THE STATE UNIVERSITY OF NEW JERSEY
RUTGERS

SUBJECT CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: Using Maackia amurensis seed lectin to target the podoplanin receptor as a functionally relevant biomarker to inhibit the growth of oral squamous cell carcinoma and precancerous lesions

Principal Investigator: Dr. Mahnaz Fatahzadeh, DMD, MSD
Professor, Rutgers School of Dental Medicine

This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the Study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Who is conducting this research study?

Dr. Mahnaz Fatahzadeh is the Principal Investigator (PI) of this research study. A Principal Investigator has the overall responsibility for the conduct of the study. However, there are often other individuals who are part of the research team.

Dr. Fatahzadeh may be reached at: 110 Bergen Street, Room D-885B , Newark NJ 07103.Phone: 973-972-1956.

The study doctor Mahnaz Fatahzadeh or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

SPONSOR OF THE STUDY: Rowan University.

Who might benefit financially from this research?

This research is designed to test a product invented by Dr. Gary Goldberg, one of the researchers in this study, and licensed to Sentrimed. Dr. Goldberg and Rowan University have an investment in Sentrimed, such as stock. The financial value of this investment might be affected by the results of this study. This means that Dr. Goldberg and Rowan University could gain or lose money depending on the results of this study.

Why is this study being done?

This study is being done to develop ways to prevent and combat oral cancer. Oral cancer is currently treated with surgery, radio/chemotherapy. Effective treatment with new drugs would be a welcome addition to available treatment options. Oral cancer cells have been shown to make a protein called "podoplanin" (PDPN). We will examine the ability of a compound called “Maackia amurensis seed lectin” (MASL) to reduce the amount of PDPN protein and inhibit the growth of cancerous and precancerous oral cells.

Why have you been asked to take part in this study?

You have been asked to take part in this study to test the effectiveness of an experimental drug known as MASL, compared to placebo on oral cancer cells. MASL is an experimental drug. This means that it has not been approved by the United States Food and Drug Administration (FDA) for the treatment of oral cancer. A placebo is a tablet, capsule or liquid that looks like the active medication but contains no active ingredients.

Who may take part in this study? And who may not?

Any patient over 18 years of age with potentially precancerous or cancerous oral mucosal abnormality who is able to provide informed consent may be asked to participate in this study.

Inclusion criteria:
1.) Males and females of at least 18 years of age who are able to give consent.
2.) Smokers and non-smokers
3.) Persons with white or red spots and/or lesions suspected or found to be oral cancer or precancer on the inner surface of the mouth.

Exclusion criteria:
1.) Patients with cognitive impairments and cannot consent for themselves.
2.) Patients with language/hearing impairments
3.) Use of a topical steroid product within the last 2 weeks.
4.) Women who are pregnant or may get pregnant during the study period (to be determined by consultation with a study physician and standard pregnancy test).
5.) Women who are breastfeeding.
6.) Men and women of reproductive potential who do not abstain or use adequate contraception during the treatment phase as explained by the study clinician

How long will the study take and how many subjects will participate?

There will be a total of 50 patients recruited for this study. If you choose to participate in this study, your participation will last approximately 2 to 6 months. However, the study may continue up to 36 months to perform laboratory experiments on your sample(s) after your participation.

What will you be asked to do if you take part in this research study?

Your lesions will be removed or biopsied by your physician and examined as necessary for your care. However, as a participant in this study, your sample will also be analyzed by the University researchers who will stain cells and grow cells from your samples to determine the content of PDPN protein in samples, the appearance of cells, and find out if these cells are sensitive to the study drug MASL. If you were referred to Rutgers or University Hospital for continuing care based on a biopsy performed elsewhere, we will request your specimen from the outside laboratory for review and PDPN staining as part of this research. Relevant personal or clinical data such as name, date of birth, contact information, and diagnosis will be obtained from you or your medical records.

You may continue participation in this study if cells grown from your samples contain large amounts of PDPN protein and you meet eligibility criteria for treatment phase..

There are two groups in this part of the study:

1) The group receiving the study drug MASL
2) The group receiving the placebo (without MASL)

You have a 50:50 chance to be randomly assigned to either group. Then, you will be asked by your physician to dissolve two small 50 mg lozenges (that will have a 50:50 chance of containing MASL or the placebo) in your mouth. You will be asked to dissolve the lozenge in your mouth for at least 5 minutes before being chewed, and refrain from spitting, eating, or drinking for at least 20 minutes after lozenge administration. You will be asked to finish chewing the lozenge within 20 minutes. Another physician will also attend the administration to assist with the evaluation of your health and response to this treatment and manage any unforeseen problems. . You may, then, undergo additional biopsies or resections as planned by your medical team if medically necessary (irrespective of your participation in this study). In other words, participation in this study will not influence your best care procedures.

The University researchers will then analyze these samples to evaluate the effects of administered study drug or placebo on the appearance of the cells and the content of PDPN protein to determine if the study drug or placebo had any effect on your tissue (lowering the content of PDPN protein and preventing growth of premalignant or malignant cells). In all cases, you will receive the best care as guided by your physicians.

What are the risks and/or discomforts you might experience if you take part in this study?

Although MASL has been used as a component in traditional medicine for many centuries without reported side effects, its safety has not been evaluated by the FDA. Therefore, unknown medical risks may be associated with the oral administration of MASL. As with any treatment, it is important that you tell your study doctor or staff about all side effects or changes in your normal health that you feel, even if you do not think that they are important or related to the study. Risk of disclosure of your personal data (name, age, gender, tumor grade, etc.) is minimal. Your samples are assigned an ID number and all private information (patient identifiers) are locked in the PI's office in a password protected computer for the duration of study. This personal information will be destroyed after the study analysis is completed.

You should not take any over-the-counter medicines, herbal products, vitamins or food supplements while taking part in the treatment phase of this study, unless you tell the study doctor and get permission from the study doctor to go on taking these medicines. You will follow the instructions of the study doctor about the use of any of these products.

You should also tell the study doctor about all medicines that other doctors may have prescribed for you to take. Your enrollment into this clinical trial might exclude you from enrolling in other clinical trials.

Reproductive risks of harm?

As a male or female participant in this study, you should abstain or use adequate contraception during the treatment phase as explained to you by the study clinician since the risks to you or to the fetus are not known. As a female participant in this study, if you become pregnant during the course of this study, you should notify the study doctor of this fact as soon as possible, since the risks to your unborn child or to yourself are unknown.

Are there any benefits for you if you choose to take part in this research study?

It is unknown whether you will personally benefit from this study and the study drugs. Your participation in this study and the study drugs given to you in the study may or may not directly benefit you. Information from this study may help the sponsor and study doctors learn things about the study drug that will help others. It is possible that you might receive no direct personal benefit from taking part in this study.

What are your alternatives if you don't want to take part in this study?

There are no alternative treatments available. Your alternative is not to take part in this study. If you do not wish to participate in this research study, you will receive treatment according to the standard practice. Your care will not suffer if you decide not to participate in the study.

How will you know if new information is learned that may affect whether you are willing to stay in this research study?

During the course of the study, you will be updated about any new information that may affect whether you are willing to continue taking part in the study. If new information is learned that may affect you after the study or your follow-up is completed, you will be contacted.

Will there be any cost to you to take part in this study?

There will be no cost to you for your participation in this study. Study drug will be provided without charge. The cost of your clinical care is not part of this project. All study procedures are performed at no cost to you.

Will you be paid to take part in this study?

You will not be paid for your participation in this research study.

How will information about you be kept private or confidential?

All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed.

Your personal information may be given out if required by law. If your oral abnormality is found to be cancerous or precancerous, a hard copy of the clinical component of the biopsy requisition form and the histopathology report for your oral abnormality (obtained from your medical record) along with other relevant clinical and personal information will be kept as part of the study records in a locked cabinet in the project PIs office (Dr. Fatahzadeh's office in Newark, NJ and Dr. Goldberg's office in Stratford, NJ). Only the study doctors and other members of the research team will have access to the research files.

A description of this clinical trial will be available on 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 website at any time.

What will happen if you are injured during this study?

Subjects in this study may be exposed to certain risks of personal injury such as potential allergic reactions to MASL. In addition, it is possible that during the course of this study, new adverse effects of MASL that result in personal injury may be discovered. Rutgers University will make appropriate referrals for treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?

Participation in this study is voluntary. You may choose not to participate or you may change your mind at any time.

If you do not want to enter the study or decide to stop participating, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled. You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to:

Dr. Mahnaz Fatahzadeh, 110 Bergen Street, Room D-885B, Newark NJ 07103

However, any samples or data that has already been sent to the research laboratory cannot be withdrawn. If you decide to withdraw from the study for any reason, you may be asked to return for at least one additional visit for safety reasons.

Who can you call if you have any questions?

If you have any questions about taking part in this study or if you feel you may have suffered a research related injury, you can call the study doctor:

Dr. Mahnaz Fatahzadeh
110 Bergen Street
Room D-885B
Newark NJ 07103
973-972-1956
If you have any questions about your rights as a research subject, you can call:

IRB Director
(973) 972-3608
Human Subject Protection Program
973-972-1149

What are your rights if you decide to take part in this research study?

You have the right to ask questions about any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

PERMISSION (Authorization) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

Information about you and your health is personal and private, so this information generally cannot be used in research without your written permission. The next few paragraphs tell you about how researchers want to use and share your health information in this research study. Your information will only be used as described here or as allowed or required by law. Ask questions if you do not understand any part of the research or the use of your health information. If you sign this consent form, you agree to let the researchers use your information in the research and share it with others as described below.

What is the purpose of the research and how will my information be used?

You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help researchers answer the questions that are being asked in the research.

This study is being done to develop ways to prevent and combat oral cancer. Oral cancer is currently treated with chemotherapy, radiation and surgery. Effective treatment with new drugs would be a welcome addition to the available treatment options. Oral cancer cells have been shown

to make a protein called "podoplanin" (PDPN). We will examine the ability of a compound called "MASL" to lower the content of PDPN protein and to inhibit the growth of oral cancer cells. The clinical information recorded on the biopsy requisition form and the biopsy report will also be included in the research data linked to your samples used in the laboratory research.

What information about me will be used?

Each patient is assigned an ID number which is used to link clinical and laboratory data. The individual's health information will not be used in this study, including any publication; however, the patient's personal identifiers (name, date of birth, etc.) are kept on file until the study closure. This time is needed to complete laboratory experiments on the collected samples and allows tracing and re-examination of the histological slides should any question regarding diagnosis arises.

Who may use, share or receive my information?

The research team may use or share your information collected or created for this study with the following people and institutions:

- Rutgers University researchers involved in the study;
- Non-Rutgers researchers on the study team: School of Osteopathic Medicine at Rowan University, 2 Medical Center Dr., Stratford, NJ 08084.
- The Rutgers University Institutional Review Board and Compliance Boards
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services
- The United States Food and Drug Administration

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I be able to review my research record while the research is ongoing?

No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I have to give my permission?

No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this research study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I say yes now, can I change my mind and take away my permission later?

Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher and tell him or her of your decision:

Dr. Mahnaz Fatahzadeh
110 Bergen Street
Room D-885B
Newark NJ 07103
973-972-1956

How long will my permission last?
There is no set date when your permission will end. Your health information may be studied for many years.

AGREEMENT TO PARTICIPATE

1. Subject consent:

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

Subject Name:_____

Subject Signature:_____ Date:_____

2. Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject and those of his/her parent or legally authorized representative have been accurately answered.

Investigator/Person Obtaining Consent (printed name):_____

Signature:_____ Date: _____

CONSENT ADDENDUM: REQUEST TO STORE TISSUE AND HEALTH INFORMATION FOR FUTURE RESEARCH

We ask your permission to store some of your tissue [a portion of the biopsy sample or excised tumor] and health information collected about you during the main study [Using Maackia amurensis seed lectin to target the podoplanin receptor as a functionally relevant biomarker to inhibit the growth of oral squamous cell carcinoma and precancerous lesions] for future research. Following are details about our request. Please know that you may still participate in the main study even if you say no to this request to store tissue for future research.

The purpose of the repository is to collect/store tissue samples and health information to be used for future research to be conducted by Dr. Goldberg and his research staff at Rowan University. Rowan University may retain, preserve, or dispose of these samples, and may use these samples and material derived from these samples in research which could result in grant applications or commercial applications.

Samples obtained from the main study may be tested immediately or may be frozen and examined later. Samples may be utilized in experiments designed to find better ways to detect, treat, and understand cancer. Some cells obtained from your body may be used to establish cell lines that may be shared in the future with other researchers. A cell line is a group of cells that will grow continuously in the laboratory. Cell lines may be useful because of special actions of the cells and/or the products they may produce. Most importantly, these samples will enable the study group to evaluate your tissues before and after administration of the study agent to determine its effect on cancer cells.

What are the risks of harm to you?

While the data developed for the main study will be coded to protect your personal information, people may develop ways in the future that would allow someone to link your medical information back to you. It is also possible that there could be violations to the security of the computer systems.

What are the benefits of participation?

You will not benefit personally from providing a sample and information for this tissue bank because research usually takes a long time to produce meaningful results. However, your participation may help investigators understand, prevent, or treat the diseases and conditions studied in the future.

How will information about you and your tissue samples be kept private and confidential?

Clinical information recorded on the biopsy requisition form and the biopsy report will be included in the research data linked to the specimen used in laboratory research. Each patient is assigned an ID number which is used to link clinical and laboratory data. Your personal information will not be used in the main study, future studies, or publications.

However, the patient's name, date of birth, gender and address on the biopsy report will be kept on file to allow tracing and re-examination of the histological slides should any question regarding diagnosis arise. Records with patient's name and birth date will be destroyed 6 years after the completion of the main study to affirm future privacy.

Is there other important information to consider?

Yes. There is no cost to you to allow us to store and use your tissue and information for future research. Nor will you be paid to participate in this repository. Should any products or services result from research using your samples and information, there is no plan to share any of the profits with you.

What are your rights if you agree to the storage and use of your tissue for future research?

You have the right to ask questions about any part of our storage and future research at any time. You should not sign this form unless you have a chance to ask questions and have been given answers to all of your questions. Your participation in the tissue bank is voluntary. You do not have to participate. If you do, you can change your mind at any time.

What are the procedures for withdrawing consent?

You may also ask to withdraw your consent for the use of specimens already collected about you, but you must do this in writing to:

Dr. Gary S Goldberg, PhD.
Associate Professor
Department of Molecular Biology
Rowan University School of Osteopathic Medicine
Science Center
2 Medical Center Drive
Stratford, NJ 08084

You can ask Dr. Goldberg to destroy any remaining tissue samples and data of yours that are currently being stored in his laboratory. You may also ask him to destroy any personal and private health information that you provided, along with the code linking you to the information you provided.

However, please note that it may not be possible to destroy samples, information, and data created from your samples that may have already been used or are in the process of being used in this research study, other research studies, or future research studies prior to your request.

Dr. Goldberg will keep records linking your identity with the sample for a period of 6 years from the end of the study. Until those records are destroyed, you may ask that your samples and materials obtained from your samples be destroyed.

Permission to Store Tissue and Health Information for Future Research Use:

Please tell us if and how you wish your samples and information to be used for future research.

Initial next to ways you permit your samples and information to be used.

Leave this section blank if you do not want your samples or information used for future research.

My samples and information may be stored and used for future research as follows:

_____ on any research topic important to researchers

OR

Only my samples and information but not identifiers (data that can identify who I am) may be stored and used for future research as follows:

_____ on any research topic important to researchers