID representatives, agents, employees, contractors, and other persons assisting in conducting, monitoring or analyzing the study
- the U.S. Food and Drug Administration
- other State and Local health authorities

17. STORING INFORMATION/DATA FOR FUTURE STUDIES

We will store information resulting from this study in a central data repository. Data is information organized for a reason, like this study. A central data repository is a place that collects and stores data from many different studies. The purpose of this collection is to make scientific information available for future studies which may help future patients. Your data may be stored indefinitely. Any information released to a central data repository will not contain traditional information such as name, birthdate, address, etc. that is considered your personal information.

18. PROBLEMS OR QUESTIONS

If you ever have questions about this study or in case of research-related injuries, you should contact Dr. *<Insert name>* at *<Telephone Number>*, or if you have questions about research subjects' rights you can call *<Insert the name and title of the appropriate country/site-specific person>* at *<Insert the number>*, or if you prefer, direct your questions to the following address*: <Insert address of IRB patient representative here>*.

SIGNATURE PAGE

(Site may use the site-specific signature page if required)

Please sign below if you agree to take part in this study.

- *you have read the informed consent and/or had it explained to you*
- *you were given the opportunity to ask questions about the information, and*
- *you voluntarily agree to take part in the study*

_____	_____	_____
Research Subject's Name *(Typed or printed)*	**Research Subject's Signature**	**Date**

Signature of person(s) explaining and obtaining the consent:

_____	_____	_____
Name and Title *(Typed or printed)*	**Signature**	**Date**

_____	_____	_____
Name and Title *(Typed or printed)*	**Signature**	**Date**

(NOTE: This consent form with the original signatures MUST be retained on file by the principal investigator. A copy must be given to the research subject. A copy should be placed in the research subject's medical record, if applicable.)

19. STORAGE OF SAMPLES and/or INFORMATION FOR FUTURE USE

(This consent is optional and agreement is not required for participation in the study)

We are asking your permission to store samples of biological specimens (e.g., cells) collected for this study to be used in the future for tests that are not yet planned. These tests may or may not be related to the study of transplantation.

Some information about a research specimen will always be linked to it (also see section 6c, Genetic Information). For example, researchers might know a sample is from a kidney transplant recipient. Because of this, allowing for specimens to be stored for future use also means allowing for the linked information to be stored and used when the specimens are needed.

Genetic Testing on Stored Samples

Your samples may be used to look at genetic information in relation to kidney transplantation (for example, the rejection process). However, your samples could also be used in studies that are not related to transplantation (for example, the immune system as a whole).

Confidentiality

All samples will be labeled with a randomly assigned unique barcode. They will not contain personal information like name, initials, or date of birth. Reports on these stored samples and genetic tests will not be given to your study doctor and they will not be in your medical record. Doctors will not know that your samples are being used for other studies and it will not affect your routine medical care.

Benefits of Stored Material and Genetic Testing

There is no benefit to you from the storage of samples and information. However, the use of your samples and information may help researchers learn more about your disease or the genetics related to a specific condition.

Samples will be stored at the core laboratories involved in this trial. If you agree, your samples and information may be stored for an unknown length of time.

Risks of Stored Material and Genetic Testing

Although your stored research samples will not be sold, the information obtained from the research performed on your samples may in the future lead to the development of commercial products. You will not receive any money from research using your stored samples and information

There may be unknown risks associated with the storage of samples and information. For example, if the future research involves genetic testing it is possible that it could be traced back to you because your genes are specific to you. We will make every attempt to protect your confidentiality and to make sure that your personal identity does not become known.

Making a Decision for Stored Human Subject Material and Genetic Testing

Your decision regarding the storage of samples or the information resulting from the analysis of your samples will not affect your ability to participate in this study.

Please indicate your response below:

Choose yes or no to allow the storage and sharing of your sample (cells) and information for genetic tests.

☐ Yes ☐ No

_____
Initials of Research Subject

Choose yes or no to allow the storage and sharing for future use of remaining sample (cells) and information for other research tests not currently planned (not genetic).

☐ Yes ☐ No

_____
Initials of Research Subject