Stanford

M. Peter Marinkovich

Associate Professor of Dermatology

CLINICAL OFFICES

- **Medical Dermatology**

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Bio

BIO

Peter Marinkovich, M.D., is an Associate Professor of Dermatology, a faculty member of the Program in Epithelial Biology and the Stanford Cancer Biology Program. He has an interest in inflammatory skin disease and is Director of the Stanford Bullous Disease and Psoriasis Clinics as well as an attending dermatologist at the VA Palo Alto Medical Center. Dr. Marinkovich's research focuses on pathogenesis and therapy of epidermolysis bullosa, psoriasis, hair disorders and skin cancers.

CLINICAL FOCUS

- Cancer > Cutaneous (Dermatologic) Oncology
- Dermatology
- Autoimmune Blistering Diseases
- Epidermolysis Bullosa
- Pemphigus

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ACADEMIC APPOINTMENTS

- Associate Professor, Dermatology
- Member, Bio-X
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Stanford Cancer Institute

ADMINISTRATIVE APPOINTMENTS

- Member, Cancer Center, Stanford University School of Medicine, (2004- present)
- Member, Medical Institutional Review Board 4, Stanford University School of Medicine, (2005- present)
- Attending Physician, Dermatology Service, Palo Alto VA Medical Center, (1995- present)
- Director, Blistering Disease Clinic, Department of Dermatology, Stanford University School of Medicine, (1995- present)

- Founding Member/Core Investigator, Program in Epithelial Biology, Stanford University, (1999- present)

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PROFESSIONAL EDUCATION

- Board Certification: Dermatology, American Board of Dermatology (1995)
- Residency: Oregon Health Science University (1994) OR
- Fellowship: Shriner's Hospital - Portland (1990) OR
- Internship: UCSF House Staff Office (1989) CA
- Medical Education: Saint Louis University School of Medicine (1988) MO

LINKS

- Marinkovich Lab: http://bmz.stanford.edu/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The extracellular matrix of epithelial tissues plays a critical role in many important biological processes such as tissue development and differentiation, wound healing, tumor invasion, cell proliferation and cell migration. A highly organized array of these molecules, termed the basement membrane, lies at the interface of epithelial tissues with surrounding stroma. Cell surface receptors termed integrins transmit the informational cues brought about by changes in the extracellular environment, and transmit them, via intracellular signaling, to effect changes in epithelial gene expression. Laminins and collagens are molecules of the extracellular matrix which play particularly crucial roles in epithelial development.

EXTRACELLULAR MATRIX IN CARCINOMA INVASION

Laminin-5 and its cell surface receptor a6b4 integrin are required for development of squamous cell carcinomas. Lack of either of these molecules results in a lack of tumor growth, whereas overexpression of these molecules correlates with increasing tumor invasiveness and a worsening patient prognosis. We have identified that laminin-5 undergoes proteolytic processing of two of its three chains, via mammalian Tolloid, a metalloprotease of the astacin family. Processing of laminin-5 promotes tumor invasion. We are currently studying the mechanisms whereby these processing events influence tumor cell invasion, migration and metastasis. Type VII collagen appears to play a key role in tumor invasion, and appears to operate through association with laminin-5. We are currently studying the mechanism of this association and its role in tumorigenesis. The laminin-5 receptor a6b4 integrin interacts with laminin-5 at one end and with intracellular protein complexes at the other end, through which it transmits important signaling information to the cell. Disruption of laminin-5 binding or binding to the intracellular protein plectin, through site directed mutagenesis results in a lack of tumor growth, indicating that integrin binding to laminin-5 and integrin binding to plectin are both critical in tumor progression. We are currently studying the mechanisms whereby these binding events promote tumor progression. The molecule collagen XVII is closely associated with laminin-5 and a6b4 integrin and also is required for tumor invasion. The C-terminal extracellular domain of this molecule appears to play a critical role in interaction with extracellular matrix molecules and in organizing cell adhesion structures. It is also a focus of our studies of the role of extracellular matrix in tumor progression.

EXTRACELLULAR MATRIX IN HAIR DEVELOPMENT

Laminin-10 is a widely expressed molecule found in a number of epithelial tissues. Lack of laminin-10 in lama5 -/- mice results in aberrant tissue development. In the skin, there is a complete lack of hair follicle development. Exogenous delivery of laminin-10 rescues hair development in lama5 -/- skin. Laminin-10 appears to act as a potent morphogen, stimulating hair follicle development in the skin of these mice. We are currently examining this system to further understand the mechanisms whereby laminin-10 facilitates hair follicle development and basal cell carcinoma invasion, a developmentally similar process.

EXTRACELLULAR MATRIX IN EPITHELIAL ADHESION

Laminin-5, a6b4 integrin, type VII collagen and type XVII collagen each promote epithelial-mesenchymal cohesion. Defects of these molecule, in the inherited group of diseases known as epidermolysis bullosa, result in profound epithelial adhesion defects, causing extensive skin and mucosal blisters and erosions. As part of a Departmental effort, in association with the Khavari laboratory, our laboratory is participating in the study of new and novel forms of extracellular matrix gene replacement in these adhesion disorders, with the goal of translating these techniques to the clinical setting.

CLINICAL TRIALS

- A Phase 1/2 Trial of PTR-01 in Adult Patients With Recessive Dystrophic Epidermolysis Bullosa (RDEB), Recruiting
- A Study of FCX-007 for Recessive Dystrophic Epidermolysis Bullosa (RDEB), Recruiting
- Characteristics of Patients With Recessive Dystrophic Epidermolysis Bullosa, Recruiting
- Characteristics of Adult Patients With Recessive Dystrophic Epidermolysis Bullosa, Not Recruiting
- Gene Transfer for Recessive Dystrophic Epidermolysis Bullosa, Not Recruiting
- Grafting of Epidermolysis Bullosa Wounds Using Cultured Revertant Autologous Keratinocytes, Not Recruiting

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Teaching

STANFORD ADVISEES

Postdoctoral Faculty Sponsor

Sucharita Boddu, Vamsi Yenamandra

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)
- Dermatology (Fellowship Program)

Publications

PUBLICATIONS

- **Chronic skin inflammation accelerates macrophage cholesterol crystal formation and atherosclerosis** *Chronic skin inflammation accelerates macrophage cholesterol crystal formation and atherosclerosis*
  Marinkovich, M. P., et al
  2018

- **Microtubules acquire resistance from mechanical breakage through intralumenal acetylation** *SCIENCE*
  Xu, Z., Schaedel, L., Portran, D., Aguilar, A., Gaillard, J., Marinkovich, M. P., Thery, M., Nachury, M. V.
  2017; 356 (6335): 328-332

- **Gentamicin induces functional type VII collagen in recessive dystrophic epidermolysis bullosa patients.** *The Journal of clinical investigation*
  Woodley, D. T., Cogan, J., Hou, Y., Lyu, C., Marinkovich, M. P., Keene, D., Chen, M.
  2017; 127 (8): 3028–38

- **Safety and Wound Outcomes Following Genetically Corrected Autologous Epidermal Grafts in Patients With Recessive Dystrophic Epidermolysis Bullosa.** *JAMA*
  Siprashvili, Z., Nguyen, N. T., Gorell, E. S., Loutit, K., Khuu, P., Furukawa, L. K., Lorenz, H. P., Leung, T. H., Keene, D. R., Rieger, K. E., Khavari, P., Lane, A. T., Tang, et al
  2016; 316 (17): 1808-1817

- **RAC1 activation drives pathologic interactions between the epidermis and immune cells** *JOURNAL OF CLINICAL INVESTIGATION*
  Winge, M. C., Ohyama, B., Dey, C. N., Boxer, L. M., Li, W., Ehsani-Chimeh, N., Truong, A. K., Wu, D., Armstrong, A. W., Makino, T., Davidson, M., Starcevic, D., Kislat, et al
  2016; 126 (7): 2661-2677

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PRESENTATIONS

- Panel Discussions: Tackling Challenges in Epidermolysis Bullosa: What Does the Future Hold - AAD 2017 Annual Meeting (March 2017)
- Prescision Dermatology: Next Generation Prevention, Diagnosis, and Treatment - Montagna Symposium on the Biology of Skin (October 2017)