Study Title: IFI16 is a Periodontitis Modulating Protein

NCT03513497

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: September 27, 2022
IRB Study # 18-0291
Title of Study: IFI16 is a periodontitis modulating protein
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What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.
You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?
The purpose of this research study is to evaluate how two specific proteins affect the mouth when inflammation is present. Understanding the expression of the proteins in the mouth will help us understand the underlying causes of periodontal disease (infections and inflammation of the gums and bone that surround and support the teeth). Ultimately, this discovery may lead to new and improved ways to diagnose and treat periodontal disease in the future.

Are there any reasons you should not be in this study?
You should not be in this study if the following apply to you:

1) You are less than 18 years of age.
2) You have fewer than 20 remaining teeth.
3) You are diabetic.
4) You have a known medical condition or take a medication (Phenytoin, calcium channel blockers, cyclosporine, Coumadin, non-steroidal anti-inflammatory drugs, Aspirin) that affects your mouth.
5) You have been treated with antibiotics within the past month.
6) You have started a new medication within the past three months.
7) You have any significant medical conditions such as kidney disease, hepatitis, HIV (AIDS), tuberculosis, any type of bleeding disorder, heart murmur, history of rheumatic fever or heart valve disease, or require prophylactic antibiotics prior to dental treatment.
8) You are a current smoker or stopped smoking less than 2 years ago.
9) You are pregnant or expect to become pregnant within the next several months.
10) You have severe unrestored cavities, or any condition in your mouth that is likely to require antibiotic treatment

How many people will take part in this study?
There will be approximately 72 people in this research study, with the goal of identifying subjects as either periodontally healthy or having periodontal disease, according to a unique classification system.

How long will your part in this study last?
Your participation in this research study will last up to 56 days and include 6 visits (with the possibility of 2 additional visits). Each visit will last between 1 to 3 hours.

What will happen if you take part in the study?

Visit 1: Screening/enrollment

- You will be given the opportunity to ask and have answered questions you have about this research. Once the study personnel have assured that you understand the implications of participating in the study, you will be asked to give consent to participate. Study personnel will provide copies of the signed informed consent forms.
- Study personnel will obtain your medical and dental history.
- Study personnel will record your race, gender, height, weight, blood pressure and pulse. *(If your blood pressure is 180/110 mmHg or higher, you will not be allowed to continue with study procedures until your blood pressure drops below this threshold or until medical clearance from your doctor has been provided to the research staff. All subjects*

that present to any study visit with an elevated blood pressure greater than 150/90 mmHg will be instructed to see his/her doctor.)

- Female participants capable of childbearing will be given a urine based pregnancy test (free of charge).
- A dental examiner (trained dentist or dental hygienist) will perform a dental examination using standard dental instruments. This examination is similar to those done in a typical dental office.
- Subjects categorized as healthy (PPC-A, PPC-B) or with severe disease (PPC-G, PPC-E), using a unique dental classification system will be considered eligible for the study.
- If you meet eligibility criteria to participate you will be invited to participate in the remaining visits of the research study. If determined non-eligible, you will be considered a screening failure, and no further study procedures or visits will be completed.
- If you meet eligibility, an area between your back teeth (also known as the interproximal region) will be selected for one gingival tissue biopsy to be completed at Visit 2.
- Study personnel will use standard dental materials to take impressions of your top teeth on one side of your mouth. This impression will be used to construct a model of your teeth and an acrylic stent (mouth guard) that you will wear only during tooth bushing, while enrolled in this research study.

Visit 2: Baseline

- Study personnel will record any changes to your medical history or medications.
- Study personnel will record your vital signs (blood pressure and pulse).
- A dental examiner will do an oral exam to verify you have had no changes in oral health.
- A dental examiner will perform a comprehensive periodontal screening examination that includes Plaque Index (PI), Gingival Index (GI), Pocket Depth (PD), Bleeding on Probing (BOP) and Clinical Attachment Levels (CAL).
- A small gingival (gum) biopsy will be taken. The biopsy procedure will include removing 2 two 4x4 mm (slightly smaller than a green pea) gum samples between two areas in the back of your mouth. Biopsies will be performed by a licensed periodontist using local anesthesia and dissolvable stiches.
- Study personnel will review oral hygiene and/or post-operative instructions with each subject, including:
    - No rinsing or spitting for 24 hours
    - Using ice packs on surgical area (side of face) for the first 24 hours
    - Using warm saltwater rinse and/or prescribed antibacterial rinse (Perioguard)
    - Eating a soft food diet and avoiding hard, sticky foods for one week
    - Avoiding warm liquids for 24 hours
- A dental examiner will collect two sub-gingival (underneath the gum) plaque samples in the same area that the gingival (gum) biopsy was completed. This will be completed by

using a standard dental instrument like your dentist or hygienist would use while cleaning your teeth.
    - Any remaining plaque samples not used in this study will be stored in an approved biorepository (storage space) for future unspecified use, with your consent. If you agree, you will be required to complete an additional consent form.
- The dental examiner will deliver 1 customized acrylic stent (tooth cover) that will be used in an area of your mouth different from where the gingival (gum) biopsy was performed. The stent is to be worn for 21 days **only** while brushing. Study personnel will review the following:
    - You will be monitored for safety every week while wearing the stent. Any site undergoing a Clinical Attachment Loss (CAL) increase of greater than 2 mm from the baseline measurement will be deemed as "progressing" and you will be exited from the study and given scaling and root planning treatment (deep cleaning) as a rescue therapy.
    - You will be instructed to not floss or use mouth rinses while using the stent.
    - You will continue to use your standard toothpaste and toothbrush.
    - You will be informed to avoid crunchy (ie: apples, carrots) or sticky (ie: gum) foods

Visit 3

- Study personnel will record changes to your medical history or medications.
- Your vital signs (blood pressure and pulse) will be recorded.
- A dental examiner will perform a comprehensive periodontal screening examination that includes Plaque Index (PI), Gingival Index (GI), Pocket Depth (PD), Bleeding on Probing (BOP) and Clinical Attachment Levels (CAL).
- A follow-up, verifying the healing of the gingival biopsy, will be done.
- Study personnel will go over oral hygiene instructions while wearing the stent.
- Adverse events will be monitored and recorded as necessary.

Visit 4

- Study personnel will record changes in your medical history or medications.
- Your vital signs (blood pressure and pulse) will be recorded.
- A dental examiner will perform a comprehensive periodontal screening examination that includes Plaque Index (PI), Gingival Index (GI), Pocket Depth (PD), Bleeding on Probing (BOP) and Clinical Attachment Levels (CAL).
- Study personnel will go over oral hygiene instructions while wearing the stent.
- Adverse events will be monitored and recorded as necessary.

Visit 5

- Study personnel will record changes in your medical history or medications.
- Your vital signs (blood pressure and pulse) will be recorded.
- You will return your acrylic stent.
- A dental examiner will perform a comprehensive periodontal screening examination that includes Plaque Index (PI), Gingival Index (GI), Pocket Depth (PD), Bleeding on Probing (BOP) and Clinical Attachment Levels (CAL).
- A small gingival (gum) biopsy will be taken. The biopsy procedure will include removing 2 two 4x4 mm (slightly smaller than a green pea) gum samples between two areas in the back of your mouth. Biopsies will be performed by a licensed dentist using local anesthesia and dissolvable stiches.
- Study personnel will review oral hygiene and/or post-operative instructions with each subject, including:
    - No rinsing or spitting for 24 hours
    - Using ice packs on surgical area (side of face) for the first 24 hours
    - Using warm saltwater rinse and/or prescribed antibacterial rinse (Perioguard)
    - Eating a soft food diet and avoiding hard, sticky foods for one week
    - Avoiding warm liquids for 24 hours.
- A dental examiner will collect two sub-gingival (underneath the gum) plaque samples using a standard dental instrument like your dentist or hygienist would use while cleaning your teeth.
- Scaling Root Planning (deep cleaning) may be started at this visit if you are in the periodontal disease group. If so, this will include the section of the mouth that is already numb due to the anesthesia used for the gingival biopsy procedure.
- You will be instructed to resume brushing all teeth. The use of mouth rinses and floss is still discouraged until told otherwise.
- Adverse events will be monitored and recorded as necessary.

Visit 6: Final Visit

- Study personnel will record changes in your medical history or medications.
- Your vital signs (blood pressure and pulse) will be recorded.
- A dental examiner will perform a comprehensive periodontal screening examination that includes Plaque Index (PI), Gingival Index (GI), Pocket Depth (PD), Bleeding on Probing (BOP) and Clinical Attachment Levels (CAL).
- A follow-up for verifying the healing of the gingival biopsy from visit 5 will be completed.
- You will receive an adult prophylaxis (dental cleaning) if you were assigned to the healthy group, **or** continuation with deep cleaning (Scaling and Root Planing).
    - Scaling and Root Planing **may involve up to 2 additional visits (visits 7 and 8)** that must be completed within 4 weeks of visit 6.
- Adverse events will be monitored and recorded as necessary.

What are the possible benefits from being in this study?
Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?

- Your gums may be uncomfortable during the routine probing exams and during and after the dental cleaning. Jaw soreness may occur following any appointments due to opening your mouth during the procedure.
- You may experience short-term gingival inflammation, halitosis or bad mouth taste, dental plaque accumulation, and bleeding of the gums from refraining from all oral hygiene procedures (i.e., tooth brushing, flossing or use of interdental aids and/or mouthwashes) in the one selected area (up to 3 teeth) for 21 days. You may continue plaque control procedures for the remaining three areas of your mouth using toothpaste with fluoride and a toothbrush. At the completion of the study, adult prophylaxis or scaling and root planing will be completed to restore gingival health eliminating gingival bleeding, dental plaque accumulation, and halitosis.
- You may experience minor pain, discomfort and bleeding during the dental exam, dental cleaning and administration of local anesthetic (numbing medicine). Upon your request a topical anesthesia can be used to reduce gum tissue sensitivity and discomfort during the dental cleaning.
- It is rare but possible to experience a reaction to the numbing medications used during the dental cleaning and biopsy procedures. Theses reactions include
- light headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, feeling of ringing in the ears, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, seizures, feeling faint, unconsciousness, slowed breathing and cardiac arrest. The numbing medications used in this study are the same medications used by licensed dentists in most modern dental clinics and practices.
- You may experience tenderness, sensitivity to hot or cold, slight bleeding or oozing, or development of a transient or permanent temporomandibular joint disorder after the dental cleaning. Some gingival recession or loss of papillae (gum tissue that fills the space between the teeth) height may occur. Subjects receiving a deeper cleaning (scaling and root planning) will be encouraged to use over the counter analgesics, according to the subject's medication tolerance, to control any post-operative pain
- There may be uncommon or previously unknown risks. You should report any problems to the researcher.
- Pregnancy tests (at no expense to you) will be done on all females who might be able to get pregnant at the start of the study.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?
For this study, your privacy and confidentiality will be protected. You will be identified with a unique number (not by name, initials or social security number) in study documents that may be linked to your dental/medical record via code. Only the listed study investigators will know how your study documents are linked to your dental/medical record. Your study records will be secured in a locked area to which only the study investigators have access.

You will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

A copy of this consent form will go into your medical record. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study.

What is a Certificate of Confidentiality?
To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project in the event of suspicion of intent to hurt yourself or others.

Will you receive results from research involving your specimens?
Most research with your specimens is not expected to yield new information that would be meaningful to share with you personally. There are no plans to re-contact you or other subjects with information about research results.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. Despite all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped. . If you decided to stop your participation in the study after visit 3, you will be offered the opportunity to receive a free dental cleaning similar to the participants completing the study.

Will you receive anything for being in this study?

- If you complete visit 1 at UNC to determine eligibility you will receive free parking vouchers for the UNC Dogwood parking deck. (If you complete visit 1 at the VIDAS or at North Carolina Implants & Periodontics you will not receive parking vouchers as parking is free at these facilities). There is no other compensation to complete this visit.
- If you complete visit 2 (includes dental exams and a gum biopsy) you will receive $75 Visa gift card.
- If you complete visit 3 you will received $25 Visa gift card.
- If you complete visit 4 you will received $25 Visa gift card.
- If you complete visit 5 (includes dental exams and a gum biopsy) you will receive $75 Visa gift card.
- If you complete visit 6 you will receive either a free adult prophylaxis (cleaning) or start the process of free SRP (deep cleaning). This dental treatment is determined by your dental health and individual need for care. If you need/receive the deep cleaning, your treatment may be started following your visit 5 study visit. ***Please note that the deep cleaning may take up to a total of 4 visit (1 SRP per quadrant) for your care to be completed.***

You will receive free parking vouchers for the UNC Dogwood parking deck for each study visit that you complete at UNC. No parking vouchers will be given if you are seen at the VIDAS Clinic in Siler City or the North Carolina Implants & Periodontics in Raleigh as these facilities have free parking.

Will it cost you anything to be in this study?

You will be responsible for your transportation to and from scheduled visits for this study.

What if you are a UNC student?
You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your university duties and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study?
This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____
Signature of Research Participant Date

_____
Printed Name of Research Participant

_____ _____
Signature of Research Team Member Obtaining Consent Date

_____
Printed Name of Research Team Member Obtaining Consent