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ACADEMIC CONTACT INFORMATION
• Alternate Contact
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Bio

BIO
Dr. Khavari only sees U.S. veteran patients at the VA Palo Alto Healthcare System

CLINICAL FOCUS
• Cancer > Cutaneous (Dermatologic) Oncology
• Dermatology
• General Dermatology

ACADEMIC APPOINTMENTS
• Professor, Dermatology
• Member, Bio-X
• Member, Child Health Research Institute
• Member, Stanford Cancer Institute
• Faculty Fellow, Stanford ChEM-H

ADMINISTRATIVE APPOINTMENTS
• Chair Department of Dermatology, Stanford University School of Medicine, (2010- present)
• Co-Director, Stanford Program in Epithelial Biology, (1999- present)

PROFESSIONAL EDUCATION
• Fellowship: Stanford University School of Medicine Registrar (1994) CA
• Residency: Stanford University School of Medicine Registrar (1991) CA
• Medical Education: Yale School Of Medicine Office of Student Affairs (1988) CT
• Internship: Yale-New Haven Hospital (1989) CT
• Board Certification: Dermatology, American Board of Dermatology (1992)
• Residency: Yale - New Haven Hospital (1990) CT
CURRENT RESEARCH AND SCHOLARLY INTERESTS

Our experimental focus is on the mammalian setting, including mouse genetics, human genetics, single cell studies, and new human tissue platforms. The latter encompass human skin regenerated on immune deficient mice as well as organotypic constructs with epithelial and stromal cells embedded within architecturally faithful mesenchyma in vitro. These new models, which we term Multi-Functional Human Tissue Genetics, allow up to 10 alleles or more to be altered simultaneously, permitting genetic experiments with an unprecedented degree of rapidity and complexity.

Stem cell biology and differentiation

In stratified epithelia proliferative basal cells adherent to the underlying basement membrane undergo cell cycle arrest then outward migration and terminal differentiation. This process is mediated by 2 mutually exclusive programs of gene expression: 1) an undifferentiated program supporting proliferation by stem cells within the basal layer and 2) a differentiation program instructing growth arrest and differentiation-associated programmed cell death in suprabasal layers. The control of this transition from epithelial stem cell to differentiated corneocyte, which is abnormal in epidermal cancers, is not well understood. We are currently pursuing studies of the dominant signaling and gene regulatory networks that control this process, including the Ras/MAPK cascade, which is required for stem cell-mediated self-renewal and the p53 transcription factor family member, p63, which is required for epidermal differentiation.

Epigenetic regulation by histone modifying proteins and noncoding RNA

In addition to classical gene regulatory networks noted above, we have recently identified a central role for additional biologic mechanisms, namely gene regulation by chromatin regulators and by noncoding RNAs. Epigenetic control of gene expression lasts through multiple cell divisions without alterations in primary DNA sequence and can occur via mechanisms that include histone modification and DNA methylation. Noncoding RNA sequences can regulate gene expression via interactions with epigenetic and other control mechanisms. The function of histone modifying epigenetic regulators and noncoding RNA as central mediators of epithelial stem cell renewal and differentiation represent major emerging areas of study in the lab.

Cancer

Skin malignancies, including epidermal squamous cell carcinoma (SCC), alone account for nearly as many cancers as all other tissues combined. Progress in understanding epithelial carcinogenesis has been hindered in the past by a lack of models that faithfully recapitulate the 3-dimensional architecture of tumor-stroma co-evolution. To address this and to also study the oncogenic potential of unregulated function of dominant regulators of epithelial homeostasis noted above, we developed Multi-Functional Human Tissue Genetics noted above which, when combined with skin tissue regeneration on immune deficient mice, has permitted the molecular reconstruction of events sufficient to trigger human cancer. These models are being used to systematically elucidate proteins required for cutaneous carcinogenesis and to test their potential role as therapeutic targets.

Molecular Therapeutics

Epithelial tissues in general and skin in particular offer an attractive site for development of new approaches in molecular therapeutics. A family of human genetic skin diseases is characterized by defective epithelial gene expression. Among the most severe of these are subtypes of epidermolysis bullosa (EB) and lamellar ichthyosis
We have developed approaches for high efficiency gene transfer to EB and LI patient skin tissue that are corrective at biochemical, histologic, clinical and functional levels. In addition to EB subtypes and LI, similar corrective efforts have also been undertaken with a number of other genetic skin disorders.

**CLINICAL TRIALS**

- Characteristics of Patients With Recessive Dystrophic Epidermolysis Bullosa, Recruiting
- Analysis of Cutaneous and Hematologic Disorders by High-Throughput Nucleic Acid Sequencing, Not Recruiting
- Characteristics of Adult Patients With Recessive Dystrophic Epidermolysis Bullosa, Not Recruiting
- Gene Transfer for Recessive Dystrophic Epidermolysis Bullosa, Not Recruiting
- Pilot Trial to Evaluate the Effect of Vitamin D on Melanocyte Biomarkers, Not Recruiting

**Teaching**

**COURSES**

2017-18

- Cancer Biology Journal Club: CBIO 280 (Win)

**STANFORD ADVISEES**

Med Scholar Project Advisor
Julia Ransohoff

Postdoctoral Faculty Sponsor
Namyoung Jung, Jordan Meyers, Smarajit Mondal, Douglas Porter, David Reynolds, Yuning Wei, Glenn Wozniak

Doctoral Dissertation Advisor (AC)
Xue Yang

**GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS**

- Cancer Biology (Phd Program)
- Dermatology (Fellowship Program)
- Molecular and Genetic Medicine (Fellowship Program)

**Publications**

**PUBLICATIONS**

- **Lineage-specific dynamic and pre-established enhancer-promoter contacts cooperate in terminal differentiation.** Nature genetics
  2017; 49 (10): 1522–28

- **CSNK1a1 Regulates PRMT1 to Maintain the Progenitor State in Self-Renewing Somatic Tissue.** Developmental cell

- **irCLIP platform for efficient characterization of protein-RNA interactions** NATURE METHODS
  2016; 13 (6): 489-?

- **The noncoding RNAs SNORD50A and SNORD50B bind K-Ras and are recurrently deleted in human cancer.** Nature genetics
2016; 48 (1): 53-58

- **Network Analysis Identifies Mitochondrial Regulation of Epidermal Differentiation by MPZL3 and FDXR** *DEVELOPMENTAL CELL*
  Bhaduri, A., Ungewickell, A., Boxer, L. D., Lopez-Pajares, V., Zarnegar, B. J., Khavari, P. A.
  2015; 35 (4): 444-457

- **Genomic analysis of mycosis fungoides and Sézary syndrome identifies recurrent alterations in TNFR2.** *Nature genetics*
  2015; 47 (9): 1056-1060

- **A LncRNA-MAF:MAFB Transcription Factor Network Regulates Epidermal Differentiation** *DEVELOPMENTAL CELL*
  Lopez-Pajares, V., Qu, K., Zhang, J., Webster, D. E., Barajas, B. C., Siprashvili, Z., Zarnegar, B. J., Boxer, L. D., Rios, E. J., Tao, S., Kretz, M., Khavari, P. A.
  2015; 32 (6): 693-706

- **Advances in skin grafting and treatment of cutaneous wounds** *SCIENCE*
  Sun, B. K., Siprashvili, Z., Khavari, P. A.
  2014; 346 (6212): 941-945

- **Recurrent point mutations in the kinetochore gene KNSTRN in cutaneous squamous cell carcinoma** *NATURE GENETICS*
  2014; 46 (10): 1060-1062

- **IQGAP1 scaffold-kinase interaction blockade selectively targets RAS-MAP kinase-driven tumors.** *Nature medicine*
  2013; 19 (5): 626-630

- **ACTL6a enforces the epidermal progenitor state by suppressing SWI/SNF-dependent induction of KLF4.** *Cell stem cell*
  Bao, X., Tang, J., Lopez-Pajares, V., Tao, S., Qu, K., Crabtree, G. R., Khavari, P. A.
  2013; 12 (2): 193-203

- **Control of somatic tissue differentiation by the long non-coding RNA TINCR.** *Nature*
  2013; 493 (7431): 231-235

- **ZNF750 Is a p63 Target Gene that Induces KLF4 to Drive Terminal Epidermal Differentiation** *DEVELOPMENTAL CELL*
  2012; 22 (3): 669-677

- **DNMT1 maintains progenitor function in self-renewing somatic tissue** *NATURE*
  2010; 463 (7280): 563-U189

- **HiChIP: efficient and sensitive analysis of protein-directed genome architecture.** *Nature methods*
  2016; 13 (11): 919-922

- **Safety and Wound Outcomes Following Genetically Corrected Autologous Epidermal Grafts in Patients With Recessive Dystrophic Epidermolysis Bullosa.** *JAMA*
  2016; 316 (17): 1808-1817

- **RAC1 activation drives pathologic interactions between the epidermis and immune cells** *JOURNAL OF CLINICAL INVESTIGATION*
  2016; 126 (7): 2661-2677
• **7SK-BAF axis controls pervasive transcription at enhancers.** *Nature structural & molecular biology*
  2016; 23 (3): 231-238

• **CALML5 is a ZNF750-and TINCR-induced protein that binds stratifin to regulate epidermal differentiation** *GENES & DEVELOPMENT*
  Sun, B. K., Boxer, L. D., Ranosoff, J. D., Siprashvili, Z., Qu, K., Lopez-Pajares, V., Hollmig, S. T., Khavari, P. A.
  2015; 29 (21): 2225-2230

• **Dissecting noncoding and pathogen RNA-protein interactomes** *RNA-A PUBLICATION OF THE RNA SOCIETY*
  2015; 21 (1): 135-143

• **A novel ATAC-seq approach reveals lineage-specific reinforcement of the open chromatin landscape via cooperation between BAF and p63.** *Genome biology*
  Bao, X., Rubin, A. J., Qu, K., Zhang, J., Giresi, P. G., Chang, H. Y., Khavari, P. A.
  2015; 16 (1): 284-?  

• **Recurrent point mutations in the kinetochore gene KNSTRN in cutaneous squamous cell carcinoma.** *Nature genetics*
  2014; 46 (10): 1060-1062

• **ZNF750 interacts with KLF4 and RCOR1, KDM1A, and CTBP1/2 chromatin regulators to repress epidermal progenitor genes and induce differentiation genes** *GENES & DEVELOPMENT*
  Boxer, L. D., Barajas, B., Tao, S., Zhang, J., Khavari, P. A.
  2014; 28 (18): 2013-2026

• **ZNF750 interacts with KLF4 and RCOR1, KDM1A, and CTBP1/2 chromatin regulators to repress epidermal progenitor genes and induce differentiation genes.** *Genes & development*
  Boxer, L. D., Barajas, B., Tao, S., Zhang, J., Khavari, P. A.
  2014; 28 (18): 2013-2026

• **Activating HRAS Mutation in Nevus Spilus.** *journal of investigative dermatology*
  Sarin, K. Y., McNiff, J. M., Kwok, S., Kim, J., Khavari, P. A.
  2014; 134 (6): 1766-1768

• **Enhancer-targeted genome editing selectively blocks innate resistance to oncokinase inhibition** *GENOME RESEARCH*
  Webster, D. E., Barajas, B., Bussat, R. T., Yan, K. J., Neela, P. H., Flockhart, R. J., Kovalski, J., Zehnder, A., Khavari, P. A.
  2014; 24 (5): 751-760

• **Quantitative analysis of mammalian translation initiation sites by FACS-seq.** *Molecular systems biology*
  2014; 10: 748-?

• **Activating HRAS Mutation in Agminated Spitz Nevi Arising in a Nevus Spilus.** *JAMA dermatology*
  Sarin, K. Y., Sun, B. K., Bangs, C. D., Cherry, A., Swetter, S. M., Kim, J., Khavari, P. A.
  2013; 149 (9): 1077-1081

• **Genomic Profiling of a Human Organotypic Model of AEC Syndrome Reveals ZNF750 as an Essential Downstream Target of Mutant TP63** *AMERICAN JOURNAL OF HUMAN GENETICS*
  2012; 91 (3): 435-443

• **Invasive three-dimensional organotypic neoplasia from multiple normal human epithelia** *Nature Medicine*
  Ridky TW, Khavari PA
  2010; 16: 1450-1455

• **Modeling Inducible Human Tissue Neoplasia Identifies an Extracellular Matrix Interaction Network Involved in Cancer Progression** *CANCER CELL*
• Use of human tissue to assess the oncogenic activity of melanoma-associated mutations *Nature Genetics*
  Chudnovsky, Y., Adams, A. E., Robbins, P. B., Lin, Q., Khavari, P. A.
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  2003; 421 (6923): 1253-1257

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  Blau, H., Khavari, P.
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