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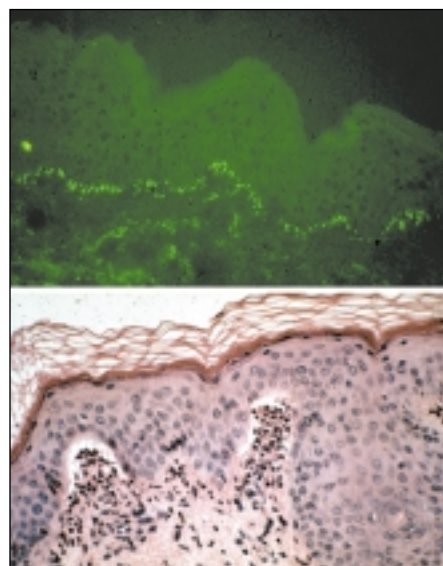
Dermatitis Herpetiformis and Dietary Gluten: Illuminating a Gut–Skin Connection

Dermatitis herpetiformis (DH) is an intensely pruritic, chronic blistering disease that often appears quite suddenly, mainly between the ages of 20 and 55, and is much more common in men than women. Overall prevalence—more frequent than the bullous pemphigoid group of blistering diseases—is estimated at somewhere between 10 to 39 cases/100,000 annually. Erythematous papulovesicular lesions are characteristically distributed symmetrically on extensor body surfaces and on the buttocks and back. Granular deposits of IgA (normally

involved in immunoprotection of the body's mucosal surfaces, especially the respiratory and gastrointestinal tracts) at the dermo–epidermal junction (DEJ) are the immunologic marker of this disease (see photo, left), and patients have a gluten-sensitive enteropathy (GSE) that is histologically apparent but generally asymptomatic.

Dapsone effectively controls cutaneous symptoms while leaving the gastrointestinal abnormalities untouched. Yet eliminating gluten from the diet controls not only these abnormalities but resolves the skin lesions as well. This highly intriguing fact suggests that solving the pathogenesis of DH will rest on unraveling the complex pathway connecting the gut's clinically asymptomatic gluten-sensitive mucosal immune response to the unusual presence of IgA in the skin and the recurrent lesions.

Russell P. Hall III, MD—chief of the Division of Dermatology and professor of immunology at Duke University Medical Center—has been pursuing the secrets of DH intently for more than 25 years, identifying clues to this pathway one by one. He stumbled across this fascinating disease unexpectedly. After completing his medical training, Hall began a research fellowship in the laboratory of Stephen I. Katz, the well-known immunodermatologist who headed the Dermatology Branch at the NCI. “I was interested in immunology and immunology research,” Hall recalls, “and within that context I wanted to explore the pathogenesis of disease. Dr. Katz was working on DH when I arrived, and I became part of that effort.” He has been at it ever since.



DH presents unique picture. DH skin is unique in the presence of granular deposits of IgA at the DEJ (top) and the neutrophilic infiltrate at the papillary tips (bottom). (Top: courtesy of Dr. Russell P. Hall III; bottom: reprint permission from M. Irwin Freedberg et al (eds), *Fitzpatrick's Dermatology in General Medicine*, 5th ed., McGraw Hill:New York, 1998, p.619.)

Focus on Research

PAF—The Skin's Early Warning System

Jeffrey B. Travers, MD, PhD

Kampen-Norins Investigator and Chair of Dermatology
Associate Professor of Dermatology, Pediatrics,
Pharmacology, and Toxicology
Indiana University School of Medicine

Travers worked in a lipid biochemistry lab during his first year of medical school. It was, unexpectedly, a transforming experience. He found a passion for research. And he was fascinated by



Jeffrey B. Travers, MD, PhD

lipids because they function in two separate worlds. They are key structural elements in the cell membrane, yet can be metabolized in oxidative reactions to form very potent signaling molecules. These lipid mediators function as cytokines, but—unlike their slower protein counterparts—are produced in only minutes. Dermatology appealed to Travers scientifically because of the skin's significant lipid content, especially the sebaceous glands, and the close resemblance between the lipid profile of keratinocytes and those in immune cells, especially neutrophils. And clinically, he would be able to practice the kind of medicine he found meaningful.

During his residency at the University of Colorado, Travers encountered the lipid that would become his life's work. He was

(Continued on page 2)

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DH: An Emerging Portrait

The first description of DH appeared in the *JAMA* 120 years ago, back in 1884, but little more was learned until a sudden flurry of investigative activity in the late 1960s set the basic defining elements in place. Cornane discovered immunoglobulin at the DEJ in patient skin which Van der Meer then characterized as IgA—a critical component of the protective immune response in mucosal barrier tissues that is normally found in the mucosal surfaces of the respiratory, gastrointestinal, and urogenital tracts. This discovery allowed identification of two patient groups within the DH clinical phenotype—the 85–90% of patients with granular IgA deposits at the DEJ, and the small remainder with linear deposits at that site. The appearance of IgA in patient skin was striking—and puzzling.

Another investigator realized that DH patients have an associated—although, intriguingly, most often asymptomatic—gastrointestinal disease that was eventually identified as GSE. The histology showed two basic features; atrophy of the normal villous architecture of the jejunal epithelium, with lamina propria and intraepithelial lymphocytic infiltrates. It was shown to be morphologically identical to, although less severe than, that seen in patients with isolated GSE (celiac sprue). And these changes were confined primarily to the small intestine, most often the jejunum. Despite this, and several laboratory studies documenting abnormal intestinal function, less than 10% of DH patients were observed to experience the typical bloating, diarrhea, and malabsorption of GSE.

During the 1970s, a high frequency of certain human leukocyte antigens (HLA-A1, -B8, -DR3, -DQ2) was documented in DH patients—but associated only with granular cutaneous IgA deposits. It became clear that, despite the clinical parallels, patients with linear deposits of IgA represent a different pathogenesis and thus a different disease, and they were recategorized as *linear IgA dermatosis*. (Linear IgA dermatosis is now known to be one of the autoimmune blistering diseases.)

Discovering the existence of GSE in DH patients prompted some of them to eliminate gluten from their diet. Doing so normalized the morphologic changes in

the small intestine and controlled their skin disease—yet another provocative observation. “It became clear that GSE plays a critical role in the pathogenesis of DH,” Hall says, “but in what way the skin disease, the cutaneous IgA deposits, and the associated GSE interact in these patients is still unknown.” The cutaneous IgA presence itself also remains a mystery—its origin, the manner in which it is deposited, and the structures to which this IgA binds.

Hall’s Perspective

“I started out asking a set of simple questions about IgA,” Hall says. “I wanted to learn what it is doing in the skin. What is its source? How does it get from there to the skin? And, what does it mean to this disease? But my focus has broadened considerably over the years,” he notes, “and I have come to find additional points about DH that make it very intriguing for an investigator.

“First, it is characterized by very severe clinical symptoms,” Hall observes. “Second, this disease has a unique histologic and immunofluorescence picture, with both neutrophils and IgA in the skin (see photos on cover). Third,” he continues, “it can be controlled exceedingly well by use of the drug dapsone, but this drug does not help normalize the associated—but asymptomatic—gut disease.

However, normalizing the asymptomatic gut resolves the skin disease in a great many patients. And reintroduction of gluten is followed by deterioration of small bowel morphology, recrudescence of cutaneous IgA deposits, and relapse of skin disease.

“And the final point,” Hall notes, “concerns the isolated GSE patients. Their gut disease looks exactly—or very closely—the same by biopsy, they are sensitive to the same wheat protein—the gliadin in gluten, and they possess the same HLA association, but contrary to DH patients, they do get lots of problems with their gut and they generally have no skin problems at all. So here is a well-characterized dietary protein that a group of people react to immunologically and morphologically in the same way,” he says. “Some of these people develop highly symptomatic gut disease, with diarrhea and

bloating, but no skin changes. The others develop extremely severe skin disease but have little to no gut disease.” The burning question is *why*—why do they go on to develop different diseases in different organs?

The implications extend beyond the DH–GSE association itself. “A number of diseases of the skin are associated with gut diseases—such as the links between pyoderma gangrenosum and erythema nodosum with inflammatory bowel disease. We do not understand the nature of this association” Hall notes, “and we have come to suspect that elucidating DH may well provide an effective model for understanding what appears to be a more general relationship between inflammation, diseases of the intestinal tract, and diseases of the skin. Hopefully we can use the DH–GSE association to understand some basic principles about how the two largest epithelial organs in the body—the skin and the gut—are related.”

And Hall is quick to point out that, despite the years of research that he and others have devoted to DH, we still do not fully understand how IgA ends up in patient skin.

Gut Instincts

With their initial focus on the mechanism for IgA’s entry in to the skin, Hall and his co-workers looked for—and found—the presence of IgA immune complexes in the serum of DH patients. But it wasn’t unique, as IgA immune complexes were also detected in the serum of patients with isolated GSE. “It was obvious that there was something more than the presence of these immune complexes that led to the development of IgA in the skin,” Hall notes, “and that’s when we realized that the gut is where we really need to look to understand this skin disease.”

Hall and his group assessed the production of antibodies in the gut secretions, finding that DH patients develop IgA antibodies against wheat protein, that they are primarily of the IgA1 subgroup, and that these distinctive antibodies enter the circulation. This suggested that the IgA in patient skin actually originates in the intestinal tract as a response to gluten, and confirmed Hall’s decision to focus on events there.

This raised additional questions: What is the critical difference between gluten-sensitive people who develop DH and those who develop celiac disease? And how does the gut relate to the development of the actual skin lesions in DH? Hall has approached these questions by



Russell P. Hall III, MD

studying tissue biopsied from the small bowel of patients in each patient group—and sometimes from normal people as well—and looking at various aspects of the gut's mucosal immune response.

Cytokine Patterns

Hall and his co-workers first turned their attention to cytokine expression in the gut. Cytokines mediate immune responses, and the pattern of local cytokine expression can determine the immunopathogenesis of an inflammatory disorder. Cytokines were already known to function in the normal gastrointestinal mucosa. Their presence often increases greatly in inflammatory enteropathies, which was suspected to play an important role in the observed tissue damage. T cells are among the cytokine-secreting leukocytes, and there was already considerable speculation due to evidence from isolated GSE patients that a T-cell-mediated immunologic response to ingested gliadin is central to their disease pathogenesis. Hall and his colleagues hypothesized that systematic variations in this gut mucosal cytokine pattern may account for the different clinical manifestations of these two gluten-sensitive diseases. A number of investigators had already identified cytokines that appear to predominate in the gut of isolated GSE patients—primarily interferon-gamma (IFN- γ), with some evidence as well for IL-2, IL-4, IL-6, IL-10, and TNF- α —but no one had yet described the gut cytokine profile in DH patients.

Hall and his team took duodenal biopsies from 3 healthy controls, 8 DH patients (7 on medication controlling their skin lesions, 1 on a partially gluten-free diet because of moderate gastrointestinal symptoms, and about to start on dapsone), and 9 isolated GSE patients (4 were asymptomatic on a gluten-free diet, 5 ingesting gluten with active gastrointestinal symptoms). The research team looked for the expression of two cytokines in particular. One was IFN- γ , already identified as prominent in GSE, and the hallmark cytokine produced by Th1 helper T cells—and thus, prominent in Th1-associated diseases (eg, delayed-type hypersensitivity). The other was IL-4, the hallmark cytokine produced by Th2 helper T cells—and thus, prominent in Th2-associated diseases (eg, allergic disease). Each type of helper T cell tends to involve a different constellation of additional cytokines, and thus a different type of inflammatory response. Th0 cells—which express both of these cytokines in relative balance—are immune-activated but have not yet differ-

entiated into Th1 or Th2.

Hall and his team found mRNA levels to discriminate between the groups (see Table 1, page 8). Symptomatic GSE patients showed a high level of IFN- γ , in line with earlier reports, while IL-4 expression was low—a Th1 pattern. Compared to these GSE values, tissue samples from DH patients showed lower IFN- γ levels and higher IL-4, although within the DH group these values were comparable—a Th0 pattern. The asymptomatic GSE patients fell in between. Their IFN- γ and IL-4 expression were equivalent, reflecting Th0 T cells. But they expressed substantially less IFN- γ than the symptomatic GSE group, yet still higher than for the DH patients. Their IL-4 levels were higher than in both of the other groups.

Reflecting on these cytokine patterns, Hall remarked on the similar Th0 pattern in both the DH group and the asymptomatic GSE patients despite continued gluten consumption in the former and a gluten-free diet in the latter. And regarding the clear cytokine difference between the DH and symptomatic GSE patients, he found it “of considerable interest that these different patterns occurred in the face of *continuing* gluten ingestion by both groups.” Although the root of these cytokine similarities despite different diets, and cytokine differences despite the same diet—all in patients with equivalent gluten sensitivity—remained to be explained, Hall believed that these differing cytokine responses to dietary gluten may play an important role in the puzzling clinical differences between DH and isolated GSE patients.

Looking at T-Cell Receptors

As these results were being prepared for publication, evidence was appearing from other labs pointing even more strongly to a significant T-cell-mediated immune event in the gut. Although both varieties of T cells— α/β T cells and γ/δ T cells—were found to be increased in the gut of DH and isolated GSE patients groups, only α/β T cells returned to normal counts when dietary gluten was eliminated, paralleling normalization of the small bowel mucosa.

Carrying this to the next step, Hall speculated that the lack of gastrointestinal symptoms in DH patients might reflect a more limited T-cell response to gluten in the gut. This, in turn, would result from a more limited repertoire of T-cell families present in the gut of these patients. Isolated GSE patients, on the other hand, may rapidly expand their gluten-associated T-cell



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response, leading to symptomatic gastrointestinal disease. Variation is a function of the T-cell receptor (TCR), which comes in a vast array of alternatives, each variant slightly different in behavior. The great many possibilities are organized into families, and the families into larger groupings, based on certain common receptor elements. Because it was the α/β T cells showing the responsiveness to the presence and absence of gluten, Hall and his co-workers compared the range of TCR families within the variable (V) region of the β -chain (ie, TCR V β families)—the appropriate TCR component in this context—between the DH and isolated GSE gut.

They obtained small bowel biopsies

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from 11 DH patients and 17 patients with isolated GSE. All of the DH patients were on medication to control their skin disease, 9 were free of GI symptoms and still consuming gluten, 1 without GI symptoms was avoiding gluten to lower medication, 1 with GI symptoms was on a partial gluten-free diet. Of the isolated GSE group, 7 were symptom-free and following a gluten-free diet. Four of the 10 with symptoms were poorly compliant, and 4 had not modified their diet. Reverse transcriptase PCR was used to assess the range of TCR V β for each individual patient. DH patients and the GSE gluten-free/symptom-free subgroup had a comparable picture—they expressed 6.6 and 5.6 of 20 V β families, respectively, with no one family predominating. The individual DH patient range was from 1 to 16 families (median = 4), with 16 identifying the single DH patient with GI symptoms, and the asymptomatic GSE patients had a range of 1 to 15, also with a median of 4. The remaining GSE patients expressed 12.6 V β families, with no single family pre-

dominating. They ranged from 6 to 20 families per patient gut, with a median of 13.

So Hall's suspicion was borne out. GSE patients without GI symptoms—whether DH patients or isolated GSE patients who religiously avoid gluten—express a small number of TCR V β families, while those with symptoms express a significantly larger number. Number of V β families is correlated with presence/absence of GI symptoms, and clearly not with gluten consumption or characteristic small bowel mucosa changes, as all but one DH patient consumed gluten and showed the impact in gut mucosal abnormalities. These results do not constitute an answer, as “the role of restricted TCR repertoire in human disease has proven controversial,” Hall notes. “But they suggest that further investigation into the TCR utilization in DH patients may provide important clues into the initiating events in GSE and the mechanisms involved in the different clinical phenotypes associated with gluten sensitivity.”

Neutrophils: Ready for Action

The skin lesions that develop in DH have a characteristic intense inflammatory infiltrate composed almost entirely of neutrophils that localize fairly exclusively to the dermal papillary tips—contiguous to the cutaneous IgA deposits. Since the pathology begins in the gut, which is also the source of the cutaneous IgA deposits, it was logical to hypothesize that changes in the gut also play a fundamental role in this neutrophil presence in the skin.

Before resting circulating neutrophils can respond fully to inflammatory or infectious events, they have to be primed. This means equipping them with the molecules enabling them to react to subsequent activation signals by extravasating and migrating to the site of chemoattractant action. Priming occurs when specific cytokines (or agents such as lipopolysaccharides)—induced by the initial pathologic event—then induce the expression of these response molecules. Activation of primed peripheral blood neutrophils by inflammation at distant sites had already been demonstrated in other situations. “So we hypothesized that the presence of an ongoing mucosal immune response in the gut of DH patients,” he explains, “may result in a priming of circulating neutrophils that would potentiate their ability to bind to vascular endothelial cells and transmigrate to the IgA deposits already present in the skin.”

Hall also knew from work elsewhere that primed neutrophils upregulate their expression of the cell surface adhesion molecule CD11b (which helps neutrophils adhere to the E-selectin molecule on endothelial cells) and minimize their expression of the adhesion molecule L-selectin (which is a lymph node homing molecule). So he and his team analyzed neutrophils from 12 normal subjects, 10 DH patients with active, ongoing disease, and 14 DH patients with quiescent disease activity. They quantified the relative expression of both relevant adhesion

HAPPY ANNIVERSARY!

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Annenberg Circle

15th Anniversary of the
Leaders Society

In 2004

40th Anniversary of the
Dermatology Foundation

PROFILES OF SUPPORT

The Dermatology Foundation—committed to maintaining the strongest possible scientific progress and professional leadership for the understanding and care of the skin—is deeply grateful for industry’s substantial and ever-growing confidence and generosity. Learning what motivates this institutional support for the DF’s agenda and impact tells us something about the individual company as well as how we are perceived in this allied community. And it puts a human face on these important relationships. (The Corporate Honor Society on page 4 lists all companies contributing at least \$50,000 annually to DF efforts.) Past profiles have included officials from Connetics, Fujisawa Healthcare, Dermik Laboratories, Galderma Laboratories, Oclassen Pharmaceuticals, OrthoNeutrogena, and Stiefel Laboratories.

*This issue spotlights the biotech company **Biogen Idec**, which has recently made a dramatic entry into dermatologic therapeutics with an immunomodulator, the very first biologic to be approved (in January 2003) for treating psoriasis. **Doug Abel**, Vice President of the Dermatology Business Unit, talks about Biogen Idec’s involvement with dermatology and the Dermatology Foundation.*

Doug Abel came to Biogen Idec in 2000 after 13 years with Allergan, a pharmaceutical company with a major focus on the skin. Because Mr. Abel had worked with the dermatology arm during many of his years there, “I had been part of Allergan’s support of the specialty,” he says, “which involved support of the Dermatology Foundation. So when I came to Biogen Idec, I carried with me a number of years of experience in dermatology and a keen

awareness of the DF and its activities. We knew that dermatology was one of the specialties we wanted to become part of, which began with our efforts to develop a psoriasis therapy.” As Mr. Abel and his colleagues planned the most effective way to bring Biogen Idec into dermatology, they identified the important commitments to make. “And one of those was a relationship with the Dermatology Foundation,” Mr. Abel emphasizes. “I identified support of the Foundation as a very worthwhile investment and decision on our part, and I had the weight of my history with the DF behind my recommendation.”

Mr. Abel points out that two elements in particular make the Dermatology Foundation especially appropriate for Biogen Idec to support. Its psoriasis drug is just the first step in addressing treatment needs in cutaneous disease. Biogen Idec is beginning to explore other applications for this drug, which include scleroderma. They also have plans for expanding their pipeline of dermatologic therapeutics. “And supporting the DF is a meaningful

way to manifest this commitment to the specialty,” Mr. Abel says.

The other aspect of the DF that appeals so strongly to Biogen Idec is “how well its mission to further research and support young investigators fits in with the cultural environment that typifies many biotech companies,” he explains. “It is an environment founded on good science, on doing cutting-edge exploratory work, and on the hope of turning that work into unique advanced therapies for patients who have unmet needs.” Biogen Idec and the Dermatology Foundation are a good fit.



Doug Abel

molecules. They also quantified the expression of Fc IgA receptor, the molecule that binds with IgA (also referred to as CD89), and they assessed the affinity with which it binds to this antibody. The results were in line with expectation. The CD11b adhesion molecule was present in much higher numbers on the neutrophils from patients with active disease, and L-selectin was reduced in both patient groups compared to neutrophils from healthy subjects. Fc IgA receptor expression did not change, but its binding affinity did. When neutrophils from each group were incubated with monoclonal human IgA, binding capacity was significantly greater for those taken from DH patients with active disease.

“Our observations suggest that limited priming of neutrophils may be occurring in

the gut of DH patients who are eating a gluten-containing diet,” Hall said at the time, “but further studies will be needed to confirm our observation.” And he concluded by adding that “further study of neutrophils and cutaneous endothelial cell expression of adhesion molecules in sites of minor trauma may provide important insights into the pathogenesis of these skin lesions.”

The Impact of Minimal Trauma

This mention of “sites of minor trauma” foreshadows the most recent study to be published from Hall’s lab. “One of the most intriguing issues for me at this point,” Hall says, “is why DH skin lesions develop, why they are uniquely localized on the elbows, knees, buttocks, across the shoulders, and on the extensor areas of the body (see photo, page 8)—and how all of

this relates to what is occurring in the gut.” A 1997 study from the Harvard-associated laboratory of Thomas Kupper, MD, had seemed to offer relevance. Kupper had found that simple mechanical deformation of human keratinocytes leads to rapid release of the primary cytokine IL-1 α , that the amount released is dependent on the amplitude of strain, and that this release of IL-1 α holds the potential to activate vascular endothelium. Kupper viewed this as a pathophysiologic mechanism that may play a role in the anatomic localization of some inflammatory skin diseases—such as psoriasis—which occur more commonly in locations where the dermis is subjected to repetitive stretch or trauma.

For Hall, Kupper’s observation offered the possible sequence of steps between the DH patients’ circulating

4 Dermatologists Honored With DF's Highest Awards

The Dermatology Foundation empowers the specialty's future through its premier Research Awards Program, which funds the investigations that advance knowledge and patient care, support the field's emerging leaders, and increase the utilization of dermatologic resources. The DF also recognizes the benchmark contributions of dermatologists whose remarkable talents and vision have defined the specialty's potential and paved the way for continued progress. This began in 1971 with the Clark W. Finnerud Award to honor exemplary clinicians/educators. The Practitioner of the Year Award, initiated in 1976, recognizes the highest levels of clinical care. The Lifetime Career Educator Award, singling out a full-time academic dermatologist dedicated to educating residents and fellows, was first conferred in 1999. The Distinguished Service Award—the highest honor the Foundation bestows upon a colleague for unique leadership and service to the specialty—is being awarded again in 2003 for only the fourth time in the past 14 years.

Clark W. Finnerud

Award. Milwaukee dermatologist **Thomas J. Russell, MD**, a “consummate clinician-educator,” is the 2003 honoree. After earning his BS and then MD at Milwaukee’s Marquette University (the School of Medicine is now called the Medical College of Wisconsin, or MCW), followed by his dermatology residency at the Mayo Clinic in Rochester, MN, Dr. Russell returned to Milwaukee in 1968, joining the Department of Dermatology at MCW as a clinical instructor and establishing a thriving private practice that is now a group of 7 dermatologists. He achieved an enormous amount in these ensuing 35 years. He was instrumental in establishing an independent Department of Dermatology at MCW, as interim chairman he sustained the department’s vitality and purpose during two extended periods, he was chosen by medical school faculty to receive the 2002 *Marvin Wagner Preceptor Award* for dedication and excellence in teaching, and he has repeatedly earned public honors as a top clinical dermatologist. Dr. Russell’s exceptional clinical and teaching strengths have long made his weekly clinics



Thomas J. Russell, MD

“a favorite of the residents.” He is also an integral member of the team that manages patients with CTCL. His active contributions to clinical photography and promulgation of high standards are widely acknowledged. Last but not least, Dr. Russell’s innovative research in the early 1970s documenting the immunogenetics of psoriasis paved the way for current advances in the genetics of this disease.

Practitioner of the Year Award.

The 2003 awardee is California dermatologist **Lenore S. Kakita, MD**, regarded as “a shining star in dermatology” and “a perfect role model and mentor.” Dr. Kakita received her BS at UC-Berkeley and her MD from UCSF, then interned at Children’s Hospital in Los Angeles, and finished her residency at UCLA in 1971. She has been with the Division of Dermatology there ever since, and maintains an active private practice. Nominators call Dr. Kakita “a caring and compassionate clinician, a superb communicator, and innovative in her treatment techniques. Her patients love her,” and she was recently named to “*Best Doctors in America*.” In addition to her private practice, academic responsibilities, and active family life, Dr. Kakita is continuously able “to take on new challenges for the betterment of a specialty she loves.” These challenges have involved important dermatology and medical organizations at the metropolitan, state, regional, national, and international levels. She has led both the California Society of Dermatology and Dermatologic Surgery and the Women’s Dermatologic Society. Within the AAD Dr. Kakita has functioned on an extraordinary number and variety of committees, task forces, panels and study groups, assumed many responsibilities on the Advisory Board, and been a liaison with the AMA. She is concerned with patient- and health care-related issues, and “her interest and participation in California and federal legislation have resulted in many favorable dermatology medical policies, enhanced reimbursement, and respect for the practice of dermatology,” one of her nominators noted. Dr. Kakita also participates in clinical trials, and finds time to write and publish, with providing the best care to her patients as her constant focus.



Lenore S. Kakita, MD

primed neutrophils, their skin lesions, and the typical appearance in areas subject to stretch and/or friction. He knew that primed neutrophils cannot migrate into tissue unless the vascular endothelium has also been altered, upregulating its expression of the selectin family of adhe-

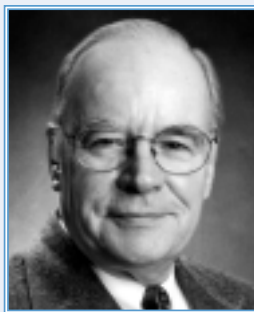
sion molecules (P-selectin and E-selectin in this instance) that enable primed neutrophils—as they prepare to leave the circulation—to tether to the endothelium and then extravasate. E-selectin expression in particular requires induction by local cytokines such as IL-1 or TNF- α .

Looking at the full sequence, Hall hypothesized that when the DH patient—in the absence of GI symptoms—continues to eat wheat protein, this continuous presence of gluten in an environment that produces anti-gluten antibodies leads to a chronic low-grade immune response in the gut.

4 Dermatologists Honored With DF's Highest Awards

Lifetime Career

Educator Award. 2003 recipient **Harley A. Haynes, MD**, has accumulated a long and distinguished track record in teaching, and is considered the “Dean of Dermatology Education” throughout the Harvard system. In 1970—after graduating from Princeton, then completing medical school, an internship and two residencies within the Harvard system, plus a 3-year research fellowship in the Dermatology Branch of the NCI—he joined the dermatology faculty at Harvard. In 1987 he also became part of what is now the Harvard–MIT Division of Health Sciences and Technology. Dr. Haynes’ enormous agenda of clinical activities within the Harvard system has been matched only by his teaching commitments and impact. His colleagues share their praise. “Dr. Haynes is a very powerful force in teaching about skin and dermatology, with great clinical judgment, the complete compassionate physician who is admired by students, residents, and faculty.” “The best evidence of his abilities as an educator is the number of dermatologists who have trained here and subsequently named Dr. Haynes as the greatest influence on their career. And each year, students from Harvard Medical School (HMS) who are interviewed for the residency program cite his influence on their choice of specialty.” HMS has recognized Dr. Haynes with the Faculty Award for Excellence in Teaching (1985 and 1987), the Sam Moschella Teaching Scholar Award from the Department of Dermatology (1997), and most recently the Daniel D. Federman Outstanding Clinical Educator Award (2000). In addition to serving as consummate teacher, mentor, advisor, and role model to students, and helping to shape the dermatology curricula at all levels, Dr. Haynes has influenced the training of all dermatology residents through contributions to national educational committees. He regularly conducts educational sessions at AAD meetings, and has published a significant number of teaching materials. Dr. Haynes is currently Professor of Dermatology at HMS, Vice Chairman of the Department of Dermatology at Brigham and Women’s Hospital, and Associate Chief, Dermatology Service, Boston VA Healthcare System.



Harley A. Haynes, MD

Distinguished Service

Award. **Eugene J. Van Scott, MD**, is only the fourth recipient of this paramount award established by the Dermatology Foundation to recognize the highest levels of dedicated and insightful leadership and service to the specialty. His greatest legacy is his role as a founder, and then guiding influence, of the Dermatology Foundation. (The three previous recipients of this award were Howard V. Dubin, MD, 1998, and Thomas B. Fitzpatrick, MD, PhD, jointly with Irvin H. Blank, PhD, 1989.) Dr. Van Scott has been a member of the specialty for more than a half century, since his residency (1949–52) at University of Chicago Clinics. After a year’s affiliation with the University of Pennsylvania, he headed the dermatology program at the NCI for the next 15 years, first the Dermatology Service of the General Medicine Branch, then the full-fledged Dermatology Branch. He was also Scientific Director for General Laboratories and Clinics at the NCI from 1965–68. Dr. Van Scott spent the next two decades as Professor of Dermatology, and then Clinical Professor of Dermatology, at Temple University. His final several years in academia were at Hahnemann University in Philadelphia. Dr. Van Scott’s publication history spans his professional career, and two hands are not enough for counting his prestigious awards over these years. Dr. Van Scott was also an eminent spokesman and man of action on many fronts in the dermatologic community, playing formative roles in the National Psoriasis Foundation and the Society for Investigative Dermatology, holding important advisory positions on a number of FDA committees and with the US Pharmacopoeia, to name just a few, and joining the AAD Board of Directors from 1961–63 and 1974–77. And most important, Dr. Van Scott was one of the 10 visionary founders of the Dermatology Foundation in 1964, helping as well to guide its early years (1964–73). Two decades later (1994) he continued to advance dermatology by bringing a new level of commitment and financial support for the Foundation as a founder of the Annenberg Circle. The Dermatology Foundation’s growth from a new idea to a membership in the thousands, a budget in the millions, substantial industry support, and a research agenda rich in breadth and depth owes this success in no small measure to Dr. Van Scott.

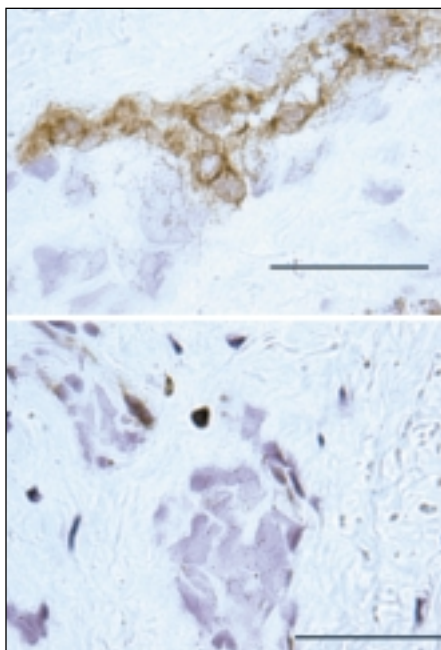


Eugene J. Van Scott, MD

This cytokine milieu partially activates inflammatory cells that traffic through the gut. Based on Kupper’s observations, Hall theorized that keratinocytes in the areas where DH lesions develop—which regularly stretch or rub—release IL-1, stimulating inflammatory mediators and initiating the

local endothelial changes enabling migration of the gut-primed neutrophils. These neutrophils would home to the source of this IL-1 release and bind with the IgA antibodies already deposited there, and the conditions for initiating lesions would all be in place.

Hall and his co-workers carried out the initial steps to test this conception. “We hypothesized that minor trauma to the skin, which does not result in any perceptible clinical or histologic change, would lead to increased expression of the adhesion molecules E-selectin and ICAM-



Minor trauma initiates pro-inflammatory changes. 4 hours after the skin was gently rubbed for a few minutes with a pencil eraser, staining for the vascular endothelial adhesion molecule E-selectin was present in the dermal blood vessels (*top*). None of the skin biopsies from unrubbed skin showed E-selectin staining (*bottom*). (Reprinted with permission from *Exp Dermatol*. See *Suggested Readings*.)

1 in the skin, which are events critical to the development of an inflammatory response," he says. "We also hypothesized that pro-inflammatory chemokines and cytokines in the skin that are known to be involved in the development of skin lesions—such as IL-8 and TNF- α —would also be expressed in the skin after such minor trauma. Such an expression of both endothelial adhesion molecules and pro-inflammatory cytokines would make skin a permissive site for the development of an inflammatory infiltrate," he adds.

The kind of minor trauma he envisioned refers to the stretching and friction that occur every day as we move and sit and reach. Hall mimicked this kind of minor trauma to the skin by gently rubbing the inner arm skin of 11 healthy adults (6 women, 5 men) with a pencil eraser for 2 minutes. Mild redness had disappeared within the first hour, and there were no evident changes of any kind in the rubbed skin by 4 hours afterward, at which point punch

biopsies were taken from both rubbed and untouched skin. This 4-hour point was chosen because of previous studies in humans showing maximum expression of E-selectin mRNA 4 hours after chemical irritation of the skin. Assessing the normal and rubbed skin for the level of mRNA for both E-selectin and ICAM-1, and for the cytokines IL-8 and IL-10, showed that the message for both adhesion molecules had increased significantly in 10 of the 11 subjects, and for the two cytokines in all 11 subjects. IL-8, a pro-inflammatory cytokine that is a neutrophil chemotactic factor, may possibly be produced by the keratinocytes themselves. IL-10—an anti-inflammatory cytokine that inhibits E-selectin expression—would appear to be the simultaneous mechanism for restraining the inflammatory reaction. Looking at E-selectin protein at 4 hours after rubbing, staining was seen in the dermal blood vessels of 3 of the 4 subjects whose tissue was evaluated with immunohistochemistry (see photos at left). There were no differences between rubbed and unrubbed skin when it came to P-selectin (also assessed) and ICAM-1.

Hall points out that "these studies demonstrate that even minor trauma to the skin—trauma that does not induce any clinical or histologic changes—can result in the expression of E-selectin, ICAM-1, and IL-8 mRNA, and the production of E-selectin protein by endothelial cells. These events would appear to predispose the skin to the development of an inflammatory infiltrate," he adds, "and if activated or partially activated inflammatory cells are traversing the skin in these areas of trauma, the skin would be poised to develop an inflammatory response that could not be blunted with the low levels of IL-10 induced by this minor trauma."

Looking Forward

Hall is continuing to characterize T-cell receptor differences between DH and isolated GSE. He finds his most recent results extremely interesting, but currently raising more questions than they have answered. He and his team are also continuing to explore the consequences of minor trauma on keratinocytes

and the inflammatory process. In addition, they are taking a much closer look at the specific T-cell responses to the different regions of the gluten protein gliadin to see if DH and isolated GSE may actually represent immune reactions to different segments of the protein molecule, and thus help to determine which organ—the gut or the skin—becomes symptomatic when the gut is inflamed.

Reflecting on the therapeutic impact for DH skin lesions that occurs from a gluten-free diet, Hall speculates that "dietary regulation of inflammation of the gut, or regulation of inflammation there by other means, may actually be a more broadly important way to look at controlling skin disease." This is something he has given thought to for some time, and intends to explore in the future. "We think that there may be a real potential for developing a model for the interaction of inflammation in the intestinal tract and the development of skin disease. And that will lead the way to new therapeutics."



DH lesions. They are uniquely localized on the elbows, knees, buttocks, across the shoulders, and on extensor surface—all areas of light friction and/or stretch. (Photo courtesy of Dr. Russell P. Hall III.)

Suggested Readings

Smith AD, Bagheri B, Streilein RD, et al. "Expression of interleukin-4 and interferon- γ in the small bowel of patients with dermatitis herpetiformis and isolated gluten-sensitive enteropathy." *Dig Dis Sci*. 1999;44:2124–32.

Hall RP III, Owen S, Smith A, et al. "TCR V β expression in the small bowel of patients with dermatitis herpetiformis and gluten sensitive enteropathy." *Exp Dermatol*. 2000;9:275–82.

Smith AD, Streilein RD, Hall RP III. "Neutrophil CD11b, L-selectin and Fc IgA receptors in patients with dermatitis herpetiformis." *Br J Dermatol*. 2002;147:1109–17.

Takeuchi F, Streilein RD, Hall RP III. "Increased E-selectin, IL-8 and IL-10 gene expression in human skin after minimal trauma." *Exp Dermatol*. 2003;12:777–83. ■

Table 1. Cytokine Expression

Cytokine	DH (Mean \pm SE)	GSE + symptoms (Mean \pm SE)	GSE – symptoms (Mean \pm SE)
IFN- γ	0.71 (0.27)	2.13 (0.93)	1.22 (0.61)
IL-4	0.64 (0.28)	0.20 (0.11)	1.09 (0.97)

DH: n=8; GSE + symptoms: n=5; GSE – symptoms: n=4. Mean ratio cytokine/CD3 expression. (Reprinted with modifications from *Dig. Dis. Sci*. See *Suggested Readings*.)

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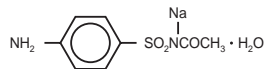
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DESCRIPTION: Sodium sulfacetamide is a sulfonamide with antibacterial activity while -sulfur acts as a keratolytic agent. Chemically sodium sulfacetamide is N-[(4-aminophenyl) sulfonyl]-acetamide, monosodium salt, monohydrate. The structural formula is:



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Each gram of Plexion SCT[®] (sodium sulfacetamide USP 10% and sulfur USP 5%) contains 100 mg of Sodium Sulfacetamide USP and 50 mg of Sulfur USP in a cream containing: Purified Water USP, Kaolin USP, Glyceryl Stearate (and) PEG-100 Stearate, Witch Hazel USP, Silicon Dioxide NF, Magnesium Aluminum Silicate NF, Benzyl Alcohol NF, Water (and) Propylene Glycol (and) Quillaja Saponaria Extract, Xanthan Gum NF, Sodium Thiosulfate USP, Fragrance.

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CLINICAL PHARMACOLOGY: The most widely accepted mechanism of action of sulfonamides is the Woods-Fildes theory, which is based on the fact that sulfonamides act as competitive antagonists to para-aminobenzoic acid (PABA), an essential component for bacterial growth. While absorption through intact skin has not been determined, sodium sulfacetamide is readily absorbed from the gastrointestinal tract when taken orally and excreted in the urine, largely unchanged. The biological half-life has variously been reported as 7 to 12.8 hours. The exact mode of action of sulfur in the treatment of acne is unknown, but it has been reported that it inhibits the growth of Propionibacterium acnes and the formation of free fatty acids.

INDICATIONS: PLEXION Cleanser, PLEXION Cleansing Cloths, PLEXION SCT and PLEXION TS are indicated in the topical control of acne vulgaris, acne rosacea and seborrheic dermatitis.

CONTRAINDICATIONS: Plexion Cleanser, PLEXION Cleansing Cloths, PLEXION SCT and PLEXION TS are contraindicated for use by patients having known hypersensitivity to sulfonamides, sulfur or any other component of this preparation. These PLEXION[®] brand products are not to be used by patients with kidney disease.

WARNINGS: Although rare, sensitivity to sodium sulfacetamide may occur. Therefore, caution and careful supervision should be observed when prescribing this drug for patients who may be prone to hypersensitivity to topical sulfonamides. Systemic toxic reactions such as agranulocytosis, acute hemolytic anemia, purpura hemorrhagica, drug fever, jaundice, and contact dermatitis indicate hypersensitivity to sulfonamides. Particular caution should be employed if areas of denuded or abraded skin are involved.

FOR EXTERNAL USE ONLY. Keep away from eyes. Keep out of reach of children. Keep container tightly closed.

PRECAUTIONS: General - If irritation develops, use of the product should be discontinued and appropriate therapy instituted. Patients should be carefully observed for possible local irritation or sensitization during long-term therapy. The object of this therapy is to achieve desquamation without irritation, but sodium sulfacetamide and sulfur can cause reddening and scaling of the epidermis. These side effects are not unusual in the treatment of acne vulgaris, but patients should be cautioned about the possibility.

Information for Patients: Avoid contact with eyes, eyelids, lips and mucous membranes. If accidental contact occurs, rinse with water. If excessive irritation develops, discontinue use and consult your physician.

Carcinogenesis, Mutagenesis and Impairment of Fertility - Long-term studies in animals have not been performed to evaluate carcinogenic potential.

Pregnancy Category C - Animal reproduction studies have not been conducted with PLEXION Cleanser, PLEXION Cleansing Cloths, PLEXION TS or PLEXION SCT. It is also not known whether these PLEXION brand products can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. These PLEXION[®] brand products should be given to a pregnant woman only if clearly needed.

Nursing Mothers - It is not known whether sodium sulfacetamide is excreted in the human milk following topical use of Plexion Cleanser, Plexion Cleansing Cloths, PLEXION SCT or PLEXION TS. However, small amounts of orally administered sulfonamides have been reported to be eliminated in human milk. In view of this and because many drugs are excreted in human milk, caution should be exercised when these PLEXION brand products are administered to a nursing woman.

Pediatric Use - Safety and effectiveness in children under the age of 12 have not been established.

ADVERSE REACTIONS: Although rare, sodium sulfacetamide may cause local irritation.

DOSAGE AND ADMINISTRATION: PLEXION Cleanser: Wash affected areas once or twice daily, or as directed by your physician. Avoid contact with eyes or mucous membranes. Wet skin and liberally apply to areas to be cleansed, massage gently into skin for 10-20 seconds working into a full lather, rinse thoroughly and pat dry. If drying occurs, it may be controlled by rinsing cleanser off sooner or using less often.

PLEXION Cleansing Cloths: Wash affected areas with cleansing cloth once or twice daily, or as directed by your physician. Wet face with water. Wet cloth with a little water and work into a full lather. Cleanse face with cloth for 10-20 seconds avoiding eyes. Rinse thoroughly and pat dry. Throw away cloth. Do not flush.

PLEXION SCT: Use once daily or as directed by your physician. Wet skin. Apply in a film to entire face, avoiding contact with eyes or mucous membranes. Wait 10 minutes or until dry. Rinse thoroughly with water and pat dry.

PLEXION TS: Cleanse affected areas. Apply a thin film of PLEXION TS to affected areas 1 to 3 times daily, or as directed by a physician.

HOW SUPPLIED: Plexion[®] (sodium sulfacetamide 10% and sulfur 5%) Cleanser is available in 6 oz. (170.3 g) tube (NDC 99207-741-06) and 12 oz. (340.2 g) bottle (NDC 99207-741-12). Plexion[®] (sodium sulfacetamide 10% and sulfur 5%) Cleansing Cloths are available in boxes of 30 cloths (3.7 g) (NDC 99207-745-30). Plexion SCT[®] (sodium sulfacetamide 10% and sulfur 5%) is available in a 4 oz. tube (NDC 99207-744-04). Plexion[®] (sodium sulfacetamide 10% and sulfur 5%) Topical Suspension is available in 30 g tube (NDC 99207-743-30).

Store at 15° - 25°C (59° - 77°F).

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Patent Pending
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Focus on Research

(Continued from cover)

a fellow in the lab of Robert C. Murphy, PhD, at the National Jewish Medical and Research Center, who studies the oxidized products of arachidonic acid (one of the major polyunsaturated fatty acids), a diverse group of molecules that play important physiological and pathophysiological roles within tissues. Arachidonic acid—from which the prostaglandins and leukotrienes are derived—results from the hydrolytic degradation of its membrane precursor by the phospholipase A2 (PLA2) enzyme. The other lipid molecule emerging from this process is the precursor molecule for the lipid mediator *platelet-activating factor (PAF)*. This precursor—called *Lyso-PAF*—is transformed into the PAF molecule by PAF-acetyltransferase. Receptors for this mediator (PAF-R) were known to exist on many cell types including platelets, vascular endothelium, neutrophils, mast cells, and monocytes, and Travers was initially studying PAF and its receptor in human lymphoblasts and B cells. Then he made the intriguing discovery that keratinocytes also possess a receptor for PAF.

His overriding interest from that point on was finding out what PAF does in the skin, and he has been pursuing this ever since.

PAF Background

The name *PAF* reflects the context in which it was very first identified decades ago, ie, platelet aggregation induced by stimulated basophils. Now it is recognized as a family of *glycerophosphocholines*, potent mediators that exert a wide range of receptor-initiated actions (from chemoattraction/activation of leukocytes in responses that include inflammation and anaphylaxis, to mitogenic effects on a variety of cells types) as well as apoptotic facilitation or protection. And the PAF system is turning out to be very important in the skin. It has not been found in normal skin, but its presence has been identified in an increasing number of conditions involving skin damage of some sort.

Based on the broad range of noxious stimuli that bring the PAF system into play, “it appears to be a primitive part of the innate immune system,” Travers explains. “PAF itself is very highly conserved across species,” he adds, “and the molecule looks the same in earthworms as it does in humans. In the skin, the PAF receptor is activated in response to direct cellular damage from physical means—such as

scratching, burns—from such assaults as UV radiation or a staphylococcal infection, from chemotherapy and radiation.” Ideally, it is a sentinel, an early warning system that responds within minutes and signals the need for the various protein mediators that will carry out the long-term response, once they have been expressed. And this is the case when PAF is biosynthesized by enzymatic pathways. It is rapidly made in very small quantities, serves its purpose, and is rapidly broken down. “Where the system can run amuck,” Travers points out, “is when potent stimuli like repeated injury (scratching) or a strong oxidative stressor (UVB) results in the massive production of PAF species by nonenzymatic routes.” Then it gains the potential for initiating a pathologic response.

The urgency behind understanding these dynamics and their various consequences is the potential for developing therapeutics that will inhibit the damaging aspects of this response.

The Skin—A Site of PAF Action

When Travers began working with PAF in the early 1990s, the receptor—cloned from guinea pig lung and human leukocytes—was known to belong to the group of seven transmembrane G-proteins. Several lines of evidence suggestive of PAF involvement in epidermal pathophysiology included detection of PAF in psoriatic scale and in blister fluid from both traumatic and bullous pemphigoid blisters. Primary cultures of human keratinocytes would synthesize PAF when stimulated with a calcium ionophore, activating calcium and—as a consequence—the enzymes that include PLA2. And in murine models of allergic and irritant contact dermatitis, both systemic and topical PAF-R antagonists had an anti-inflammatory effect.

Travers used a set of polyclonal antibodies raised against the PAF-R in human leukocytes and demonstrated binding in primary cultures of human keratinocytes harvested from neonatal foreskins, and in two immortalized keratinocyte cell lines. In sections of human skin, the antibodies bound within the epidermis in a granular, cellular membrane pattern. He determined that these keratinocyte-bound receptors are functional by treating the cells with PAF and recording the presence of intracellular calcium mobilization within the appropriate time frame. Travers also learned that neither fibro-

blasts nor melanocytes express the PAF-R.

Travers’ study appeared in 1995. “The demonstration of a functional keratinocyte PAF-R suggests that PAF may have direct effects on keratinocyte function,” he said at the time, “but the nature of this role is not at all clear.” He suspected that this lipid mediator would turn out to be important in normal keratinocytes or inflammatory processes, and thus possibly provide a path to better treatment strategies for inflammatory dermatoses. Travers would eventually learn that PAF is important in both arenas.

PAF: What Induces It in Keratinocytes

Travers gradually learned that keratinocytes will produce PAF, and less potent analogs, in response to a variety of stimuli that include the classic calcium ionophore A23187 (which directly mobilizes intracellular calcium) and the peptide growth factor endothelin-1. Cytokines and UV-radiation also induce keratinocytes to synthesize PAF. And—in a positive feedback loop—PAF produced in the keratinocyte can then bind with its receptor and stimulate additional PAF production.

Travers and his co-workers also explored the effect of exposure to signals induced by oxidative stress, because this kind of stress results in the mobilization of intracellular calcium in keratinocytes as well as other cell types. They used a model system that his lab had created by modifying the human KB epithelial cell line, which normally lacks PAF receptors (KBM-*M* for MSCV retroviral vector). They used a retroviral carrier to transduce some of these cells with the PAF-R gene and called the resulting cells—now expressing the missing receptor—KBP (*P* for PAF-R). When both sets of cells are stimulated and the results compared, any observed differences are clearly due to the newly added receptor. This highly focused comparison enabled Travers to document a dramatic receptor-related drop in threshold for the response to oxidative stress (from a potent pro-oxidant lipid hydroperoxide), ie, synthesis of a PAF-R agonist within 10 minutes following exposure. This response was negated when either PAF-R inhibitors or the antioxidants vitamin E or 1,1,3,3-tetramethyl-2-thiourea were added to the mix. Travers noted that responding to oxidative stress by synthesizing additional PAF-R-activat-

Leaders Society: News and Views

The Leaders Society—began in 1989 as a bold step to increase the Dermatology Foundation's financial resources for funding quality research in dermatology—is celebrating its 15th anniversary. Its founding has proved to be a wise move.

That first year, even though less than 100 dermatologists stepped forward to contribute the \$1,000 required for annual DF membership at that new level, the Career Development Award program was able to make a nominal start, providing \$40,000 a year for up to three years to bridge the transition from research training to independent researcher. In 2003, the annual Leaders Society campaign attracted nearly 1,200 dermatologists. The total annual LS contribution has reached over \$1.1 million, now funding a substantial number of three-year career grants that provide \$55,000 annually.

Dermatology itself has also been changing dramatically during this time. An explosion of research-driven knowledge has fueled gratifying progress in understanding, diagnosing, and treating skin diseases and conditions. Cosmetic and surgical dermatology are achieving new recognition. As a result, the specialty has attained

a significant level of respect and is sought out by patients desiring expert care for a wide range of problems affecting the skin.

The Dermatology Foundation's Research Awards Program—the *raison d'être* for its existence—has played an increasingly prominent role in fueling this tremendous growth. But the Foundation is determined to provide an even greater stimulus to progress and will not be content until its annual fund-raising efforts enable it to support *all* of the research projects deemed worthy by the review committee.

To help accomplish this goal, the Foundation is changing its membership dues structure. The DF has never increased the annual Leaders Society or Scientific Society commitments despite inflation's continued encroachment on their purchasing power. By the end of 2002, what \$1,000 had bought in 1989 was costing \$1,493,80. The time to catch up with inflation has arrived. So starting in 2004, the annual LS commitment is \$1,500 and the Scientific Society dues are \$750. Bringing these dues in line with current purchasing power will benefit the specialty and its patients for years to come.

ing stimuli might well explain why cells equipped with PAF receptors respond more intensely to oxidative stress signals.

Then Travers turned his attention to the possible role of PAF in modulating the consequences of damage to the skin's barrier function. Acute keratinocyte damage that disrupts the cutaneous barrier function occurs in response to inflammatory dermatoses and to exogenous toxic insults that include thermal and chemical injury. Such toxic injuries as thermal burns can be associated with significant morbidity and even mortality, yet the inflammatory mediators precipitated by epidermal damage were still unknown. Travers' results with oxidative stress pointed to the possible involvement of the PAF system. So he and his team expanded these earlier results by exposing HaCaT cells—an immortalized, nontumorigenic human keratinocyte cell line—to acute heat or cold as well as to the potent pro-oxidant lipid used previously.

Again, the HaCaT cells regularly synthesized PAF and less potent PAF species. "With such diverse toxic stimuli all resulting in the accumulation of these biologically active lipids," Travers said, "these findings provide evidence that the PAF system may well be involved in the inflammatory response that follows acute epidermal

damage." And the fact that PAF levels generated in all of these studies were far above the picomolar concentrations at which PAF is effective gave further support for possible pathophysiological effects *in vivo*. "An understanding of the mediators involved in epidermal cytotoxicity/cutaneous inflammation holds the potential for improved treatment strategies," Travers points out.

PAF—Not the Only Ligand for PAF-R

Next, Travers turned his attention to a very different kind of potential PAF system activator in the skin—a ligand that is neither PAF, nor one of its analogs. Evidence was appearing for the PAF-R on other cell types that a variety of ligands—including staphylococcal bacterial toxins—could bind and activate it. Keratinocytes had not yet been assessed, even though the skin is a primary site of significant *Staphylococcus aureus* infection and colonization. "These skin infections are not only an important cause of morbidity and even mortality," Travers points out, "they are thought to serve as initiation and/or persistence factors for numerous inflammatory skin diseases, including psoriasis and atopic dermatitis. Significant evidence is accumulating," he adds "that the keratinocyte may be an important target for such *S. aureus*-derived

proteins as superantigens, Protein A, and α -toxin. And an understanding of the interactions of these proteins with target cells has important therapeutic implications."

To gauge the role of the keratinocyte PAF-R in these cutaneous interactions, Travers and his colleagues recently exposed his HeCaT and KB cell lines to α -toxin, a cytolytic compound that forms a transmembrane pore to breach the target cell membrane. This mediates intracellular calcium mobilization, stimulating the release of both arachidonic acid and PAF. Exposing HeCaT cells to α -toxin produced a large increase in both mediators. To gauge any PAF-R-associated contribution to this impact, Travers either pretreated cells with PAF-R antagonists or overexpressed the PAF metabolizing enzyme acetylhydrolase II. All of these receptor-inhibiting conditions blunted arachidonic acid release by approximately one-third.

Then Travers examined samples of his KBM and KBP cell lines. Some of each type were left alone for 30 minutes, while the remainder were stimulated with purified α -toxin for that period. Then the amount of arachidonic acid released into the supernatant—an index of receptor activation—was measured (see bar graph, page 13). Because α -toxin causes arachi-

donic acid production via calcium mobilization, some presence of arachidonic acid was expected in both groups of exposed cells. The amounts released in the receptor-positive cells, however, were far greater, reflecting receptor participation. And pretreating both cell groups with a receptor antagonist reduced production only in receptor-positive cells. In unpublished studies, his group has found that the staphylococcal cell-wall product lipotechoic acid can actually signal directly via the PAF-R.

“Our growing awareness of the diversity of ligands recognized by the PAF-R,” Travers says, “may mean that the PAF system is actually involved in a wide range of pathologic conditions going significantly beyond oxidative damage and bacterial infection.”

....And What Does PAF Do?

PAF does a lot. It is a pleiotropic mediator—it has a variety of effects, some of them working in opposite directions—depending on the immediate circumstances. This great span of activity stands to reason. PAF production is stimulated by an impressive variety of endogenous and exogenous assaults, in the skin as elsewhere. And by now it has been recognized that the PAF receptor is linked to numerous signal transduction pathways that include NF- κ B, mitogen-activated protein kinases, and intracellular calcium mobilization, and the receptor can transactivate the epidermal growth factor receptor.

One of the more dramatic examples of its opposing actions involves apoptosis. PAF can enhance it or inhibit it, depending on the cause. When UVB radiation produces severe keratinocyte damage—from oxidative stress and cytokine production—cells that are beyond the capabilities of endogenous repair mechanisms undergo programmed cell death. Travers used his KBM/KBP system to discover that the ensuing apoptosis of unreparable cells occurs much more rapidly when PAF is able to participate. More recently, Travers examined the effect of PAF on chemotherapy-induced apoptosis. Again, he exposed KBM and KBP cells to chemotherapy agents (etoposide, mitomycin C). He also created a modified HaCaT cell line by ablating the PAF-R with an antisense vector. With both types of keratinocytes, receptor-positive cells were much more likely to

apoptose than their receptor-lacking counterparts. Travers believes that PAF plays a supportive role to NF- κ B here, and that this important pathway is stimulated to induce the death of cells that are no longer able to synthesize proteins adequately. He sees this type of cooperative partnership between PAF and NF- κ B as offering a potential strategy for increasing the impact of chemotherapy without increasing dose, and thus systemic toxicity.

And on the other hand, Travers and his group documented PAF’s protective anti-apoptotic effect when it comes to the cytokines TNF- α (tumor necrosis factor- α) and TRAIL (TNF-related Apoptosis-inducing Ligand-induced Apoptosis). Travers links this to NF- κ B as well, explain-

ing beyond the world of cell cultures. “For a while we were simply looking at our receptor-positive and receptor-negative cells,” he notes. “But more recently, we have begun working with two types of *in vivo* model systems.” Travers and long-term collaborator Dan Spandau, PhD, use retroviruses to overexpress the PAF-R in human keratinocytes and grow this transgenic skin in SCID mice. So far, as in the cell cultures, we see an increased responsiveness to UVB-induced programmed cell death and cytokine production in tissue made up of keratinocytes carrying many more PAF receptors than normal,” Travers says. He has recently acquired knockout mice totally lacking the PAF-R, and has begun looking at their cutaneous response to UV light.

He has not done any clinically associated work with humans since identifying PAF and a related species in blister fluid from bullous pemphigoid patients. But existing evidence leads him to suspect that the PAF system has a role in modulating AD. He is also looking toward a broad utility from the development of more effective PAF-R antagonists, and an area that particularly interests him is treatment to prevent burn-induced shock. There are reports that PAF-R antagonists have been protective in several animal models, and Travers is preparing to explore this using his knockout mice. He is hoping that muting the impact of this lipid mediator will eliminate the risk of shock.

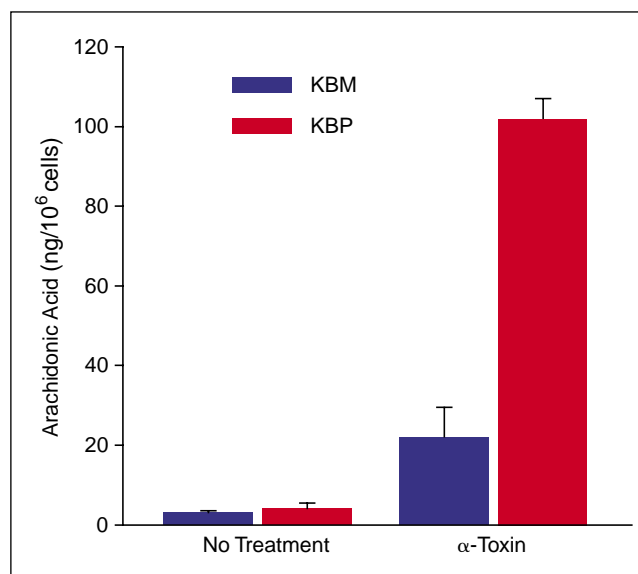


Figure 1. Staphylococcal α -toxin binds with PAF-R. When exposed to this bacterial protein for 30 min., receptor-bearing epidermal cells (KBP) release substantially more arachidonic acid than identical cells lacking the receptor (KBM). (Reprinted with permission from *JID Symp Proc*. See *Suggested Readings*.)

ing that these cytokines do not damage cells to the point of impairing their basic ability to manufacture proteins, and thus NF- κ B has a protective effect in part through the production of anti-apoptotic proteins.

Travers and his team have also shown that the epidermal PAF-R stimulates cytokine (IL-1, -6, -8, -10, TNF- α) production and ICAM-1 expression.

Current Work

Improving our understanding of the PAF system in the context of keratinocyte biology and cutaneous inflammation holds the potential for therapeutic interventions specifically designed around this lipid mediator. Toward this goal, Travers and his co-workers are now pro-

Suggested Readings

Travers JB, Murphy RC, Johnson CA, et al. “Identification and pharmacological characterization of platelet-activating factor and related 1-palmitoyl species in human inflammatory blistering diseases.” *Prost Lipid Mediators*. 1998;56:305–24.

Travers JB. “Oxidative stress can activate the epidermal platelet-activating factor receptor.” *JID Symp Proc*. 1999;112:279–83.

Travers JB, Norris DA, Leung DYM. “The keratinocyte as a target for staphylococcal bacterial toxins.” *JID*. 2001; 6:225–30.

Alappatt C, Johnson CA, Clay KL, et al. “Acute keratinocyte damage stimulates platelet-activating factor production.” *Arch Dermatol Res*. 2000; 292:256–9. ■

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Where Are They Now?—DF Profiles Research Award Recipients

From Old-Fashioned Scientist to PAF Expert

This column, written by Medical Editor Ponciano D. Cruz, chronicles the level of return on the DF's research investments over the years, ie, the progress that ensures the health of our patients—and our specialty.

Jeffrey B. Travers, MD, PhD, Kampen-Norins Investigator and Chair of Dermatology at Indiana University, brought a background in organic chemistry to his medical studies, and began working in a lipid biochemistry laboratory during his first year. His experiences there radically altered his initial desire to become a small-town physician, and his recently discovered interest in working in an academic environment led him to study for his PhD in pharmacology as well. Dr. Travers' new fascination with lipids in particular influenced his choice to specialize in dermatology, as lipids are particularly important in keratinocytes. He realized as well that dermatology would allow him to combine the kind of clinical practice he desired with highly stimulating work in academic medicine.

During his residency at the University of Colorado, Dr. Travers concomitantly spent two years as a research fellow in the laboratory of Robert Murphy, PhD, at the National Jewish Medical and Research Center. Dr. Murphy studies lipid mediators, and for years has been celebrated for his use of mass spectrometry in investigating them. "So I found myself doing mass spectrometry work," Dr. Travers recalls, "but I began to realize that the kinds of questions I really wanted to ask about lipid mediators—and especially about PAF—could not be answered this way." While working in Dr. Murphy's lab, Dr. Travers had made the surprising discovery that keratinocytes express a receptor for PAF. "And I wanted to find out what that receptor does! But," he adds, "I needed the tools of molecular biology to pursue these studies. And I had never learned them. That revolution had passed me by."

Dr. Travers first step was finding a congenial faculty position at the University of Indiana. "Then I was very fortunate in finding a position here in the lab of David Williams, MD, a Howard Hughes investigator." If Dr. Travers could find funds, Dr. Williams would teach him everything he knew about retroviruses, and about molecular biology and the tools and techniques for studying it. In 1975, Dr. Travers applied for a grant from the Dermatology Foundation, and received a three-year Career Development Award beginning in July 1976 to study *The Role of Platelet-Activating Factor in Keratinocyte Function*. He used only the initial year of his DF award, because the following year he received one of the coveted NIH KO8 grants (their *Mentored Clinical Investigator Award*).

In the years since then, Travers has fundamentally established much of the existing knowledge initiating our understanding of the functions and importance of the platelet activating factor system in the skin, beginning to outline its critical roles—both protective and pathological—in both innate and adaptive immunity and its potential as a therapeutic target. "My DF award was crucial to my ability to get started," Dr. Travers points out. Without this bridge funding, he would not have been able to gain his formative education and the experience and credentials enabling him to support his research with NIH funds.

Ponciano D. Cruz, Jr., MD
Medical Editor



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