

**STATEMENT OF THE SOCIETY FOR INVESTIGATIVE  
DERMATOLOGY**

**ON**

**FISCAL YEAR 2007 APPROPRIATIONS FOR THE  
VETERANS AFFAIRS MEDICAL RESEARCH PROGRAM**

**BEFORE THE**

**HOUSE APPROPRIATIONS SUBCOMMITTEE ON MILITARY  
QUALITY OF LIFE AND VETERANS AFFAIRS**

**PRESENTED BY**

**ALICE P. PENTLAND, M.D.**

**PRESIDENT-ELECT, THE SOCIETY FOR INVESTIGATIVE  
DERMATOLOGY**  
820 W. Superior Avenue  
7<sup>th</sup> Floor  
Cleveland, Ohio 44113-1800

**MARCH 1, 2006, 10:00 AM**

Mr. Chairman, and Members of the Subcommittee — I am very grateful for this opportunity to testify today on behalf of the Society for Investigative Dermatology in support of the VA Medical Research Program. I am Dr. Alice Pentland, Professor and Chair of Dermatology, University of Rochester School of Medicine and Dentistry. I have been awarded a grant from the VA to study the causes of skin cancer, and what preventive measures might be taken. I have provided dermatology services to Veterans through the VA health system, and given financial support to Veteran's Outreach to extend veteran benefits in my community beyond what the Veterans Administration is able to provide. I also serve as President-Elect of the Society for Investigative Dermatology, and I am here before you today, on their behalf.

### Background

The Society for Investigative Dermatology has over 2000 members worldwide dedicated to the advancement and promotion of science relevant to skin health and disease through scholarly exchange of scientific information, education and advocacy. Members include scientists and physician researchers from universities, hospitals and industries committed to the science of dermatology. Much of the research conducted by our members addresses the needs of our veterans, and is funded by the VA Medical Research Program and performed at VA research facilities.

### Burden of Skin Diseases

Mr. Chairman, in 2005, along with the American Academy of Dermatology Association (AADA), SID released the most comprehensive report to date on the prevalence, annual economic burden and quality of life implications of the 21 most common skin diseases in the United States, selected from over 3000 varieties of skin disease identified in the medical literature. The economic burden of this sampling of skin diseases amounts to nearly \$39 billion.

Our veteran population is particularly susceptible to certain skin diseases. Treatment rates for skin cancer and other skin diseases associated with chronic diseases are significantly higher for Veterans than for the U.S. population as a whole. A number of factors contribute to the disproportionate rate of skin cancer and other skin diseases in the Veteran population.

While on active duty, soldiers may be subject to extreme temperatures, extensive sun exposure, unsanitary living conditions, poor nutrition, combat wounds, chemical agents and many other challenges known to contribute to skin disease. Add to these the delay in diagnosis and lack of therapeutics in the field, and the result is more severe skin disease. In previous wars, and in the current conflict in Iraq, 10 -15% of evacuations from the combat theatre are due to skin disease; skin infections due to prolonged wearing of combat protective gear, bites causing infections such as leishmaniasis, skin wounds and caustic burns to skin from chemical agents, etc. Once manifested in war, these problems can become life-long service-connected medical problems.

Basic research examining skin structure and barrier function and studies examining genetic and immunological disorders that disrupt skin and its barrier function have been and continue to be important in expanding our understanding of skin injury, skin infection and strategies to prevent these problems, or produce more rapid healing. Among these problems, the wound healing category is of special concern to both soldiers and veterans and includes the threat of ultraviolet

light and chemical exposure. This category of skin diseases accounts for \$12 billion alone in economic burden each year, including the costs for Veterans in nursing homes and long-term care facilities due to such conditions. The VA Medical Research Program conducts and supports a vigorous scientific effort to study and reduce the suffering associated with all of these service-related skin conditions.

#### Meeting the Need

Recent articles in *Stars and Stripes*, a Department of Defense-authorized daily newspaper distributed overseas for the U.S. military community document the frustration of wounded veterans in seeking better treatments for UV exposure, the threat of parasitic infections, amputated limbs and wound treatment.

Steady support of skin research through the VA system over time builds a base of researchers that can fulfill this area of chronic need. However, skin research does not benefit skin disease alone. Skin serves as an excellent interdisciplinary model for disease research and is an area where research dollars meet the goals of many disease areas at once.

Given this array of facts, it is crystal clear that additional funding for skin disease research is needed to produce improved treatments, cures and preventive measures to better protect our armed forces from these threats to their personal health and safety, and offer them improved long-term health.

#### Recommendations for the VA Medical Research Program

Mr. Chairman, your support for the VA Medical Research Program is deeply appreciated. In spite of lukewarm support from the Administration for this critical, patient-focused research, we urge continued growth for this program so that it can address the intense needs in this area. The Society for Investigative Dermatology is pleased to join our sister organization in the Friends of VA Medical Research (FOVA) in supporting a Fiscal Year 2007 appropriations level of \$399 million for the VA Medical and Prosthetics Research Program.

Thank you again for the opportunity to present the views of the Society for Investigative Dermatology. I will be pleased to answer any questions you may have.

**HOUSE COMMITTEE ON APPROPRIATIONS  
SUBCOMMITTEE ON MILITARY QUALITY OF LIFE AND VETERANS AFFAIRS  
Witness Disclosure Requirement - "Truth in Testimony"**

Your Name: Alice P. Pentland, M.D.

1) Other than yourself, please list what entity or entities you are representing:

Society for Investigative Dermatology

Friends of VA Medical Research

- 2) Are you testifying on behalf of a Federal, State, or Local Government entity? No
- 3) Are you testifying on behalf of an entity other than a Government entity? Yes
- 4) Please list any federal grants or contracts (including subgrants or subcontracts) which you have received since October 1, 1999: Please see biosketch below:

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel in the order listed on Form Page 2.

<u>NAME</u> <b>Alice P. Pentland, M.D.</b>	<u>POSITION TITLE</u> Chair and Professor of Dermatology Director, Center for Future Health		
<i>EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include</i>			
<u>INSTITUTION AND LOCATION</u>	<u>DEGREE</u>	<u>YEAR(s)</u>	<u>FIELD OF STUDY</u>
University of Michigan Medical School Ann Arbor, Michigan  eRA COMMONS USER NAME APENTLAND	B.S., M.D.	1972-1978	Biology and Medicine

*postdoctoral training.)*

**A. POSITION AND HONORS**

**Professional Experience**

- 1978-1979 Medical Internship, University of North Carolina, Chapel Hill, NC
- 1979-1983 Dermatology Residency, University of Michigan, Ann Arbor, MI
- 1980-1982 Postdoctoral Fellow, University of Michigan, Ann Arbor, MI
- 1984-1986 Postdoctoral Fellow, Dept of Pharmacology, Washington University, St. Louis, MO
- 1984-1986 Instructor in Medicine (Dermatology), Washington University, St. Louis, MO
- 1986-1992 Assistant Professor of Medicine (Dermatology) & Pharmacology, Washington University, St. Louis, MO
- 1992-1996 Associate Professor of Medicine (Dermatology) & Pharmacology, Washington University, St. Louis, MO
- 1996-present James H. Sterner Professor and Chair, Dermatology, University of Rochester, Rochester, NY
- 1997-present Director, Center for Future Health

**Honors and Awards**

Diplomat of American Academy of Dermatology, 1983, Society for Investigative Dermatology,  
American Academy of Dermatology, American Dermatology Association, American Society of Clinical Investigators, MD Future of Health Technology Awardee, 2002,

**Advisory Committees**

Member of Dermatology Foundation Grant Review Board, 1990-1993, 1991-1992, Editorial Board Journal of Investigative Dermatology, Member of GMA-1 Study Section, 10/1994 - 10/1998, Board of Directors, Society for Investigative Dermatology 1998-2003, Board of Directors, Dermatology Foundation 2000-2003, Board of Scientific Counselors, NCI 2001-2005, President Elect, Society for Investigative Dermatology, 2005-2006, American Professors of Dermatology Board of Directors

## **B. PUBLICATIONS (SELECTED)**

1. Pentland A and Needleman P. Modulation of keratinocyte proliferation in vitro by endogenous prostaglandin synthesis. *J Clin Invest.* 77:246-251, 1986.
2. Holtzman MJ, Turk J, Pentland A. A regiospecific monooxygenase with novel stereopreference is the major pathway for arachidonic acid oxygenation in isolated epidermal cells. *J Clin Invest.* 84(5):1446-53. 1989.
3. Pentland AP, Mahoney M, Jacobs SC, Holtzman MJ. Enhanced prostaglandin synthesis after ultraviolet injury is mediated by endogenous histamine stimulation. A mechanism for irradiation erythema. *J Clin Invest.* 86(2):566-74. 1990.
4. Pentland AP, Morrison AR, Jacobs SC, Hruza LL, Hebert JS, Packer L. Tocopherol analogs suppress arachidonic acid metabolism via phospholipase inhibition. *J Biol Chem.* 267(22):15578-84, 1992.
5. Kang-Rotondo CH, Miller CC, Morrison AR, Pentland AP. Enhanced keratinocyte prostaglandin synthesis after UV injury is due to increased phospholipase activity. *Am J Physiol.* 264(2Pt 1):C396-401, 1993.
6. Shapiro SD, Kobayashi DK, Pentland AP, Welgus HG. Induction of macrophage metallo-proteinases by extracellular matrix. Evidence for enzyme-and substrate-specific responses involving prostaglandin-dependent mechanisms. *J Biol Chem.* 268(11):8170-5, 1993.
7. Saarialho-Kere UK, Kovacs SO, Pentland AP, Olerud JE, Welgus HG, Parks WC. Cell-matrix interactions modulate interstitial collagenase expression by human keratinocytes actively involved in wound healing. *J Clin Invest.* 92(6):2858-66, 1993.
8. Miller CC, Hale P, Pentland AP. Ultraviolet B injury increases prostaglandin synthesis through a tyrosine kinase-dependent pathway. Evidence for UVB-induced epidermal growth factor receptor activation. *J Biol Chem.* 269(5):3529-33, 1994.
9. Sudbeck BD, Parks WC, Welgus HG, Pentland AP. Collagen-stimulated induction of keratinocyte collagenase is mediated via tyrosine kinase & protein kinase C activities. *J Biol Chem* 269:30022-29, 1994.
10. Gresham A, Masferrer J, Chen X, Leal-Khoury S, Pentland AP. Increased synthesis of high-molecular-weight cPLA<sub>2</sub> mediates early UV-induced PGE<sub>2</sub> in human skin. *Am J Physiol.* 270 (4 Pt 1):C1037-50, 1996.
11. Malaviya R, Morrison AR, Pentland AP. Histamine in human epidermal cells is induced by ultraviolet light injury. *J Invest Dermatol.* 106(4):785-9, 1996.
12. Konger R, Malaviya R, Pentland AP. Growth regulation of primary human keratinocytes by prostaglandin E receptor EP<sub>2</sub> and EP<sub>3</sub> subtypes. *Biochim Biophys Acta.* 1401:221-234, 1998.
13. Buckman S, Gresham A, Hale P, Hruza G, Anast J, Masferrer J, Pentland AP. COX-2 Expression is Induced by UVB Exposure in Human Skin: Implications for the development of skin cancer. *Carcinogenesis.* 19:5:723-729, 1998.
14. Pentland AP, Schoggins JW, Scott GA, Khan KNM, Han R. Reduction of UV-induced skin tumors in hairless mice by selective Cox-2 inhibition. *Carcinogenesis* 20:1939-44, 1999.
15. Buckman SY, Koki AT, Edwards DA, Pentland AP. Immunohistochemical analysis of cyclooxygenase expression in human skin. *Methods Mol Biol* 120:35-43, 1999.
16. Rys-Sikora KE, Konger RL, Schoggins JW, Malaviya R, Pentland AP. Coordinate expression of secretory phospholipase A<sub>2</sub> and cyclooxygenase-2 in activated human keratinocytes. *Am J Physiol - Cell Physiol* 278:C822-C833, 2000.
17. Scott G, Deng A, Rodriguez-Burford C, Seiberg M, Han R, Babiarz L, Grizzle W, Bell W, Pentland, A. Protease activated receptor-2, a receptor involved in melanosome

- transport, is upregulated in human skin by ultraviolet irradiation J Invest Dermat 117:1412-20, 2001.
18. Konger RL, Scott GA, Ladenson JH, Landt Y, Pentland AP. Loss of the EP<sub>2</sub> Prostaglandin Receptor Results in an Invasive Epithelial Phenotype and Decreased Paxillin Expression. Amer J Path 161(6):2065-2078, 2002.
  19. Rys-Sikora KE, Pentland AP, Konger, RL. Pertussis toxin-sensitive secretory phospholipase A2 expression and motility in activated primary human keratinocytes. J Invest Dermatol 120(1):86-95, 2003.
  20. Tripp CS, Blomme EAG, Hardy MM, LaCelle P, Pentland AP. Epidermal COX-2 induction following UV irradiation: Suggested mechanism for the role of COX-2 inhibition in Photoprotection. J Invest Dermat 121(4):853-861, 2003.
  21. Pentland AP, Scott G, VanBuskirk J, Tanck C, LaRossa G, Brouxhon S. Cyclooxygenase-1 Deletion Enhances Apoptosis but Does Not Protect Against Ultraviolet Light-Induced Tumors. Cancer Res. 64: 5587-5591, 2004.
  22. Scott, G, Jacobs, S, Leopardi, S, Anthony, FA, Learn, D, Malaviya, R, Pentland, A. Effects of PGF<sub>2</sub> $\alpha$  on human melanocytes and regulation of the FP receptor by ultraviolet radiation. Experimental Cell Res 304:407-16, 2005.
  23. Konger, RL, Billings, SD, Thompson, AB, Morimiya, A, Ladenson, JH, Landt, Y, Pentland, AP, Badve, S. Immunolocalization of low affinity prostaglandin E2 receptors, EP1 and EP2, in adult human epidermis. J Invest Dermat 124:965-70. 2005.
  24. DeLouise, L. A.; Fauchet, P. M.; Miller, B. L.; Pentland, A. A. "Hydrogel-Supported Optical-Microcavity Sensors" Advanced Materials 17(18): 2199-2203, 2005.
  25. Konger, RL, Brouxhon, S, Partillo, S, VanBuskirk, J, Pentland, AP. The growth inhibitory EP<sub>3</sub> receptor stimulates release of pro-differentiation mediators ceramide & sn-1,2-diacylglycerol. Exp Dermat 12:914-22, 2005.
  26. Rodriguez-Burford, C., Mercurio, M., Tu, J.H., Carey, D., Han, R., Gordon, G., Niwas, S., Bell, W., Elmetts, C.A., Grizzle, W., Pentland, A.P.: Selective COX-2 inhibition produces heterogeneous erythema response to UV-irradiation. J Invest Dermat. 125(6):1317-20, 2005.

## C. RESEARCH SUPPORT

### CURRENT:

#### **PGE2 Receptor Function in Skin**

Principal Investigator: Alice Pentland, MD

9/1/05 - 8/31/10

Agency: NIIH RO1CA117821

Determine signaling pathways by which prostaglandin receptor function to moderate keratinocyte proliferation differentiation and apoptosis.

#### **Training Program in Dermatological Research**

Principal Investigator: Alice Pentland, MD

5/1/99-4/30/09

Agency: NIH/NIAMS 2T32AR07472

The major goals of this project are to provide fundamental training at the predoctoral and postdoctoral level in basic and clinical research as it relates to skin.

#### **Annual Dermatology Resident Retreat**

Principal Investigator: Alice Pentland, MD

6/1/01-5/31/08

Agency: NIH AR47991

The long-term objective of this meeting is to increase the pool of physician-scientists in dermatology.

**In-Vivo Clinical Coherence Confocal Microscope**

Principal Investigator: James Zavislan, Ph.D. 6/1/04-5/31/07  
Sub-Investigator: Alice Pentland, MD  
Agency: NIH

Research to optimize in vivo confocal microscopy. I provide access to patients under my clinical care.

**In-Vivo Clinical Coherence Microscope**

Principal Investigator: James Zavislan 2005-2006  
Sub-Investigator; Alice Pentland, MD  
Agency: Nystar

**COMPLETED:**

**Cyclooxygenase and PGE2 Receptor Function in Skin Cancer**

Principal Investigator: Alice Pentland, MD 4/1/00 – 3/31/05  
Agency: NIH RO1AR46828

Determine signaling pathways by which prostaglandin receptor function to moderate keratinocyte proliferation differentiation and apoptosis.

**Phase II/III Clinical Trials of Celecoxib in Subjects with Actinic Keratosis**

Sub-Investigator: Alice Pentland, MD 9/1/00-3/15/05  
Agency: NCI Searle

Determine efficacy of celecoxib in prevention of actinic keratoses. Enrollment now completed.

**Regulation and Function of CPLA2 in UV Injury**

Principal Investigator: Alice Pentland 7/1/90-11/30/00  
NIH, R01AR40574

**Fatty Acid Mechanisms of UV Carcinogenesis**

Veterans Administration Research Award  
Principal Investigator: Alice Pentland 6/30/96-99



Signature: Alice P. Pentland, M.D.

Date: March 1, 2006

**Alice P. Pentland, M.D.**

**President-Elect, Society for Investigative Dermatology  
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