Division of The Skin Sciences Institute

DIVISION PROFILE	
Number of Faculty	13
Number of Joint Appointment Faculty	
Number of Fellows	
Research Fellows	2
Number of Graduate Students	7
Number of Other Students (full and part-time)	1
Number of Support Personnel	2
Number of Peer Reviewed Publications	23

FACULTY LISTING

Steven B. Hoath, MD, Professor of Pediatrics, Medical Director
Marty O. Visscher, PhD, Research Director, The Skin Sciences Institute
Raymond E. Boissy, PhD, Professor of Dermatology and Cell Biology, Director, National Vitiligo Association
Steven T. Boyce, PhD, Professor of Surgery, Associate Professor of Biomedical Engineering, Director, Department of Tissue Engineering, Shriners' Burns Institute
Charles L. Heaton, MD, Professor of Dermatology, Director, Sexually Transmitted Diseases Clinic and Training Program, Department of Health
Gerald B. Kasting, PhD, Associate Professor of Skin Pharmaceutics and Cosmetic Science
W. John Kitzmiller, MD, Associate Professor of Surgery, Head, Division of Plastic and Reconstructive Surgery; Director of Wound Care, Drake Hospital
Zalfa Abdel-Malek, PhD, Associate Professor of Dermatology
Diya F. Mutasim, MD, Professor of Dermatology, Chairman, Department of Dermatology
Vivek Narendran, MD, Associate Professor of Pediatrics, Director, Newborn Nursery Christ Hospital, Director, NICU University Hospital, Director, Perinatal Outreach Program
James J. Nordlund, MD, Professor Emeritus of Dermatology, Director, Vitiligo Clinic
Neville G. Pinto, PhD, Professor of Engineering, Assistant Dean of Graduate Studies
R. Randall Wickett, PhD, Professor of Skin Pharmaceutics and Cosmetic Science, Director, Cosmetic Science Graduate Program

OVERVIEW

The Skin Sciences Institute (SSI) is an interdisciplinary research group of investigators from CCRF, the Shriners' Burns Institute, the Departments of Dermatology and Surgery, and the Colleges of Pharmacy and Engineering. The institute's goals are to conduct basic and translational skin research, to provide the basis for evidence based skin practices, while recognizing the skin as an important aspect of primary health care delivery, and to establish effective research partnerships with the skin and health care industries and international academic institutions.

Retention of vernix caseosa on the infant skin at birth results in increased skin hydration and more rapid acid mantle formation, necessary for antimicrobial function, compared to skin treated to remove the vernix. Recent studies have demonstrated that films of vernix caseosa provide a protective barrier to the penetration of exogenous irritating agents, i.e., species such as chymotryptic enzyme. This finding further emphasizes the beneficial effects of vernix and indicates utility as a skin protectant during the newborn period. Parents and health care providers can be encouraged to view vernix as a naturally occurring cream that may facilitate adaptation to a dry environment. Vernix biology is a relatively unexplored field of perinatal biology with practical implications for translational physiology, infection control, bathing practices, temperature management and surface adhesion. Two paracrine melanogenic cytokines, stem cell factor (SCF) and endothelin-1 (ET-1), have been shown to play pivotal roles in skin pigmentation including UVB-induced pigmentation and senile lentigo. However, little is known regarding their interactive effect on skin pigmentation. Their roles were examined in vivo using the human xenograft model. The combination of SCF

and ET-1 demonstrated a statistically significant increase in tyrosinase gene expression substantiated by the enhancement of melanin content and skin pigmentation compared to treatment with either alone. In addition, SCF and ET-1 in combination induce proliferation, melanogenesis and dendritogenesis of melanocytes. These data suggest that SCF administered locally in combination with ET-1 may have a potential therapeutic effect for the treatment of melanocytopenic disorders such as vitiligo by inducing melanocyte migration, proliferation and restoration of function in the depigmented lesion.

Investigator expertise in epidermal barrier formation, quantitation of skin surface biomarkers, vernix biology, pigment cell research and treatment of hyperpigmentary disorders, skin restoration, tissue engineering and wound healing, transdermal drug delivery and stratum corneum transport, and quantitative biophysical characterization of skin characteristics forms the basis of the SSI's scientific strategy and areas of ongoing collaboration.

Left to Right: S. Hoath, M. Visscher, V. Narendran

HIGHLIGHTS

Epidermal Innate Immunity

Epidermal innate immunity involves pro and anti-inflammatory cytokines, structural proteins, and specific antigen presenting cells. Host defense proteins (HDPs) and an intact skin barrier are essential. There are reports of skin neuroendocrine activity constituting an equivalent of the HPA, referred to as the Skin Stress Response System (SSRS). The SSRS responds to infection, trauma, and UV radiation causing release of interleukins which trigger CRH and POMC. Cortisol release by the hair follicles has been shown, suggesting local stress mediation at the level of the skin. We investigated epidermal innate immunity by characterizing the spectrum and ontogeny of HDP secreted by newborn infants by measuring HDPs from skin surface samples. Major host defense proteins, lactoferrin and lysozyme, were found in samples from adults and neonates, with evidence of functional lysozyme activity and concentrations 5-6-fold higher in neonates. These data support an important role for lysozyme in neonatal innate immunity.

Second, multiple biomarkers were quantified from the skin of premature infants, full-term infants and adults using a high throughput bead array system. Differences were observed between infants and adults and between preterm and full-term infants. Cortisol was significantly higher for preterms versus full-terms. Inflammatory cytokines IL6, IL8, and IL1B were higher in preterms than full-terms and could potentially stimulate cortisol release. IL1a and involucrin were higher in both infant groups than in adults and higher in preterms than full-terms. The infant variation may be due to differences in SC maturation and integrity, but the higher level for full-terms versus adults is not explained on this basis.

Epidermal Barrier Response to Repetitive Hand Hygiene Procedures

Reduction in healthcare acquired infections is an important patient safety goal. Compliance with hand hygiene practices is effective for preventing infections, but compliance rates are about 30%. The primary reason for compliance failure is skin irritation. Frequent, repetitive soap and water exposure has significant negative effects on the epidermal skin barrier, e.g. inflammation, lipid disruption, and increased permeability. In response, epidermal repair is up-regulated, leading to hyperproliferation, insufficient hydration and inadequate desquamation. Damaged skin has higher levels of colonizing microflora. We determined the epidermal response during the exposure to and regression (after time off) from repetitive hygiene procedures in spring and winter among intensive care nurses. We used high resolution digital photography and quantitative imaging to measure irritation and erythema. Higher levels of dryness in winter than in spring indicated greater stratum corneum barrier damage, i.e., hyperproliferation and aberrant desquamation. Paired comparison of the images showed significantly greater changes in skin irritation during the work cycle in winter compared to spring. Self-assessment scores showed improvement over the cycle in spring and worsening in winter. Examination of the skin response during spring regression indicated that it was more irritated after 2-3 days of work than at the start of the next work cycle (after time off). In contrast, the skin at the end of the cycle in winter was less irritated than after regression. Epidermal barrier recovery occurred to some extent in spring but not in winter. Repetitive, high frequency hand hygiene practices lead to chronic, unresolved irritation in nearly all subjects. There is a substantial need for practices that disinfect the skin without compromising epidermal barrier integrity.

Modulation of Skin Pigmentation

We analyzed the effects of deoxyArbutin (dA) and the second-generation derivatives, deoxyFuran, thio-dA, and fluoro-dA on melanocyte function and viability. At safe concentrations, they reversibly down-regulated melanogenesis by competitively inhibiting tyrosinase and had higher competitive inhibitor potencies than the current gold standard, hydroquinone (HQ). Concentrations that did compromise melanocyte viability inhibited cell proliferation (i.e., cytostatic). Unlike HQ, they but did not induce apoptosis (i.e., cytotoxic). The melanogenic enzymes tyrosinase and TRP-1 mediated the cytostatic effects of dA and its derivatives. A minimal amount of Reactive Oxygen Species (ROS) was generated upon treatment with dA and derivatives, in contrast to the dramatic amount induced by HQ. This increase in ROS triggered an increase in activity of the endogenous antioxidant catalase in treated melanocytes. Endogenous catalase was sufficient to protect cells against ROS generated by the dA compounds, but not HQ. Therefore, dA and second-generation derivatives demonstrate great potential for therapeutic use in hyperpigmentary disorders because they are effective tyrosinase inhibitors and less toxic relative to hydroquinone.

TRAINING

Ivan Abril-Ramirez, MD	PL-II
Valencia Walker, MD	PL-III
Jennifer Davis, BS	Yr 1
Dina Said, BS	Yr 2
Jennifer Canning, BS	Yr 3
Smita Chawla, BS	Yr 4
Santosh Yadav, BS	Yr 4
Anyarporn Tansirikongkol, BS	Yr 4
Marisa Robinson, BS	Yr 5

PUBLICATIONS

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14. Kasting GB, Miller MA. Kinetics of finite dose absorption through skin 2: volatile compounds. J Pharm Sci 2006;95(2):268-80.
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16. Miller MA, Bhatt V, Kasting GB. Dose and airflow dependence of benzyl alcohol disposition on skin. J Pharm Sci 2006;95(2):281-91.
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18. Wang TF, Kasting GB, Nitsche JM. A multiphase microscopic diffusion model for stratum corneum permeability. I. Formulation, solution, and illustrative results for representative compounds. J Pharm Sci 2006;95(3):620-48.
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