PI: Gil Yosipovitch
IRB Study Number: 20200857
NCT04717466
Version 9, Date: 21Mar2024

1) Protocol Title

Brain morphological changes accompanied by effective biologic treatments for psoriasis and their associations with the improvement of well-being, itch, and pain

2) IRB Review History*

N/A

3) Objectives*

The purpose of this study is to assess the effect of a biologic drug targeting the IL-17 pathway (secukinumab) on brain plasticity and examine whether the plastic changes correlate with the improvement of perception of well-being, itch, and pain in patients with psoriasis.

4) Background*

Psoriasis is a chronic skin inflammatory disease, affecting 2 % of people in the US. Following Interleukin-17 (IL-17) neutralization, patients with psoriasis experience rapid changes in their well-being and mood. Though IL-17 neutralization-induced improvement in plaques and Psoriasis Area and Severity Index (PASI) score takes weeks, patients often state they feel significantly less pain and itch, and note improved mood after only one injection (Yosipovitch et al., 2019). It is currently unknown how IL-17 neutralization affects the improved perceptions of patients with psoriasis so rapidly as the drug does not cross the blood–brain barrier. Previous drug trials using DMARDS and TNF inhibitors for psoriatic and inflammatory joint disease have shown neuroplastic changes in the brain (Baliki et al. 2005, Harvey et al. 2012). The potent new generation of biologic drugs targeting IL-17 have more robust and rapid effect on psoriasis than the drugs mentioned above (Yosipovitch et al., 2019). Therefore, assessing the effect of these drugs on brain plasticity and correlating it to the improvement of itch, pain and perception of well-being is a timely topic to investigate.

The aim of this study is to elucidate brain mechanisms associated with perceptions of well-being and improvements in itch and/or pain after use of a potent effective treatment for psoriasis using IL-17 neutralization.

5) Inclusion and Exclusion Criteria*

Inclusion:

1) Between 18 and 65 years of age.
2) Psoriasis patients (with/without psoriatic arthritis): Psoriasis Area (BSA) is more than 5%.

3) Psoriasis patietns must have had a TB test in the past 8 months (if a patient has not had one, the study will provide one).
4) Healthy subjects: in general, good health without history of neurological and psychiatric diseases. No chronic itch, pain, skin or systemic conditions currently or in the past.
5) Women of child bearing potential will be administered a pregnancy test to verify that they are not pregnant.
6) MRI Compatibility: No major contraindication for MRI (pacemaker, vascular stents, metallic ear tubes, and absence of metal implants or braces) as assessed by MRI technologist using site approved screening form.
7) Participants have to be able to speak and read English fluently.
8) Participants must have signed a written informed consent before being enrolled in the study

Exclusion:

1) Individuals under 18 or over 65 years of age.
2) Inability to complete the required measures.
3) Participants who use antihistamine drugs for itch relief
4) Suffering from any disease state or physical condition, which would increase their health risk by study participation.
5) Patients with chronic infectious diseases (e.g., mycobacterial and fungal infections and chronic tuberculosis) or inflammatory bowel disease.
6) Patients without a negative TB test in the past 12 months.
7) Hypersensitivity or anaphylaxis to biologics
8) Patients with treatment of biologics should not receive live vaccines. Thus, age appropriate immunizations according to current immunization guidelines must be completed before the experiment.
9) Patients with primary immunodeficiet lacking IL-17, patinets with autoantibiobodies against IL-17
10) Currently enrolled in any investigational study in which the subject is receiving any type of drug, biological, or non-drug therapy.
11) Recent initiation (within last 3 months) or change in dose of centrally acting agents such as antidepressants, neuroleptics or neuropathic medications.
12) Patients who were previously treated with drugs targeting IL-17
13) Patients who have used biologics in the past in the past 8 weeks or Otezla in the past 4 weeks.

14) Patients who use centrally acting agents only when they need. The purpose is to avoid a risk of acute effect of these agents on brain activity.
15) Current treatment with opioid analgesics.
16) Uncontrolled thyroid disease.
17) Use of illicit drugs or history of opiate addiction.
18) Diagnosis of a major psychiatric disorder such as schizophrenia, major depression or bipolar disorder that is active currently.
19) Morbid obesity
20) Weight: 250 lb or more
21) Any known diseases or disorders that may affect conducting the experiments (e.g., intracranial pathology, claustrophobia, severe respiratory or cardiovascular problems, active fibromyalgia) or diseases that have potential risks of infections (e.g., HIV, Hepatitis C, etc).
22) Inability to speak and read English.
23) Pregnant.
24) Incarcerated.

6) Number of Subjects*

This is an exploratory study to elucidate brain mechanisms associated with perceptions of well-being and improvements in itch and/or pain after use of a potent effective treatment for psoriasis using IL-17 neutralization. We will enroll 15 psoriasis patients and 15 healthy subjects with an approximately equal gender distribution, in order for 10 psoriasis patients and 10 healthy subjects to complete the study.

Psoriasis patients will be recruited from the Department of Dermatology Clinics. An approximately equal number of men and women between 18 and 65 years of age will be recruited using IRB-approved advertising. All participants will be required to consent and to fulfill the inclusion and exclusion criteria. Healthy subjects (similar age and gender ratio to the patient group) will be recruited through IRB-approved advertisement. UM students or employees may be enrolled in this study as long as they fulfill the inclusion and exclusion criteria.

7) Recruitment Methods*

Patients seen for their routine care at the Dermatology Outpatient Clinics at the University of Miami Hospital, South Miami satellite site, and Lennar Medical Foundation satellite site will be identified for possible study eligibility by any of the dermatologists in our practice. If the treating dermatologist is a study team member, they will ask the potential subject if they would be interested in being contacted by the study team to learn

more about a research study on chronic itch. A partial HIPAA waiver is needed, so that if the patient gives permission to be contacted, they will then be approached by a member of the study team while they are in clinic or if that is not feasible then the treating dermatologist will ask if the patient would like to be contacted by telephone. If the treating dermatologist is not a study team member, they will ask the potential subject to contact the study team for more information by providing the study team's contact information and/or the study flyer. If it is then determined that they are interested in participating, they will be scheduled for a visit at our research site where informed consent and all other study procedures will take place. The risks/benefits of the study will be presented to the subjects, as well as the disclaimer that refusal to participate in the study will in no way, shape, or form alter the type or quality of their care.

Patients with the diagnosis of psoriasis who sign the University of Miami's Consent to Contact consent during their routine medical care will be identified using research IT and URIDE. Each of those individuals will then be contacted by phone by a study team member and asked if they would be interested in learning more about a research study for psoriasis (see phone script). If they are interested in participating, they will be scheduled for a visit at our dermatology clinical research site where informed consent and all other study procedures will take place. The risks/benefits of the study will be presented to the subjects, as well as the disclaimer that refusal to participate in the study will in no way, shape, or form alter the type or quality of their care.

Furthermore, using the approved flyer, we will announce this study on the Facebook page of the University of Miami Department of Dermatology and Cutaneous Surgery to recruit patients and healthy subjects. Emails of the approved flyer will also be sent to the Miami Society for Dermatology and Cutaneous Surgery list serve and Palm Beach County Society for Dermatology list serve to inform community clinicians about this study. We will also post fliers at designated locations throughout University of Miami buildings and in our dermatology clinics for recruiting patients and healthy subjects.

For recruitment purposes, we will advertise our study through the national psoriasis foundation and social media to distribute study advertisement.

8) Study Timelines*

This project is expected to last 24 months. There will be 3-4 study visits and 1 follow up visit for psoriasis patients and 3 study visits for healthy subjects. Each study visit will last approximately 2 hours.

9) Study Endpoints*

The primary endpoints:

Identify changes in brain anatomy (gray matter density) in psoriasis patients after injection of Sucukinumab using use voxel-based morphmetory (VBM) between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

Identify changes in baseline brain activity in psoriasis patients after injection of Secukinumab using and arterla spin labeling MRI (ASL) between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

The secondary endpoints:

Assessment of how an effective biologic treatment of psoriasis (Secukinumab) improves itch by using a Numerical Rating Scaling (NRS) ranging from 0 (no itch) to 10 (the worst itch imaginable) to assess severity of itch between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

Assessment of how an effective biologic treatment of psoriasis (Secukinumab) improves pain by using a Numerical Rating Scaling (NRS) ranging from 0 (no pain) to 10 (the worst pain imaginable) to assess severity of itch between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

Assessment of how an effective biologic treatment of psoriasis (Secukinumab) improves severity of psoriasis by using the Psoriasis Area and Severity Index (PASI) to assess severity of psoriasis ranging from 0 to 100, with a higher score indicating more severe psoriasis between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

Assessment of how an effective biologic treatment of psoriasis (Secukinumab) improves the patient's well-being by using the 5-item World Health Organization Well-Being Index (WHO-5) ranging from 0 to 25 with a higher score indicating better well-being between baseline, 1

week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

Assessment of how an effective biologic treatment of psoriasis (Secukinumab) improves the patient's quality of sleep by using the Numerical Rating Scaling (NRS) rainging from 0 to 10, with a higher score indicating lower sleep quality between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

Assessment of how an effective biologic treatment of psoriasis (Secukinumab) improves the patient's physical activity by using the 7-days physical activity recall (7D-PAR) ranging from 0 to 27, with a higher score indicating more physical activity between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

Assessment of how an effective biologic treatment of psoriasis (Secukinumab) improves stress in daily life in psoriasis patients by using the Perceived Stress Questionnaire (PSQ) ranging from 0 to 1, with a higher score indicating more stress between baseline, 1 week (visit 2), and 4 weeks (visit 3) as well as by comaparing between the patient and healthy control group.

10) Schedule of Assessments

10 patients with psoriasis and 10 healthy controls will participate in this study. The patient group will have 3-4 study visits and 1 follow up visit, while the healthy control group will have 3 study visits (Fig. 1). Patients can be rescreened in a washout period is needed.

Pre-Study visit (Patients only)

*Patients that have not had a TB preformed in the past 8 months will have to attend this pre-study visit to undergo a TB test

- Patients will fill out an informed consent
- Assessment of Body Surface Area (BSA) to show percent of psosiais involvement from 0 to 100%.
- Blood (~4ml) will be drawn for the Quantiferon TB Gold test
    - Subjects can not proceed to the 1st study baseline visit until results are received

- If an indeterminate result is received, the subject will be offered to repeat the test once
- If a positive result is received, the subject will be excluded from the study and refered to their primary care physician for further assessment and/or treatment
- If a negative result is received, the subject may continue with the study

1st study visit (Baseline measurements)

- All participants will be asked to fill out an informed consent (if not completed at the prestudy visit), and a form for demographic information including health information. Medical history and current medications will be documented from medical records chart review. Females of childbearing potential will undergo an hCG pregnancy test.

- MRI measurments of brain anatomy and activity using voxel-based morphmetory (VBM) and arterial spin labeling (ASL). MRIs in the study do not involve the use of contrast for all study visits.

-Assessment of Body Surface Area (BSA) to show percent of psosiais involvement from 0 to 100%.

- Assessment of severity of itch and pain using numerical rating scale (NRS) ranging from 0 (no itch/pain) to 10 (the worst itch/pain imaginable).

- Assessment of wellbeing using The 5-item World Health Organization Well-Being Index (WHO-5) (Topp et al., 2018)

- Assessment of severity of psoriasis using Psoriasis Area and Severity Index (PASI) (Fredriksson and Pettersson, 1978)

- Assessment of the quality of sleep using the sleep NRS- Assessment of excerise using 7-days physical activity recall (7D-PAR) (Young et al., 2013).

- Assessment of stress using Perceived Stress Questionnaire (PSQ) (Levenstein et al., 1993).

- At the end of the above measurements and assessments, injection of Secukinumab to psoriasis patients. That is, 2 Sensoready pens, dose: 150 mg/ml per pen, will be applied to different locations (i.e., 150 mg/ml x 2). A medically qualified study team member will explain how to do the injection and patients will inject by themselves in front of the study team member.

∗: Healthy controls will perform only VBM and ASL measurements, WHO-5, Sleep-NRS, 7D-PAR and PSQ. No injections will be performed to healthy controls.

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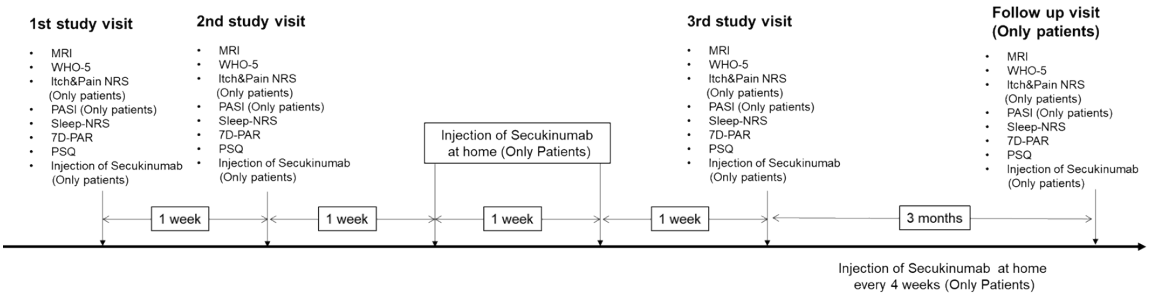
Fig. Time course of experiment for each participant



2nd study visit (1 week (± 3 days) after the initial injection of Sucukinumab)

- hCG pregnancy test
- MRI measurements of brain anatomy and activity using VBM and ASL.
- Assessment of severity of current itch and pain using NRS
- Assessment of wellbeing using WHO-5
- Assessment of severity of psoriasis using PASI
- Assessment of the quality of sleep using the sleep NRS
- Assessment of excersise using 7D-PAR
- Assessment of stress using PSQ
- At the end of the above measurements and assessments, injection of Secukinumab to psoriasis patients (Patients will inject by themselves) (150 mg/ml x 2).

∗: Healthy Controls will perform only VBM and ASL measurements, WHO-5, Sleep-NRS, 7D-PAR and PSQ. No injections will be performed to healthy controls

Between 2nd and 3rd study visits

Psoriasis patients will inject Secukinumab (150 mg/ml x 2) once a week (± 2 days) at home for 2 weeks (i.e., twice before the third study visit). Study staff will confirm whether patients have injected by phone call or email.

3rd study visit (4 weeks (± 3 days) after the initial injection of Sucuknumab)

- hCG pregnancy test
- MRI measurements of brain anatomy and activity using VBM and ASL.
- Assessment of severity of current itch and pain using NRS
- Assessment of wellbeing using WHO-5
- Assessment of severity of psoriasis using PASI
- Assessment of the quality of sleep using the sleep NRS
- Assessment of exercise using 7D-PAR
- Assessment of stress using PSQ

- At the end of the above measurements and assessments, injection of Secukinumab to psoriasis patients (Patients will inject by themselves) (150 mg/ml x 2).

∗: Healthy controls will perform only VBM and ASL measurements, WHO-5, Sleep-NRS, 7D-PAR and PSQ.

Between 3rd study visit and Follow up visit

After the 3rd study visits, psoriasis patients will continue injections of Secukinumab until the follow up visit (3 months after the 3rd study visit). However, the interval of injection will be changed from 1 week (± 2 days) to 4 weeks. That is, patients will inject (150 mg/ml x 2) every 4 weeks before the follow-up visit (i.e., twice before the follow-up visit).. Study staff will confirm whether patients have injected by phone call or email.

Follow up visit ONLY for patients (3 months (± 3 days) after the 3rd study visit)

- hCG pregnancy test
- MRI measurements of brain anatomy and activity using VBM and ASL.
- Assessment of wellbeing using WHO-5
- Assessment of severity of current itch and pain using NRS
- Assessment of severity of psoriasis using PASI
- Assessment of the quality of sleep using the sleep NRS
- Assessment of excersise using 7D-PAR
- Assessment of stress using PSQ

11) Data Management*

Data analysis

We will use statistical parametric mapping (SPM, https://www.fil.ion.ucl.ac.uk) and voxel-based morphometry (VBM, http://www.neuro.uni-jena.de) for the MRI data analyses. We will compare the whole brain gray matter density (VBM) and baseline brain activity (ASL) obtained at the first study visit between psoriasis patients and healthy controls to identify brain regions that show significant changes in the gray matter density and activity in psoriasis patients. We will investigate compare the gray matter density and activity in the identified brain regions alter overtime between the 1st study visit and other study visits as well as follow up visit in psoriasis patients. We will conduct the same analysis in healthy controls. Statistical significance applied to the MRI data analysis (VBM and ASL) will be set at FWE $p < 0.05$ corrected for the whole brain. For the correlation analyses, statistical significance will be set at $p < 0.05$.

We will compare itch NRS, pain NRS, WHO-5, NRS, PASI, Sleep-NRS7D-APR, and PSQ between the 1st study visit and other study visits as well as follow up visit in psoriasis patients. We will conduct the same analysis in healthy controls. 2-way ANOVA followed by Bonferroni correction will be used for data analysis (statistical significance: $p < 0.05$).
We will also conduct whether time course changes in brain anatomy (VBM) and brain activity (ASL) throughout the whole visits correlate with time course changes of itch NRS, pain NRS, WHO-5, NRS, PASI, sleep-NRS 7D-APR, and PSQ in psoriasis patients. Similar analysis will be done with healthy controls. Statistical significance: $p < 0.05$.

All of the data, including records of subjects, source documents, and informed consent will be kept in the study center (1600 NW 10th Ave, RMSB 7097 & 7099, Miami FL 33136) under lock for 6 years after the study finished. Data will be kept on UM procured, password protected computers of UM approved cloud storage.

12) Provisions to Monitor the Data to Ensure the Safety of Subjects*

The study team will be responsible for protecting the safety, rights, and well-being of study participants. The participants' vital signs (e.g., communication with participants in the MRI scanner) will be monitored.

Recording and reporting of adverse events that occur during the course of the study will help to ensure the continuing safety of participants. Local and systemic adverse events will be monitored during the study.

In case an adverse event does take place, a documentation system will be used to record the following information: description of event, time/date of onset, duration of reaction, relationship to study proceedures/drug, and seriousness/severity (based on Common Terminology Criteria for Adverse Events v4).

Study stoppage will occur if 40 subjects complete the study or if a severe adverse event related to the study occurs.

The PI will be responsible for monitoring ongoing activates to ensure compliance with regulator ad protocol requirements, data quality, and participant safety.

For MRI measurement

Privacy: Subjects to be scanned in the Imaging Facility are given a unique identifier, consisting of the first four letters of the investigator's PSY login name, a five-character study code, and the subject's participant number (up to 8 digits) as assigned by each research team. For example, AJHA_

_MIND_03, JBRI_ _ABMT_40001 codes may be used. This Facility code is the "name" to be entered in the MR computer file. No actual name nor any other identifying information is to be entered in the MR computer file, to make certain that subject privacy can be fully observed. Individual investigators are responsible for keeping records in order to identify the raw data collected in the Facility.

Safety screening: In Zone II (bathroom and waiting area of the MRI environment), research participants will complete a metal screen and remove all metal objects. Women must remove their underwire bras. Gowns are provided, if desired. After reviewing these forms, the MRI technologist will determine if the research participant is eligible to scan. The original forms will be kept in a locked file cabinet and filed according to date in the MRI facility and a copy will be given to the investigator.

Incidental findings: Dr. Efrat Saraf Lavi (Associate Professor of Radiology, Neuroradiology section and Medical Director of the Applebaum Diagnostic Imaging Center) will review a baseline structural scan from each subject that undergoes an MRI for any incidental findings. She will generate a summary report and the PI will communicate any results of clinical significane to the subject. Also a copy of this MRI summary report will be provided to the subject to all them in order to communicate the findings with their medical doctor. The subject may also request a DVD of their brain images.

13) Withdrawal of Subjects*

All subjects are free to withdraw from participation in this study at any time, for any reason, and without prejudice.

Subjects must be withdrawn from the study if:

1) A subject withdraws consent.
2) The Investigator believes it is in the best interest of the subject to be removed from the study.
3) If the subject experiences greater than a mild adverse event. (Subjects that experience a mild adverse event will be asked if they would like to continue the study. The occurrence of a severe adverse event will trigger the study to stop for safety purposes.)
4) Failed COVID-19 checks, including COVID-19 screening questionnaire and temperature check, required by the MRI facility.

The data collected before the withdrawal will still be used in data analysis.

14) Risks to Subjects*

1. MRI.

There are no foreseeable risks to a participant as all measures have been taken to ensure their safety. The participant may only run the risk of feeling claustrophobic when they are within the MRI scanner. All participants will be given the opportunity to experience the scanner in a mock environment.
Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. If the participant has a cardiac pacemaker or any other biomedical device in or on your body, it is very important they you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that they notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on their body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed. In addition, watches and credit cards should also be removed as these could be damaged. The participant will be provided a way to secure these items. If the participant has any history of head or eye injury involving metal fragments, if they have ever worked in a metal shop, or if they could be pregnant, they should notify the operator/investigator.

There is a possibility the participant will experience a localized twitching sensation due to the magnetic field changes during the scan. This is expected and should not be painful. Dizziness or nausea may occur if you move your head rapidly within the magnet.

IF THE PARTICPANT FEELS DISCOMFORT AT ANY TIME, THEY CAN NOTIFY THE OPERATOR AND CAN DISCONTINUE THE EXAM AT ANY TIME.
The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. The investigators for this project may not be trained to perform medical diagnosis. The investigators are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. When this occurs, a physician will be consulted as to whether the findings merit further investigation, in which case the investigator will contact you and your primary care physician and inform you of the finding

(NeuroscienceMRI_Notification form). The decision as to whether to proceed with further examination or treatment lies solely with you and your physician. The investigators, the consulting physician, and the University of Miami are not responsible for any examination or treatment that you undertake based on these findings. Because the images collected in this study may not comprise a proper clinical MRI scan, these images will not be made available for diagnostic purposes.

Women of Childbearing Potential: If any participant is pregnant or currently breast-feeding, they may not participate in any of our studies involving MRIs. The participant must understand that if they are pregnant or become pregnant, or if they are breast-feeding during this study, themselves or their child may be exposed to an unknown risk.

2. **Injection of Secukinumab**: The injection of Secukinumab may increase the risk of infection. Patients may experience nasopharyngitis, diarrhea, and upper respiratory tract infection.

3. **Protected Health Information (PHI).** Protected Health Information (PHI) will be collected during the study. Every attempt will be made to ensure that this PHI is kept secure. All study data will be kept in a locked office and kept under password protection on a computer that is only accessible by study personnel.

15) Potential Benefits to Subjects*

Psoriasis patients will receive a potent anti-psoriatic biologic.

16) Vulnerable Populations*

No vulnerable populations will be enrolled in this study.

17) Setting

The pre-study visit will be conducted at the Dermatology Clinical Trial Unit at the University of Miami Medical campus.

Research will be conducted in the neuroscience annex at the University of Miami, Florida. Data acquisition will be conducted using 3T MRI located within the neuroscience annex.

Potential subjects will be identified and recruited through IRB approved flyers.

18) **Resources Available**

The principle Investigator (PI) Gil Yosipovitch, MD, is a Professor from the Department of Dermatology & Cutaneous Surgery at the University of Miami and Director of the Miami Itch Center. Dr. Yosipovitch's primary research interest is in pruritus (itch) and the neurophysiology and innervation of skin in chronic itch. Dr. Yosipovitch has conducted research in the field of skin physiology, pharmacology, and neurophysiology of itch over the past 25 years. His research activities have centered on basic and clinical studies on itch neurophysiology, itch psychophysics and neuroimaging and developing topical and systemic formulations of anti-pruritics and clinical studies on different types of itch. Dr. Yosipovitch will assist with recruitment, study procedures, manuscript writing and assess adverse events.

Sub-PI Hideki Mochizuki, PhD, is an Assistant Professor from the Department of Dermatology & Cutaneous Surgery at the University of Miami and Director of the Brain imaging unit of the Miami Itch Center. Dr. Mochizuki has conducted psychophysical and neurominging studies with healthy subjects and patients with skin diseases, with focus on the mechanisms of itch. He will be the main person to conduct protocol design, data collection, data analysis, and manuscript writing.

Co-Investigator Leigh A. Nattkemper, PhD, is an Assistant Professor from the Department of Dermatology & Cutaneous Surgery at the University of Miami. Dr. Nattkemper uses advanced molecular biology and genetic approaches to understand the patho-mechanisms of chronic itch, with a special interest in the neurological processes. She has conducted research in the field of chronic itch for over 9 years and will act as Study Coordinator. She is also involved in protocol design and writing, data collection, data analysis, and manuscript writing.

Co-investigator Paolo Romanelli, MD, is a Professor from the Department of Dermatology & Cutaneous Surgery at the University of Miami. Dr. Romanelli is a director of psoriasis clinic at the University of Miami. He is Board Certified in Dermatology and Dermatopathology, his main interests are Psoriasis and Dermatopathology and he has special expertise in histopathology of Wound Healing. He will assist with recruitment, study procedures, and manuscript writing.

Research Fellows and Student Researchers from the Department of Dermatology & Cutaneous Surgery at the University of Miami will assist in subject recruitment, and study procedures, and data entry. They will be CITI certified and approved in the IRB system.

All study personnel will complete their CITI training and be adequately informed about the protocol and study procedures. All duties and functions are appointed and overseen by the PI.

19) **Confidentiality**

Protected Health Information (PHI) will be collected, but will not be disclosed. Therefore, a HIPAA authorization form will be collected. Every attempt will be made to ensure that this PHI is kept secure. All study data will be kept in a locked office and kept under password protection on a computer that is only accessible by study personnel.

All data, documents, reports, and scans (not including consent and demographic documents) will be kept de-identified and coded with a link between the code and subject's identity maintained separately from the data. Only the PI will have access to the code sheet. PHI (name and DOB) will be kept on UM's Velos system in order to track the subject's study status.

Data will be stored on a UM electronic device (encrypted, password-protected computer) and no data, documents, reports, or scans will be sent outside of UM.

EMR or PHI without obtaining a signed HIPAA authorization from the subject will be accessed to identify potential subject for recruitment purposes only. The PI confirms that the information collected for this will be destroyed or de-identified at the earlier opportunity. Information collected for this purpose will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study or for other research for which the use of disclosure of PHI is permissible.

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Choose the statements below that are applicable to this research:

26(a). Will the research collect protected health information or personally identifiable information from the EMR or from subjects at UHealth and/or JHS?

☒ Yes (If checked go to 26(b))

☐ No (If checked, go to Section 27)

26(b). Check the box next to the correct statement below

☒ Research Subjects will sign a HIPAA Authorization before the research will collect this data.

☐ Research Subjects will not sign a HIPAA Authorization for this data collection and the research is requesting a waiver of HIPAA authorization from the IRB.

26(c). How will the research store the data?

☒ On a University of Miami electronic device (e.g. encrypted, password-protected computer)

☒ On a cloud-based storage system that is approved by the University of Miami

☐ On the secured JHS SharePoint environment

26(d) Select one of the following:

☐ The Principal Investigator (and/or Study Team members) will record (e.g. write down, abstract) data acquired in a manner that does not include any indirect or direct identifiers (listed in the instructions for Section 26 of this protocol), and the recorded data will not be linked to the individual's' identity.

OR

☒ The Principal investigator (and/or Study Team members) will record (e.g. write down, abstract) the data collected in a manner that does not include any direct identifiers (see list in the instructions for Section 26 of this protocol) of any subject. Instead, the Principal Investigator and/or Study Team members shall will assign a code (that is not derived in whole or in part from any direct or indirect identifiers of the individual) to each study subject and link the code to the study subject's identity. The link to each subject's identity and/ or other identifiable information will be maintained on a document separate from the research data.

26(e) Additional requirement for Jackson Health System Data:

☒ Not-applicable, no data will be acquired from JHS under a waiver of authorization.

☐ JHS data, including Protected Health Information (PHI) and/or Personally Identifiable Information (PII), acquired from JHS for this research under a waiver of authorization shall only be stored on the secured JHS SharePoint environment made available by JHS. I and the Study Team members shall not copy or store the JHS sourced personally identifiable

information (PII), including protected health information (PHI) data to any other system, including any systems maintained or provided by the University of Miami. I and the Study Team shall only copy or transfer JHS-sourced data that has been properly de-identified in accordance with all requirements contained in the HIPAA Rules by removing all of the identifiers listed in the instructions for Section 26 of this protocol.

20) Biospecimens

☒ Not applicable. No biospecimens will be collected

☐ *Bio*-Specimens obtained for this research will be stored without any direct or indirect identifiers.

☐ *Bio*-Specimens obtained for this research will be stored in a de-identified coded manner.

☐ When required to transport data or bio-specimens for this research, the research team will transport the data and bio-specimens in a de-identified (or anonymous) manner with a link to the individual subject's identity maintain separately from the data and/or bio-specimen.

21) Provisions to Protect the Privacy Interests of Subjects

Study subjects will only be asked to provide personal information to approved study personnel, who will ensure the subject is at ease with the situation. Study personnel will clearly explain that the subject does not have to answer any questions or provide any sample they are uncomfortable about.

22) Compensation for Research-Related Injury

There is no available compensation in the event of research related injury.

23) Economic Burden to Subjects

There will be no charges to the subjects that agree in participating in this study.

24) Consent Process

The research team will follow the "HRP-090 SOP: Informed Consent Process for Research" to obtain informed consent and the "HRP-091 SOP: Written Documentation of Informed Consent" to document informed consent in writing.

Study personnel will meet with each potential subject to discuss the study in detail, answer questions, and allow the subject to read the entire consent form. The informed consent form explicitly states the rationale for the study and requirements for participation, both before and during the session. The informed consent form states that subjects may discontinue participation or be terminated from the study at any time.

All pertinent aspects of the study will be explained to the subject before he or she signs the informed consent form. A signed informed consent form will be obtained from the subject before any activity or treatment is undertaken as part of the study.

Non-English Speaking Subjects will not be enrolled. Subjects who are not yet adults (infants, children, teenagers), cognitively impaired adults, and adults unable to consent will not be enrolled.

This trial will be registered on ClinicalTrials.gov.

25) Process to Document Consent in Writing

The research team will follow the "HRP--091 SOP: Written Documentation of Informed Consent" to document informed consent in writing.

26) Authorization for Use and Disclosure of Protected Health Information (HIPAA)

Type of Request:

☒ Waiver of Authorization for access to medical record for subject identification/recruitment.

☐ Waiver of Authorization for access to medical record to obtain data for the research.

Confirm that you will destroy the Protected Health Information (PHI) you and/or your Study Team acquire receive from JHS and/or UHealth at the earliest opportunity.

☒ ***I confirm***

Confirm that the Protected Health Inform (PHI) you acquire from JHS and/or UHealth will not be re-used or disclosed to any other person or entity, except as required by law or for authorized oversight of the research study or for other research for which the use or disclosure of PHI is permissible.

☒ ***I confirm***

☒Not applicable. This research will not collect data from JHS record under a waiver of authorization

Notwithstanding the preceding "I confirm" statements above, I agree that neither I nor any member of the study team listed on the IRB submission for this Protocol shall ever re-use or re-disclose any of the information acquired from Jackson Health System in any format, whether **identifiable or de-identified,** to any individual or entity without first obtaining written permission from Jackson Health System, even if such re-use or re-disclosure is permissible by law (e.g., HIPAA).

27) **Drugs or Devices**

Secukinumab will be given to psoriatic subjects as per the FDA approved label.

28) **References**

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