PANAMERICAN SOCIETY for PIGMENT CELL RESEARCH

PASPCR Newsletter

Volume 6 Number 4 **December,1998**

Introduction . . .

The **PASPCR** ***Newsletter*** is published quarterly and is intended to serve as a means of communication for the members of our Society. As such, we invite our membership to actively contribute to it; if you attend a scientific meeting at which you heard work which you think will be of interest to the membership of the **PASPCR**, please write a few paragraphs summarizing what was presented and share it with us. If you should have a change of affiliation or address, we'd like to know that, too. This is **your *Newsletter***, and we depend upon you to help us make sure it best serves the Society's needs. Contributions and comments can be sent to Vince Hearing, preferably by Email to **hearingv@nih.gov**.

The **PASPCR** ***Web*** page is the major, up-to-date source of current information for the **PASPCR** membership. The home page page has a new URL address which will result in faster transfer of information to your computer than before. The new address is http://www.cbc.umn.edu/paspcr. Please update your existing **PASPCR** link to this new address (the old one will disappear in a few months). We have now included a page that has positions available and positions wanted. Postings for Positions Available will be open to all individuals so long as the position is related to pigment cell research. Postings for Positions Wanted will be open only to members of the **PanAmerican Society for Pigment Cell Research** or its sister societies (**JSPCR** and **ESPCR**). Send postings to Bill Oetting at **bill@lenti.med.umn.edu**. Please provide an expiration data for any submitted postings. The **PASPCR Web** page also contains information on the goals, ByLaws and Rules of the Society, future meetings, past issues of the **PASPCR** Newsletter as well as links to other related sites including the InterPig DataBase, the International Federation of Pigment Cell Societies (**IFPCS**) and the regional Pigment Cell Societies from Europe and Japan. In addition, the **PASPCR** membership directory is available on the **PASPCR Web** page; please notify us if you wish any or all of your information to be deleted or modified on that site. If there is additional information that you wish to have added to this web page, please let us know. Send any comments and/or suggestions to the **PASPCR** WebMaster, Bill Oetting at **bill@lenti.med.umn.edu** or to Vince Hearing at

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PanAmerican Society for Pigment Cell Research

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Calendar of Events :

Dec 5 - 6, 1998 13th JSPCR Annual Meeting, to be held in Kobe, Japan (contact: Dr. Masamitsu Ichihashi, Department of Dermatology, Kobe University School of Medicine, 5-1 Kusunoki-cho, 7-chome, Chuo-ku, Kobe 650 Japan; FAX: +81 78 382-2497)

Dec 12 - 16, 1998 American Society for Cell Biology, Annual Meeting to be held in San Francisco, CA (contact: http://www/faseb.org)

May 5 - 9, 1998 Society for Investigative Dermatology, Annual Meeting to be held in Chicago, IL (contact: http://www/sidnet.org)

Oct 30 - Nov 3, 1999 XVIIth International Pigment Cell Conference, to be held in Nagoya, Japan (contact: Dr. Shosuke Ito, Fujita Health University School of Health Sciences, Toyoake, Aichi 470-11, Japan; Phone: +81-562-93-2595; Fax: +81-562-93-4595; Email: sito@fujita-hu.ac.jp)

Jun 25 - 28, 2000 IXth Annual Meeting of the PanAmerican Society for Pigment Cell Research, to be held in College Station, TX (contact: Dr. Lynn Lamoreux, Department of Veterinary Pathobiology, The Texas Veterinary Medical Center, Texas A & M University, College Station, TX 77843-4467; Phone: (409) 845-6084; FAX: (409) 845-9972; Email: LLAMOREUX@VETMED.TAMU.EDU)

Welcome to New Members

by James J Nordlund / Raymond Boissy

We welcome the following new member to the **PASPCR** . . .

Shirley M Bartido

If anyone is interested in joining our Society or wishes to sponsor a member, application forms can be obtained from Dr. James J. Nordlund at the PASPCR Secretary/Treasurer's office.

Corporate Sponsors

by James J Nordlund / Raymond Boissy

The PASPCR would like to acknowledge and thank our Corporate Sponsors; the list below reflects contributions over the past 2 years. Financial gifts from these sponsors have allowed our Society to increase benefits to the membership far out of proportion to the actual dues collected from members. Monies contributed by these sponsors have been used over the years to support various PASPCR functions including our Young Investigator Award program, meeting travel stipends, annual meeting expenses and this Newsletter.

GOLD Corporate Patrons	*SILVER Corporate Patrons*	*Corporate Patrons*
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Letter from the President

by Sally Frost-Mason

Greetings colleagues:

This marks my last correspondence as President of the PASPCR. It has been an extremely eventful three years for me, both personally and professionally, and certainly the most significant events were my simultaneous ascendancy to the deanship of our College of Arts & Sciences here in Lawrence, Kansas, and to the presidency of the PASPCR.

I feel privileged to have served as President of this society, and, as I mentioned in my closing remarks at our annual meeting in Snow Mass this year, although I have little time for "bench science" in my current job, I still plan to be an active attendee at our meetings and to support the society in ways that I hope are meaningful. Perhaps the best contribution that I can make at this time is to reconstruct the 10+ year history of the PASPCR in writing and photographically. I have indeed begun this project and thank those of you who have sent me photographs from recent and past national and international events. I would urge those of you who have special memories to please share those with me, either in written or photographic form, and I will gratefully add such information to the archive that I am assembling.

As we approach a new millenium, one that by many is being hailed as the "century of biology," we have much to be thankful for and much to look forward to. The advances in the field of pigment cell biology over the past two decades have truly been astonishing, and there is no reason to believe that the pace of new discoveries will slow any time soon.

We also have much work to do, students to train, postdocs to mentor, and new faculty to hire. Those of you associated with institutions of higher learning are perhaps beginning to realize that the face of our academic departments is changing more rapidly now than it has since post-World War II. The cost of such change is enormous, but we owe it to future generations to ensure that the legacy we leave behind is a strong and lasting one, so I would argue that the cost is one that we simply must find a way to pay.

Dick King will be the next President of the PASPCR. He is an outstanding choice to lead our Society as we transition past the year 2000. Dick, Jim Nordlund, Vince Hearing, Ray Boissy and many others helped me tremendously during the past three years, for which I will be forever grateful. I wish Dick all the best as our next President and thank all of you for your patience and support during my tenure as your leader.

Sincerely, Sally Frost Mason

1998 PASPCR Elections

You should be receiving ballots for the 1998 **PASPCR Elections**; please remember to vote in time! This is an especially important election since we are not only electing 3 Council Members, but we are electing the President-Elect whose term begins in 2002 and follows that of Richard A King (who takes over this January)

Along with that ballot you should receive your **Dues Notice** for next year and the **Subscription Form** for reduced prices for ***Pigment Cell Research***. You should remit those forms as soon as possible so as not to miss any issues in 1999. All subscribers in 1999 will receive advance copies of the Program and Abstracts for the 17th International Pigment Cell Conference to be held in Nagoya next fall, along with any published Proceedings that emanate from that Conference, and of course all the regular issues of the journal.

Finally, you should also receive application forms for the **IFPCS Travel Stipends**. There are 3 such Stipends available to PASPCR members and any unused funds will be turned over on August 1, 1999 to Prof Ito to support travel to the IPCC in Japan. Don't waste this valuable opportunity.

In Memoriam - T. T. Tchen (1924 - 1998)

by John D Taylor

Tche Tsing (*aka* T. T.) passed away on August 26, 1998 at Saint Francis Memorial Hospital in San Francisco. A week earlier he was stricken while playing squash, lost consciousness, and never emerged from a coma. His squash opponent revealed that T. T. had just beaten him and was expressing a smug smile of victory at the time he was stricken.

T. T. was born in Beijing, China in 1924, and most of his early life was spent in Shanghai. He was educated in French schools; and it is for this reason that his last name is spelled Tchen rather than Chen. His father was a mathematics professor so T. T. was exposed to academic rigor early. He received a B.S. in chemistry from Auroa University in Shanghai in 1948. He matriculated to the biochemistry doctoral program at the University of Chicago and graduated in 1954.

In 1954, Konrad Block left the University of Chicago for an appointment as the Higgins Professor of Biochemistry in the Department of Chemistry at Harvard University. As a post-doc, T. T. accompanied Block to Harvard to work with him on the mechanism and regulation of the cholesterol and fatty acid metabolism for which Block and Feodor Lynen were awarded the Nobel Prize in Medicine or Physiology in 1964.

T. T. left Block's laboratory and arrived at Wayne State University in 1958 as an Associate Professor. His early years to the early '60s were spent with research dealing with various aspects of cholesterol biosynthesis. He next ventured into prokaryotic systems up to the early '70s, in which he studied developmental cellular biological principles that would remain with him during the rest of his research career. Seeking a eukaryotic model, he found one with Walter Chavin's ACTH-induced melanogenesis in the goldfish. Walter, at the time, was a professor of biology, and some of T. T.'s early pigment cell work was conducted in collaboration with him. Later, some significant findings dealing with goldfish melanophore emerged in collaboration with Funan Hu, who at the time was with the Michigan Cancer Foundation. The most prominent being that the hormone-induced melanogenesis resulted in an obligatory mitosis of the melanoblast yielding two daughter cells -- another stem cell and a differentiating melanocyte (*Ann N.Y. Acad. Sci*., 100:708, 1963).

It was also during the early '70s that T. T. discovered the electron microscope. Suddenly, a biochemist was given the gift of sight! With his new gift, he spent thousands of hours looking at specimens on our scopes. He knew enough about the operation of the scope in order to examine specimens, and then he would tell the student to take pictures of this or that. He took great delight in telling his chemistry colleagues about the wonders of ultrastructure -- many seemed impressed.

In my view, it was the electron microscope and the pluripotency of the chromatoblast that shaped T. T.'s research interest for the next decade. It all started with indications that pterinosomes from goldfish xanthophores were tyrosinase positive. This was followed by ultrastructural studies of chromatophores from some amphibians and reptiles, which revealed pigmentary organelles common to more than one chromatophore. At the time, Joseph T. Bagnara (University of Arizona) took the lead with the pluripotency story which later climaxed with a paper appearing in *Science* (**203**:410, 1979). T. T. was one of several co-authors as he had made major contributions to the story. The discovery of mosaic chromatophores was focal to the pluripotency concept, but the role of the multivesicular body in goldfish melanosome formation as discovered by one of my doctoral students, William A. Turner Jr. (deceased), set the stage for the concept of a common precursor organelle. T. T. made major contributions to our understanding as to how tyrosinase, found in Golgi-derived vesicles, could insert and invert themselves into larger endoplasmic reticulum-derived vesicles, and then finally engage in melanin synthesis (*J. Ultrastruct. Res*., **51**:16, 1975). Hours spent on the electron microscope were beginning to pay off.

T. T. and I were fortunate that first Masataka (*aka* Matt) Obika and then Jiro Matsumoto, both from Keio University in Yokohama, decided to spend their sabbaticals with us. Matt brought us up-to-speed with the latest developments in pigmentary organelle translocations research; so as a result, we followed Matt's lead. Several important papers (*Cell Tiss. Res.*, **105**:417 & *J. Exp. Zool.*, **205**:95) represented the culmination of this important work.

Several interesting papers involving melanosome translocations came out of that collaboration; but it was the translocations of the carotenoid droplets found in xanthophores that would focus our attention in years to come. One of my doctoral students, John Lo (National Yang-Ming University, Taipei) started his studies by purifying goldfish xanthophores. Purified xanthophores were cultured, hormone-induced, and dissected ultrastructurally and biochemically by John and then later by a number of students who followed. Toward the end of these studies, Tom J. Lynch and Robert J. Palazzo (University of Kansas) had focused our interests on the pathways affecting intracellular signaling responsible for carotenoid droplet translocations (*J. Biol. Chem*., **261**:4204,1986 & **261**:4212, 1986; *Cell Motil. Cytoskel*., **13**:9, 1989 & **13**:21, 1989). The goldfish xanthophore research ended with Victoria A. Kimler (University of Detroit Mercy). She, using our newly designed whole mount transmission electron microscope technique, demonstrated that carotenoid droplets were not isolated; but instead, were protrusions that were continuous with the smooth endoplasmic reticulum -- overall appearance similar to a cluster of grapes. Also of interest was that the membrane limiting the carotenoid was a lipid monolayer rather than a lipid bilayer. Tracing the continuum of the lipid monolayer back to the SER, it became a lipid bilayer at the carotenoid droplet-SER junction (*J. Exp. Zool.*, **267**:510, 1993.

Jiro Matsumoto's sabbatical focused us on a number of interesting cell lines that he brought with him from Keio University. With Jiro's guidance, we explored the goldfish erythrophromoma cell line in terms of cellular differentiation against their normal counterparts. A *Science* paper (**217**:1149, 1982) represented the culmination of several important papers that resulted from this research

T. T. was generous with his time. He particularly enjoyed spending time with students. He was always challenging their thinking processes with a goal to make them creative thinkers. He graduated 15 masters students and 30 doctoral students. He received the Distinguished Graduate Faculty Award in 1990.

T. T. retired in 1993 and moved to a home in Oakland, California overlooking San Francisco and its bay. What surprised me was that he gave up science completely -- stopped reading journals. Gave up the pipe and reduced coffee intake drastically. He focused his attention on gardening, Chinese cooking and squash. He felt that his knees would not allow him to be competitive in tennis and he would rather not play than not be competitive. He would return to Detroit at least once a year to visit one of his sons. Ken and I would get caught up on his activities over a dinner at one of T. T.'s favorite restaurants. T. T. and his wife, Ina, were well-known gourmet cooks and were close friends with the top chefs in the Metro-Detroit area.

T. T. is survived by his wife, Ina, and his two sons, Terence and Vincent. T. T Tchen, 1924 to 1998. Scientist, educator, tennis and squash player, gourmet cook and friend. We are diminished.

In Memoriam - Bengt Larsson (1942 - 1998)

by Patrick A Riley

It is with deep regret that we report the death of Bengt Larsson. He died suddenly at home in Uppsala on 8th October 1998.

Bengt Larsson was born in Umea in 1942. He was proud of his Northern roots but had settled in Uppsala where he was Professor of Toxicology in the Biomedical Centre of Uppsala University. He entered the University of Uppsala in 1965 to read philosophy, literature and the humanities and went on to study mathematics, chemistry and geology. He had a deep interest in nature, especially in birds, and was also a gifted musician.

His career began when he joined the Department of Toxicology in 1973 to work with Nils Gunnar Lindquist and Sven Ullberg at which time he switched his attention to biology and medicine and was awarded his PhD in 1979. His knowledge of chemistry led him to pioneer the development of X-ray film that could be used for tritium autoradiography (now sold widely for this purpose as Tritiumfilm, Ultrofilm ^{3}H and Hyperfilm ^{3}H).

Autoradiographic techniques were then being introduced for the detection of the biodistribution of materials and Bengt applied this to a wide variety of systems. His main research work work was related to the interaction between chemicals and melanin. He demonstrated the selective accumulation of drugs in melanogenic tissue and became a world authority in this field. He published many original papers pertaining to this topic and was frequently asked to review progress in this area, particularly in respect of the possible diagnostic or therapeutic potential in melanoma of agents selective for melanogenically active cells. His pre-eminence in his field also led to his involvement in many international research ventures and he was widely respected and admired.

Not only did Bengt Larsson's studies demonstrate melanin binding by a wide spectrum of compounds but the reasons for the affinity were explained in detail. His work emphasized the relative importance of electrostatic interactions and the formation of charge-transfer complexes in the binding of chemicals to melanin. He also showed the contribution of hydrophobic interactions to the melanin-affinity of compounds such as polycyclic hydrocarbons and aflatoxin B_1. The important cytotoxic consequences of melanin affinity to the ear and the extrapyramidal system (as in MPTP-induced Parkinsonism) was investigated with Lindquist and Annika Lyden-Sokolowski.

Bengt Larsson, together with Lennart Dencker, demonstrated the covalent uptake of thiols by melanogenic tissues and, in studies with Ulrik Ringborg, showed that radioiodine-labelled thiouracil has clinical potential as a diagnostic aid in melanoma. He was also involved in the possibility of using this vehicle for boron neutron capture therapy (BNCT) and, in collaboration with Amilcar Roberto and Ulla Mars, had developed a radiographic technique based on boron-thioureylenes. He was actively pursuing this area of radiopharmacology at the time of his death.

Bengt Larsson organised a most successful ESPCR Scientific Meeting in Uppsala in 1989. He was very proud of the important biological tradition centred on Uppsala, the home of Linnaeus, and enjoyed showing visitors round the museum at Hamarby. The Conference Reception was held on a warm summer's evening in the Botanical Gardens founded by Linnaeus. In 1991 he was elected to the Secretaryship of the ESPCR. At that time the Secretary of the Society was also the Treasurer and Bengt Larsson was very successful in building up the finances and was the first to obtain Industrial sponsorhip for the Society.

Bengt Larsson was elected President of the ESPCR in 1994 and carried out his official duties with distinction. He was unfailing in his support for the membership and his able and benign Chairmanship was greatly appreciated by the Council. He served on the Council of the IFPCS and was instrumental, as a member of the Publications Committee, in guiding the Federation through several difficult times. He was, at the time of his death, Treasurer of the IFPCS. His patient and undemonstrative style was widely admired and he was painstaking and diligent in discharging his responsibilities.

Bengt was a deeply reflective man who felt most comfortable in the solitary grandeur of the natural world. He grew up in a liberal household and as a boy overheard many political conversations between his parents and visiting Party leaders and members of the parliament (Riksdag) which may have influenced his broadminded view of life. His childhood summers were spent on the small island of Holmon at peace in the contemplation of nature, and he returned there regularly with his family in later years. His love for the woods and the silent waters of his homeland seemed to be reflected in his quiet and generous nature. He was, in every sense, a gentleman. We have lost a fine scientist, a loyal servant of the ESPCR, and, most of all, a true and beloved friend.

He is survived by his wife, Pia, and daughter, Liselott, to whom we offer our deepest condolences.

Invitation to the XVIIth IPCC (International Pigment Cell Conference) by Shosuke Ito

Invitation to the XVIIth International Pigment Cell Conference Nagoya Congress Center
Nagoya, Japan October 30 - November 3, 1999

Dear Colleague:

After the inauguration of the International Federation of Pigment Cell Societies (IFPCS) in Kobe in 1990, the International Pigment Cell Conferences (IPCC) rotate among the European, American, and Asian continents, hosted by one of the three regional societies: the ESPCR, the JSPCR, and the PASPCR. The 15th IPCC was thus held in London in 1993, chaired by Professor Patrick A. Riley, and the 16th IPCC was recently held in Anaheim, California, chaired by Professor Frank L. Meyskens, Jr.

It is our great honor and real pleasure to inform you that the next 17th IPCC will be held in Nagoya, Japan in 1999, co-organized by the IFPCS and the JSPCR. We heartily hope that pigment cell biologists and clinicians will join together in Nagoya in October 1999 to present their latest achievements in the exciting world of pigment cell research. Your participation will be most important for the scientific success of this meeting.

The city of Nagoya, the 4th largest in Japan, enjoys a rich history of traditional culture and a reputation for world-renowned high-tech industries. Nagoya is located at the center of Japan and is easy to access: the Nagoya International Airport is directly connected with 30 cities around the world. The conference site, the Nagoya Congress Center, is newly built and has ample spaces for the participants to discuss and exchange ideas, which we believe will certainly bring about fruitful collaborations.

We will follow the good tradition of the IFPCS leadership in directing scientific programs to unify the three regional societies. Within such a framework, we wish to place special emphasis on poster presentations. We hope to provide a certain number of travel grants for young investigators to attend this meeting. In order to be eligible for such a grant, an applicant has to be a member of one of the three regional societies for at least one year prior to the meeting. We are also planning banquet and social activities in such a way to make your visit to Nagoya most enjoyable and memorable. It will be our great privilege to welcome you and your colleagues to Nagoya in 1999.

Shosuke Ito, Ph.D. — *Chair,* IPCC Nogoya

Kazumasa Wakamatsu, Ph.D. — *Secretary-General,* IPCC Nagoya

For further information please contact us at: Fujita Health University School of Health Sciences, Toyoake, Aichi 470-11, Japan; *Phone*: +81-562-93-2595; *Fax:* +81-562-93-4595; *Email*: sito@fujita-hu.ac.jp

Positions - Wanted and Available :

Postdoctoral Positions. in the Department of Cell Biology at the NYU School of Medicine are available to study the biogenesis of melanosomes using a combined cellular, molecular and genetic approach. Prior experience in molecular or cell biology required. Applications from those with prior experience with yeast, Drosophila etc. interested in applying their skills to a mammalian system with strong genetics are especially welcome. A track record of productivity is essential. Send CV, brief description of experience and names of 3 references to: Seth J. Orlow, MD, PhD, NYU Medical Center, 560 First Avenue Room H-100, New York, NY 10016. Fax 212-263-5819, email: orlows01@mcrcr.med.nyu.edu

Postdoctoral Research Associate - Position available to study the biology of human inherited disorders of pigmentation using mouse knockout technology. The successful applicant will have a Ph.D. and/or M.D. with experience in cell biology and molecular biology. Experience with production of knockout mice using ES cell technology preferred. Please send curriculum vitae along with the names of three references to Dr. Richard King, Division of Genetics, Department of Medicine, Box 485 Mayo, 420 Delaware St. S.E., University of Minnesota, Minneapolis, MN 55455. Equal Opportunity Employer.

Postdoctoral Position - Ph.D. in molecular biology, biophysics, genetics or biochemistry. Position available to conduct research on molecular mechanisms of cellular response to oxidative stress in human melanocytes and melanoma cells and its regulation for preventive and therapeutic indications. Contact Dr. Frank L. Meyskens Jr., Director, University of California-Irvine, Chao Family Clinical Cancer Research Center, 101 The City Drive, Orange, CA 92668, USA. Fax (714) 456-5039 Email flmeyske@uci.edu

Meeting Report - by Vincent Hearing, Alan Moshell, Nobuhiko Kobayashi, and David Sliney

NIH Research Workshop on Risks and Benefits of Exposure to Ultraviolet Radiation and Tanning

September 16-18, 1998 Bethesda, Maryland

David Sliney chaired **Session A on "Ultraviolet Radiation: Sources and Measurement"**. He gave a brief overview of optical radiation measurement in the UV spectral region. He emphasized that any measurement in photobiology was related to action spectra. So he quickly defined action spectrum and explained the effects upon an action spectrum by pre-filtering of incident radiation. He spoke of radiometric quantities, the Bunsen-Roscoe Law of Photochemistry, the limits to the inverse-square law and related basics. He also emphasized that because of the nature of a photochemical reaction requiring a minimal photon energy, it was typical for action spectra to have a sharply ending efficacy at longer wavelengths, with the result that resolution of that rapidly changing function with wavelength was difficult to achieve without a very narrow spectral bandwidth probe source such as a laser. He illustrated this by showing the same action spectrum resolved with 1, 2 and 5-nm full-width-half-maximum (FWHM) monochromators and how the slope changed significantly. He showed an example of the influence of the

slit-width and stray light (out-of-band radiation) upon the action spectrum or spectroradiometric measurement. He also explained the difference of radiant exposure (surface exposure dose for a cosine-response, from one direction) from fluence (radiation arriving from all directions including backscatter--with no cosine factor), which both had the units of J/cm^2 or J/m^2.

Sliney then spoke on the measurement of UVA and UVB. He pointed out that the CIE Report on the Division of UVA and UVB (which recommended maintaining the definitive break at 315 nm) noted that these terms were merely for shorthand notation and should not be used in place of action spectra for describing the effects at a given wavelength or for excluding the possible effects at a given effect. Merely because one effect is dominant at one wavelength does not mean that another effect does not exist. He then spoke of broad-band meters and the importance of looking at spectral response errors and how those errors had a different effect depending upon source spectrum. One had to look at spectral response and emissions over orders of magnitude, and semi-log plots of emission spectra, spectroradiometer slit functions and action spectra over several orders of magnitude was of great importance. He described the importance of matching field-of-view with a source and the value of a cosine-response detector. He then mentioned other measurement factors such as alignment, etc.

Edward DeFabo spoke on different lamp sources commonly used in photodermatological research. He described the spectral power distributions (SPDs) of Philips F40 and Westinghouse FS Sunlamps which have similar emission spectra which appear on a linear plot to be very similar and emitting only in the UVB. However, on semilog plots, he showed significant UVA radiation. Again, the PUVA lamps also showed significant radiation out of the UVA band for which they were designed to emit. He also showed the SPD of a Philips TL01 lamp with a strong emission at 300 nm, with longer emissions in the UVA and visible region. Another lamp, the Philips TL10R R-UVA Lamp had virtually no UVB radiation, but at wavelengths in the visible there was still emission. He then showed the SPD of a Sylvania F40/CW Cool White Lamp used in an animal house emitted UVR that could "contaminate" an experiment. He showed that the GE F40GO Gold Lamp was superb as a light source not emitting UVR of any significance. He showed the spectral irradiance of a 2500-W xenon lamp used in a solar simulator. He showed how xenon-arc/filter combinations could be used in experiments if the filters were properly chosen. One could also use narrow-band spectral band-pass filters with a xenon-arc to produce combinations of UVB and UVA emissions. Using these approaches, DeFabo and Frances Noonan were able to produce action spectra of contact hypersensitivity in the mouse.

Robert Sayre spoke on UV sources used for artificial tanning of the skin. He noted that most lamps varied in output characteristics, and his remarks would be for example only. He explained that he and other physicists made measurements of the emission spectra of sunlamps to determine safety, establish timer maximum and the initial exposure. He showed the nearly similar erythemal and melanogenesis action spectra in the UVB and UVA. He explained that he employed spectroradiometry with 1 nm bandwidths and 1 nm increments to obtain the SPD. He also noted that UVC, UVB and UVC were employed to determine the erythemal and melanogenesis exposure times Te and Tm. He showed a representative label for a sunlamp based upon the FDA standard. He then gave a typical solar noon spectrum stating that the Te would be about 29 minutes and Tm would be about 85 minutes. He showed a photograph of the SPERTI sunlamp used since the 1930s that would not meet the FDA standard. More recently, fluorescent sunlamps were developed and used in clam-shell-array sunbeds which had Te and Tm of about 10 and 30 minutes. Stand-up units and clamshell (bed) units used arrays with different lamps, such as PUVA lamps. Another, more recent unit used high pressure lamp arrays with UV irradiances of 725 W/m^2 and shorter values for Te and Tm. The power of fluorescent units has increased and not standard unified bulbs, units, user directions and labeling. He argued that the issues to be addressed should describe measurement procedures and instrumentation, that simplified labeling including a universal exposure schedule and develop a better defined concept of bulb compatibility.

C. Eugene Moss spoke on sources of inadvertent skin exposure to UVR in the occupational environment. He explained that NIOSH was interested in future research on occupational hazards from UVR and had a program with a goal to reduce occupational exposure to solar UVR as well. He estimated that 120 million workers were exposed to optical radiation, and many were exposed to solar radiation in their work outdoors. He listed a range of artificial sources. He showed a photograph of a welder and the reflections encountered in a close workspace, and he emphasized that the welder was well protected by industrial clothing, an apron and welding helmet. He stated that some welders even sustained erythema through clothing. He showed representative arc spectra, such as the strong UVC emission from aluminum gas tungsten arc welding (GTAW). He showed examples of different types of transparent welding curtains and how their spectral transmittance varied. He described some geometrical factors, such as the increased irradiance measured in the position of an observer standing in the direction of the movement of the welding arc. He thought that with the advent of robotics and automated welding, the exposure to UVR could be better controlled and reduced. He stated that there were about 500,000 welders in the US. He also showed examples of exposure to UVR from other industrial sources such as metal furnaces, glass furnaces, thermal-arc spraying, plasma-arcs, solar simulators, xenon lamps, photocuring units, non-destructive-testing lamps and germicidal lamps. He stated that accidents had occurred when maintenance personnel were changing germicidal lamps. He cited the AWS Book on the UVR reflectance of paints and other materials. He explained that UVC also produced ozone--another occupational hazard. He described the problem of performing

measurements in real work conditions and the variation in output. Viewing ports were sometimes found that were not safe in a research facility. He concluded that adequate eye and skin protection were worn in industry both to prevent acute effects and because of OSHA compliance work, that infrared could also be a hazard, and finally, that the presence of photosensitizers in the workplace had not been adequately addressed.

Panel Discussion - The speakers and four additional experts were then called to a panel to discuss the topic of the session and to answer questions from the audience. Donald Forbes was asked by Sliney to present 3 slides which compared the CIE TC 6-32 Action Spectrum for Photocarcinogenesis with the CIE erythemal action spectrum. There were wide-ranging discussions relating to UV lamps, skin cancer and the relative role of UVA and UVB.

On Thursday morning, Irene Kochevar opened **Session B on "Ultraviolet Interactions With and Effect on the Skin"**, and she briefly described the molecular basis of photocarcinogenesis. She briefly described the effects of UV photons upon DNA. She distinguished between direct DNA lesions which dominates from UVB exposure and oxidative stress produced by UVA exposure.

Frank DeGruijl spoke on nucleotide excision repair by either transcription-coupled repair (TS), which was a problem for people who sunburn easily, and global genome repair (NTS), which was deficient where cancer was involved. He showed the strong correlation of the p53 gene and carcinomas. He described several possible pathways, but noted that UVA1 did not generate p53 gene mutations but did produce cancer (papillomas). He also described skin tumors in repair deficient XPA mice.

Vincent A DeLeo spoke on the multistage process of UV carcinogenesis. He stated that the UV mechanism of photocarcinogenesis had analogies with the mechanism of phorbol esters promoting carcinogenesis. He described the cascade of events in signal transduction which led to gene expression. He stated that UVC was clinically irrelevant as a carcinogen in human, but some of the basic in-vitro studies of gene expression. He reviewed the reports related to UVA induced epidermal growth factor (EGF) in a number of studies, but this was not a DNA damage event. He went on to describe a host of studies of the effects of UVA, B and C in producing various cellular responses, but many not related to carcinogenesis. Although the data suggest that non DNA events by UV play an important role in the response of cells to sunlight, these for the most part are not playing a direct role in photocarcinogenesis, but may effect the cell's ability to deal with the DNA damage.

Richard P Gallagher spoke on epidemiological studies of childhood exposure to sunlight and different skin cancers. He mentioned the Australian studies of skin cancer incidence differences between those who were born in Australia vs. those arriving after childhood who came from countries of low UV exposure. The increased risk from nine studies of large childhood sunlight exposure for melanoma was 1.95. He also mentioned high odds ratios shown by the Westerdahl data for sunbed exposure at a young age (less than 30) and melanoma. Basal cell carcinoma (BCC) was shown to be related to increased childhood studies; however this did not show up for studies of squamous cell carcinomas (SCC) except a single study suggesting a possible correlation with severe sunburn, but even that conclusion was questionable. Certainly five out of six studies showed an increase of nevus density with childhood sunlight exposure.

Margaret Tucker reviewed the epidemiological studies of the risk related to adult exposure. She admitted that it was very difficult to find individuals who had predominant UV exposure in adulthood, inasmuch as most who experience heavy exposure in adulthood also had heavy exposure during childhood. She described an NCI study of melanoma-prone families, where they examined the skin of children at ages 10 and periodically thereafter. They found that sunlight exposure was an independent factor which increased the incidence of nevi development and cutaneous malignant melanomas (CMM). She gave an example of melanomas induced by one of the susceptible individuals disobeying clinical guidance to minimize sunlight exposure and actually began using a sunbed. She stated that there was no real way to distinguish between UVA and UVB exposure or sunlight vs. artificial tanning sources. There was difficulties in quantifying actinic damage. Nevertheless, the number of epidemiologic studies consistently showed increased risk from CMM and probably BCC, for intense periods of leisure time sun exposure. She described a recent case-control study of CMM which had over 1000 controls for 716 cases of CMM. This showed a relative risk of 5-7 for excessive sun exposure. They did not see an increased risk for sunburns sustained prior to age 10, but then the risk was 1.3 for teenage exposure. She noted that those subjects who recalled sunburns, generally showed that the number of sunburns in childhood were the same or more than in adulthood. The data were quite complex, but she concluded that the data showed that cumulative childhood and adult exposure increased the risk, showing a cumulative effect. She showed data suggesting that more than 300 minutes of sunbed exposure led to an increased risk of CMM of about 2. She described efforts to estimate the average annual UVB exposure based upon location using latitude altitude and cloud cover. She recognized the many problems requiring further research to improve exposure estimates for individuals.

Paul Bergstresser spoke on immunological effects. He rapidly described the immune response in the skin and the fact that the impact of sunlight exposure upon immune response was "invisible." He described studies in hamsters by employing DNFB to challenge skin immune response following UV exposure. The down response was maintained by T cells. A variety of cells were responsive to the effect. He differentiated between local and systemic immune suppression, but both lead to systemic suppression. Systemic suppression suggested IL-10, TNF-α and cis-UCA; whereas local immunosuppression might be irradiated APC or some other local factor. He cited the strong evidence showing that three possible photoreceptors: DNA, urocanic acid and cell membranes, were

involved. To better isolate the different roles, action spectra, such as those of DeFabo and Noonan, could be used. He cited the study of Yoshikawa et al., (J. Invest. Derm., 95:531, 1990) to show in humans that individuals with skin cancer did have a susceptibility to immune suppression as shown in testing. He cited the Kripke studies to show that DNA was a receptor as well. He also noted the study of Roberts and Beasley relating good sunscreen application to protection. He cited the recent study in J Immunol, 160:4263, 1998 from a group in Muenster, Germany. He then cited a number of studies to show how very complicated the picture of immunosuppression really was, but that despite the several photoreceptors, the effect was always to suppress.

Gary J Fisher spoke on the molecular basis for photoaging in humans. He showed the familiar clinical picture of accelerated aging by contrasting unexposed abdominal skin with that of the forearm. He explained that 90 percent of dry weight of skin was collagen, and with increased aging and sunlight exposure the concentration of collagen decreased. He showed a complex signal cascade which related to collagen synthesis and collagen destruction to lead to the collagen deficiency which led to imperfect repair ("solar scar") and the appearance of photoaging. Using FS40 lamps filtered by Kodacel to eliminate UVC, they experimented in human subjects by histological studies with fluorescent markers and procollagen I gene expression. He showed evidence of collagen synthesis stimulated by levels of only 0.01 to 0.02 MED and how repeated sunlight exposure decreased the production of procollagen I. He showed that the greatest effects occurred with UV B and UVA spectra.

Panel Discussion - In the panel discussion, Joseph Stanfield was delighted that studies had now shown that sunscreens were effective if matched to the source, and that early studies showed ineffectiveness only when the UVC was included. Ken Kraemer spoke briefly on xeroderma pigmentosa and the age of onset of cutaneous symptoms in infancy and onset of the first cutaneous cancers (median age of 8 years) because of defective repair in XP. He emphasized that all exposed tissues were effected, including the cornea (but not the retina because UV "did not reach the retina." Normally functioning DNA repair mechanisms provide a 1,000-fold level of protection. He concluded that sunlight exposure is responsible for the induction of melanoma as well as non-melanoma skin cancer, although the mechanism of induction of non-melanoma skin cancers was different between XP and normal patients. Noonan took the opportunity to show some recent data from her laboratory in the laboratory and compared this to the data from Kevin Cooper showing the same dose threshold of about 220 J/m^2. Janusz Beer remarked that the public's perception of UVR has changed in time. One hundred years ago it was bad, then 50 years ago it was good as it prevented rickets and provided a "beautiful" tan, then UVB was good in the 1970s, bad in the 1980s, but UVA was good, but now both UVA and UVB are considered bad. He explained that the Framingham Heart study cost $40 million over 50 years, thus why not propose a Framingham UV study? He asked whether solar tanning carry less or more risk of cancer from artificial lamps. Gallagher showed Canadian epidemiological showed decreasing age-adjusted skin cancer incidence in the past decade and this might be due to more effective sunscreens. Martin Weinstock took issue with an earlier statement about "compensation" of increased sun exposure time with increased sunscreen SPF. Sullivan argued that UVA and UVB were really only shorthand notations and that the oxidative damage could occur in the UVB and in the visible and direct damage is not limited to the UVB. There was discussion as to whether oxidative damage was really important, and if so, then should not sunscreens also block short-wavelength light. When Sayre asked the Panel whether the current FDA tests for photosensitization were adequate, the Panel agreed that they were adequate. With regard to the epidemiological evidence linking sunlight exposure with CMM, Gallagher thought that the evidence was really quite good and just as robust as that for SCC and BCC. There was a spirited discussion which was quite technical with regard to whether special patient susceptibility to skin cancers was being correctly interpreted or a red herring. Schweiger noted that in 40 years of treating vitiligo patients, he never saw a single case of skin cancer in a vitiliginous area, and yet these patients quite readily sunburn in those areas; DeLeo thought this an interesting observation and other dermatologists agreed and CHS was not the same in that area, although one suggested that these patients avoided sun exposure to those areas. There was a question relating to the role of melanin vis-a-vis immunosuppression, and the Panel agreed that there weight of evidence showed no effect of the presence of melanin (as from tanning) in reducing the immune suppression. Another dermatologist from Germany asked about the role of photoimmunology from the perspective of evolution. DeFabo suggested that it served a positive role to protect the skin from an autoimmune attack, but it served a negative role only at very high doses. Tucker explained that about half of one's solar UV exposure occurred in childhood, hence the epidemiological data relating to childhood exposure cannot be used to promote a theory of an initiation stage in childhood and a promotion stage in adulthood, but a cumulative exposure risk model was more acceptable in her mind.

Jan van der Leun opened **Session C on Beneficial Effects of UV Exposure**. He noted that the century opened with the concentration on beneficial effects led by the Nobel Laureate, Finsen, of Denmark. Today, the focus has evolved to studies of harmful effects, perhaps because they are easier to study.

Martin A Weinstock spoke on an epidemiologic approach to melanoma and tanning. He opened his talk by noting the a priori rationale for effect modification, that frequent sun exposure protects against subsequent sunburn. He noted that Dubin et al some years ago cited effect modification was present in several studies, but their study was biased selection of the study population and biased data collection from the study population. He also cited the "synergy" claimed by Holman. He reviewed his study of nurses (Weinstock et al., Am J Epidemiol, 134:462-470, 1991), where they hypothesized that individual susceptibility played a role in risk. They developed a sun

susceptibility index based upon skin type and sensitivity to burn, fair hair, etc. Looking at the risk of CMM skin cancer, the sun sensitive women had increasing risk with increasing number of exposures and had a risk of 3.5 if out suntanning more than 31 times per year; whereas the sun resistant women had a decreasing risk for more exposures per year, and dropped to 0.3 for greater than 31 per year. He stated that the results were repeated in other subsequent studies, but not in all studies.

Michael Hollick spoke on the Vitamin D. He explained that 750,000 iguanas had been imported into the US since the success of the film, "Jurassic Park," and thousands were dying by being kept indoors away from sunlight. He showed an advertisement for Repta-Sun full spectrum lamps with Vitamin D for Iguana cages. He emphasized that vitamin D was essential for utilizing dietary calcium. Up to 21 percent of "Vitamin-D" skim milk had no detectable Vitamin D when tested in his laboratory and by the FDA. Significant D deficiency (Lancet,351, 1995) was found in large fractions of the elderly population. Their studies showed that only 6% of the body surface needed sunlight exposure and one MED over the full body surface was needed to achieve 10,000 IUs of Vitamin D. Since Vitamin D synthesis required UVB exposure, he suggested that sunscreens reduced this production and labeling of sunscreens should warn the user of that.

George Studzinski stated that UV produced benefits as a protection against cancer as well as causing skin cancer. He stated that solar UV produced vitamin D levels depending upon the amount of melanin and black women had less serum vitamin D presumably because of UV attenuation by melanin. He showed the results of some *in vitro* and biochemical studies which he stated supported the effect that vitamin D improved immunological defenses.

Cedric Garland showed cancer mortality data for the more than 3,000 counties of the USA for different cancers. While some cancers were distributed quite randomly, but colon cancer did not show any red "hot" zones south of 37 degrees North. Rectal cancer also showed this distribution. He showed a rather strong correlation with sunlight. The acidity level in lakes showed the same trend as did acid rain and the acid haze filtered vitamin D. He showed that the risk of colon cancer was strongly depending strongly with the absence of serum vitamin D. Above 30 ng/ml there were very little risk of colon cancer. They also showed the same correlation for breast cancer. He also showed the greater survivability with greater serum vitamin D as in Hawaii vs. Connecticut.

Norman Rosenthal spoke on Seasonal Associated Disorder (SAD) which correlated very well with reduced sunlight. He described the well known symptoms of SAD which were very evident in the winter. He showed the data for phototherapy of this winter depression. Current phototherapy is not as effective as summer sunlight. Marked mood improvement was also shown for patients visiting sunbed salons several times, and vitamin D was also shown to reduce SAD symptoms in some studies.

Panel Discussion - In the panel session which took place after lunch, W Howard presented some prepared remarks by a CDRH *ad hoc* Committee on Sunlamps which had been evaluating UV emitting sunlamps. He explained that in 1994 FDA received a request from the medical community to ban sunlamps because of the melanoma risk, In addition, they received a citizens' petition in 1997 to ban tanning accelerators, set maximal annual doses, demand melanoma warning statements go after false claims, etc. In 1994 CDRH felt that the epidemiological evidence was suggestive but not convincing that sunbed exposure was a major causative factor in CMM. He explained that to respond to these concerns, the FDA recognized that there were many scientific questions which needed resolution in order to answer these inquires. Alan Fleisher noted that his group found that sunbeds were effective in treating the symptoms of psoriasis and he suspected that there were many patients self-treating their skin problems in community based tanning salons. Robin Hornung was interested in optimizing health promotion campaigns to minimize UV exposure; she argued for targeting different groups (e.g., children) with different messages. Kraemer showed how strong efforts to protect XP patients against sunlight exposure could lower the serum levels of vitamin D, but they found that they still were in the normal range, and maintaining this level was presumably due to diet. James Spenser noted that moderated fragmented UV exposure was less dangerous, but he concluded that tanning was worse than burning. Antony Young showed the results of his study which showed that tanning afforded very little protection against the production of erythema in both Type II and Type III skin types--with a maximal added protection factor of about 2, and yet there was little difference in this factor between Types II and Type III. van der Leun described various efforts to educate and warn the public of the dangers of excessive UV exposure, and cooperative campaigns were more successful than warning campaigns. In answer to a question about children engaged in tanning, Beth Whitmore commented that circulating T-suppressor cells actually increased after ten exposures in tanning salons. They measured many serum factors showing significant changes which could be labeled both as adverse and positive. Gallagher stated that in his studies, the protection factor afforded by tanning was less related to the tan than to the "ability to tan." Weinstock asked Hollick about how much solar exposure was really needed to assure adequate production of vitamin D. He stated that although elderly people had impaired ability to produce vitamin D, but it was still quite possible in tanning beds. The level required for production was sub-erythemal, and a black person (Type 6) requires about ten times the UVB dose of Type II skin and Hollick stated that from his experience most African-Americans had a vitamin D deficiency. Hollick felt that 1,000 to 1,500 IU of vitamin D would be necessary for dietary intake per day if sunlight exposure (e.g., among submariners), whereas the current rule is to limit dietary intake to 800 IU. Hollick stated that orally administered vitamin D was clearly sufficient to maintain bone calcium; however, it was not clear that this was equivalent for other roles of vitamin D, e.g., with regard to cell proliferation.

Barbara Gilchrest opened **Session D on Methods of Producing / Enhancing the Tanning Process**. She gave a very nice overview of melanogenesis and how it depended upon the number of melanocytes (which double after a tanning episode), the melanin synthesis rate, which is increased after UV exposure, and melanocyte dendricity and finally by melanin transport. She stated that melanins was the major recognized factor in cutaneous photoprotection. Keratinocytes released by UV exposure, e.g., BFGF, ET-1, α-MSH, and NGF, stimulated melanocytes to produce melanin. Fibroblasts also stimulated through NT3 the dendricity of melanocytes.

Vincent J. Hearing spoke on the molecular and enzymatic events of the tanning process. He explained that melanins were synthesized within melanosomes--which some termed fancy lysosomes. He described how melanocytes transferred their melanin granules to keratinocytes. However, UV stimulated both keratinocytes and melanocytes. UV worked indirectly on keratinocytes to produce ET1, ET1R and POMC, which in turn stimulate melanocytic activity. He showed a very complex diagram of the pathway for melanogenesis and the three main types of melanins DHICA-melanins, DHI-melanins and Pheo-melanins. He felt the weight of evidence showed that melanocytic activity was stimulated through MSH receptors. The pheomelanin rate of production was hardly affected, whereas the eumelanins were produced upon MSH stimulation. He then summarized the current knowledge of the absorption factors and cytotoxicity of melanins. The pheomelanins produced cytotoxicity when exposed to UVR, whereas the others provided protection, with DHICA being the best compromise. He also showed the supranuclear melanin cap produced in some cells. The picture of cellular regulation of melanin production was quite complex and there were many factors playing a role.

Rox Anderson argued that melanin did not originate in the evolutionary chain for solar protection, but for marking, as in lizards, zebras, and other primates. He explained that darker races had singly packed more uniformly distributed melanosomes in keratinocytes, whereas light skinned races have melanosomes with smaller particles. Using confocal microscopy, they were studying the dynamics of melanogenesis. He argued that there were data suggesting that melanin was photoprotective and some just the opposite (e.g., Hill et al study in guinea pigs). He then described Immediate Pigment Darkening (IPD) from UVA exposure at 365 nm in the first hours. True melanogenesis is seen after about 24 hours and UVB erythema is strongly evident; but, after ten days the UVA tan is stronger and different from the UVB tan. He indicated that IPD was an oxygen-dependent process and requires pre-formed melanin, and he argued that IPD was not photoprotective. He stated that UVB tans were photoprotective and UV tans were not. While the melanogenic action spectrum was very similar to the erythemal action spectrum, they were not the same in the UVA. Natural photoprotection in the UVC occurred from proteins and urocanic acid, whereas proteins and melanin were the primary absorbers in the UVB and only melanin played a big role in the UVA. The skin has evolved different photoprotective responses appropriate to the stimulus, since epidermal thickening worked well in the UVC, UVB provided both thickening and melanin, and only melanin was protective in the UVA (Beck-Thomsen, Photochem. Photobiol., 1996).

Jan van der Leun then spoke on UVA tanning. He showed the tanning action spectrum produced by Parrish et al., some years ago. He noted that even if a lamp source contained 99% UVA and 1% UVB, the dominant effect would be from UVB. Historically, he explained that the German National Committee to the IEC Committee dealing with sunlamp products argued that the UVA was ineffective as a carcinogenic agent and in 1986 proposed lamps that strongly emitted UVA, but their proposed curve for carcinogenesis was never accepted. Instead, the SCUP curve was accepted shortly thereafter as a realistic effort. He stated that UVC was the most effective in tanning with the least erythema and carcinogenic risk, but UVC is not used for tanning in practice, and the result is that UVA and UVB are used. However, today, he argued that there was not a strong argument for one band or another. UVB provided more tolerance to sunlight, increased vitamin D, but UVA produced less sunburn. However, it was not clear whether photoaging or melanoma risk was increased more by UVA or UVB. He felt that the original move of the 1980s to move to the UVA was a poor choice, and that considering current knowledge, he personally thought UVB was a better choice.

H. Gordon Ainsleigh presented his view of the scientific data supporting the benefits of UV tanning, but he was quite negative about UVA-only tan which he argued did not produce vitamin D and did not reduce the risk of non-dermal cancers. He argued that the increased incidence of basal cell and squamous cell skin cancers in users of sunscreens. He claimed that for every person who dies of skin cancer, there were 16 persons who died of internal cancers which he alleged were reduced in incidence from UVB exposure. He claimed that a tan reduced the initiation of melanomas and melanomas did not progress in tanned individuals, citing the epidemiological studies which all show reduced melanoma incidence in outdoor workers (who maintain a tan). He stated that the lowest melanoma incidence was in Hawaii and the District of Columbia, and he claimed that this was due to uniform UV exposure as a function of season. He argued the best preventive measures would be to shave the head and neck and to maintain a tan. He claimed that they could eliminate 58,000 cancer deaths a year by adding oral vitamin D to the diet and universal tanning.

Robert A Stern discussed tanning accelerators, such as psoralens. He considered tanning a response to injury, and the benefit of tanning as a protector did not outweigh the risks. He asked the question of whether tanning could not be achieved without this risk? He mentioned PUVA, topical psoralens and emollients (e.g., baby oil) were tan accelerators. He remarked that not all tans are equally photoprotective. He stated that the risk of NMSC from tan accelerators was greater in the person most likely to use them--persons most likely to use them. He stated that

while the risk of NMSC could be reduced with the photoprotection of a tan and potentially increased risk for CMM. He has been following 1380 patients treated by PUVA and these patients now have over 1700 tumors. He gave detailed statistics and time of development but the overall RR of SCC was 5.1 for the low PUVA dose group and 68.5 for more than 337 treatments. The incidence of CMM has been recently increasing, suggesting a long period of delay--several decades.

Barbara Gilchrest returned to the podium to speak on the use of DNA fragments or other methods to turn on the cellular tanning process. She explained that her group had been studying the pathway that began tanning and could they imitate that to produce tanning. They argued that UV-induced membrane damage and UV-induced DNA damage would initiate melanogenesis, based upon their studies with shaved guinea pigs. They applied 1-oleyl-glycerol to achieve a tanning response, since diacylglycerol was released when cell membranes were damaged by UVR. She also showed again the 1982 Parrish action spectrum for erythema and tanning with the efficiency of induction of thymidine dimers. Noting that the SOS response in bacteria irradiated by UVR resulted from the signal originating from the removed DNA single strand excised during excision repair. Treating the guinea pig skin with pTpT thymidine dinucleotide also led to a tan. They tried other oligonucleotides on pigmentation in cell cultures and found that single-stranded DNA was the most effective.

David A Brown spoke on melanogenesis stimulated by diol compounds. He noted that propylene glycol, the typical carrier, was mildly melanogenic itself. Some compounds even thickened the epidermis. He went through many compounds, showing some more effective in producing the tyrosinase activity than others and some more penetrating into the epidermis than others. The skin had to be treated five times per week to maintain the tan. He then spoke about the nitric oxide pathway and how nitric oxide pathway inhibitors could be used to determine the mechanism.

Panel Discussion - In the panel discussion, Gilchrest listed the variety of tanning accelerators. She stated that DNA fragments increase tyrosinase and α-MSH binding; that T4N5 increases thymine dimer excision rate after UV damage and the resulting DNA fragments act as tyrosinase; that diacylglycerols activate PKC to activate tyrosinase; that Diols affect the nitric oxide cycle; that tyrosine is the substrate for melanin production; that plant extracts apparently increase CAMP levels. Patricia Agin noted that since the FDA monograph in 1993, there had been an increase in the use of artificial tanners and she argued for an FDA warning statement on tanning. Andrija Kornhauser asked what would happen if these agents would help to protect in non-pigmented vitiligo skin or in Type I skin. Joseph Levy, the executive director of the Smart Tan Network, spoke on the activities of his organization and stated that their Golden Rule of Tanning was "never to burn." He stated that their customers were happy, reported fewer cases of sunburn, that they recommended use of sunscreens and "intelligent tanning." Robert Wagner, President of Aegis Inc, thanked the organizers for inviting panelists representing the indoor tanning industry and he argued that some of the risks discussed in the workshop did not fit with the scientific data coming from the real country of origin of indoor tanning: Germany. He recommended that some of the scientists should visit a UV Tanning trade show in Germany to get the contrary scientific information. Cedric Garland showed a plot of the annual increase in melanocytic skin cancer which had been steadily increasing since 1930, and fit the increasing sales of sunscreens, hence he asked whether UVA being poorly screened based upon the Setlow action spectrum for fish melanomas. Weinstock felt the argument was weak, and Gallagher thought that there were enormous social changes which took place in the 1930s and 1940s which increased childhood exposure might explain the graph. Gallagher took strong issue with the arguments of Ainsleigh, suggesting that the weight of evidence was against his hypothesis that tanning would reduce the incidence of internal cancers. Forbes tested a number of off-the shelf tanning agents and found them to be innocuous and ineffective. Noonan stated that she came from Queensland, Australia, where they had a high UV exposure, but she was unaware of a greatly reduced risk of breast or colon cancer. Garland thought that Australians were not that heavily exposed; however, Noonan disagreed, noting the epidemic of skin cancer there. Garland stated that no correlation was perfect. In answer to a concern raised by Stern, van der Leun estimated that the increased risk for UVB therapy was an order of magnitude less risky than PUVA and their limited check of clinical patients showed this; however, Stern argued for a larger study, considering that UVB therapy was now far more common than PUVA to treat skin diseases. There was an extensive discussion relating to the most effective means to educate teenagers about the risk of tanning if Skin Type I or Type II. There was a range of opinion about the potential long term risks of the experimental tanning accelerators, as Hearing was concerned about all of the cell proliferative activity being turned on; whereas Anderson thought it very exciting and probably better than tanning in a UV box. Beer asked about how many salons were members in the tanning industry active in groups such as Smart Tan Network; the reply was 1,700 members.

On Friday morning, Frank Gasparro chaired **Session E on "Sunburn as a Surrogate Marker of Later Biologic Events"**. He opened with some remarks about DNA photochemistry. He noted that the p53 gene had a peak absorption spectrum of 275 nm. He also noted that thymidine dimers were actually produced in greater numbers that pyrimidine dimers, but were not as significant. He noted that both cytosine and 5-methyl-cytosine were red shifted from the 265-nm peak of DNA. He suggested that the workshop not aim for a simple solution, but to have all of the best science and from that formulate the best public health messages.

Kays Kaidbey viewed some early changes as markers for delayed effects. He viewed the following as UVA damage markers: epidermal thickening, sunburn cell induction, depletion of Langerhans cells, lysozyme deposition, and an inflammatory response shown by a leukocyte as a common antigen. His objective was to develop a method to measure the efficacy of UVA sunscreens. He argued that the IPD method to measure sunscreen efficacy was seriously flawed because the action spectrum was quite different. Using a strongly filtered UV lamp that was almost completely UVA radiation, they tested twelve human subjects with three sunscreens. They measured visible epidermal thickening, lysozyme, leukocyte common antigen (LCA), sunburn cells and p53. He recommended that the term "broad-spectrum sunscreen" be limited to those which block UVA1 as well as UVB.

Margaret Kripke spoke on her group's studies on the role of immunological events in skin cancer with a solar simulator. They tested the impact of using different sunscreens on mice exposed to the simulated solar spectrum. They used specially formulated sunscreens with an SPF of 15 (except for one broad absorber with an SPF of 22) with widely different spectral filtering. All of the sunscreens showed a level of protection by using a measure of the p53 gene mutations, and also looked at tumor induction showed great protection and only one tumor in one mouse showed up very late and at a very high dose. She stated that one could develop a means to test sunscreens on mice using the p53 marker gene. She also described their use of the method of testing CHS suppression (as described earlier by Noonan) with DNFB. She showed the difference in the dose response curves for UVB-induced immune suppression as measured by systemic CHS and local CHS with different challenging agents. She argued for performing a complete dose response curve in order to see the slope. Using CHS to DNFB test with four different sunscreens they found an actual immune protection factor (IPF) ranging from 1.5 to 3.2 for the SPF of 15-22. Using another test (DTH to *C. albicans*), they found IPF values of 2.0 to 5.6. She concluded that murine tests were possible, but they did not show levels of IPF close to the SPF.

Marianne Berwick spoke on epidemiological studies relating to sun exposure and sunscreens. She distinguished between the intermittent sun exposure experienced by office workers and the continuous exposure of farm workers. The meta analysis of epidemiological studies show a higher risk for outdoor workers for fewer years of exposure and greater for indoor workers over a lifetime (she cited a study of Rassow). There were three studies (Holman, Osterlind, Berwick) which showed no association of the use of sunscreens and CMM; however, one Austrian study showed a negative impact of sunscreens, and two studies showing an apparent benefit of sunscreen use. She spoke of the enormous problems of this type of epidemiological study which tried to associate recall of sunburns and use of sunscreens many years prior to the onset of symptoms. She noted that only the sunburn phenotype was likely to use sunscreens and that the use of sunscreens only became very popular by 1978. She suggested that "residual confounding" was likely to explain the positive association of melanoma incidence and increased use of sunscreens. The studies attempting to show the impact of previous sunburns and CMM had mixed results, but she concluded that the weight of evidence favored the association of sunburns with CMM. There was about a 6-fold risk associated with having many nevi and being sun sensitive.

Douglas Brash spoke on other surrogate markers of skin cancers. He stated that for SCC, there were the following pre-cancer markers: p53 mutant clones, actinic keratosis and carcinoma *in situ*; for CMM: moles, dysplastic nevi, radial growth, pre-invasive melanoma; and for BCC he had none. He showed clinical examples of these markers. He argued that UVR leaves mutational signatures that distinguishes it from other carcinogens: the CC to TT and the C to T change. With regard to the p53 gene, he noted that there was an application for studying effects with time. Within hours following sunlight exposure, the p53 protein assay will show the effect of the sunlight exposure--the apoptotic sunburn cells. Within weeks of chronic UV exposure, one can measure p53-mutant clones and p53 mutations in mouse skin. Months later, one can detect keratoses (SCC precancers). The problem of using these surrogate markers was that patients did not like to have skin bioassays and one needed to see new lesions appearing. Furthermore, there was a spontaneous regression of old lesions and problems of the subjects following the UV-exposure regimen. He raised the question of whether tumors arise from precancers as opposed to the possibility that precancers and the cancers really only have the same precursors. He emphasized that precancers do not always proceed to cancers; only one mole in 7,000 proceeds to a cancer and only one precancer in 1,000 proceeds to SCC. He was worried that the FDA and the sunscreen industry could unwittingly establish a test employing a marker that would prevent the development of one item, but not prevent all types (e.g., with a different initiation action spectrum. He asked whether giving sunscreens to adults, was it too late. He also raised the hypothetical possibility that protection against one maker might increase the incidence of something else.

Panel Discussion - In the Panel Discussion, Gasparro summarized the work of Lorraine Kligman on accelerated skin aging. She had studied glycosaminoglycans as a marker of collagen changes which led eventually to accelerated skin aging. She had emphasized that some UVB and UVA radiation reached the important layers of the skin even with sunscreens she tested, but broad-spectrum sunscreens were clear superior in moderating the adverse effect. Colin F. Chignell, made the first remarks from the panel; and spoke about the experience with para-amino-benzoic acid (PABA) which has been widely used in sunscreens, but despite its apparent protective qualities, it also could produce unwanted effects. He also noted the problems of patients taking photosensitizing medications at the time that they are a client in an indoor tanning salon. Richard Gallagher remarked that information needed to be specific for people with different types of skin, and that tan should be avoided by persons

with skin types I and II. Lee Peeler commented on the importance of advertising and promotional materials being well understood by the consumer. With regard to health or medical products, claims should generally be supported by clinical trials. She explained that the FTC took action against four tanning salons making misleading claims and against some manufacturers marketing sunscreen products. Margaret Tucker remarked that freckling was not a perfect indicator, but the presence of nevi--and particularly dysplastic nevi) was a better indicator (for CMM), but the presence of both freckles and dysplastic nevi was an excellent indicator of sun sensitivity. Antony Young showed slides of propidium iodide staining of DNA to identify nuclei as well as monoclonal antibody staining to identify DNA lesions. He showed a very revealing comparison of TT action spectra at different layers in the basal layers and compared these action spectra with the Parrish erythemal action spectrum, and they diverged exactly as would expected in the 275 nm region, showing the greatly reduced penetration of short wavelength UVB and UVC radiation. He also showed data that revealed that immunosuppression has a much lower SSR dose threshold than erythema in skin type III; hence, he concurred with the conclusions of Kripke, that IPF was indeed much lower than SPF. Kripke argued that the lack of immunosuppression from the low IPF was really not important if there were no UV damaged skin or precancerous lesions; and it was important that the SPF indeed reflect the protection against DNA damage. Annie Fourtenier briefly described her studies which showed that a higher IPF really did reduce the p53 markers. J. A. Johnson, University of Nebraska, Omaha, briefly described his work with dihydroxyacetone (DHA) which induced skin pigmentation that would increase the SPF of other sunscreens by about threefold. Chignall was asked whether photosensitizing medications could not be grouped into seriously effective compounds, Chignall could not think of a solution to this problem, other than for salon operators to obtain the Physician's Desk Reference. Physical sunscreens were discussed with regard to IPF, but there seemed to be little or no information. Weinstock argued that sunscreen labeling should require some information about how frequently the sunscreen needed to be re-applied. Weinstock suggested that public health messages should not focus on dysplastic nevi since half those patients who develop CMM did not have this indicator, and he thought the messages should be broader. Robin Hornung noted that girls and young women historically have been more cautious in sun behavior, but also were most favorable toward tanning. John Sutherland asked about what was really known about the long-wavelength tail of immune-suppressive action of UV, and whether that would explain the very low IPF values. No one knew, but DeFabo noted that sunscreens did not really seem to block the isomeration of urocanic acid, which was also present in the stratum corneum. Gilchrest suggested a two-step immune suppressive experiment whereby the sunscreen was applied during a test of the UV suppression during the promotion stage of carcinogenesis. She raised the question of whether the mouse immune system was not quite different in its response to UV from human skin, but Noonan and others suggested that there was little difference when tests had been conducted.

General Discussion - Vincent A DeLeo led an open discussion on topics. He opened the discussion by asking about public health campaigns and what was done in other countries. Sliney noted that the World Health Organization and ICNIRP had held meetings on this subject and two years ago the USACHPPM and WHO had organized a meeting in Baltimore of health education experts on how to prepare public health information campaigns on UV sunlight hazards, and a booklet had been drafted on this. DeLeo asked about whether a sun-simulating suntanning was better, and there was a range of views, with Schroepl noting that sunlight was best because humans evolved under sunlight. Gilchrest noted that one should be very skeptical about the use of the fish action spectrum for CMM, and using the XP patient experience, she thought that UVB is still the primary actor, and she noted a study using human foreskin transplanted into immune-suppressed mice reported recently in the Am. J. Pathol. that showed UVB sensitivity. Ainsleigh noted that very study with human foreskin showed that "tanning was protective." This led to a discussion on potential positive effects of UV exposure. Weinstock stated that there were too little data to draw any conclusion and that this meeting was not really set up to answer that question. Kripke noted that there were indeed indicators that some cancers were more frequent in areas of high insolation and she thought that non-Hodgkin lymphomas might meet that criterion, and Donald Forbes recalled a report some years ago by Davies which showed life shortening with UV. Gallagher stated that there had been a study showing no latitudinal gradient for non-Hodgkin lymphomas. Beer again asked the question what was the minimum tanning dose and the needed frequency. The answer from Kaidby was 15 J/cm^2 of UVA, but it was more than 1 MED in the UVB. James Spenser stated that it was impossible question, since it varied so much by individual. Gilchrest also stated that it was a very individual question and that skin had a "memory," inasmuch as skin that had been tanned in the past more readily tanned. Antony Young stated that 0.7 MED was better than 0.5 MED. Cyr asked about whether a tanning dose response curve had been performed. Michael Caswell described a study of 14 subjects which showed that repeated exposures (at 3-day intervals) first led to a visible tan after 10-15 days and steadily increased in darkness over two months. Using a ChromaMeter to measure tanning curve was very similar. A question was raised about the treatment of psoriasis patients in tanning salons. US dermatologists did not refer patients to a salon. Barth stated that many patients go to tanning salons, but dermatologists do not refer them normally to a tanning salon.

Closing Session - The closing session on Friday afternoon was chaired by DeLeo. Sliney briefly summarized the major points made during his session on measurement of UV and the physical characteristics of sources. He pointed out that useful measurements could be made with broad-band meters if the action spectrum were known, and yet some action spectra may be flawed due to finite bandwidth sources used in their derivations. He also

summarized the points of DeFabo, Sayre and Moss. Irene Kochevar summarized the major points form her session. She stated that the action spectrum for dimer formation was really not known in the longer wavelength UVA, and there was a potential for other reactions to dominate in that region. There was also discussion of the lack of an action spectrum for CMM, but much speculation. Some conclusions could be drawn from XP patients and from epidemiological studies of risk factors such as nevi. She summarized the limits of epidemiological studies and recommendations for further prospective studies beginning with children. She also discussed markers and pathways and the growing concerns about UVA exposure. Jan Stolwijk summarized the four beneficial effects of UVR exposure. He explained that Weinstock summarized knowledge about preconditioning of skin by repeated exposure to sunlight or artificial UVR, but in sun-sensitive people the risk increased rather tan decreased with repeated outdoor exposure. He summarized the studies on UV production of vitamin D in the skin. One report of the benefit of vitamin D to protect against internal cancers was met with some disbelief. He noted the work of Rosenthal SAD and phototherapy, and upon sunlight and mood. Gilchrest spoke on the tanning session and she summarized the genetic determinants and the molecular studies, but she emphasized that it was unknown whether tanning actually reduced the risk of skin cancer or whether the very determinants of ability to tan was an indicator of good cellular defenses with or without the pigmentation level. She noted that melanin alone was not the protective factor. Tan was a word that meant several things and not all tans are the same. She concluded that there was no clear evidence for tanning preferentially with UVA or UVB. Studies of PUVA patients show a clearly increased incidence of all skin cancers decades later. This might be true for other UVR exposures as well. She also described the problems associated with current tanning promoters. She then described various techniques now under research to stimulate tanning without UVR exposure. It was concluded that the benefits of such topical agents would have to be evaluated for possible unknown adverse effects of artificially manipulating molecular machinery of the melanocytes to produce pigmentation. Francis Gasparro summarized his session on various biological markers. These markers, such as p53, were being used to assess the effectiveness of sunscreens. The different markers had been employed to show effectiveness to reduce both carcinoma risk and skin aging risk. He argued for the need for further research, and he felt that basing too much on a nocturnal animal--the hairless mouse required caution. He made a plea to be careful about public health messages based upon limited scientific data. There may be benefits as well as risks. DeLeo summarized his closing session on all aspects of UV exposure and tanning.

After the workshop finished, the NIH and FDA organizers, and session chairs met to discuss research needs and other actions which were thought appropriate in light of the workshop. The following research needs were listed.

a. Action Spectrum of Melanogenesis
b. Waveband interactions
c. The role of visible light
d. Better model systems
e. Standardizing exposure means as sources and meters (CIE activity)
f. Action spectrum for photoaging
g. The need for a Framingham UV Study
h. Cohort study of children solar exposure and nevus density
i. Prevalence studies of basal/squamous cell cancers and melanomas in high and low areas of insolation
j. International prevalence study
k. Prospective study of sun vs. tanning salons
l. Biopsies of heavy tanning bed users or UVB phototherapy
m. Study of genes involved (surrogate markers depend upon establish
n. Dose response curve of human skin cancer
o. Testing the Garland hypothesis by another retrospective study, e.g., using the Haines data
p. Tanning action spectrum and how effective is this in photoprotection
q. Is the skin a receptor for many other effects, e.g., endorphins, etc.

With regard to non-research items, the following were discussed:

a. IEC WG16 on sunlamp products: should the US participate more actively?
b. Sunlamp standard could use groupings.
c. Guidelines for sunscreens and substantivity; reapplication guidelines; develop a standard label on the back with spectral attenuation vs wavelength.

Summarizing statement: Much is known, but much is yet to be learned, about the effects, both beneficial and adverse, of human exposure to UV light, both on the skin itself and on the person as a whole. Much additional research needs to be done in many areas in order to provide the basis of public health actions. Sunburn prevention alone is not the only answer. A combination of adjustment of time of day for outdoor activities, structured shade, clothing and other physical blockers, and sunscreens are necessary to allow prudent people to enjoy the benefits of outdoor activities while minimizing the risks.

Meeting Report - **by Sheila Mac Neil**

VIIIth Annual Meeting of the ESPCR September 23-26, 1998 Prague, Czech Republic

This meeting was held at the time of the 650th Anniversary of Charles University, Prague and was organised by the 1st Faculty of Medicine, Charles University. The spirit of the city of Prague and of Charles University was evident in every aspect of the meeting. A strong sense of history and of continuity graced the proceedings, the kindness and gentle humour of our Czech hosts made this an extremely pleasant meeting.

Unfortunately just a few weeks after the meeting it was with deep sadness that the ESPCR members learned of the sudden death of our previous ESPCR President, Bengt Larsson. Bengt contributed enormously to the European family of the ESPCR and had participated only recently in August in a meeting in Colorado to the planning for the International Federation Pigment Society meeting in Japan in 1999. Bengt and his wife, Pia, were at the ESPCR meeting enjoying the unique atmosphere of Prague. All who knew him were shocked by his sudden death and our thoughts are with his wife and family for their loss.

Who was there? The ESPCR meeting was attended by 142 participants from 17 different countries. In 2½ days there were 10 scientific sessions and 6 plenary lectures and 54 posters. A busy time but still with plenty of time for excellent music and food and wonderful beer and time to catch up with friends and colleagues.

Nature of report Several colleagues have kindly contributed a summary of the highlights of sessions they chaired and have also identified particular talks or posters that they found raised their pulse rate. In this respect there was one particular plenary lecture which stood out above all others - **John Pawelek** and colleagues provided new experimental evidence that could change how we think about metastatic melanoma ... For details, see a fuller description later in this report (under "Our favourite things").

SESSION I - - - Melanin-synthesis, properties and function - - - by Prof Patrick Riley

Six papers were presented in this Session and 3 posters (P1, P3 and P52) were included in the discussion. The first talk was a brief and lucid exposition by **Prof Christopher Ramsden** of a series of chemical studies inspired by some new reactions found as a result of work on tyrosinase oxidation of analogue substrates. In this he outlined the production of the indoliumolate betanes and described work which led on to the study of the facile formation of quinomethanes from orthoquinones under conditions in which the α-carbon has acidic character. This latter characteristic of these reactions enabled a reinterpretation of the famous Gates' synthesis of morphine. In the discussion of this paper **Dr. Edward Land** briefly mentioned the poster display P1 devoted to the generation of orthoquinones by pulse radiolysis, a technique that permits the measurement of the rate constants of subsequent reactions, such as cyclisation or isomerisation to form the corresponding quinomethanes.

Dr. Allesandra Napolitano then presented some new chemical evidence enabling a more detailed description to be given of the intermediates in the oxidation of cysteinyl dopa leading to the formation of benzothiazines. This talk was followed by a discourse by **Prof Bruno Nicolaus** concerning the fundamental structural features of melanins. In this he emphasised the importance of the chemical "backbone" of conjugated double bonds permitting the possibility of semiconductor properties of melanins. He pointed out that the melanisation of deep-sea vertebrates for example, where no light-absorbing function would be expected, have evolutionary value and leads to the expectation that there are other functions of melanins that are important. Whether melanin should be considered as jewel or garbage remained, however, an open question.

Dr. Jim Gallas then gave a spirited exposition of work on neutron diffraction analysis of experimental melanin solutions. He showed that there were specific aggregation patterns with a 3.4 Angström stacking characteristic, suggesting a layering phenomenon. These aggregates could be disrupted by hydrogen peroxide. **Prof Milan Elleder** then gave a brilliantly illustrated talk showing UV irradiation-induced fluorescence in pigmented tissue. This was also shown to be a feature of synthetic melanin and could be stimulated by prior treatment with hydrogen peroxide. The following talk by **Dr. Luciana Mosca** illustrated similar fluorescence in material generated by the oxidation of tyrosyl residues in opiate peptides. In discussion, the possibility that the fluorescence was dependent on degradation which involved Fenton chemistry, and thus bore similarities to the methodologies employed in posters P3 by **Donato** et al. and P52 by **Wakamatsu, Ito** and **Koch** was proposed. However, caution in the interpretation of the autofluorescence phenomena was urged by **Prof Tadeusz Sarna** who pointed out that, at least *in vivo*, there were a number of other compounds that could undergo autofluorescence and might be influenced by melanin in the micro-environment. **Prof Karin Schallreuter** strongly suggested that the fluorescence was related to other compounds that were known to be present in melanosomes such as the pterins, an interpretation that was not accepted by Professor Elleder who pointed that this could not be the case with synthetic melanins. The interesting differences between the case of induction of autofluorescence between eumelanins and phaeomelanins was also briefly mentioned, but lack of time prevented a full discussion of this interesting new data which may have diagnostic significance in view of the apparent increase in phaeomelanin synthesis in dysplastic naevi (a topic mentioned in a later session of the meeting).

SESSION II - - - Melanogenesis - - - by Prof Anthony Thody

This contained 4 talks, most controversial of these was that presented by Prof Karin Schallreuter. "One would have expected a little more on the MSH peptides in view of the current controversy concerning their significance as pigmentary hormones in humans (see Session IX for MSH and immunomodulation). The topic was at least touched on by **Karin Schallreuter** in her plenary lecture on pterins and pigmentation. It is now clear from her work that 6-tetrahydrobiopterin (6-GH_4) has an important role in melanogenesis by regulating the availability of L-tyrosine and tyrosinase activity. She now has new data which suggests that α-MSH figures in this control through its ability to bind 6-BH_4 and the implications are that α-MSH is able to regulate melanogenesis through activation of the MC-1 receptor and also through actions which are independent of the receptor. This is an extremely novel idea and hopefully we shall hear more on the subject at future ESPCR meetings".

Nico Smit presented work on the flavonenzyme DT-diaphorase suggesting that this enzyme may enhance oxidative stress by generating redox cycling catecholes and depletion of NAD(P)H unless other detoxifying enzymes are present.

Messod Benathan and colleagues looked at the effects of thiol-modulating agents on melanogenic activity of normal and malignant pigment cells. Their results suggested that the balance between cysteine and glutathione may play an important role in regulating melanogenic activity of pigment cells. **Ullrich Schraermeyer** et al. presented evidence that melanosomes in retinal pigment epithelial cells are active lysosomes involved in the degradation pathway of rod outer segments of the eye.

SESSION III - - - Microphthalmia encoded Transcription Factor and Melanogenesis - - - by Vincent Hearing

Vincent Hearing and **Anthony Thody** co-chaired this brief but interesting session which centred around the role of MITF (Microphthalmia encoded Transcription Factor) and other transcription factors that regulate mammalian melanogenesis. It has been known for some time that MITF, a basic helix-loop-helix transcription factor, regulates tyrosinase gene expression (as well as TRP1/TyrpI and/or TRP2/Dct, although these have been disputed) through binding to the E-box upstream regulatory region present in all 3 encoded genes. In this session, we heard that at least one, and probably many other, factors also play important roles in this regulation. Initially, **M. Furumura** reported his studies looking at transcriptional modulation of TRP genes by murine ITF2, another bHLH transcription factor originally identified by him as being upregulated during pheomelanogenesis. ITF2 was able to trans-activate the TRP1 gene as strongly as MITF, stimulated tyrosinase gene expression somewhat, and TRP2 expression not at all. Interestingly, ITF2 was able to inhibit MITF stimulation of TRP gene expression, probably by generating inactive heterodimers between MITF and ITF2.

J. Vachtenheim next reported on the role of MITF in human melanoma cells; they showed that expression of MITF is repressed in some cultured melanoma cells, and that this was associated with downregulation of tyrosinase, TRP1 and TRP2 genes in those cells. They directly demonstrated MITF regulation of those genes in human melanocytes by transfecting MITF back into those cells and demonstrating consequent upregulation of one or more of those TRP genes in the transfected cells. Their data support the critical nature of MITF expression in the pigmented phenotype of human melanocytes, and further suggest that repressors may be present in unpigmented cells which may also play important roles in regulating expression and catalytic function of those enzymes. Finally, **S. Olaizola-Horn** reported on the regulation of MITF and tyrosinase genes. Tyrosinase expression can be regulated via the cAMP and PKC pathways, but intracellular signalling pathways regulating MITF expression are not yet known. This study showed that treatment of melanocytes with forskolin to stimulate cAMP levels induced MITF gene expression within 4 hours and tyrosinase gene expression within 48 hours. Depletion of PKC by prolonged TPA treatment resulted in a decrease in pigmentation but was accompanied by increased MITF mRNA levels. These results suggest that tyrosinase and MITF gene expression are both regulated via cAMP and PKC pathways, but independently. This study further shows that factors other than MITF regulate tyrosinase gene expression and thus human pigmentation. The general conclusion of this session is that MITF is an important regulatory factor in controlling TRP gene expression, but that one or more other transcription factors are also important at this level of regulation.

SESSION IV - - - UV light, Photoprotection, Phototherapy - - - by Prof J.P. Césarini

This session was chaired by **Prof Tad Sarna** and **Prof Césarini.** The session was composed of 11 formal oral presentations to which 4 posters can be linked and were briefly discussed at the end (the programme of the session was organised in co-operation with the European Society for Photobiology). Three major topics were exposed: photoprotection, progress in photodynamic therapy and some insights in melanoma cell biology.

J.P. Césarini and **H.C. Wulf** presented the natural photoprotection offered by melanins for different phototypes and the acquired photoprotection after serial exposures to UVA + B radiations. Topical sunscreens (Sun Protection Factor based on protection against erythema) are able to suppress the actinic erythema but other UV effects like immunosuppression or indirect evidence for genotoxicity, are still present in the absence of erythema. The importance of skin-vehicle interaction was emphasised by **B. Gabard** and the skin penetration of UV filters seems a critical point for the quality of sunscreens. **R. Pedeux** had shown p53 expression in melanoma

cells in culture. In work presented by **E. Wencz**, the association of UVA sensitivity and phaeomelanogenesis was found phototoxic, the melanin content being strongly correlated with UVA-induced single strand breaks in melanocytes.

The second part of the session was devoted to photodynamic phototherapy. **S.B. Brown**, after a review of the literature, explained how light source dosimetry and treatment protocols can be improved, and pointed also the need for more basic studies. **G. Jori** found that the tumour response (pigmented melanoma in mice) was affected by a variety of parameters and that hyperthermal conditions (43-44°C) contributed to the damage to the tumour, the photo bleached tumour being more susceptible to the PDT treatment. **M. Jiraskova** emphasised the red fluorescence observed after intralesional injection of PDT, the fluorescence being of great help for the evaluation of tumour extent. **G.M.J. Biejersbergen-van-Henegouwen** suggested that photobinding of chemical with DNA or proteins is a pre-requisite to obtain specific suppression of hypersensitivity in extra-corporeal phototherapy with UVA. The induced singlet oxygen produces immune suppression.

The third part was more specifically devoted to some biological aspects of melanoma. **H.Z. Hill** found that serum-free conditioned medium of cultured melanoma cells, following irradiation with ionising radiations, contains some antigenic proteins that increases the survival of melanoma cells. This may explain some drawback of radiotherapy and chemotherapy of melanoma. **E.M. Link** demonstrated that UV and ionising radiations may trigger the melanoma metastasis. Some "physiological" factors, like eicosanoids, may trigger the metastatic cascade. The production of eicosanoids was accompanied by the activation of ACTH and α-MSH mediated immune system (adrenal axis feedback loop).

SESSION V - - - Pigment Cell Cultivation - - - by Prof Sheila Mac Neil

Ullrich Schraermeyer reported on experience with both explant and enzymically dispersed culture of porcine and human iridial melanocytes. **Roger Bowers** reported on premature death of avian melanocytes in Barred White Leghorn feathers. He was able to induce premature death *in vitro* by the addition of L-dopa plus α-MSH or by not changing medium. Both led to an increase in oxygen radical accumulation and development of apoptosis in melanocytes. Using this model, he was then able to look at strategies to "rescue" melanocytes from oxygen radical accumulation. Addition of superoxide dismutase was particularly effective and he suggested that this avian *in vitro* system could be used to study premature ovarian melanocyte cell death analogous to that found in vitiligo.

Next was a presentation from **M. Regnier** from L'Oreal on the use of keratinocyte-melanocyte co-cultures and pigmented reconstructed human epidermis to study modulation of melanogenesis. Dr. Regnier demonstrated that co-seeding melanocytes and keratinocytes on acellular human dermis gave a model in which UV induction of pigmentation could be observed and the efficacy of topical applications of pro or de-pigmenting agents could be followed. In question time, I asked whether α-MSH induced pigmentation in these models and whether the model had ever been constructed with fibroblasts present. Dr. Regnier replied that MSH was not melanogenic in this model in their experience and the contribution or otherwise of the fibroblast had not been examined in this model.

This related to a presentation by **Paula Eves** et al. (from my own laboratory) where we found that the addition of fibroblasts to such a reconstructed 3D skin composite (based on sterilised human de-epidermised acellular dermis to which melanocytes and keratinocytes and fibroblasts were added) actually reduced the spontaneous pigmentation of the skin composites. In agreement with Dr. Regnier, however, we also find MSH to be without effect on pigmentation in this model irrespective of the presence or absence of fibroblasts.

Using this model we demonstrated that, in collaboration with **Prof Ghanem**, the human melanoma cell line (HBL), which is poorly invasive on its own, could be demonstrated to traverse the basement membrane when keratinocytes were also present. Keratinocytes on their own did not invade the basement membrane. This suggests some interaction between the melanoma cell line and keratinocytes which may be relevant to initial escape of melanoma cells from the primary tumour.

Sviderskaya et al. then reported on the establishment of 3 unpigmented lines of a new cell type from neonatal murine skin. These cells appear to be neural crest-like.

Aranberger et al. then gave a brief video (in the absence of any of the authors) of grafting of melanocytes and keratinocytes for patients with vitiligo.

SESSION VI - - - Pigment cells and Oxidative Stress - - - by Prof Sheila Mac Neil

For several years now pigment cell melanoma cell biologists have been asking whether melanocytes and melanoma cells differ in their handling of oxidative stress and indeed whether a failure to handle oxidative stress might contribute to melanocyte failure and their ultimate removal (as in vitiligo) or even to melanocytic transformation.

Continued work on this theme from the group of **Prof Frank Meyskens** focused on differences in the basal levels of the superoxide anion and hydrogen peroxide in cutaneous metastatic melanoma cells and cultured melanocytes (I am indebted to **Dr. John Haycock** for this summary of this work). These authors found that metastatic melanoma cells have higher levels of both superoxide anion and hydrogen peroxide than normal human melanocytes as determined by FACS analysis etc.

Next, he reported that melanocytes did not respond to an oxidative stress with an increase in NF-kB DNA binding activity, whereas metastatic melanoma cells did. Also, the level of constitutive NF-kB activity in

metastatic melanoma cells was higher than in melanocytes. This could be reduced by incubating the cells with two types of antioxidants: (i) pyrrolidine dithiocarbamate or (ii) 1, 10-ortho phenathroline (a metal ion chelator which acts as antioxidant by removing transition metal ions, thereby preventing metal catalysed oxidation proceeding by the Fenton reaction).

He speculated that an NF-kB response might be seen if a high enough oxidative stress were given. The absence of a response, he thought, was due to a high level of intracellular antioxidant protection.

The interest in NF-kB Rel family members was extended to include various heterodimer formations, identified in the two cell types by immunoprecipitation. These included various combinations of p50, p65, p75 and p52. Under basal (unstimulated) conditions some combinations of Rel dimers were either very low or undetectable in the metastatic melanoma cells in contrast to the melanocytes.

Mauro Picardo and colleagues gave a presentation continuing their work into investigating the anti-oxidative status of patients with melanoma. They presented evidence that whereas in normal subjects, there was a correlation between epidermal and peripheral blood mononuclear cell levels of superoxide dismutase, catalase and vitamin E, this correlation was not seen in melanoma patients suggesting that some patients with melanoma may have a constitutive metabolic alteration. This, in turn, may contribute to their susceptibility to external oxidative stress.

In a second presentation from this group, **Dr. V. Maresca** presented evidence that the potent inflammatory cytokine, TNF- α, can itself generate pro-oxidative stress in melanoma cells. The response of cells to TNF- α may differ depending on the levels of intracellular antioxidants and peroxidisable compounds in the cells.

The final talk from **Roger Bowers** and colleagues continued Roger's work in trying to (a) deliberately drive to the point of destruction his chicken melanocytes and then (b) rescue them from impending death by paying attention to their ability to cope with oxidative stress. In this study, he showed that the addition of iron to the failing melanocytes increased their mortality rate significantly and that, as expected, drugs which compromised the ability of the cell to cope with oxidative stress (via buthionine sulphoximine addition, a glutathione inhibitor) and a superoxide dismutase inhibitor (diethyldithiocarbamate) both increased mortality rate in the feather melanocytes of the Barred White Leghorn.

SESSION VII - - - Neuromelanogenesis - - - by Prof Sheila Mac Neil

This was chaired by **Prof M.G. Peter** and **Prof Bengt Larsson**. The first presentation by **Vincent Hearing** concerned macrophage migration inhibitory factor (MIF). This was originally identified as a lymphocyte-derived protein that inhibited monocyte migration. More recently it has been found to catalyse the conversion of dopaminechrome and norapenaphrinechrome, toxic quinone products of the neurotransmitters dopamine and norapenaphrine to indole quinone derivatives that may serve as precursors in neuromelanin. He demonstrated that MIF rescue cells from dopaminechrome-induced death *in vitro* and speculated that as MIF was highly expressed in human brain, it may participate in a detoxification pathway for catacholamine products and could, therefore, have an important protective role for neural tissues.

M. Miranda et al. then presented data of possible relevance to Parkinson's disease. In Parkinson's disease there is degeneration of the dopaminergic cells in the nigro-striatum system. A low level of tyrosine hydroxylase prevents transformation of L-tyrosine to L-dopa. A common therapy has been the administration of the dopamine precursor (L-dopa) but it does have severe side-effects. An alternative approach of stereotactic injection of liposome-entrapped tyrosinase was used to significantly increase the levels of dopamine in the rat brain.

SESSION VIII - - - Gene Expression in Pigment Cells - - - by Sheila Mac Neil

This Session was chaired by **Friedrich Beermann** and **Sheila Mac Neil**, and contained 5 talks. In the first from **Richard King** and colleagues, transcripts of the Hermansky Pudlak Syndrome (HPS) chain were mapped. They identified several mutations and polymorphisms in this gene in individuals with HPS.

G. Kraehn and colleagues then presented work on differential expression of receptor tyrosine kinases in melanocytic skin lesions.

Staying with differentially expressed genes, the next presentation from **R. Hipfel** et al. searched for differentially expressed genes in malignant melanoma and congenital nevi biopsies. Using the technique of differential display more than 120 melanoma-specific and about 100 nevi-specific products were cloned and screened. Of these, 10 melanoma-specific transcripts were confirmed and sequenced. Three of these genes were singled out for particular interest as they concerned a cysteine protease, a protein proteinase inhibitor and a gene product that is mainly expressed in the brain and may function as a transcription factor.

The next presentation from **J. Utikal** et al. focused on c-myc oncogene expression and reported over-expression of c-myc with late stage melanoma which the authors speculated might be due to an increased number of c-myc - chromosome-8 copy number.

The last presentation from **U. Leiter** et al. concerned the apoptotic pathway in melanoma. These authors concluded that bcl2 gene expression increases in malignant melanoma which might reflect an increased malignant potential caused by an inhibition of apoptosis conferring a growth advantage in melanoma metastasis.

SESSION IX - - - Melanoma - Experimental Aspects - - - by Sheila Mac Neil

This was chaired by **Prof Doré** and **Prof Garbe.** It contained the most exciting presentation of the meeting (not just my opinion but resoundingly confirmed by **Tony Thody, Frank Meyskens, Jan Borovansky** and no doubt many others). For details of this presentation by **John Pawelek**, please see under "Our favourite things".

There were 6 other talks in this very lively session. **Friedrich Beermann** and colleagues have used transgenic mice methodology to develop animals with tumours of the retinal pigment epithelium. This has been achieved using SV40 transforming sequences directed to the developing RPE using the promoter of tyrosinase-related protein-1 (TRP-1) in transgenic embryos. Work has advanced to the stage that primary tumour cell lines and metastasis derived from these have now been established and characterised.

Ruth Halaban and colleagues presented work in which they have examined to what extent the retinoblastoma tumour suppressor protein (RB) contributes to tumourigenicity in melanocytes. They were able to neutralise RB function and this led to releasing melanocytes from their normal cell cycle constraints but these melanocytes remained phorbol ester dependent and underwent accelerated cell death in the absence of phorbol ester. Thus, it appears that loss of this protein is insufficient for melanocytic transformation but clearly contributes to regulation of melanocytes by external growth inhibitory signals.

The next talk was from my own laboratory **(B. Richardson)** on the influence which sex steroids can exert on melanoma cell invasion (at least *in vitro*). Epidemiological studies show female survival benefit in advanced metastatic melanoma which is largely unexplained. Using a very simple model of a melanoma cell line (A375-SM cells) invading through a layer of human fibronectin over 20 hours, we were able to show that the female steroid 17β-oestradiol and, to an even greater extent, oestrone, significantly reduce invasion of cells. Other androgenic and adrenal steroids were ineffective. This *in vitro* data begins to offer an explanation to the apparent female survival advantage in metastatic melanoma.

The next talk was from **Dr. J. Haycock** from my laboratory working in collaboration with **Prof Ghanem**. Jointly, the two laboratories have previously shown that α-MSH is able to oppose the actions of the pro-inflammatory cytokine TNF-α in both melanocytes and melanoma cells. The current study progresses this work to show that α-MSH can be demonstrated to oppose the actions of TNF-α at the level of activation of the transcription factor NF-kB. Thus, TNF-α would normally activate NF-kB to a maximal degree within 1-2 hours in cutaneous and ocular melanocytes and melanoma cells. We have demonstrated that α-MSH can reduce this activation by 50% on average, demonstrating for the first time in melanocytes and melanoma cells that the immunomodulatory action of α-MSH may rise by inhibiting the normal cytokine induced activation of NF-kB in both melanocytes and melanoma cells.

The next talk from **P. Parsons** et al. concerned the anti-tumour activity of agents which affect acetylation of histone. Cell killing was accompanied by hyperacetylation of histone H4.

The last talk in this session was from **Stan Pavel** and colleagues. They presented evidence that the composition of melanin in melanosomes of dysplastic naevi is very abnormal with increased concentrations of sulphur and, hence, phaeomelanin. According to Frank Meyskens - "they are building a compelling case that the naevi are under chronic oxidative conditions and, hence, internal genotoxic stress".

SESSION X - - - Melanoma - Clinical Aspects - - - by Prof Frank Meyskens

Progress in the clinical area lags behind that of the tremendous advances occurring in our basic understanding of melanoma. There were, however, a couple of novel observations reported. **Blum** and his colleagues (Tuebingen) reported on a large comparative study of clinical examination to ultrasound evaluation of regional lymph nodes. Comparison to histopathological analysis indicated that ultrasound was more effective than palpation. Also, from the same group **(Blaheta)** was presented the results of another large study showing that sentinel node evaluation and biopsy combined with RT-PCR for tyrosinase in apparently negative cases increased the diagnostic accuracy. If the results of these two studies can be confirmed, their usage will be important in determining who might and might not benefit from adjuvant interferon, a difficult and expensive intervention. The Ulm group **(Kaskel)** also reported a large series in which S-100 was evaluated as a marker of disease. Its elevation in serum was found to correlate with high frequency with the appearance of metastatic disease; however, more extensive studies will need to be done to determine its usefulness as a prognostic or response (to therapy) marker. The remainder of the presentations of the papers in this session dealt with the epidemiology of melanoma in Germany and, although of interest to workers and the public in Germany, did not provide new or unexpected information about the disease.

OUR FAVOURITE THINGS The presentation which attracted most attention and probably has caused many of us to go away and re-evaluate some of our ideas was that from **John Pawelek** in which he showed that experimentally mouse melanoma cells can fuse with macrophages to form hybrids, many of which are more aggressive metastatically *in vivo* than the parent cell line. *In vitro*, these cells were found to be more heavily pigmented and responsive to MSH than the parent cell line. The hybrids also responded to MSH with increased chemotaxis - a property not noted in the parent cell line.

John took great pains to point out that this is not a new idea - fusion of cancer cells with macrophages has been previously noted for other cancers including melanoma (**Munzarova** and colleagues, Lancet 1987 and Melanoma Research 1992) and it offers another explanation for how melanoma cells acquire metastatic success. Quoting

from Munzarova et al. "We are of the opinion that the rapid assimilation of multiple properties from various populations of cells (and especially those of macrophages) obtained by fusion and processes after it are a better explanation of many of these qualities than the requirement of a single cell lineage to undergo sequentially so numerous mutagenic alterations" (Munzarova et al. Neoplasma 1992; 39: 70-86). This fusion behaviour which John and colleagues demonstrated can happen reproducibly *in vitro* (**Rachkovsky** et al. Clinical Experimental Metastasis, 1998, 16: 299-312) offers a new paradigm for the study of melanoma cells and their host interactions. It has implications for detection of metastatic melanoma, for drug resistance and, down the line, it may offer new avenues for therapeutic and preventive intervention.

Does this occur clinically? Is this what is going on with advanced metastatic melanoma? It was unfortunate that John's talk was delivered near the end of the meeting so that there was less opportunity for discussion of the import of this work which is potentially enormous.

Other plenary lectures

In addition to **John Pawelek** and **Karin Schallreuter** (already mentioned in this report), we had excellent contributions from **Prof Pat Riley, Prof Tadeusz Sarna, Dr. Nico Smit** and **Prof M. Elleder**.

Prof Riley gave a plenary lecture explaining that the unusual kinetic behaviour of tyrosinase is due to its activation by dihydric phenol substrates which are formed indirectly (including dopa which is not a direct product of the tyrosinase reaction) as previously proposed by Raper and his co-workers (my thanks to Jan Borovansky for this succinct summary of Pat Riley's talk).

Prof Sarna looked into the complex question of whether melanins act as antioxidants and how phototherapy of pigmented tissues must take into account the ability of melanin to bind photosensitisers. Also, oxidative degradation of melanin can significantly reduce its antioxidant efficiency. Professor Sarna's talk underlined once more that the exact role of melanin in photoprotection remains unclear.

Dr. Nico Smit, in a plenary lecture emphasising how much the culture conditions can influence the pigmentary biology of the melanocyte, made a plea for some standardisation of culture conditions in order to be able to compare results obtained in different laboratories.

Finally, **Prof Elleder** gave an excellent review of lipopigments. Frustratingly, the chemical nature of lipopigments is still unknown despite serious analytical effort in this area. He pointed out that lipopigments may contain a number of associated compounds, one of which may be melanin although this is the subject of some debate. The best understood lipopigment is that occurring in a fatal neurodegenerative disease where the origin of the pigment is an agregate of extremely hydrophobic proteins (enzyme subunits of a mitochondrial enzyme).

We were also delighted at this meeting to, as a Society, offer honorary life membership to **Profs Riley** and **Duchon** in recognition of their considerable achievements to research in pigment biology and their unflagging support of the European Society for Pigment Cell Research.

Prize-winning posters

First prize went to "Expression of the epidermal growth factor receptor (EGFR) gene and chromosome-7 aneuploidy in cutaneous neoplasias and metastasis" - Authors: M. Udart, J. Utikal, R.U. Peter and G. Krahn.

Second prize went to "Molecular characterisation of c-kit from the Mexican axolotl" - Authors: K.A. Mason, N.B. Parker, D.M. Parichy and S.R. Boss.

Third prize went to "Chemical characterisation of dopamine-melanin: application to identification of melanins in butterfly wing" - Authors: K. Wakamatsu, S. Ito and P.E. Koch.

Meeting Report -

Ultraviolet Irradiation and Photoprotection August 18 - 22, 1998 Snowmass, Colorado

Summary of an open discussion at the 47th Annual Montagna Symposium on the Biology of Skin "Photobiology: the Molecular and Biologic Effects of Light and Their Impact on Skin and Skin Diseases"

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Background The 47th Annual Montagna Symposium on the Biology of Skin was organized around the topic: "Photobiology: the Molecular and Biologic Effects of Light and Their Impact on Skin and Skin Diseases." When it was learned that the NIH was convening a Workshop with a similar focus the following month, Symposium organizers invited all attendees to provide input on the major Workshop topics. In this way, thoughts of this expert

group could be introduced into the Workshop, which only a few planned to attend due to competing commitments. The final 90 minutes of the Symposium was conducted as an open group discussion of selected Workshop themes and involved approximately 50 dermatologists, photobiologists, and cellular-molecular biologists, all of whom are actively engaged in related research. The following are points on which there was unanimous agreement as ascertained by group votes.

Sunlight, photons, and the action spectrum Sunlight as well as artificial sources of ultraviolet radiation emit photons with a wide spectrum of energies (determined by wavelength). For photons from such sources to cause biologic effects, they must first be absorbed by molecules (chromophores) within the skin. Because each molecule absorbs certain wavelengths preferentially, the effects of light on skin are highly dependent on the wavelengths that are included in a source. By measuring the relative ability of photons in a spectrum of sunlight (or ultraviolet light from an artificial source) to produce a specific effect one establishes an action spectrum (such as for cancer development or immunosuppression). Each action spectrum, therefore, is a function of the molecules whose modification by absorbed photons causes a specific effect. Thus, action spectra differ for various effects, for example for the development of the different types of skin cancer.

Skin cancer is caused by sunlight Exposure of skin to sunlight is the cause of the vast majority of the major types of skin cancer: basal cell carcinomas, squamous cell carcinomas, and melanomas. Because the three types of skin cancer are different, statements about the role of sunlight (including ultraviolet radiation from sunlight), as well as the possible benefits of protective measures, must carefully identify the type of cancer that is under consideration. Despite modest knowledge about many effects of sunlight on skin cancer and the benefits of sun protection, several facts are relatively certain:

1. Among the three types of skin cancer, there is greatest certainty about the role of ultraviolet radiation in promoting development of squamous cell carcinomas and their precursors, actinic keratoses.
2. Minimizing exposure to sunlight and the use of other sun protective measures decreases the frequency of all types of skin cancer.
3. Experience with patients having genetic defects in the repair of sunlight-induced damage to DNA (and a high frequency of all types of skin cancer) demonstrate conclusively that a comprehensive program of sunlight avoidance prevents skin cancer development.

Tanning: Tanning is an injury response in skin.

Photoaging: Sunlight exposure and exposure to ultraviolet radiation from artificial sources (tanning devices) has unwanted "premature aging" effects on skin; this is termed photoaging. Avoiding exposure will delay and minimize photoaging.

Photoprotection and Sunscreens: Reducing one's exposure to sunlight and to artificial sources of ultraviolet radiation (photoprotection) will decrease the frequency of skin cancer and will delay and minimize photoaging. Sunscreens have the capacity to attenuate sunburn and to decrease the incidence of actinic keratoses and squamous cell carcinomas. Consistent with the goal of reducing ultraviolet radiation exposure, sunscreens are an important element in a comprehensive program of sun light protection. There is no evidence that by increasing sunlight exposure one can prevent or retard the development of skin cancer or that developing a “tan” offers more protection than minimizing sunlight exposure in the first place. Epidemiologic studies to determine the effectiveness of sunscreen use in preventing human skin cancers are likely to be confounded by the fact that persons at greatest risk of skin cancer are also most likely to use sunscreens. As well, cancers develop typically after many years of sun exposure and the recent emphasis on sunscreen use may be as yet largely irrelevant to risk.

Practical approach to photoprotection:

1. Avoid exposure to sunlight during the middle of the day. A useful practical guide is to minimize exposure whenever one’s shadow is shorter than one’s height (45° solar angle).
2. Wear protective clothing, including a wide-brimmed hat.
3. Conduct outdoor activities in the shade of trees and buildings.
4. Use a broad-spectrum (UVA + UVB) sunscreen. The use of sunscreens is only one element in a comprehensive program of sunlight protection.

Immunosuppression: Ultraviolet radiation causes a disruption of normal immune responses in skin, most commonly leading to immunosuppression. The action spectrum for this effect, particularly in humans, is uncertain. Moreover, the action spectrum is likely to vary substantially, depending on the type of immune response that is under consideration. Photoprotection can prevent immune disruption, but the effects can be quantified only with knowledge of the action spectrum. Studies of immunosuppression and its prevention have been compromised by the use of UV sources with output spectra often very different from sunlight (see prior paragraph).

Research Needs:

1. The action spectrum for the induction and promotion of basal cell carcinomas and melanomas is unknown.
2. The action spectrum for photoaging is unknown.

3. The action spectrum for immunosuppression is unknown.
4. The photochemistry and photobiology of sunscreens is incompletely known. We do not yet have the perfect sunscreen.
5. The genetic and environmental risk factors (in addition to ultraviolet radiation) in the development of skin cancer are only now beginning to be uncovered.
6. Genes that determine susceptibility to basal cell carcinoma, squamous cell carcinoma, and melanoma must be identified. Additional model systems are needed.

Members in the News -

Kenneth Mason - won the Silver Melanocyte Poster Award at the ESPCR Meeting held in Prague this past October. His poster title was "Molecular Characterization of c-kit from the Mexican Axolotl"

Ruth Halaban - is the Keynote Speaker of the JSPCR Meeting to be held in Kobe, Japan this month. The title of her lecture is "The Rb/E2F Pathway in Normal and malignant Melanocytes"

John Pawelek - was a Keynote Speaker of the ESPCR Meeting held in Prague, Czech Republic; the title of his lecture was "Supermelanotic and Metastatic Melanoma x Macrophage Fusion Hybrids: Altered N-Glycosylation as an Underlying Mechanism" (his lecture was the '**HIT**' of the meeting, cf the ESPCR Meeting Report - congratulations John)

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The Bibliography published in this issue covers the period August, 1998 through October, 1998. If you notice a paper that was not detected by this search that should be included, please send it to us and we will include it in the next issue. We have attempted to highlight any publications which include a member of the PASPCR with a star (*sorry if we missed you but let us know and you'll get a free marked repeat in the next issue*).

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