Institutional Review Board
Human Research Protections
Protocol Narrative ~ Expedited/Full Committee
Biomedical/Clinical Research
Version 2015

Upload this completed narrative and any supplemental documentation to the IRB Application.	**IRB USE ONLY – HS#: 2017-3518**
Lead Researcher Name: Anand K. Ganesan, M.D., Ph.D.	
Study Title: Evaluating the Efficacy of the Melanocyte Keratinocyte Transplantation Procedure in the Treatment of Vitiligo	

CLINICAL TRIAL MASTER PROTOCOL AND INVESTIGATIONAL BROCHURE INFORMATION *

	Master Protocol	**Investigator Brochure:** <Specify Drug/Device>	**Investigator Brochure:** <Specify Drug/Device>	**Sponsor Consent Form Template(s)**
Version #:				
Version Date:				

[x] This study is investigator-authored (investigator developed the study and is conducting the study at UCI and/or with other non-UCI sites).

* Add columns as applicable

NON-TECHNICAL SUMMARY

Provide a brief non-technical summary or synopsis of the study that can be understood by IRB members with varied research backgrounds, including non-scientists and non-affiliated members.

Vitiligo is a dermatologic disease characterized by depigmentation of skin. While the loss of melanocytes observed in vitiligo is driven by the immune system, repigmentation of the skin that occurs during UV light treatment is driven by melanocytes that migrate out of the hair follicle and into epidermis or the activation of stem cells within the epidermis. Unfortunately, some skin areas affected by vitiligo have very few hair follicle melanocytes and an indeterminate number of epidermal melanocytes and therefore unable to respond to light therapy.
This pilot study seeks to establish a relatively new procedure- the melanocyte keratinocyte transplant procedure (MKTP)- at UC Irvine Healthcare as a method to treat depigmented skin in vitiligo patients.

In addition, this study will utilize single cell RNA sequencing technology to identify the different population of melanocytes in cells harvested for the transplant procedure in an effort to identify the specific type of melanocyte that is responsible for vitiligo repigmentation.

Patients in Dr. Ganesan's clinic at UCI Department of Dermatology will approach for participation in the study. The study will include both men and women and will not be limited by race or ethnicity. We will exclude less than 18 years old for the study as we believe it would be difficult for these subjects to tolerate the melanocyte keratinocyte transplant procedure. Patients offered a melanocyte keratinocyte transplant procedure. This procedure is a method to transplant a large area of skin with a suspension of melanocytes and keratinocytes that is generated from 1-3/10th the surface area of epidermis.
This study has three arms:

1- MKTP with Surgical Blade

2- MKTP with Negative Pressure Instrument (suction blistering device).

3- Suction blister grafting without cell dissociation

On the first arm of the study, A normally pigmented area on the patient was anesthetized with 1% lidocaine with epinephrine. Using a surgical knife, we removed a small portion of the epidermis that is unaffected by vitiligo from a small area (2cm^2) on the patient's thigh to obtain donor cells. Epidermis that was harvested with the surgical knife was washed with Lactated Ringers solution three times, and then dissociated using trypsin to separate the cells into a single cell suspension. The recipient area to be grafted was ablated with an Erbium YAG laser. Half of the dissociated single cells from the donor area (thigh)was then transplanted on to the area affected by vitiligo that the patient is interested in grafting (5 cm^2 area).

We then evaluated response to treatment in the transplanted areas at 1 day, 1 week, 1 month and 3 months, and 6 months by both photography and quantifying the VASI score.

VASI is the percentage of vitiligo involvement and is calculated in terms of hand units. One hand unit is approximately equivalent to 1% of the total body surface area.

On the second arm of the study, we are using a minimally invasive procedure (suction blister grafting) to sample the grafted skin and donor skin- this method can separate the epidermis from the dermis without inducing a scar. A normally pigmented area on the upper thigh is anesthetized with 1% lidocaine with epinephrine. Using a suction blister technique, we remove a small portion of the epidermis that is unaffected by vitiligo from a small area (4 cm^2 or 0.6 inch^2) on the patient's thigh to obtain donor cells. Epidermis that was harvested is washed with Lactated Ringers solution three times, and then dissociated using trypsin to separate the cells into a single cell suspension. The recipient areas to be grafted is used to harvest epidermis using a suction blister device. Half of the dissociated single cells from the donor area (thigh) are then transplanted on to the area affected by vitiligo that the patient was interested in grafting (5 cm^2 area or 0.7 inch^2). The suction blister skin from the recipient sites is simultaneously dissociated into a single cell suspension. A portion of the remainder of the cells (from both the donor and recipient site) is subjected to flow sorting to quantify the populations of melanocytes and keratinocytes. Another portion of the remainder cells are submitted for single cell RNA-sequencing at the genomics and high throughput facility to identify the spectrum of different types of melanocytes and keratinocytes in the epidermis using single cell RNA-sequencing technology. We then evaluated response to treatment in the transplanted areas at 1 day, 1 week, 1 month and 3 months, and 6 months by both photography and quantifying the VASI score. This arm of the study is nearly complete, with only 2-3 more patients to enroll to complete the statistical evaluation of efficacy.

VASI is the percentage of vitiligo involvement and is calculated in terms of hand units. One hand unit is approximately equivalent to 1% of the total body surface area.

On the now proposed third arm of the study, we use a minimally invasive procedure (suction blister grafting without cell dissociation) to sample the grafted skin and donor skin- this method can separate the epidermis from the dermis without inducing a scar. A normally pigmented area on the upper thigh will be anesthetized with 1% lidocaine with epinephrine. Using an epidermal harvesting system which is a suction blister technique, we will remove multiple small portions (about 128 blisters-1.8 mm in diameter) of the epidermis unaffected by vitiligo from a small normal area (5 cm^2) on the patient's thigh to obtain donor cells and using a regular negative pressure instrument for removing four samples for histopathological study (two from the vitiligo area and two from the normal donor skin). The epidermis from the donor area (thigh) will then be transplanted on to the area affected by vitiligo that the patient is interested in grafting. Also, the four portions from the normal skin and the recipient site will be sent for the histopathological evaluation.

We will then evaluate response to treatment in the transplanted areas at 1 day, 1 week, 1 month and 3 months, and 6 months by both photography, quantifying the change in depigmented surface area, and the VASI score. Also, we will evaluate the two vitiligo samples and two normal skin samples through histopathology to assess where the unique populations of cells identified in our RNA-seq analysis are localized. We hypothesize that our transplant procedure will yield excellent to good repigmentation, resulting in a mean of 60% reduction in surface area (SD=30%) from baseline to 6-month follow up. With a sample size of 5 patients, this study will achieve 90% power to test this hypothesis based on a two-sided paired t-test at p=0.05 significance level. In addition, we will compare the results from the 7 patients harvested using the surgical blade technique (procedure already completed and follow up results pending) with the results from 7 patients harvested with the suction blisters (almost completed) and seven patients from the newly proposed experimental group.

SECTION 1: PURPOSE AND BACKGROUND OF THE RESEARCH

1. Provide the scientific or scholarly rationale for the research. Describe the relevant background information and the specific gaps in current knowledge that this study intends to address.

Vitiligo is a dermatologic disorder characterized by depigmented areas of skin caused by immune-mediated melanocyte destruction.[1] This disease has an estimated prevalence of 0.5-4 percent worldwide; however, the prevalence can reach as high as 8% in certain parts of the world.[1] The visual appearance of vitiligo can have serious social, mental and emotional impact on patients with this disease, leading to a poor quality of life and increased incidence of depression and suicide.[2] In addition, the disease has many unique biologic aspects that make it very interesting to study. While the process is initiated by the immune system, repigmentation is driven by melanocyte stem cells that migrate to and repigment the epidermis.[3] This is not a static process but a dynamic one—areas of skin are constantly losing pigment and new melanocytes are migrating to repigment the area. It is not known why this depigmentation initiates only in certain areas, or how the repigmentation occurs. Nothing is known about how many melanocyte populations there are in the skin, and which one of these contribute to repigmentation. Answering this basic question will not only give insight into the disease and its treatment, but also elucidate mechanisms that underlie epithelial regeneration itself.

There are limited treatments for vitiligo and no known cure. The gold standard for treatment of vitiligo is narrow band UVB light therapy, which induces follicular epidermal melanocytes to migrate to the epidermis.[4] This is not a uniformly successful treatment and requires often greater than 50 treatments for an adequate therapeutic response, which takes up to three months to see.[4] Unfortunately, this treatment does not work if the affected skin lacks a melanocyte stem cell reservoir, such as occurs in segmental vitiligo.

Standard surgical management of vitiligo involves transplanting normal melanocytes into depigmented areas. While the UCI Dermatology Clinic currently performed punch grafting transplantation procedures, recent advances have established the melanocyte-keratinocyte transplant procedure (MKTP) as a more effective way to treat the disease.[5] The procedure involves harvesting a small area of epidermis from normal skin (usually the thigh), destroying the epidermis in an affected area of skin, and transplanting the single cell epidermal suspension onto the affected area. This method has the advantage of harvesting only small pieces of skin to treat large affected areas (can treat an area 10x as large as the donor site). It has a 70% success rate as documented by recent studies after specialized training.[5] Dr. Ganesan, the PI on the study, completed a course to learn the procedure at Henry Ford Hospital, the first site that performed this procedure in the United States. The procedure is currently performed at UT Southwestern, U Mass Amherst, and Henry Ford Hospital. Upon completion of this pilot study to collect preliminary outcome data on the procedure at UCI, UC Irvine will become the first institution on the west coast to offer the treatment to patients. In a desire to continuously innovate and develop an even better procedure, we are harvesting skin from the donor site and skin from the recipient site using a surgical blade in the first arm of the study, blister grafting technique with dissociation of the cells in the second arm of the study and transplanting the blisters without dissociation of the cells in the third arm of the study. Suction blistering method is a more uniform way to remove the epidermis without inducing a scar, making it safer than the original published MKTP technique. One of the issues with current grafting methods is the need for specialized equipment for cell dissociation, which can often be tedious and time consuming. We ask the question whether this dissociation really results in a better outcome in the third arm of the study. In the third arm of the study, we will use Cellutome suction blister grafting without cell dissociation. With Cellutome, we can harvest more grafts in a shorter time. As each blister is smaller in size, there is a smaller risk of scarring after the procedure.

Blister grafting without cell dissociation has been tested by many researchers in the past with good results [11,12].
In a study by Budania et al, suction blister epidermal grafting was compared with autologous noncultured epidermal cell suspension. Most of the subjects in this study showed >75% repigmentation[13]. In another study by Li J et al, suction blister epidermal grafting was performed for one thousand one hundred subjects with stable vitiligo [14]. Excellent repigmentation was observed in > 80% of the patients [14]. Babu et al conducted a comparison study between punch grafting and suction blister epidermal grafting in the treatment of stable lip vitiligo [15]. In this study, more than half of the patients in both groups showed more than 50 % repigmentation [15].

Cellutome epidermal harvesting system can harvest more grafts in a shorter time in comparison to the Negative Pressure Instrument which makes the transplantation easier, faster and more efficient.

2. Provide relevant preliminary data (animal and/or human).

Melanocyte-Keratinocyte Transplant Procedure (MKTP) has been performed in many institutions in Europe, Asian and throughout the Middle East.[5] It has also recently been established in the United States at Henry Ford Hospital Multicultural Dermatology Center. Recent publication of result following MKTP shows it to be an effective and well-tolerated treatment option for vitiligo. (5) Dellatorre et al demonstrated that Suction Blister Epidermal Graft is a low cost and effective option (65 to 100% repigmentation can be achieved in up to 80% of patients).
(6) In another study, Jeong H S et al proved that Non-cultured epidermal suspension grafting is a useful surgical intervention in patients with stable vitiligo, capable of promoting repigmentation in areas refractory to medical intervention and allowing a donor-to-recipient ratio of up to 1:10.
(7) In another study Ashique KT et al demonstrated that suction blister epidermal graft continues to be a good, cost-effective, surgical method of treating vitiligo especially on the face and lip. The donor site also tends to show good healing tendency with minimal scarring and post inflammatory pigmentation. (8) Also in another study by Gou D et al found that Blister grafting is successful in most patients with vitiligo, with a high graft survival rate (9). Also, Strassner JP et al demonstrated that suction blistering technic does not increase the risk of vitiligo on the blister areas. (10)

3. Describe the purpose, specific aims or objectives. Specify the hypotheses or research questions to be studied.

The purpose of this study is to compare the result of suction blister grafting without cell dissociation versus suction blister grafting with cell dissociation and MKTP with blade technique and determine whether cellular dissociation impacts the outcome. In the first arm of this study, seven patients were enrolled, and the procedure was done successfully without complication. Follow up was accomplished and outcomes will be analyzed at the end of the study. In the second arm of the study, we have conducted the MKTP with suction blistering in 7 patients and then will compare the results with previous study. In the third arm of the study, we are planning to perform suction blister grafting without epidermal cell dissociation on a total of seven patients. We want to evaluate the importance of cell dissociation on the outcome of this procedure.

This information and experience will be important worldwide for the vitiligo community, as it is the only study that compares the efficacy of these three methods in a single study. This will help us better advice and counsel patients on the best procedure for them when we discuss the options. UCI is the only center on the west coast offering this procedure, so ensuring the efficacy of the methods is important.
In addition, we want to use the unique opportunity of this three-arm pilot study to characterize the different melanocyte and keratinocyte populations that exist in the epidermis, populations that may be important in the pathogenesis of vitiligo itself. The MKTP procedure works to repigment vitiligo yet does not involve transplantation of hair follicle melanocyte stem cells, as only the epidermis is harvested during the procedure. To identify what this migrating population might be, we will first seek to identify the different populations of melanocytes that are present in the normal epidermis using single cell RNA-seq. In addition, we will perform RNA-seq on the affected skin to examine the contributions of keratinocytes to the pathogenesis of the disease. In the third arm, we will harvest tissue for spatial localization of the different cell types, which will really allow us to determine which cells are contributing to vitiligo pathogenesis. With the new modification, we are also adding in methods to sort the transplanted cells to both monitor the success of the procedure and develop methods to identify the right cells to transplant.

4. Describe the primary outcome variable(s), secondary outcome variables, and predictors and/or comparison groups as appropriate for the stated study objectives/specific aims.

Primary Outcome Variable:

We will then evaluate response to treatment in the transplanted areas at one day, 1 week, 1 month and 3 months, and 6 months by both photography to measure the change in surface area (image J) and quantifying the VASI score. In addition, we will evaluate how long it took the patient to heal at both the donor and graft site and record any complications of the procedure itself. We hypothesize that our transplant procedure will yield excellent to good repigmentation, resulting in a mean of 60% reduction in the VASI scores (SD=30%) from baseline to 6-month follow up. With a sample size of 5 patients for each arm, this study will achieve 90% power to test this hypothesis based on a two-sided paired t-test at p=0.05 significance level. After conducting the three arms of the study, we also want to compare the results of three techniques together.

5. List up to ten relevant references/articles to support the rationale for the research. Do not append an extensive NIH-grant-style bibliography.

1. Ezzedine, K, Eleftheriadou V, Whitton M, van Geel, N. Vitiligo. *Lancet* 2015; 386: 74-84.
2. Nogueira LS, Zancanaro PC, Azambuja RD. Vitiligo and emotions. *An Bras Dermatol*. 2009;84(1):41-5.
3. Cui J, Shen LY, Wang GC. Role of hair follies in the repigmentation of vitiligo. *J Invest Dermatol*.1991;97(3):410-6.
4. Kishan Kumar YH, Rao GR, Gopal KV, Shanti G, Rao KV. Evaluation of narrow-band UVB phototherapy in 150 patients with vitiligo. *Indian J Dermatol Venereol Leprol*.2009;75(2):162-6.
5. Huggins R, Henderson M, Mulekar S, Ozog D, Kerr H, Jabobsen G. Melanocyte-keratinocyte transplantation procedure in the treatment of vitiligo: the experience of an academic medical center in the United States. *J Am Acad Dermatol*. 2012; 66:785-93.
6. Dellatorre G, Bertolini W, Castro C, Optimizing suction blister epidermal graft technique in the surgical treatment of vitiligo. An. Bras. Dermatol. Vol.92, No.6, Rio de Janeiro Nov./Dec. 2017
7. Jeong H. S, Vandergriff T, Pandya A. G. Use of Suction Blisters for Nonculture Epidermal Suspension Grafting in patients with Vitiligo. Dermatol Surg. 2016 May;42(%):688-91
8. Ashique KT, Kaliyadan F. Long-Term Follow-Up and Donor site changes Evaluation in Suction Blister Epidermal Grafting Done for Stable Vitiligo: A Retrospective Study. Indian J Dermatol. 2015 Jul-Aug;60(4):369-72
9. Gou D, Currimbhoy S, Pandya AG. Suction blister grafting for vitiligo: efficacy and clinical predictive factors. Dermatol Surg., 2015 May; 41(5):6633-9
10. Strassner JP, Rashighi M, Ahmed Refat M, Richmond JM, Harris JE. Suction blistering the lesional skin of vitiligo patients reveals useful biomarkers of disease activity.j Am Acad Dermatol. 2017 May;76(5):847-855
11. Koga M. Epidermal grafting using the tops of suction blisters in the treatment of vitiligo. Arch Dermatol. 1988 Nov;124(11):1656-8
12. WYM Tang, LY Chan, KK Lo. Treatment of vitiligo with autologous epidermal transplantation using roofs of suction blisters. Hong Kong Med J. 1998; 4:219-24
13. Budania A, Parsad D, Kanwar AJ, Dogra S. Comparison between autologous noncultured epidermal cell suspension and suction blister epidermal grafting in stable vitiligo: a randomized study. Br J Dermatol. 2012 Dec; 1295-301

14. Li J, Fu WW, Zheng ZZ, Zhang QQ, Xu Y, Fang L. Suction blister epidermal grafting using a modified suction method in the treatment of stable vitiligo: a retrospective study. Dermatol Surg. 2011 Jul; 37(7): 999-1006
15. Babu A, Thappa DM, Jaisankar TJ. Punch grafting versus suction blister epidermal grafting in the treatment of stable lip vitiligo. Dermatol Surg. 2008 Feb; 34(2): 166-78

SECTION 2: ROLES AND EXPERTISE OF THE STUDY TEAM

1. List all research team members who will interact or intervene with human subjects or will have access to identifiable private information about human subjects. *Include additional rows for Co-researchers and Research Personnel, as needed.*
2. For each research team member, indicate all applicable research activities the individual will perform. *Finalizing informed consent is reviewing, answering/asking questions, confirming competency, as necessary, and signing/confirming the informed consent.*
3. If applicable, list the Faculty Sponsor as a Co-Researcher who will have research oversight responsibilities.

Lead Researcher:

Name and Degree: Anand K. Ganesan, M.D, Ph.D.

Position/Title and Department: Associate Professor in UCI Department of Dermatology

Team Member will: **[x]** Screen/Recruit **[x]** Finalize Informed Consent

[x] Perform Research Activities *(describe below)* **[x]** Access subject identifiable data

List the research activities/procedures to be performed and the individual's relevant qualifications (training, experience): Dr. Ganesan is a board-certified dermatologist with over ten years of experience in clinical and basic science research. He leads his own research lab at UCI, which focuses on dermatologic disorders of pigmentation and skin cancers. He has completed a course in MKTP at Henry Ford, and he also has 10 years' experience in performing punch graft transplantation for treating vitiligo.
He will develop this research project as well as the research protocol and be responsible for training and oversight of the study team. He will have access to PHI and subject identifiable data. He will perform study procedures and train the co-researchers. He will analyze study data, as well as prepare and present the study findings for publication and presentation. Dr. Ganesan will be performing the collection of the skin graft and the cell transplant procedure.

Co-Researcher:

Name and Degree: Pezhman Mobasher, MD

Position/Title and Department: Research assistant in UCI Department of Dermatology

Research Fellow in the Department of Dermatology

Team Member will: **[x]** Screen/Recruit **[ ]** Finalize Informed Consent

[x] Perform Research Activities *(describe below)* **[x]** Access subject identifiable data

List the research activities/procedures to be performed and the individual's relevant qualifications (training, experience): Pezhman is a dermatologist who trained in Iran and Bulgaria. He will assist in the development of this research project as well as the research protocol, assist with study procedures, and coordinate patient visits. He will also be responsible for analyzing images and study data and prepare results for publication.

Co-Researcher:

Name and Degree: Jessica Shiu

Position/Title and Department: Resident in UCI Department of Dermatology

Research Fellow in the Department of Dermatology

Team Member will: **[x]** Screen/Recruit **[x]** Finalize Informed Consent

[x] Perform Research Activities *(describe below)* **[x]** Access subject identifiable data

List the research activities/procedures to be performed and the individual's relevant qualifications (training, experience): Jessica Shiu is a physician scientist trained resident in the Department of Dermatology at UC Irvine. She completed at her MD and PhD at the University of Maryland Medical Scientist Training Program. She will be active in all aspects of the study and have access to PHI and subject identifiable data. She will perform study procedures and help analyze study data, as well as prepare and present the study findings for publication and presentation.

SECTION 3: SUBJECT POPULATION(S) (INDIVIDUALS/RECORDS/SPECIMENS)

A. Subjects To Be Enrolled on this UCI protocol (Persons/Records/Biospecimens)

1. Complete the table of subject enrollments below. *Include additional rows for subject category/group, as needed.*
2. If the study involves the use of existing records or biological specimens, specify the maximum number to be reviewed/collected and the number needed to address the research question.

Category/Group (e.g., adults, controls, parents, children)	**Age Range** (e.g., 7-12, 13–17, adults)	**Maximum Number to be Consented or Reviewed/Collected** (include withdrawals and screen failures)	**Number Expected to Complete the Study *or Needed to Address the Research Question***
1-First Arm-Harvesting with surgical Blade(adults)	18 years and older	10	7 completed
2- Second Arm-Suction Blistering Method (adults)	18 years and older	10	7
3-Third Arm-Suction Blister grafting without cell dissociation	18 years and older	10	7
		Total: 30	

B. Overall Study Sample Size

If this is a multi-site study, provide the total number of subjects to be enrolled from all sites.

[x] Not applicable: This study will only take place at UCI, and does not involve other sites.

Total number of subjects across all sites: <Type here>

C. Eligibility Criteria

1. Identify the criteria for inclusion and exclusion.

Inclusion Criteria:

1. Verified diagnosis of vitiligo by board-certified dermatologist
2. Candidate for vitiligo treatment as determined by lead researcher
3. Has a 5 cm^2 area of vitiligo and an area on the upper thigh that is not affected by the disease
4. Over 18 years of age at time of signing informed consent form
5. Ability to understand, abide by and participate in study procedures

Exclusion Criteria:

1. Inability to understand or abide by instructions for participation in study and procedure
2. Pregnant or lactating women
3. Less than 18 years old at time of signing informed consent form
4. Current use of tobacco products or within 1 month prior to procedure date
5. History of coagulation disorder, platelet dysfunction disorder, platelet count less than <150,000 platelets per microliter
6. History of poor wound healing or condition that would compromise optimal healing of graft site as deemed by lead researcher
7. History of keloids

2. If eligibility is based on age, gender, pregnancy/childbearing potential, social/ethnic group, or language spoken (e.g., English Speakers only), provide a scientific rationale.

[ ] Not applicable: Lidocaine is pregnancy class B, and as there is more than minimal risk. We will exclude pregnant patients. The ideal patients for the procedure are those with stable vitiligo. As children often have less stable disease, they are being excluded from the pilot study to remove any additional confounding variables.

SECTION 4: RECRUITMENT METHODS

Check any of the following methods that will be used to recruit subjects for this study:

[ ] This study involves no direct contact with subjects (i.e., use of existing records, charts, specimens).

Specify database or IRB-approved protocol number (HS#), if applicable: <Type here>

[ ] Advertisements, flyers, brochures, email, Facebook, and/or other media.

Specify where recruitment materials will be posted: <Type here>

If subjects will be recruited by mail, e-mail, or phone, specify how their contact information will be obtained: <Type here>


Submit recruitment materials for IRB approval.

[X] The study will be listed on Clinicaltrials.gov. *All clinical research must be registered.*

[ ] The study will be listed on the UC Irvine Health Clinical Trials web page.


Submit the UCIMC Standard Research Recruitment Advertisement for IRB approval.

[ ] The UCI Social Sciences Human Subjects Lab/Sona Systems will be used.


Submit the Social Science Human Subject Pool Recruitment Advertisement for IRB approval.

[ ] Referral from colleagues

- Study team will provide colleagues with UCI IRB-approved recruitment materials for distribution to potential subjects (e.g., recruitment flyer, introductory letter);
- An IRB-approved recruitment letter will be sent by the treating physician. The letter will be signed by the treating physician and sent to his/her patients to inform them about how to contact study team members; and/or
- Colleagues obtain permission from interested patient to release contact information to researchers.
- Study team does not have access to patient names and addresses for mailing.
- If colleagues will screen their patients' medical records to determine subject eligibility and approach patients directly about study participation: *Complete Appendix T to request a partial waiver of HIPAA Authorization.*


Submit recruitment materials for IRB approval.

[ ] Study team will contact potential subjects who *have given prior permission to be contacted* for research studies.

Specify when and how these individuals granted permission for future contact: <Type here>

Specify database or IRB-approved protocol number (HS#): <Type here>

[x] Study team members will approach their own patients, students, employees for participation in the study.

[ ] Study team will screen UCIMC medical records to which they have access to determine subject eligibility. The patients' physicians will approach patients directly about study participation.


Complete Appendix T to request a partial waiver of HIPAA Authorization.

[ ] Other Recruitment Methods: <Indicate the recruitment method(s) here>

SECTION 5: INFORMED CONSENT PROCESS

A. Methods of Informed Consent

1. Indicate all applicable informed consent methods for this study. *Submit the consent/assent document(s) with your e-IRB Application (e.g., Study Information Sheet, Recruitment script, Consent Form, etc.). Only IRB approved consent forms (containing the IRB approval footer) may be used to consent human subjects at UCI.*

[x] Written (signed) informed consent will be obtained from subjects. Signed informed consent, parental permission, and/or child assent will be obtained from subjects, as applicable.

[ ] Requesting a waiver of written (signed) informed consent. Signed consent will not be obtained; consent will be obtained verbally or via the web. Informed consent, parental permission and/or child assent will be obtained from subjects, as applicable.


Complete Appendix P.

[ ] Requesting to seek surrogate consent from a legally authorized individual. Surrogate consent may be considered only in research studies relating to the cognitive impairment, lack of capacity or serious or life-threatening disease and conditions of the research subjects.


Complete Appendix E.

[ ] Requesting a waiver of informed consent. (i.e., consent will not be obtained). *Skip to Section 5.B.*


Complete Appendix O.

2. Indicate where the consent process will take place.

[x] In a private room
[ ] In a waiting room
[ ] In an open unit
[ ] In a group setting
[ ] The internet
[ ] In public setting
[ ] Over the phone
[ ] Other (specify): <Type here>

3. Specify how the research team will assure that subjects have sufficient time to consider whether to participate in the research.

[x] Subjects will be allowed to take home the unsigned consent form for review prior to signing it.

[ ] Subjects will be allowed <Type here> hours to consider whether to consent.

[ ] Other (specify): <Type here>

4. If children are enrolled in this study, describe the parental permission process and the child assent process.

[x] Not applicable:

5. Some subjects may be vulnerable to coercion or undue influence, such as those who are economically or educationally disadvantaged, mentally disabled, or students (undergraduate, graduate, and medical students) and employees of UCI (administrative, clerical, nursing, lab technicians, post-doctoral fellows and house staff, etc.), describe the procedures to ensure the voluntary participation of these individuals.

    1. **[ ]** Not applicable: Potential subjects are informed that no matter what they will decide regarding participation, their care received from their physician will not be affected. They will also be offered the alternative punch grafting procedure.

[ ] Other (specify): <Type here>

B. Health Insurance Portability and Accountability Act (HIPAA) Authorization

Indicate all applicable HIPAA authorization methods for this study.

[ ] Not applicable: Study does not involve the creation, use, or disclosure of Protected or Personal Health Information (PHI).

[ ] Requesting a Total waiver of HIPAA Authorization. HIPAA authorization will not be obtained at all for the study.

Complete Appendix T.

[ ] Requesting a Partial waiver of HIPAA Authorization. HIPAA authorization will not be obtained for screening/recruitment purposes. However, written (signed) HIPAA research authorization is obtained for further access to personal health information.

Complete Appendix T.

[x] Written (signed) HIPAA Research Authorization will be obtained from subjects. Signed authorization, parental authorization, and/or child assent will be obtained from subjects, as applicable.

Complete the HIPAA Research Authorization form.

C. Methods of Informed Consent for non-English Speakers

1. Indicate the applicable informed consent method for non-English speakers.

[ ] Not applicable: Only individuals who can read and speak English are eligible for this study. *Scientific justification must be provided in Section 3.C.2.*

[x] The English version of the consent form will be translated into appropriate languages for non-English speaking subjects once IRB approval is granted. *The translated consent form must be submitted to the IRB for review prior to use with human subjects. Only IRB approved consent forms (containing the IRB approval stamp) may be used to consent human subjects at UCI.*

[ ] Requesting a short form consent process.


Complete Appendix Q.

The short form process will be used for the following occasional and unexpected languages:

[ ] All non-English languages
[ ] All non-English languages except Spanish
[ ] Other languages (specify): <Type here>

2. Explain how non-English speaking subjects will be consented in their language and who will be responsible for interpreting and facilitating the informed consent discussion for the non-English speaking subjects.

[ ] At least one member of the study team is fluent in the language that will be used for communication, and that study team member(s) will be available during emergencies.


For all members of the study team responsible for obtaining informed consent from non-English speaking subjects, provide their qualifications to serve in this capacity (i.e. language fluency) in Section 2.

[x] The study team has 24-hour access to a translation service with sufficient medical expertise to discuss the research in this study.

[ ] Other (explain): <Type here>

SECTION 6: RESEARCH METHODOLOGY/STUDY PROCEDURES

A. Study Location

Specify where the research procedures will take place (e.g. UCI Douglas Hospital – Cardiac Care Unit, UCI Main Campus Hewitt Hall, UCI Health – Pavilion II, UCI Family Health Center, Anaheim, Irvine High School).


If research activities will also be conducted at non-UCI locations (e.g., educational institutions, businesses, organizations, etc.), Complete Appendix A. Letters of Permission or other documentation may be required (e.g. Off-site Research Agreements or IRB Authorization Agreements).

UCI Gottschalk Medical Plaza, Department of Dermatology

B. Study Design

1. Include an explanation of the study design (e.g., randomized placebo-controlled, cross-over, cross-sectional, longitudinal, etc.) and, if appropriate, describe stratification/ randomization/blinding scheme.

This study is a longitudinal study to measure response to MKTP treatment versus baseline pigmentation in the grafted area. We will evaluate response to treatment in the transplanted areas at 1 week, 1 month and 3 months, and 6 months by both photography to measure change in surface area and quantifying the VASI score.

2. Provide precise definitions of the study endpoints and criteria for evaluation; if the primary outcomes are derived from several measurements (i.e., composite variables) or if endpoints are based composite variables, then describe precisely how the composite variables are derived.

Study Endpoints:
We hypothesize that our transplant procedure will yield excellent to good repigmentation, resulting in a mean of 60% reduction in surface area and VASI scores (SD=30%) from baseline to 6-month follow up. With a sample size of 5 patients, this study will achieve 90% power to test this hypothesis based on a two-sided paired t-test at p=0.05 significance level. This will be measured by both the physician and captured via digital photography. In the second arm of the study, we will compare the results with skin harvested with a blade as compared to a suction blister method. In the third arm of the study, we will compare the results skin harvested with a blade as compared to a suction blister with dissociation and suction blister without dissociation.

C. Research Procedures

1. Provide a detailed chronological description of all research procedures.

Subjects will undergo a vitiligo surgical treatment consisting of melanocyte-keratinocyte transplantation with surgical blade, with suction blistering device with cell dissociation and suction blister grafting without cell dissociation.

This procedure is described in detail below:

1-First arm:
An unaffected area of the subject's body was selected for a donor site. This site is usually on the lateral aspect of the leg or gluteal region and for the purposes of this study will be 2 cm^2. The site was cleaned with povidone iodine and ethanol and an anesthetic block was performed with 1% lidocaine and 1:200,000 epinephrine with sodium bicarbonate. The area was sterilely draped. Lubrication was applied and a 200-micrometer thick layer of skin was removed with a silver skin grafting knife. This donor site was covered with a hydrocolloid dressing, gauze, and an adhesive dressing.

The donor site skin sample was placed in a Petri dish, with the epidermis upward and immersed in 8ml trypsin, 0.25% EDTA tetrasodium and incubated at 37 degrees Celsius for 20-30 minutes. After this incubation, the trypsin solution was disposed of and the skin sample was rinsed with a nutrient medium. The dermis was mechanically separated with forceps from the epidermis. The epidermis was then separated into multiple, smaller pieces, washed with the medium and put into a centrifuge tube. Medium

was added to bring total volume to 4ml. This tube was inverted for approximately 5 times and then centrifuged for 5 minutes at 2000 rpm to separate the cell pellet with the melanocytes and keratinocytes from the other epidermal components. The remaining components were disposed of and the cell pellet with the melanocytes and keratinocytes in suspension were then transferred into a 1 ml syringe. This solution was used for grafting, where the leftover suspension was used for single cell RNA-sequencing.

The recipient site was selected as a single area with between 5 cm^2 and 10 cm^2 in any area of body locations other than the eyelids, lips, palms, soles, or nail beds. The recipient site was prepped and draped in usual sterile fashion. The recipient transplant sites were prepped with povidone iodine and 70% ethanol. An anesthetic block was achieved with 1% lidocaine with sodium bicarbonate. This area then underwent full thickness epidermal ablation with an Erbium-YAG laser. The previously described epidermal suspension was then applied evenly to the denuded area. This recipient site was then covered with collagen matrix dressings, sterile gauze and occlusive dressing.
Subjects were then able to be discharged to home but avoided disturbing dressing or soaking the dressing.

Subjects scheduled follow up post-operative appointments to the UCI dermatology clinic for evaluation by the lead researcher 1 day and 7 days after the procedure. In addition, the patient scheduled follow ups at 1 month, 3 months, and 6 months after treatment to evaluate treatment response.

2-Second arm:
An unaffected area of the subject's body is selected for a donor site. This site is usually on the lateral aspect of the leg or gluteal region and for the purposes of this study is 4 cm^2. The site is cleaned with povidone iodine and ethanol and an anesthetic block is performed with 1% lidocaine and 1:200,000 epinephrine with sodium bicarbonate. The area is sterilely draped. Then, we create 8 blister areas each about 5mm^2 with the suction blister device. The suction blister device is a self-contained instrument package to successfully creates suction blisters on skin. Blisters will be created by skin being drawn through the openings of a warmed aluminum orifice plate that is fitted to a suction chamber. The orifice plate is removable and interchangeable, and various plates can be produced with various orifices and sizes to meet specific needs.

The lightweight chambers are attached to the patient by Velcro® straps. The instrument console contains the power source, vacuum pump, temperature and vacuum controls to operate multiple suction chambers. The suction chambers are connected to the console via flexible tubing that supplies the chamber's vacuum and heating circuits. Each of the chambers has an individual temperature controller in the console and all chambers share a common adjustable vacuum system.

For convenience and improved blister success, each chamber has a transparent viewing window so that the actual blister formation process can be monitored.

After creating blisters, we unroof the blisters and use the roof skin for transplantation.
Then, the donor site is covered with a hydrocolloid dressing, gauze, and an adhesive dressing.
The donor site skin sample is placed in a Petri dish, with the epidermis upward and immersed in 8ml trypsin, 0.25% EDTA tetrasodium and incubated at 37 degrees Celsius for 20-30 minutes. After this incubation, the trypsin solution is disposed of and the skin sample is rinsed with a nutrient medium. The dermis is mechanically separated with forceps from the epidermis. The epidermis is then separated into multiple, smaller pieces, washed with the medium and put into a centrifuge tube.

Medium is added to bring total volume to 4ml. This tube is inverted for approximately 5 times and then centrifuged for 5 minutes at 2000 rpm to separate the cell pellet with the melanocytes and keratinocytes from the other epidermal components. The remaining components is disposed of and the cell pellet with the melanocytes and keratinocytes in suspension is then transferred into a 1 ml syringe. This solution is used for grafting, where the leftover suspension is used for single cell RNA-sequencing.

The recipient site is selected as a single area of 5 cm^2 in any area of body in locations other than the eyelids, lips, palms, soles, or nail beds. The recipient site is prepped and draped in usual sterile fashion. The recipient transplant site is prepped with povidone iodine and 70% ethanol. An anesthetic block is achieved with 1% lidocaine with sodium bicarbonate. This area then is removed with a suction blister (10 blisters each 5 mm2). This tissue is used to make another single cell suspension. The epidermal suspension from the donor site is then applied evenly to the denuded area. This recipient site is then covered with collagen matrix dressings, sterile gauze and occlusive dressing. The recipient cell suspension is also used for single-cell RNA-sequencing. A portion of the remainder of the cells (from both the donor and recipient site) is subjected to flow sorting to quantify the populations of melanocytes and keratinocytes.

Subjects are then discharged to home but advised avoiding disturbing dressing or soaking the dressing.

Subjects were scheduled follow up post-operative appointments to the UCI dermatology clinic for evaluation by the lead researcher 1 day and 7 days after the procedure. In addition, the patients were scheduled follow ups at 1 month, 3 months, and 6 months after treatment to evaluate treatment response.

3-Third arm:

An unaffected area of the subject's body will be selected for a donor site. This site is usually on the lateral aspect of the leg or gluteal region and for the purposes of this study will be 5 cm^2 or 0.77 $inch^2$. The entire harvesting procedure usually takes less than one hour. The site will be cleaned with povidone iodine and ethanol and an anesthetic block will be performed with 1% lidocaine and 1:200,000 epinephrine with sodium bicarbonate. The area will be sterilely draped. Then, we will create multiple micro domes(blisters) with the cellutome epidermal harvesting system which is an FDA approved suction blister device with FDA Regulation # 878.4820.
The cellutome epidermal harvesting system is a self-contained instrument package to successfully creates suction blisters on skin. The CELLUTOME™ Harvester will be strapped to the donor site. The graft development process is usually completed in 30-45 minutes. Use of the system, provides a ready to apply array of autologous epidermal micro grafts that are 1.8 mm in diameter. These are spaced and oriented at 2.5 mm from edge to edge and 4.3 mm from center to center, yielding a significant expansion ratio. A 5-by-5-cm size yields 128 microdomes. When the grafts are ready for harvesting, the CELLUTOME™ Control Unit is turned off. The grafts are placed onto a transparent dressing and are then are ready to be applied to the recipient site. Then, the donor site will be covered with a hydrocolloid dressing, gauze, and an adhesive dressing. Also, a small area from the recipient site and also a normal skin on the donor area will be removed with a regular suction blister device (4 blisters each 5 mm^2). The regular suction blister device is a self-contained instrument package to successfully creates suction blisters on skin. Blisters will be created by skin being drawn through the openings of a warmed aluminum orifice plate that is fitted to a suction chamber. The orifice plate is removable and

interchangeable, and various plates can be produced with various orifices and sizes to meet specific needs.

The lightweight chambers are attached to the patient by Velcro® straps. The instrument console contains the power source, vacuum pump, temperature and vacuum controls to operate multiple suction chambers. The suction chambers are connected to the console via flexible tubing that supplies the chamber's vacuum and heating circuits. Each of the chambers has an individual temperature controller in the console and all chambers share a common adjustable vacuum system.

For convenience and improved blister success, each chamber has a transparent viewing window so that the actual blister formation process can be monitored.

After creating four blisters, we will unroof the blisters and use the roof skin for histopathological evaluation. The two blisters from the normal skin and two blisters from the recipient site will also be used for histopathological study

The recipient site will be selected as a single area of 5 cm^2 to 10 cm^2 in any area of body in locations other than the eyelids, lips, palms, soles, or nail beds. The recipient transplant sites will be prepped with povidone iodine and 70% ethanol. An anesthetic block will be achieved with 1% lidocaine with sodium bicarbonate.

The rest of recipient site will then undergo full thickness epidermal ablation with an Erbium-YAG laser. The micro domes(blisters) produced by Cellutome epidermal harvesting system from the donor site will be transferred and put on the recipient site. This recipient site will then be covered with collagen matrix dressings, sterile gauze and occlusive dressing.

Subjects will then be discharged to home but will avoid disturbing dressing or soaking the dressing.

Subjects will schedule follow up post-operative appointments to the UCI dermatology clinic for evaluation by the lead researcher 1 day and 7 days after the procedure. In addition, the patient will schedule follow ups at 1 month, 3 months, and 6 months after treatment to evaluate treatment response.

2. Describe the duration of a subject's participation in the study. If there are sub-studies, include duration of participation in each sub-study.

Up to 6 months for each arm of transplant procedure and appropriate follow up.

3. List data collection instruments (e.g., measures, questionnaires, interview questions, observational tool, etc.).

Investigator-authored, non-standardized, or un-validated measures must be submitted for review.

<Type here>

D. UCIMC Supplementary Clinical Services

If a UCIMC clinical unit/department (e.g., phlebotomy for blood draws, pharmacy for dispensing study drug(s), radiation services for X-rays, MRIs, CT scans, and Neurology for lumbar punctures) will perform research-related procedures:

1. List the research procedure (e.g. lumbar puncture, MRI, CT Scan), and
2. Identify the unit/department that will perform the procedure.

[ ] Not applicable: This study does not involve the services of a UCIMC clinical unit/department.

Treatment for vitiligo will occur at UCI Department of Dermatology.

Dr. Ganesan and his staff will perform the melanocyte-keratinocyte transplant procedure and follow-up evaluations.

E. Privacy

Privacy is about the subject's ability to control how much others see, touch, or collect information about the subject. Indicate all of the following methods that will be used to assure subject privacy. *Violations of privacy include accessing a subject's private information without consent, asking personal sensitive information in a public setting, being audio recorded or photographed without consent.*

[x] Research procedures (including recruitment) are conducted in a private room.

[x] Use of drapes or other barriers for subjects who are required to disrobe.

[x] Only sensitive information directly related to the research is collected about subjects.

[ ] When information is collected from internet sources, the internet site's privacy statement will be reviewed and followed.

Provide a copy of the Data Use Policy to the IRB.

[ ] Other (specify): <Type here>

F. Use of Existing Biological Specimens and/or Existing Information/Data

1. For studies that involve use of existing (i.e. on the shelf; currently available) specimens:
   a. Indicate the source of the specimens and whether the specimens were originally collected for research purposes.
   b. Explain how the existing specimens will be obtained.

[x] Not applicable: This study does not involve use of existing biological specimens.

Source: Indicate <u>all</u> that apply:

[ ] UCI/UCIMC

Originally collected for research purposes: **[ ]** YES; UCI IRB number (i.e. HS#): <Type here>

[ ] NO; explain: <Type here>

[ ] UCIMC Pathology Biorepository will provide specimens.

[ ] Non-UCI Entity; specify: <Type here>

Originally collected for research purposes: **[ ]** YES

Submit a copy of the IRB Approval Notice and Consent Form for the original collection.

[ ] NO; explain: <Type here>

[ ] Other; explain: <Type here>

2. For studies that involve use of existing (i.e. on the shelf; currently available) clinical data:
   a. Specify the source of the clinical data.
   b. Explain how the study team will access the clinical data. *Access to UCI Medical Center medical records for research purposes outside the capacity of the Honest Broker Services, such as access to physician notes, must be obtained from the Health Information Management Services*.

For investigator initiated/authored studies <u>only</u>, submit a data abstraction sheet that includes a complete list of data elements/information that will be collected from (existing) records or submit the case report form (CRF; eCRF).

[ ] Not applicable: This study does not involve use of existing clinical data. *Skip to Section 6.G.*

Source: Indicate <u>all</u> that apply:
[x] UCI/UCIMC.
[ ] non-UCI Entity; specify: <Type here>

How Obtained: Indicate <u>all</u> that apply:
[ ] The study team will request specific patient information/data from UCIMC Health Information Management Services.

[x] The study team will review their patients' records and abstract data directly from those records.

[ ] The study team will request specific patient information/data from UCI Health Honest Broker Services. Describe the following:

Cohort selection criteria (e.g., use the available Clinical Terms from the Cohort Discovery Tool such as Demographics: Gender, Diagnoses: Asthma, Procedures: Operations on digestive system): <Type here>

Expected cohort size/patient count: <Type here>

Cohort attributes or data elements (e.g., lab test values, medication, etc.): <Type here>

[ ] Other; explain: <Type here>

3. For studies that involve use of existing (i.e. on the shelf; currently available) clinical data, specify the time frame of the clinical data to be accessed (e.g. records from January 2002 to initial IRB approval).

The duration of the study.

G. Collection of Photographs, or Audio/Video Recording

1. Describe all procedures involving the use and/or collection of photographs, or audio/video recording.

[ ] Not applicable: This study does not involve photographs or audio/video recording. *Skip to Section 6.H.*

2. Specify if photographs or audio/video recording will include subject identifiable information (e.g., name, facial image). If so, indicate which identifiers will be collected.

No photographs will be taken that include subject identifiers. The areas taken will include the donor site and recipient site of the graft at each clinical visit (1 day, 4 days, 1 month, 3 months, and 6 months).

3. Explain whether the photographs or audio/video recording will be included in subsequent presentations and/or publications and, if so, whether subject identifiers will be included.

No presentation or publications from this research will include photographs that will include subject identifiers.

H. Sharing Results with Subjects

1. Describe whether individual results (results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with subject or others (e.g., the subject's primary care physician). *Only tests ordered by a physician and conducted in a CLIA certified lab may be shared.*
2. Explain what information will be shared and how the results will be shared.

[x] Not applicable: Individual results will not be shared with subjects.

<Type here>

3. Describe whether overall study results will be shared with subjects.
4. Explain how results will be shared.

[x] Not applicable: Final study results will not be shared with subjects.

<Type here>

I. Statistical Considerations *(This section is required for Investigator-Authored Research)*

1. Statistical Analysis Plan: Describe the statistical method(s) for the stated specific aims and hypotheses. *Your analysis plans should match the stated study specific aims and hypotheses in Section 1.*

[ ] Not applicable

This is an observational study to examine response to therapy using change in surface area and VES score. There will be no measurement other than improvement in surface area and VES score as a measure of improvement before and after the procedure.

2. Describe the primary statistical method(s) that will be used to analyze the primary outcome(s) or endpoints.

We will measure the VES score and surface area change in the transplanted area before and after the procedure. The rate of change in surface area and VES will be measured as an outcome measure. This study is powered to examine if the initial procedure induces significant repigmentation (10 patients for each arm) and is also sufficient to compare the initial procedure to the procedure with the blister grafting technique.

3. Describe the secondary statistical method(s) that will be used to analyze the secondary outcome(s) or endpoints.

N/A

4. If appropriate describe secondary or post hoc analyses of primary outcome(s) or other exploratory analysis.

N/A

5. Sample Size Determination**:** Explain how the overall target sample size was determined (e.g., power analysis; precision estimation), providing justification of the effect size for the primary outcome based on preliminary data, current knowledge/literature and/or cost consideration; if appropriate, provide sample size justification for secondary outcomes. Power analysis should (at least) match the primary outcome/endpoint.

With a sample size of 5 patients in each arm, this study will achieve 90% power to test the hypothesis for each arm based on a two-sided paired t-test at p=0.05 significance level.

SECTION 7: RISK ASSESSMENT AND POSSIBLE BENEFITS

A. Risk Assessment

1. Indicate the appropriate level of review of this study, based upon your risk assessment.

[x] This study involves greater than minimal risk to subjects and requires Full Committee review. *Skip to Section 7.B.*

[ ] This study involves no more than minimal risk and qualifies as **Expedited research**.

2. If this study involves no more than minimal risk, provide justification for the level of review and for all applicable Expedited Categories you have chosen.

B. Risks and Discomforts

1. Describe and assess any reasonably foreseeable risks and discomforts — physical, psychological, social, legal or other. Include an assessment of their expected frequency (e.g., common – 65%, less common – 40%, unlikely – 5%, rare - <1%) and the seriousness (mild, moderate, severe). *A bullet point list is recommended. If this study will involve the collection of identifiable private information, even temporarily, for which the disclosure of the data outside of the research could reasonably place the subjects at risk, include the risk of a potential breach of confidentiality.*

Common:

- Pain secondary to surgical procedure. This will be alleviated with appropriate anesthetic and analgesic preparation. Post-surgically, subjects will be provided standard of care post-operative care and medications.
- Hyperpigmentation at the donor site is a common side effect of the therapy. An area on the thigh that will be covered will be specifically selected for the donor site so it is not visually obvious.
- Scarring- As with any procedure there is always a risk of scarring at either the donor or recipient site

. Slow process- Time required to create blisters is usually 45 to 90 minutes.

-

Rare:

- Infection. All surgical procedures involve some infection risk. All standard of care surgical sterile techniques will be strictly adhered to and subjects will be monitored at three post-operative visits for any signs of infection or complications.
- Psychological distress: treatment is not a guaranteed successful. Subjects might experience psychological distress or a heightened emotional response to failed re-pigmentation. Appropriate pre-treatment counseling and the development of reasonable expectations will be discussed prior.

2. Discuss what steps have been taken and/or will be taken to prevent and minimize any risks/ potential discomforts to subjects. *Examples include: designing the study to make use of procedures involving less risk when appropriate; minimizing study procedures by taking advantage of clinical procedures conducted on the subjects; mitigating risks by planning special monitoring or conducting supportive inventions for the study; implement security provisions to protect confidential information.*

Proper surgical standard of care for anesthetic, analgesic care as well as sterile technique.
Appropriate follow up for post-operative care.
Appropriate and compassionate counseling on treatment expectations.

C. Potential Benefits

1. Describe the potential benefits subjects may expect to receive from participation in this study. *Compensation is not a benefit; do not include it in this section.*

[ ] There is no direct benefit anticipated for the subjects.

Subjects will have the opportunity for MKTP grafting of an affected area as part of the study, which is more effective than the currently used punch grafting technique.

2. Specify the expected potential societal/scientific benefit(s) of this study.

This study will establish the use of melanocyte-keratinocyte transplant procedure for the treatment of vitiligo at the University of California, Irvine and potentially identify the molecular characteristics of melanocytes that repigment the skin.

SECTION 8: ALTERNATIVES TO PARTICIPATION

Describe the alternatives to participation in the study available to prospective subjects. Include routine (standard of care) options as well as other experimental options, as applicable.

[ ] No alternatives exist. The only alternative to study participation is not to participate in the study.

[x] There are routine standard of care alternatives available; specify: subjects can elect to not undergo this study and undergo the punch grafting procedure for vitiligo.

[ ] There are other alternatives to study participation; specify: <Type here>

SECTION 9: SUBJECT COSTS

1. Indicate below if subjects or their insurers will be charged for study procedures. Identify and describe those costs.

[ ] Not applicable: This study involves no interaction/intervention with research subjects. *Skip to Section 10.*

[x] This study involves interaction/intervention with research subjects; however there are no costs to subjects/insurers.

[ ] This study involves interaction/intervention with research subjects, and there are costs to subjects/insurers: <Type here>

2. If subjects or their insurers will be responsible for study-related costs, explain why it is appropriate to charge those costs to the subjects or their insurers. Provide supporting documentation as applicable (e.g., study procedures include routine (standard of care) procedures; FDA IDE/HDE/IND letter that supports billing to subjects).

[x] Not applicable: The study involves no costs to subjects for study participation.

[ ] Study related costs will be billed to subjects or their insurers for the following reasons: <Type here>

SECTION 10: SUBJECT COMPENSATION AND REIMBURSEMENT

1. If subjects will be compensated for their participation, explain the method/terms of payment (e.g., money; check; extra credit; gift certificate).

[ ] Not applicable: This study involves no interaction/intervention with research subjects. *Skip to Section 11.*

[x] No compensation will be provided to subjects.

[ ] Compensation will be provided to subjects in the form of cash/gift certificate.

[ ] Compensation will be provided to subjects in the form of a check issued to the subjects through the UCI Accounting Office. The subject's name, address, and social security number, will be released to the UCI Accounting Office for the purpose of payment and for tax reporting to the Internal Revenue Service (IRS).

[ ] Other: <Type here>

2. Specify the schedule and amounts of compensation (e.g., at end of study; after each session/visit) including the total amount subjects can receive for completing the study. *Compensation should be offered on a prorated basis when the research involves multiple visits.*

   For compensation ≥ $600, subject names and social security numbers must be collected. This information must be reported to UCI Accounting for tax-reporting purposes.

[x] Not applicable: This study involves no compensation to subjects.

3. Specify whether subjects will be reimbursed for out-of pocket expenses. If so, describe any requirements for reimbursement (e.g., receipt).

[x] Not applicable: This study involves no reimbursement to subjects.

Subjects will be reimbursed; specify: <Type here>

SECTION 11: CONFIDENTIALITY OF RESEARCH BIOSPECIMENS/DATA

A. Biospecimens/Data Storage

1. Indicate all subject identifiers that may be included with the biospecimens or collected for the research study. *If any study-related data will be derived from a medical record, added to a medical record, created or collected as part of health care, or used to make health care decisions the HIPAA policy applies. The subject's HIPAA Research Authorization is required or a waiver of HIPAA Research Authorization must be requested by completing Appendix T.*

[ ] This study does not involve the collection of subject identifiers.

Check all the following subject identifiers will be used, created, collected, disclosed as part of the research:

[x] Names	**[x]** Social Security Numbers	**[ ]** Device identifiers/Serial numbers
[x] Dates*	**[x]** Medical record numbers	**[ ]** Web URLs
[x] Postal address	**[ ]** Health plan numbers	**[ ]** IP address numbers
[x] Phone numbers	**[ ]** Account numbers	**[x]** Biometric identifiers
[ ] Fax numbers	**[ ]** License/Certificate numbers	**[ ]** Facial Photos/Images
[ ] Email address	**[ ]** Vehicle id numbers	**[ ]** Any other unique identifier

[ ] Other (Specify all): <Type here>

* *birth date, treatment/hospitalization dates*

Indicate how data will be stored and secured, including electronic data as well as hardcopy data paper records, electronic files, audio/video tapes, biospecimens, etc. *If the research data includes subject identifiable data and/or Protected Health Information, the storage devices or the electronic research files must be encrypted. [For guidance on the use of cloud services, please review the UCI OIT policy.]*

Electronic Data/Files (check all that apply):

[ ] Anonymous data will be maintained; no subject identifiers

[x] Coded data; code key is kept separate from data in secure location.

[ ] Data includes subject identifiable information. Provide rationale for maintaining subject identifiable info)**:** <Type here>

[x] Data will be stored on secure network server.

[ ] Data will be stored on standalone desktop computer (not connected to network/internet)

[ ] Other (specify here): <Type here>

Hardcopy Data (Records, Recordings, Photographs) and Biospecimens (check all that apply):

[ ] Anonymous biospecimens/data will be maintained; no subject identifiers

[x] Coded data; code key is kept separate from biospecimens/data in secure location.

[ ] Biospecimens/Data includes subject identifiable information (Provide rationale for maintaining subject identifiable info)**:** <Type here>

[x] Data will be stored in locked file cabinet or locked room.

[ ] Biospecimens will be stored in locked lab/refrigerator/freezer.

[ ] Other (specify here): <Type here>

2. List the location(s) where the data and/or biological specimens will be stored**.**

UCI Dermatology Clinical Research Center
Ganesan Lab in UCI Sprague Hall

3. If subject identifiable data will be transported or maintained on portable devices, explain why it is necessary use these devices. *Only the "minimum data necessary" should be stored on portable devices as these devices are particularly susceptible to loss or theft. If there is a necessity to use a portable device for the initial collection of identifiable private information, the research files must be encrypted, and subject identifiers transferred to a secure system as soon as possible.*

[x] Not applicable: Research data will not be transported or maintained on portable devices.

Research data will need to be maintained on the following portable device(s) for the following reason(s): <Type here>

B. Data and/or Biological Specimens Access

Specify who will have access to subject identifiable data and/or biological specimens as part of this study.

[ ] Not applicable: No subject identifiers will be collected.

[x] Authorized UCI personnel such as the research team and appropriate institutional officials, the study sponsor or the sponsor's agents (if applicable), and regulatory entities such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP), and the National Institutes of Health (NIH).

[ ] Other: <Type here>

C. Data and/or Biological Specimens Retention

Indicate how long subject identifiable data and/or biological specimens, including the subject code key will be retained. *If more than one of the options below is applicable (e.g., the study involves children), records must be kept for the longer period.*

[ ] Not applicable: No subject identifiable research data will be retained.

[ ] Separate code key will be destroyed or subject identifiable information will be removed from the biospecimens and/or data at the earliest convenience, consistent with the conduct of this research. Specify timeframe: 1 year after completion of study

[ ] Destroyed once research data is analyzed.

[ ] Destroyed after publication/presentation.

[ ] Will be maintained; specify time frame and provide the rationale: <Type here>

[x] Will be stored and maintained in a repository for future research purposes.

Complete Appendix M

[x] Will be retained for six years as this research involves Protected Health Information (PHI) (e.g., IRB documentation, consent/assent forms – NOT the actual PHI). *Investigators must destroy PHI at the earliest opportunity, consistent with the conduct of this study, unless there is an appropriate justification for retaining the identifiers or as required by law.*

[ ] Will be retained for seven years after all children enrolled in the study reach the age of majority [age 18 in California] as this study includes children.

[ ] Will be retained 25 years after study closure as this study involves in vitro fertilization studies or research involving pregnant women.

[ ] Will be retained for two years after an approved marketing application, as this is a FDA regulated study. If approval is not received, the research records will be kept for 2 years after the investigation is discontinued and the FDA is notified.

[ ] Other: <Type here>

D. Photographs, Audio/Video Recordings Retention

1. If subject identifiable audio or video recordings will be collected, specify the timeframe for the transcription and describe retention/destruction plans.

[x] Not applicable: Subject identifiable audio/video recordings will not be collected.

[ ] Audio or video recordings transcribed; specify time frame: <Type here>

[ ] Audio or video recordings will be maintained; specify time frame: <Type here>

[ ] Audio or video recordings maintained indefinitely; provide the rationale: <Type here>

[ ] Audio or video recordings destroyed; specify time frame: <Type here>

2. If subject identifiable photographs will be collected, describe retention/destruction plans**.**

[ ] Not applicable: Subject identifiable photographs will not be collected.

[ ] Photographs will be maintained; specify time frame:

[x] Photographs maintained indefinitely; provide the rationale: photographs will be maintained by the lead researcher indefinitely for evaluation of study outcomes, rationale for further study development, and research presentation and publication. However, all photographs will not include subject identifiable information or specific individual characteristics.

[ ] Photographs destroyed; specify time frame: <Type here>

E. Certificate of Confidentiality

1. Indicate whether a Certificate of Confidentiality (COC) has been or will be requested.

[ ] Not applicable: No COC has been requested for this study.

[ ] A COC will be or has been requested for this study. *The COC application must be submitted to the IRB staff for review after IRB approval.*

[x] A COC has been obtained for this study. The expiration date of this COC is: <Type here>

Provide a copy of the COC Approval Letter.

2. Explain in what situations the UCI study team will disclose identifiable private information protected by a COC.

To help us protect the subject's privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, researchers cannot be forced to disclose information that may identify the subjects in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings or be used as evidence, for example, if there is a court subpoena, unless the patient has consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if the patient has consented to the disclosure, including for his/her medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States

federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). The subjects should understand that a Certificate of Confidentiality does not prevent them from voluntarily releasing information about themselves or their involvement in this research. If they want their research information released to an insurer, medical care provider, or any other person not connected with the research, they must provide consent to allow the researchers to release it.

UNIVERSITY OF CALIFORNIA, IRVINE
CONSENT TO ACT AS A HUMAN RESEARCH SUBJECT

Evaluating the Efficacy of the Melanocyte Keratinocyte Transplantation Procedure in the Treatment of Vitiligo (Arm 3)

You are being asked to participate in a research study. Participation is completely voluntary. Please read the information below and ask questions about anything that you do not understand. A researcher listed below will be available to answer your questions.

RESEARCH TEAM
Lead Researcher
Dr. Anand Ganesan, M.D., Ph.D.
Department of Dermatology Telephone Number:
949-824-0606 24-Hour Telephone Number/Pager: 714-506-3967

Other Researchers
Dr. Jessica Shiu, M.D, Ph.D.
Department of Dermatology Telephone Number:
949-824-0606 24-Hour Telephone Number/Pager: 714-506-3967

STUDY LOCATION(S):
UC Irvine Dermatology Clinical Research Center
UC Irvine Health Gottschalk Medical Plaza Department of Dermatology

STUDY SPONSOR(S):
UC Irvine Health Department of Dermatology

WHY IS THIS RESEARCH STUDY BEING DONE?

The purpose of this research study is to understand how effective suction blister grafting without cell dissociation is at treating vitiligo and identify characteristics of the pigment cell that migrates to the skin during the process of repigmentation. This procedure is experimental. The study doctor will offer participants the opportunity to undergo melanocyte keratinocyte transplant procedure, which is one of the possible treatments for vitiligo. This procedure is a method to transplant an area of skin affected by vitiligo with a mixture of prepared pigmented and non-pigmented skin cells that are harvested from the top layer of the skin in an area that is not affected by vitiligo.

If you agree, A normally pigmented area on the upper thigh will be numbed with 1% lidocaine with epinephrine. Using a superficial skin harvesting system which is a suction blister technique, we will remove multiple small portions of the superficial layer of the skin unaffected by vitiligo from a small normal area (5 cm2) on your thigh to obtain the transplantation cells and also using a regular negative pressure instrument for removing four samples, two from the vitiligo area and two from the normal skin. The superficial layer of the skin from the normal skin area (thigh) will then be transplanted on to the area affected by vitiligo that you are interested in grafting. Four samples (two from the normal skin and

two from the vitiligo skin) generated by the negative pressure device will then be sent to identify specific characteristics of the migrating cells responsible for repigmentation.

A dressing will be placed on the grafted area and the area the cells were taken from. You will return to clinic in 1 day, and 1 week for follow up. Then you will return at 1 month, 3 months, and 6 months for follow up photography to quantify your response to the treatment.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 30 participants will take part in this research at UCI.

AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?

Inclusion Requirements

You can participate in this study if you have been diagnosed by a dermatologist with vitiligo and are a candidate for vitiligo treatment as determined by the lead study doctor. In addition, you need to:

- Be over 18 years of age at time of signing consent form
- Have the ability to understand and agree to participate with the study procedures

Exclusion Requirements

You cannot participate in this study if you:

- If you are not willing or able to understand and carry out the study procedures
- Pregnant or breastfeeding
- Are under 18 years of age at time of signing informed consent form
- Have a history of keloid scars
- Use tobacco products currently
- Have a medical condition that would make it dangerous for you to participate, such as:
    - Poor clotting of your blood. This is the way your body stops bleeding after you have a cut or injury to one of your blood vessels.
    - Difficulty or problems with your healing ability after you have surgery
    - or a medical condition that would make it dangerous for you to participate as determined by the study doctors

HOW LONG WILL THE STUDY GO ON?

The study will take six months in total as you will need to return after six months for follow up photography to determine the response rate.

WHAT PROCEDURES ARE INVOLVED WITH THIS STUDY?

If you choose to participate, you will come to see the study doctor and he will determine the appropriate areas for your skin grafts.

The study doctor will first identify an unaffected area on your body that will be selected for a ***donor(normal skin using for transplantation)*** site. This site is usually on the side of your upper leg or on your buttocks and will be approximately 5 cm^2. This site will be sterilely cleaned and draped (covered) with sterile surgical towels. The entire harvesting procedure usually takes less than one hour. An anesthetic block (Numbing) will be performed with 1% lidocaine and 1:200,000 epinephrine with sodium bicarbonate. The area will be sterilely draped(covered). Then, we will create multiple micro domes(blisters) with the Cellutome epidermal harvesting system which is an FDA approved suction

blister device. The cellutome epidermal harvesting system is a self-contained instrument package to successfully creates suction blisters on skin. The CELLUTOME™ Harvester will be strapped to the donor site (Normal skin used for transplantation). The graft development process is usually completed in 30-45 minutes. The grafts are placed onto a transparent dressing and are then are ready to be applied to the area affected by vitiligo. Then, the donor site will be covered with a hydrocolloid(synthetic gelly) dressing, gauze, and an adhesive dressing. As part of the study, a small area from the recipient (vitiligo) site and also the normal skin of the donor site will be removed with a regular suction blister device (4 blisters each 5 mm^2). After creating four blisters, we will unroof (cut and remove the top of) the blisters and use the roof skin for histopathological evaluation(pathology lab studies).

The recipient (vitiligo) site will be selected as a single area of 5 cm^2 to 10 cm^2 in any area of the body in locations other than the genitals. The recipient transplant (vitiligo) sites will be prepped (cleaned) with povidone iodine and 70% ethanol. The area affected by vitiligo will be anesthetized (numbed) with 1% lidocaine with epinephrine.

The recipient (vitiligo) site will then undergo full thickness epidermal ablation(full superficial skin removal) with an Erbium-YAG laser to remove all the cells affected by vitiligo. The micro domes (blisters) produced by Cellutome epidermal harvesting system from the donor (normal skin for transplant) site will be transferred and put on the recipient (vitiligo) site. This recipient site will then be covered with collagen dressings, sterile gauze and occlusive dressing. The four blisters from the donor site and normal skin will also be used for histopathological study.

You can go home the same day but will need to protect your dressing and avoid soaking it in water. You will follow up with the study doctors in the outpatient clinic in 2 days after the procedure and then again 7 days later to see how you are healing and your response to the transplant treatment. You will return for a final follow up 1 month, 3 months, and 6 months after the procedure.

WHAT ARE THE POSSIBLE SIDE EFFECTS OR RISKS RELATED TO THE STUDY?

Side Effects or Risks of Suction blister grafting without cell dissociation

This is a surgical procedure and involves removing multiple blisters of the top of your skin that will be applied to a vitiligo area on your body. The procedure has the risk of infection, poor wound healing, pain, bleeding, decreased or increased pigmentation, redness or skin rash, and scarring. There is also a risk that your body will not accept the skin graft and it will not work to treat your vitiligo. This is known as graft failure. The study doctors will make every effort to avoid infection, which includes sterile preparation, appropriate post-surgical site dressings, follow up care, and if necessary, antibiotics. You will receive local anesthetic medicine when you undergo the surgical procedures and post-surgical analgesics, if necessary.
The risks of the local anesthetic medicine are very rare but include the possibility of as follows:
headache, slow heart rate, low blood pressure, allergic reaction, and tremor.

Breach of Confidentiality

There is a small chance of a breach of confidentiality involving research data. All identifiable information that will be collected about the subject will be removed and replaced with a code. A list linking the code and subject identifiable information will be kept separate from the research data.

Unknown risks:
There may be risks related to the research that we don't know about yet. However, you will be informed of any additional risks to which you may be exposed, and any changes that are made to the study, as a result of any newly-identified risks.

Reproductive Risks:
You should not get pregnant while in this study. The Lidocaine used in this study could harm an unborn baby.

ARE THERE BENEFITS TO PARTICIPATING IN THIS STUDY?

Participant Benefits
Taking part in this study may or may not make your health better. However, it is already known that the melanocyte keratinocyte transplantation is an effective way to treat vitiligo.

Benefits to Others or Society
There may be benefits such as demonstrating that the melanocyte keratinocyte transplant procedure is a useful treatment for vitiligo. Also, we may identify which melanocyte population migrates to repigment the skin. This could lead to improvements in grafting and transplantation or to the development of better drugs to stimulate this population of cells to migrate.

WHAT OTHER CHOICES DO I HAVE IF I DON'T WANT TO PARTICIPATE?
If you decide not to participate, or if you withdraw from this study before it is completed, your other choices may include:

Getting no treatment Getting standard treatment for your condition without being in a study (punch grafting, light therapy).

Getting a different experimental treatment/taking part in another study.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?
You will not be paid for taking part in this study.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?
There is no cost to you or your insurer for your participation in this study. There are no medical and research procedure-related costs to you for participation in this study. You and /or your health plan/insurance will be billed for the costs of any standard medical care you receive to diagnose and/or treat any medical condition(s) outside of this study. You will also be responsible for any deductibles or co-payments that would normally be associated with these standard medical costs.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?
It is important that you promptly tell the researchers if you believe that you have been injured because of taking part in this study. You can tell the researcher in person or call him/her at the number listed at the top of this form.

If you are injured as a result of being in this study, UCI will provide necessary medical treatment. The

costs of the treatment may be covered by the University of California or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about this, you may call UCI Human Research Protections (949) 824-6068 or (949) 824-2125 or by e-mail at IRB@research.uci.edu

WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?

You are free to withdraw from this study at any time. **If you decide to withdraw from this study, you should notify the research team immediately**. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits or your safety and welfare are at risk.

If you elect to withdraw or are withdrawn from this research study, you may choose to terminate the continued use or disclosure of your protected health information (PHI) for research purposes. The request to end the use or disclosure of your PHI should be made in writing.

If you experience any of the side effects listed above, if your health worsens, or if you are injured during the research, you may need to be withdrawn from the study, even if you would like to continue. The research team will make this decision and let you know if it is not possible for you to continue. The decision may be made to protect your safety and welfare, or because the research plan does not allow people who develop certain conditions to continue to participate.

If you withdraw or are removed from the study, the researcher may ask you to attend a final follow-up visit to complete your participation in this study.

HOW WILL INFORMATION ABOUT ME AND MY PARTICIPATION BE KEPT?

Subject Identifiable Data

All identifiable information that will be collected about you will be removed and replaced with a code. A list linking the code and your identifiable information will be kept separate from the research data.

Data Storage

Data will be stored on research computers and laptops (all secured with passwords). Only authorized individuals will have access to it. There will be no hardcopy data.

Study data might be processed, analyzed and kept on laptops besides the desktop computer but subject identifiable data will not be stored on portable devices.

Data Retention

The researchers intend to keep the research data until the research is published and/or presented. The data associated with this study will be retained for 6 years.

WHO WILL HAVE ACCESS TO MY STUDY DATA?

The research team, authorized UCI personnel and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to your study records to protect your safety and welfare.

Any information derived from this research project that personally identifies you will not be released or disclosed by these entities without your separate written consent, except as specifically required by law. Research records provided to authorized, non-UCI entities will not contain identifiable information about

you. Publications and/or presentations resulting from this study will not include identifiable information about you.

While the research team will make every effort to keep your personal information confidential, it is possible that an unauthorized person might see it. We cannot guarantee total privacy.

ClinicalTrials.gov ClinicalTrials.gov is a Web site that provides information about clinical trials. 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.

Certificate of Confidentiality
To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, researchers cannot be forced to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIH which is funding this project 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 from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

Medical Care
If you agree to participate in this research study, a signed copy of this consent document and the privacy authorization form may be filed in your electronic medical record (EMR) and your study participation may be added to your EMR. This information will be used for your care and treatment and for healthcare operations, which may include billing and payment.

ARE THERE OTHER ISSUES TO CONSIDER IN DECIDING WHETHER TO PARTICIPATE IN THIS STUDY?

Use of Specimens
Biospecimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

Genetics
In the event of an unexpected breach of confidentiality, a federal law called the Genetic Information Non-Discrimination Act (GINA) will help protect you from health insurance or employment discrimination based on genetic information obtained about you. In California, state law (CalGINA) requires that

employers with 5 or more employees may not use your genetic information, obtained from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment. However, these laws do not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.
If you would like more information about the federal GINA law go to:
http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf or CalGINA:
http://www.leginfo.ca.gov/pub/11-12/bill/sen/sb_0551-0600/sb_559_bill_20110906_chaptered.pdf

Investigator Financial Conflict of Interest
No one on the study team has a disclosable financial interest related to this research project.

Request for Donation of Specimens and/or Data for Future Use
This is a request for donation of your tissue for medical research. Please read each sentence below and think about your choice. After reading each sentence, put your initials in either the "Yes" or "No" box. If you have any questions about this request for donation, please talk to the researchers. If you choose not to donate your specimens, any leftover tissue or blood that is not needed for this study will be thrown away.

1. You may keep my tissue for future research related to vitiligo. My tissue will be stored in a way that does not directly identify me.

YES	NO

2. You may keep my tissue for future research to learn about, prevent, or treat other health problems such as skin cancer or pigmentary disorders in dermatology. My tissue will be stored in a way that does not directly identify me.

YES	NO

3. You may share my tissue with other researchers. My tissue will be stored in a way that does not directly identify me.

YES	NO

So long as your specimens remain identifiable, you are free to withdraw the use of your specimens kept for future research. If you decide to withdraw your specimens from such use, you should notify the research team immediately. Specimens previously provided to researchers and any data generated will continue to be used.

4-UCI researchers may contact me in the future to ask me to take part in other research studies.

YES	NO

WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?
If you have any comments, concerns, or questions regarding the conduct of this research, please contact the research team listed at the top of this form.

A 24-hour number is also listed on the top of this form to report any health concerns or unanticipated problems you may experience after normal hours or on weekends.

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any suggestions, problems or concerns you may have about the study, please contact UCI's Office of Research by phone, (949) 824-6068 or (949) 824-2125, by e-mail at IRB@research.uci.edu or at to 160 Aldrich Hall, Irvine, CA 92697-7600.

What is an IRB? An Institutional Review Board (IRB) is a committee made up of scientists and non-scientists. The IRB's role is to protect the rights and welfare of human subjects involved in research. The IRB also assures that the research complies with applicable regulations, laws, and institutional policies.

HOW DO I AGREE TO PARTICIPATE IN THIS STUDY?
You should not sign and date this consent form until all of your questions about this study have been answered by a member of the research team listed at the top of this form. You will be given a copy of this signed and dated consent form, and the attached "Experimental Subject's Bill of Rights" to keep.
Participation in this study is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your future relationship with UCI or your quality of care at the UCI Medical Center.

If, during the course of this study, significant new information becomes available that may relate to your willingness to continue to participate, this information will be provided to you by the research team listed at the top of the form.

Your signature below indicates you have read the information in this consent form and have had a chance to ask any questions you have about this study.

Note: If the research described in this form involves your protected health information (PHI), you will be asked to sign separate UC HIPAA Research Authorization form for the use of your PHI.

I agree to participate in the study.

_____ _____

Subject Signature **Date**

Printed Name of Subject

Signature of Person Obtaining Informed Consent **Date**
(Individual must be listed on Page 1 of this consent)

Printed Name of Person Obtaining Informed Consent

A witness signature is required on this consent form only if: (Researchers: check which one applies)

☐ Consent is obtained from the subject via the Short Form process, as approved by the IRB.
☐ The subject has decision-making capacity, but cannot read, write, talk or is blind.
☐ The subject's guardian/legally authorized representative (LAR) cannot read, write, talk or is blind.
☐ The IRB specifically mandated a witness signature for this study (e.g., high risk and/or invasive research procedures).

Note: The witness must be impartial (i.e. not a member of the subject's family, not a member of the study team).

For the witness:

I confirm that the information in this consent form was accurately explained to and understood by the subject or legally authorized representative and that informed consent was given freely.

_____ _____

Witness Signature **Date**

(If no witness signature is required, this witness signature section of the consent form may be left blank).

_____

Printed Name of Witness

UNIVERSITY OF CALIFORNIA, IRVINE
Experimental Subject's Bill of Rights

The rights listed below are the right of every individual asked to participate in a research study. You have the right:

1. To be told about the nature and purpose of the study.

2. To be told about the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. To receive a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. To be told of any benefits that you may reasonably expect from the participation in the study, if applicable.

5. To receive a description of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. To be told of what sort of medical treatment, if any, will be available if any complications should arise.

7. To be given a chance to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. To refuse to participate in the research study. Participation is voluntary. You may refuse to answer any question or discontinue your involvement at any time without penalty or loss of benefits to which you might otherwise be entitled. Your decision will not affect your right to receive the care you would receive if you were not in the experiment.

9. To receive a copy of the signed and dated written consent form and a copy of this form.

10. To be given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study you should contact the research team listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research subject, please contact the UCI's Human Research Protections unit in the Office of Research by calling (949) 824-6068 or (949) 824-2125 Monday – Friday, 8 am – 5 pm; or by e-mail at IRB@research.uci.edu; or by writing us at to 160 Aldrich Hall, Irvine, CA 92697-7600.

University of California Irvine Health

Permission to Use Personal Health Information for Research

Study Title (or IRB Approval Number if study title may breach subject's privacy):

Melanocyte Keratinocyte Transplantation- Defining the Characteristics of Migrating Melanocytes

Principal Investigator Name:

Anand Ganesan

Sponsor/Funding Agency (if funded):

none

A. What is the purpose of this form?

State and federal privacy laws protect the use and release of your health information. Under these laws, the University of California or your health care provider cannot release your health information for research purposes unless you give your permission. Your information will be released to the research team which includes the researchers, people hired by the University or the sponsor to do the research and people with authority to oversee the research. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that health care providers can share your information with the researcher, research team, sponsor and people with oversight responsibility. The research team will use and protect your information as described in the attached Consent Form. However, once your health information is released by UC Irvine Health it may not be protected by the privacy laws and might be shared with others. If you have questions, ask a member of the research team.

B. What Personal Health Information will be released?

If you give your permission and sign this form, you are allowing your health care provider to release the following medical records containing your Personal Health Information. Your Personal Health Information includes health information in your medical records, financial records and other information that can identify you.

☐ Entire Medical Record

☐ Ambulatory Clinic Records

☒ Progress Notes

☐ Other Test Reports

☐ Other (describe):

☒ Lab & Pathology Reports

☐ Dental Records

☐ Operative Reports

☐ Discharge Summary

☐ Consultations

☐ Emergency Department Records

☐ Financial Records

☐ Imaging Reports

☐ History & Physical Exams

☐ Psychological Tests

_____

(Description of Other Health Information)

C. Do I have to give my permission for certain specific uses?

Yes. The following information will only be released if you give your specific permission by putting your initials on the line(s).

_____I agree to the release of information pertaining to drug and alcohol abuse, diagnosis or treatment.

_____I agree to the release of HIV/AIDS testing information.

_____I agree to the release of genetic testing information.

_____I agree to the release of information pertaining to mental health diagnosis or treatment.

D. Who will disclose and/or receive my Personal Health Information?

Your Personal Health Information may be shared with these people for the following purposes:

1. To the research team for the research described in the attached Consent Form;
2. To others at UC with authority to oversee the research
3. To others who are required by law to review the quality and safety of the research, including: U.S. government agencies, such as the Food and Drug Administration or the Office of Human Research Protections, the research sponsor or the sponsor's representatives, or government agencies in other countries.

E. How will my Personal Health Information be shared for the research?

If you agree to be in this study, the research team may share your Personal Health Information in the following ways:

1. To perform the research
2. Share it with researchers in the U.S. or other countries;
3. Use it to improve the design of future studies;
4. Share it with business partners of the sponsor; or
5. File applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

F. Am I required to sign this document?

No, you are not required to sign this document. You will receive the same clinical care if you do not sign this document. However, if you do not sign the document, you will not be able to participate in this research study.

G. Optional research activity

If the research I am agreeing to participate in has additional optional research activity such as the creation of a database, a tissue repository or other activities, as explained to me in the informed consent process, I understand I can choose to agree to have my information shared for those activities or not.

☐ I agree to allow my information to be disclosed for the additional optional research activities explained in the informed consent process.

H. Does my permission expire?

This permission to release your Personal Health Information expires when the research ends and all required study monitoring is over.

I. Can I cancel my permission?

You can cancel your permission at any time. You can do this in two ways. You can write to the researcher or you can ask someone on the research team to give you a form to fill out to cancel your permission. If you cancel your permission, you may no longer be in the research study. You may want to ask someone on the research team if canceling will affect your medical treatment. If you cancel, information that was already collected and disclosed about you may continue to be used for limited purposes. Also, if the law requires it, the sponsor and government agencies may continue to look at your medical records to review the quality or safety of the study.

J. Signature

Subject

If you agree to the use and release of your Personal Health Information, please print your name and sign below. You will be given a signed copy of this form.

_____

Subject's Name (print)—*required*

_____ _____

Subject's Signature Date

Parent or Legally Authorized Representative

If you agree to the use and release of the above named subject's Personal Health Information, please print your name and sign below.

Parent or Legally Authorized Representative's Name (print)	Relationship to Subject
Parent or Legally Authorized Representative's Signature	Date

Witness

If this form is being read to the subject because s/he cannot read the form, a witness must be present and is required to print his/her name and sign here:

Witness' Name (print)	
Witness' Signature	Date