

OFFICERS 1997-1998

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PRESIDENT'S MESSAGE

It was an honor and privilege being the president of the Society this year. Something one learns as president is you must remember many details and make sure to thank everybody. So I would like to take this opportunity for a few thanks. First, I'd like to thank each and every member for their continuing support, creating vitality for the Society which will soon be celebrating its 100th anniversary. Second, I'd like to thank the faculty and staff at each institution for their efforts and co-operation. Finally, I'd like to thank anybody whom I didn't thank that thinks they should be thanked. Thanks!

THE YEAR IN REVIEW

The 1997-98 year of the Chicago Dermatological Society brought many renowned guest speakers to the meetings despite the consistently bad weather we experienced. As usual, the faculty and residents of the major host institutions provided fascinating cases. What follows is the year in review. (The October meeting was reviewed in the previous newsletter, so is omitted here.)

NOVEMBER 19, 1997

Hosted by the University of Illinois

Max and Vera Pinski Memorial Lecture

Guest Speaker: Antoinette Hood, M.D.

Dr. Hood discussed her original work which examined the correlation of clinical with histologic diagnosis of three common entities: benign appearing nevi, fibroepithelial polyps, and seborrheic keratoses. The findings demonstrated that a dermatologist's clinical impression is more accurate in predicting the benign nature of fibroepithelial polyps than with seborrheic keratoses. If a seborrheic keratosis has unusual features, it might be a good idea to get a pathological analysis.

There were some fascinating cases:

- Cutaneous Atypical Mycobacterial Infection (presented by Drs. Brieva, Hoag, and Alaiti)
- Scleroderma vs. Acrodermatitis Chronica Atrophicans (presented by Drs. Aronson and Diamond)
- PPD+ Associated Panniculitis and/or Cytophagic Histiocytic Panniculitis (presented by Drs. Aronson, Dworin and Wong)

DECEMBER 10, 1997

Hosted by the Chicago Medical Society

Day of Learning

Silas Wallk Memorial Lecture

The Guest Speaker: A. Bernard Ackerman, M.D.

Dr. Ackerman gave two lectures:

1. The Evolution of Melanoma. Dr. Ackerman discussed the historical perspective and concept of how melanomas evolve. In his opinion almost all melanomas evolve in a regular and orderly fashion starting with increase in melanocytes in the basal layer, then atypical melanocytes moving to upper levels of the epidermis and down hair follicles and extending as single atypical melanocytes along a broad front of epidermis and finally involving the dermis. The non-dermal stages are melanoma-in-situ, and these same changes can be seen in conjunction with most melanomas that involve the dermis.
2. Pitfalls in Diagnosis of Melanoma. Dr. Ackerman showed difficult cases and common pitfalls in diagnosis of melanoma. The audience participated in the discussion.

In addition to the lectures, a self assessment examination was given. It was organized by Jeffrey Draluck, M.D. The participants looked at twenty fascinating slides that were submitted by Drs. Barsky, Braniecki, Bronson, Eng, Fretzin, Fronda, Guitart, Reddi, and Ronan. After the lectures, Dr. Ackerman looked at the slides "cold" and gave

his diagnosis. Videotapes of the lectures and meeting were given to all the institutions, and a copy is available at the Society, should any member wish to borrow it.

JANUARY 21, 1998

Coding Seminar

Not even a blizzard could deter a standing room only crowd from attending a coding seminar given by the Diva of Documentation and Czarina of Coding...Inga Ellzey. The main topics concerned necessary documentation for E/M coding. Other changes for 1998 were discussed. Inga is always a dynamic, entertaining and very informative speaker. She will be back again next year to give us more "good" news.

MARCH 18, 1998

Hosted by Cook County Hospital

Samuel Zakon Lecture

Guest Speaker: Timothy Johnson, M.D.

Dr. Johnson is the director of the University of Michigan Cutaneous Oncology Division. He gave us an update on diagnosis and treatment of melanoma. Some points of interest were: 1) Melanoma free margins on sun damaged skin of the face (lentigo maligna melanoma) may be very difficult to determine. Dr. Johnson and his colleagues use a modified type of micrographic surgical technique on some of these lesions; 2) He discussed his experience with sentinel node biopsy. For melanomas over 1mm in depth, sentinel node evaluation can be an important prognostic tool as well as determining whether to recommend interferon as an option for those patients. It appears that interferon may improve the prognosis, but it's still too early to tell in which cases it might have the greatest benefit; 3) In melanoma-in-situ he recommended margins 1/2 to 1cm but only deep enough to remove all the adnexal structures. Therefore, except where the hair follicles go to the fat, such as in the scalp, the excision, in his opinion, need only go into the fat. Dr. Johnson provided a useful handout of U of M treatment protocols that is frequently updated. I asked him to send the CDS updates. Anybody who wishes a copy of the handout contact Mindy at the CDS.

Fascinating Cases:

- Lymphedema Praecox (presented by Drs. Remlinger and Vallurupalli)
- Histoid Hansen's Disease (presented by Drs. Ortiz-Ferrer, Bronson, and Miller)

APRIL 8, 1998

Hosted by the University of Chicago

Allan Lorincz Lecture

Guest speaker: Amir Mehregan, M.D.

Dr. Mehregan discussed the Pinkus family, Felix and Herman and their contributions to the field of Dermatology. We often lose sight of the fact most skin diseases were described and defined by a relatively small group of pioneers in our field, within a period of less than 150 years. It was because of these few that the field was nurtured and developed. The specialty continues to grow due to the many colleagues they mentored, such as Dr. Mehregan. Dr. Mehregan reminded us all of the gratitude we owe these colleagues, and his reflections on his mentors are a tribute to them and a humbling reminder to us all.

Fascinating cases:

- B-cell Lymphoma presenting as solid facial edema and exophthalmous (presented by Drs. Shaw and Dragon)
- Granulomatous process associated with deletion of chromosome 20 (presented by Drs. Pezen and Applebaum)
- Hypertrichosis Universalis (presented by Drs. Pezen, Dragan, and Melamed)

Bruce Bennin, M.D.

AWARDS

The Awards Committee of the Society has chosen the recipients of the Practitioner of the Year and the Founders Award for 1998.

PRACTITIONER OF THE YEAR

Awarded each year to an individual for exemplary service as a practitioner of dermatology:

MORTON D. BARNETT, M.D.

FOUNDERS AWARD

Awarded each year to an individual who has devoted extraordinary time and talent as a teacher and clinician:

ANA M. ENG, M.D.

MORTON D. BARNETT, M.D.

Morton D. Barnett, M.D., along with his twin sister, Nancy, was born in Chicago and raised in Oak Park. Upon graduation from Oak Park-River Forest High School, he attended the University of Illinois at Champaign for his pre-medical education. While at the University of Illinois, Mort was a member of Alpha Epsilon Pi fraternity.

Mort earned his doctor of medicine degree from Stritch School of Medicine of Loyola University in 1963. He then completed a one year rotating internship at San Bernardino County Hospital, San Bernardino, California. After his internship, Mort volunteered for the United States Air Force and was stationed at Minot Air Force Base, Minot, North Dakota. He was assigned to the 5th Fighter Interceptor Squadron as their flight surgeon. One of the "highlights" of his Air Force career was the opportunity to fly Mach II (twice the speed of sound) in an F-106 Delta Dart fighter aircraft.

Following his Air Force days, Mort began his dermatology residency at Cook County Hospital under the guidance of, initially, Theodore Cornbleet, M.D. and then Sidney Barsky, M.D. One of the many things that stands out in his mind from residency days is the requirement that they present patients at every monthly meeting of the Chicago Dermatological Society. "By the month of May, we were really scrounging for cases."

Mort set up his practice of Dermatology in Joliet, Illinois. He fondly remembers that when he first started, he would schedule all of the patients at about the same time so that it would appear to the patients that the waiting room was full. Something must have worked because his practice grew and, in 1992, Matthew R. Kelleher, M.D. joined Mort and, in 1995, Steven W. Neubauer, M.D. was added to the staff of Dermatology Limited. Throughout his thirty years of practice, Mort has strived to maintain the highest of standards in the care of his patients.

He is currently on the active staff of both Provena Saint Joseph Medical Center and Silver Cross Hospitals in Joliet and is a volunteer physician for the Will-Grundy Medical Clinic. Mort is a member of the American Medical Association, Illinois State Medical Society and Will-Grundy County Medical Society where he serves on the Peer Review Committee. Additionally, he is a member of the Chicago Dermatological Society, serving as its Vice-President in 1988-1989, the Illinois Dermatological Society, the Leader's Society of the Dermatology Foundation and is a fellow of the American Academy of Dermatology. Mort is certified by the American Board of Dermatology.

Being an avid sports fan, and especially a die-hard Cub fan, Mort enjoys watching a variety of sporting events and optimistically feels that one of these days the Cubbies will win a pennant and be in the World Series. Within the last several years, he has taken up fishing and looks forward to his annual trek to Canada to catch the really BIG walleyes and northerns.

Mort feels that behind every good man is a wonderful woman. His wife and best friend of thirty-nine years is Harriet, whom he met at the University of Illinois while they were both attending undergraduate school. They are the proud parents of two children and three grandchildren. Their daughter, Julie, a commercial artist, resides in Southern California with her husband and three-year-old daughter, Alyssa. Their son, Brian, is an anesthesiologist at Rush-Copley Hospital in Aurora and lives in Naperville with his wife and fifteen-month-old identical twin sons, Matthew and Andrew.

Mort is truly honored and deeply touched to be the recipient of the 1998 Chicago Dermatological Society Practitioner of the Year Award. He feels that he has joined an extremely elite group of dermatologists and will continue to uphold the standards as set forth by this award.

ANA M. ENG, M.D.

As a child growing up in the Philippines, Ana Eng, M.D. attended two different schools: English and Chinese, because that was how Chinese children in the Philippines were brought up at the time. Her mother was a physician, and one of her brothers, who is now an orthopedic surgeon, was in medical school. She thought that medicine was the only path to follow.

In medical school, Ana never cared much for dermatology. All rashes looked alike, and all tumors of the skin seemed pretty much to resemble each other. In fact, her lowest grades in medical school were in dermatology. She learned dermatology through forced memory. After a rotating internship in Vermont, she decided to apply for a pathology residency. It seemed to her at the time that every physician looked to the pathologist for the final answers. She began a pathology residency in Madison, Wisconsin. After doing more than 100 autopsies as a first-year pathology resident in Madison, that was it! She gave up! She thought to herself, "Maybe I should go back to dermatology and figure out all those skin rashes and tumors, and face the challenge of learning both the clinical aspects and the pathology of skin diseases."

Ana was accepted into the dermatology residency program at the University of Chicago. It was there that she came under the guidance of Dr. Allan Lorincz. Dr. Lorincz screened every case, no matter how simple. He influenced everyone by his wide-ranging ideas. He was a good influence on Ana.

Ana expressed her new-found interest in dermatopathology to Dr. Lorincz, who arranged for her to spend time in Monroe, Michigan, with Dr. Herman Pinkus. She traveled to Michigan many times during her residency and during vacation times, learning dermatology and dermatopathology from Dr. Pinkus. When Dr. Pinkus would read slides, he would scrutinize every single detail given in the case. Every microscopic component of the skin seemed alive to him. He would do an acid orcein Giemsa stain on most slides, which gave him an extra perception of other elements of the specimen — elastic fibers, mast cells, etc. His questioning mind led him to think and to be a detective. Dr. Pinkus and Ana would often ride on a bus from Monroe to Detroit, where they would discuss dermatopathology.

Dr. Pinkus loved nature, and would often show Ana photographic slides of flowers and landscapes. Throughout her residency, and as an instructor at the University of Chicago, both Dr. Pinkus and Dr. Mehregan would advise Ana on diagnostic problems through the mail. E-mail was non-existent, so it was a lot like a correspondence school. She is quite grateful for the precious experience.

A more recent interest for Ana has been nail pathology. She wondered, "Who would have the most specimens?" Dr. Bernie Ackerman came into her mind. When she expressed an interest to him, he generously agreed to let her sort and scrutinize any nail specimens he had. She also came to deeply appreciate his experience not only in dealing with slides, but his keen insights and sensitivity into different situations.

Ana would like to extend a special thank you to Drs. Lorincz, Pinkus, Mehregan, and Ackerman for their guidance, teaching, and for sharing their love of medicine and dermatology with her.

Ana realizes how fleeting the short moments of this lifetime are. Van Gogh once said, "The best way to know God is to love many things."

Her favorite hobby is floral design, where she has passed six sets of examinations, judged five shows and won five blue ribbons. She has qualified to be a judge for the Garden Club of Illinois. She enjoys showing the beauty of our Creator (nature, flowers, plant materials, branches) through the principle of floral design, much as a make-up artist shows the best of facial features. Some of her designs have been displayed at the Elmhurst Art Museum, Navy Pier, and at the Chicago Botanical Gardens. Another hobby is Polynesian dancing — doing the hula and dressing as a hula dancer. She realizes this is rather odd for a physician, but no one knows she is a physician when she dances.

Ana served as a docent for the Chicago Architecture Foundation for eight years, giving river tours, walking tours, elevated train tours, and sculpture tours. Chicago becomes a much more friendly city when you know what the city is all about. She takes great satisfaction in conveying the history, art, and architecture of Chicago to the public.

Ana belongs to the Fox Valley PC Association, a computer club where everybody is helpful and friendly. "Knowledge can be gained so quickly through CD-Rom disks or the internet rather than going through pages of a book in a huge library," she feels. She also thinks that our brains are very much like a computer, and our minds much like files stored on a disk. The good files are: Loyalty, Perseverance, Smiles, Preparation, Determination and Love. The corrupted files are: jealousy, selfishness, laziness, gossip, griping and dishonesty.

Ana's academic affiliations have been with the University of Chicago, University of Illinois, Hines VA, and Loyola. Her publications number 47 (mostly in the area of dermatopathology). Another commitment has been giving lectures on dermatology for the Olser Institute. She has two children: Oliver, and Tanya. Oliver, recently finished his Ph.D. in mathematics in Madison, Wisconsin. He's chosen to stay on in Madison, working with Epic, a computer company in the health care business. Tanya is an actuarial with Delouche and Touche in their Los Angeles offices. She moved to L.A. hoping to meet more oriental boys.

Hopefully, when time permits, Ana would like to get more involved with investments. "To do it in a disciplined and educated way, not only makes one save and multiply those savings, but it helps one to keep up with what is going on in different industries — banking, oil, technology, restaurants, airlines, etc. Wouldn't it be nice to organize a club for pre-teens and get them involved?"

1998 SERVICE AWARDS

25 YEARS

Thomas O. Chua, M.D.
Chester Danehower, M.D.
Trudy F. Eisenman, M.D.
Taraneh S. Firoozi, M.D.
Thomas L. Fisher, M.D.
Adarsh A. Kumar, M.D.
A. Lertsburapa, M.D.
Marvin H. Margolis, M.D.
Eva V. Page, M.D.
Keyoumars Soltani, M.D.
Katherine A. Wier, M.D.

30 YEARS

Morris Meister, M.D.
Charles H. Patton, M.D.
Edward S. Peterka, M.D.
Francis M. Sellers, M.D.

35 YEARS

Martin L. Gecht, M.D.
Murray Nierman, M.D.

40 YEARS

Charles Camisa, M.D.
George J. Dickison, M.D.
Robert Pittelow, M.D.

45 YEARS

Clarence Livingood, M.D.
Joel Taxman, M.D.

50 YEARS

Sidney J. Kaplan, M.D.
Milton Robin, M.D.

ANNOUNCEMENT

Michael D. Tharp, M.D., the Clark W. Finnerud, M.D., Professor and Chairman, Department of Dermatology at Rush-Presbyterian-St. Luke's Medical Center, is investigating the use of a new topical and oral retinoid (Targretin) in an open label, multicenter, clinical trial for early and advanced stages of cutaneous T-cell lymphoma. As you know, CTCL can be a devastating disease that has few approved effective therapies. These clinical trials are being conducted to evaluate the antitumor efficacy of Targretin for different stages of this disorder. Treatment is intended to be administered for a minimum of 16 weeks. These patients would be seen at Rush in the Dermatology Patient Services Clinic, room 264 Professional Building. The study coordinator, Annette Morales, R.N., will arrange appointments and can be contacted at 312-942-2197.

INCLUSION CRITERIA

- 1) A clinical diagnosis of cutaneous T-cell lymphoma, stage IA, IB, or IIA for early stage and stage IIB, III, IVA or IVB with no CNS involvement for advanced stage.
- 2) Refractory to, intolerant to, or reached a response plateau for at least six months on at least two prior therapies from the following list: PUVA, UVB, EBT, photopheresis, interferon, systemic cytotoxic chemotherapy, cyclosporine, topical nitrogen mustard or topical carmustine (BCNU). At least one of these qualifying prior treatments must have been topical nitrogen mustard, topical carmustine or a phototherapy. Topical steroids and systemic retinoids do not qualify.
- 3) Complete avoidance of systemic or topically-applied antihistamine and antipruritic agents for at least one week or, if such agents cannot be avoided, systemic and topically-applied antihistamine and antipruritic agents must be using a stable dose regimen for at least one week prior to initiation of study drug treatment and throughout the study, unless it is determined that a discontinuation or a reduction in dose is indicated.
- 4) Age 18 years or older and a Karnofsky performance score of 60 or more.
- 5) Free of serious concurrent illness.

EXCLUSION CRITERIA

- 1) Topical therapy for CTCL including nitrogen mustard, carmustine, corticosteroids and others within 2 weeks of entry.
- 2) Psoralen plus UVA or UVB irradiation therapy within three weeks of entry.
- 3) Electron beam therapy, photopheresis therapy and systemic anticancer therapy of any kind within 30 days of entry.
- 4) Oral retinoid therapy for any indication within 3 months of entry.
- 5) Oral etretinate therapy for any indication within 1 year of entry.
- 6) T-cell Lymphoma involving the central nervous system.
- 7) Pregnancy or active breast feeding.
- 8) Serious intercurrent medical illness or infection, including HIV, which could potentially present a safety risk and/or prevent compliance with the requirements of the treatment program.

NEW CHAIRMAN AT LOYOLA UNIVERSITY

June K. Robinson, MD will become Director of the Division of Dermatology within the Department of Medicine of Loyola University Chicago Stritch School of Medicine in May, 1998. She is also the Program Leader of the Skin Cancer Clinical Program of the Cardinal Bernardin Cancer Center, a position in which she integrates the clinical care of patients with non-melanoma skin cancer and melanoma with Dr. Brian Nickoloff's basic research laboratory group. By directing a multidisciplinary center for melanoma patients, Dr. Robinson will coordinate their medical and surgical oncologic care. In her clinical practice in the Cardinal Bernardin Cancer Center, she will continue to perform the resection of non-melanoma skin cancer with Mohs surgery. Dr. Robinson joins Drs. David Eilers, Edward Keuer, Tehming Liang, Mary Massa, Jeffrey Melton, and James Swan of the dermatologic clinical faculty at Loyola University and Hines Veterans Administration Hospital.

A native of Pennsylvania, Dr. Robinson graduated cum laude from the University of Pennsylvania in Philadelphia and attended medical school at the University of Maryland. She completed a medical internship in Baltimore, a dermatology residency at Dartmouth Hitchcock Medical Center in Hanover, NH, and a fellowship in Mohs micrographic surgery and dermatologic surgery at New York University Skin and Cancer Clinic. She is board certified in dermatology and Mohs micrographic surgery. She taught for 19 years in the Department of Dermatology at Northwestern University Medical School, where she was Professor of Dermatology and Surgery. Dr. Robinson has authored or co-authored over 100 papers, 21 abstracts, 19 book chapters, and co-edited four textbooks. Her chief interest is the prevention, early detection and treatment of non-melanoma and melanoma skin cancer. She is currently the Secretary Treasurer of the American Academy of Dermatology.

She is married to William Barker, who practices corporate litigation with the primarily Chicago based law firm of Sonnenschein. They enjoy living in Chicago and find juggling the schedules of a two career couple stimulating.

After May 15, 1998, Dr. Robinson can be reached at telephone (708) 327-3363 and FAX (708) 327-3364. Her mailing address is:

June R. Robinson, MD
Director, Division of Dermatology
Program Leader of the Skin Cancer Clinical Program
Cardinal Bernardin Cancer Center
Loyola University Medical Center
2160 South First Ave., Room 341
Maywood, IL 60153

1998 MIDWEST CLINICAL CONFERENCE

The 54th Midwest Clinical Conference was held at Navy Pier February 20 through 22, 1998. The dermatology course this year took place on Sunday, between 8:00 a.m. and noon, and was titled "Dermatology for Primary Care Physicians." There were four outstanding presentations: Debra Bakal, M.D. discussed Common Skin Disorders; Gisela Yingst, M.D. spoke about Benign and Malignant Neoplasms of the Skin; Julie Moore, M.D. covered Cutaneous Manifestations of HIV/AIDS; and Anthony J. Mancini, M.D. closed the session with Neonatal and Pediatric Dermatology.

The room held about 300 seats; they were all taken and there was standing room only! Questions were entertained after each presentation, moderated by Fern P. Nelson, M.D. The dermatologists were surrounded by conference attendees at the end of the session, answered questions and received thanks from many.

I would like to personally thank the presenters for their time, efforts, and for making this year's dermatology session a resounding success.

Fern P. Nelson, M.D.

OUR VICE-PRESIDENT

Anne Solomon was in awe of the USA from a very young age when her family received their first trunk full of food and clothes from her grandparents in New York. She and her brothers were brought up in a busy general practitioner's household in the South of England at a time when doctors still made house calls and the office was in the house. Anne understood early the privilege of being a physician and being allowed to share in the lives of others at crucial moments. It seemed only natural that she should have a career in medicine. At seventeen, she was studying 12-18 hours a day at the University of Birmingham Medical School. Saturday nights were spent dancing to the Beatles. Sundays were spent hiking in the Malvern Hills.

While working in the British Health Service, she learned a lot about physical examination and clinical freedom. After obtaining her MRCP (internal medicine boards), she spent three years in renal medicine during the early days of dialysis and transplantation. That is, until she saw the light. She took the advice of her mother, a long time psoriasis sufferer, and went into dermatology, beginning in Dr. Lyell's department in Scotland. She then travelled to America. During a year in Dr. Stoughton's laboratory in La Jolla, Anne soon realized that as an unlicensed foreign doctor she sorely missed clinical contact. She set about taking the appropriate exams, and became a dermatology resident at the University of Chicago, with which she has been intimately associated ever since.

It was at the University of Chicago where she met and married Edward Laumann, a professor of Sociology. She discovered the rewards, as well as the trials, of inheriting two teenage children, both of whom are now grown. (Eric is a litigator at Jenner and Block, while Lisa is a Ph.D. candidate in psychology at the University of Virginia.) Her own two sons, now teenagers, and her two grandchildren are together at the University of Chicago Laboratory School.

Since 1979 she has been in a group practice on the South Side of Chicago which has been at the forefront of the "Managed Care" revolution. Through her association with Michael Reese Hospital she has served as an active teacher and faculty member at the University of Illinois. She has become an American citizen, of which she is very proud. Now she is extremely honored to have been chosen to be vice-president of the local society she values most dearly.

NEW OFFICERS FOR CHICAGO DERMATOLOGICAL SOCIETY

The following slate of officers has been chosen for 1998-1999:

President Kathleen Remlinger, M.D.
President-Elect Keyoumars Soltani, M.D.
Vice-President Tony Fu, M.D.
Secretary David Lorber, M.D.
Treasurer Amy Paller, M.D.

NEW OFFICERS FOR ILLINOIS DERMATOLOGICAL SOCIETY

The following slate of officers has been chosen for 1998-1999:

President Samuel Solomon, M.D.
President-Elect Darryl Bronson, M.D.
Secretary/Treasurer Harry Goldin, M.D.

SOCIETY RESEARCH AWARDS

The Chicago Dermatological Society, through its Research and Education Fund, awarded three research grants for 1997-1998. Research must be conducted in the United States. Any regular member of the Society may be eligible, as well as fellows, residents, and Ph.D. degree holders, whose major appointment is in an academic dermatology department. Applicants in the latter three categories who are not members of the Society must be sponsored by a dermatology department or divisional preceptor who is a regular member of the Society.

The three award winners for the year were:

- 1) Jean-Christophe Lapiere, M.D. – Northwestern University; Strategies Toward Gene Therapy For Dystrophic Epidermolysis Bullosa; \$5,000 award.
- 2) Li-Feng Li, M.D. – University of Illinois; Role of Protein Kinase C In The Regulation of Hair Growth; \$5,000 award.
- 3) I-Ja Chan, Ph.D. – Rush-Presbyterian-St. Lukes Medical Center; Studies Of The Mechanism Of Chymase-Induced Apoptosis; \$5,000 award.

Two award winners have provided us with an abstract of their research:

Principle Investigator: Jean Christophe Lapiere, M.D.

Title: Development and Characterization of a Recombinant Truncated Type VII Collagen "Minigene": Implications for Gene Therapy of Dystrophic Epidermolysis Bullosa

Address: Dept. of Dermatology, Northwestern Univ. Chicago, IL.

Dystrophic epidermolysis bullosa (DEB) is an inherited mechano-bullous disorder of skin caused by mutations in the type VII collagen gene and perturbations in anchoring fibrils. The lack of therapy for DEB provides an impetus to develop gene therapy strategies. However, the full-length 9 kb type VII collagen cDNA exceeds the cloning capacity of current viral delivery vectors. Gene therapy for DEB may necessitate the use of a truncated type VII collagen "minigene". In this study, we constructed a recombinant type VII collagen minigene, comprising the sequences coding for the N-terminal 1253 AAs and the C-terminal 161 AAs of the noncollagenous domains (NC1 and NC2 respectively) and 880 AAs of the central collagenous domain minus a 2 Kb in frame deletion. The "minigene" had intact NC1 and NC2 domains which are required for interactions with extracellular matrix components and for initiation of the antiparallel dimer formation of type VII collagen. The construct was placed under the control of a cytomegalovirus promoter and transfected into 293 cells. The 293 cell clones secreted 2-5 mg/L of the 240 kDa recombinant type VII "minicollagen" (mini VII). Characterization of purified mini VII demonstrated the following: Like NC1, mini VII bound to fibronectin, laminin-5, type I collagen and type IV collagen. In cell attachment assays using both fibroblasts and keratinocytes, mini VII supported greater cell-matrix adhesion than NC1 alone. Mini VII promoted human keratinocyte migration. Biochemical studies showed that mini VII was N-linked glycosylated, like NC1, and was secreted as correctly-folded, disulfide-bonded trimers resistant to protease degradation. Further, like authentic type VII collagen, mini VII appeared to undergo conversion from procollagen to collagen in 293 cells. Finally, transfection of the "minigene" into immortalized RDEB keratinocytes (in which the expression of type VII collagen was absent) resulted in synthesis and secretion of mini VII. We conclude that mini VII may provide a therapeutically active product to correct the gene defects of RDEB and reverse their consequences.

Principle Investigator: I Ja Chan, Ph.D.

Title: Studies of the Mechanism of Chymase-Induced Apoptosis

Address: Department of Dermatology, Rush-Presbyterian-St. Luke's Medical Center, Chicago IL.

It has been well established that human basal cell carcinomas have increased numbers of mast cells. Previous studies from our laboratory have shown that mast cells can kill tumor cells in vivo and in vitro. In addition, connective tissue mast cell-derived chymase induces cell death in a number of tumor cell lines. Biochemical analysis of this pathway of cytotoxicity in our laboratory revealed that chymase-induced cell death is initiated by spe-

cific cell surface receptor binding, mediated by dephosphorylation of nuclear protein pp82 and alteration of four nuclear protein expressions. Agarose gel electrophoresis of chromosomal DNA also revealed that chymase induces nuclear DNA fragmentation in a susceptible cell line FL. It appears that chymase-induced cell death is a programmed cell death (apoptosis). Thus, we have investigated the mechanism of chymase-induced apoptosis. We hypothesized that during certain times in the cell cycle might make tumor cells more susceptible to chymase killing. Therefore, chymase-sensitive FL cells and chymase-resistant K562 were synchronized and arrested in G₁, S, G₂ and M phases, and then exposed to chymase for 0, 4, 8, 18 hrs. DNA terminal transferase nicked endlabeling (TUNEL) assay was used to monitor chymase-induced DNA fragmentation at each phase of the cell cycle. Chymase did not cause significant DNA fragmentation at G₀, G₁, and S phases (0.3% to 3.4%), but did induce a greater percentage of FL cells to undergo DNA fragmentation and death (20.3% to 28.6%) at G₂ and M phases. In addition, chymase did not induce DNA fragmentation in the chymase-resistant cell line K562 in G₀, G₁, S and M phases. These results suggest that chymase disruption of mitosis leads to apoptosis and therefore this serine protease may play an important role in anti-tumor activity.

1998-99 PROGRAMS AND SPEAKERS

SEPTEMBER 16, 1997

Cases from the Community

OCTOBER 21, 1998

Samuel Bluefarb Lecture
Northwestern University

NOVEMBER 18, 1998

Allan Lorincz Lecture
University of Chicago

Paul Khavari, M.D.

DECEMBER 9, 1998

Silas Wallk Day of Learning
University of Illinois

William James, M.D.

JANUARY 20, 1999

Coding Seminar
Chicago Medical Society

Inga Ellzey

FEBRUARY 17, 1999

Samuel Zakon Memorial Lecture
Cook County Hospital

APRIL 21, 1999

"Seminars-In-Depth" Pediatric Dermatology
Chicago Medical Society

Amy Paller, M.D.

Barbara Reed, M.D.

Ilona Freiden, M.D.

MAY 19, 1999

Max & Vera Pinski Memorial Lecture
Rush-Presbyterian-St. Lukes Medical Center
Annual Awards Luncheon
Charles Camisa, M.D.

NEW MEMBERS

ROBIN L. HORNING, M.D., M.P.H.

Dr. Horning was born in Santa Rosa, California, and then later moved to Bakersfield, CA. After spending the first 7 years of her life in California, she moved to northern Idaho where she completed her elementary and high school education. She then went to Yale University for her college education, majoring in geology and geophysics. After working one year in the area of exploratory petroleum geology, she decided to pursue a career in the medical sciences. She then worked in an immunology laboratory as a research assistant at the Yale University School of Public Health for two years. After that, she obtained her medical degree in 1990 at the Yale University School of Medicine. She then pursued a pediatrics internship at Duke University, followed by her dermatology residency at the same institution.

Given her interest in research and public health, Dr. Horning then pursued a two year fellowship in the national Robert Wood Johnson Clinical Scholars Program at the University of North Carolina-Chapel Hill. During this fellowship, she also obtained a Master's Degree in Public Health from the Department of Epidemiology, UNC School of Public Health. She was also able to complete a residency in General Preventive Medicine and Public Health during this same period of time. She just became board-certified in this specialty in February, 1998. Currently, she is an Assistant Professor at Northwestern University in the Departments of Dermatology, Pediatrics, and Preventive Medicine.

Dr. Horning's research interests have been in the area of preventive medicine and health services research. Her concentration is in skin cancer prevention, with a special focus on the childhood population. She recently was awarded the Dermatology Foundation's Clinical Career Development Award in Health Policy.

On the social side of life, Dr. Horning loves various outdoor activities such as camping and hiking, and she loves to travel. This summer she will travel to Costa Rica with her fiancé, Peter Lennon, after their wedding on June 6, 1998.

THOMAS R. BRANDER, M.D.

Dr. Brander received his undergraduate degree from Calvin College in Grand Rapids, Michigan. He subsequently attended medical school at the University of Illinois at Chicago. He completed his internship in internal medicine at the University of Chicago and his dermatology residency at the University of Illinois. He is currently in private practice in Bloomington, Illinois with James Seehafer, M.D.

RACHEL SCHACHT, MD.

Dr. Schacht is a Chicago native. She received her B.A and M.D. in 1993 through a combined 6-year program at Lehigh University and The Medical College of PA (now Allegheny University Health Sciences) in Philadelphia, Pennsylvania. Upon completion of the combined program, she returned to Chicago for her internship at Northwestern University and dermatology residency at Cook County Hospital. She is currently in private practice with Ruth Nesavus-Barsky, M.D. and Marcia Johnson, MD., Ph.D at Barsky Dermatological Associates in Oak Brook, Illinois.

RHONDA S. GANANSKY, M.D.

Dr. Ganansky was born in central Illinois and raised on a farm with her five sisters (no brothers). She received her B.S. in biology from the University of Illinois at Urbana-Champaign in 1985. She received her medical education from Chicago Medical School in North Chicago, graduating in 1989. After an internal medicine internship at Rush-Presbyterian-St. Luke's in Chicago, she began a dermatology residency. Her first year was spent in Marshfield, Wisconsin, at the Marshfield Clinic. The next two years were spent at the University of Wisconsin in Madison, Wisconsin. After finishing her residency, she then spent 4½ years in private practice in a multispecialty clinic in Evansville, Indiana. In order to move closer to her identical twin sister who lives in the Chicago area, she recently relocated her practice to the Rockford Clinic. She enjoys general adult and pediatric dermatology and dermatologic surgery.

Happily married to Ron for eleven years, they have three children and live in the country near Belvidere, Illinois.

ABDUL HAFEEZ, M.D.

Dr. Abdul Hafeez was born in Yemen and grew up in Pakistan. He immigrated to Illinois in 1980 and went to Elgin High School in Elgin, Illinois. He received his undergraduate, medical education, and dermatology residency all at the University of Illinois in Chicago. After spending a year in a dermatology group practice in a town near Charlotte, North Carolina, he moved back to Illinois where most of his family resides. He is currently in practice in La Grange, Illinois, with Dr. Shelley Halper, and part time at Ravenswood Clinic in Chicago. He is happily married for two years.

GERTA JANS, M.D.

Dr. Jans is a graduate of the University of Illinois Medical School. After an internship at Northwestern Memorial Hospital, she completed her dermatology residency at the University of Illinois. Dr. Jans is the third generation in her family to become a physician. Her mother, a native of Spain, came to the U.S. to complete a residency where she met her husband (also a physician). Dr. Jans has been in private practice in the suburban Chicago area for the past seven years, working in established dermatology practices in Crystal Lake, Elk Grove Village, and Wilmette. She is now in a solo private practice in Kenilworth, Illinois. Gerta is married to Joan Guitart, M.D., a dermatopathologist at Northwestern University Medical School. Gerta and Joan have four children: Hanna age 7, Joan Ramon (Jr.) age 5, Francis Xavier (Xavi) age 3, and Gerta Emma (Gigi) age 6 months.

CAROLYN MERRITT, M.D.

Dr. Merritt attended college at Howard University in Washington, D.C. After teaching school for two years, she went to medical school at George Washington University in Washington, D.C. She then completed an internship, dermatology residency, and dermatology fellowship all at the University of North Carolina in Chapel Hill. Her fellowship was based on an in-vitro model of immune complex mediated basement membrane zone injury using bullous pemphigoid as the primary disease.

Carolyn moved to Chicago in 1991 to become a dermatologist with Humana Health Care in Evanston, Illinois. She had been in private practice in Petersburg, Virginia, but after the death of her first husband, she chose to move to Chicago where she had family and many friends. Chicago was her favorite city because it offered the adventures found in a large city along with a warm, friendly spirit. After seven years at Humana, Carolyn has decided to experience managed care from a different perspective — private practice. She has joined Fern P. Nelson, M.D. and Donna Stockton, M.D. in Joliet, Illinois.

Carolyn's two sons, Marty and Brian, have spent their formative years in Chicago and consider Chicago their home. She has happily remarried and in July will be celebrating her 2nd anniversary. In her spare time, she participates in her favorite pastime — singing. For the past five years she has been a part of a three hundred member women's choir as well as a smaller group called SPIRIT. They sing gospel music in churches, at weddings, in hospitals, and in nursing homes.

ANITA PEDVIS-LEFTICK, M.D.

Dr. Pedvis-Leftick graduated from McGill Medical School in Montreal, Canada. She completed a year of pediatrics at the Montreal Children's Hospital, followed by a year in internal medicine at the Jewish General Hospital. After that, she completed a three year residency in dermatology at the University of Illinois Medical Center in Chicago, Illinois. Dr. Pedvis-Leftick is Board Certified in dermatology in both the United States and Canada. Before coming to the U.S., she was in private practice in dermatology in Ottawa, Canada. She also was on staff at the Children's Hospital of Eastern Ontario as a consultant in dermatology. She has a particular interest in the treatment of patients with psoriasis, and was the Chairman of the Medical Advisory Board of the Canadian Psoriasis Foundation. Her husband, Dr. Marvin Leftick, is a rheumatologist. They have three children. She is in private practice at the Samaritan Health Partners in Danville, Illinois.