PASPCR
*Newsletter*

Volume 2 Number 4 December,1994

## Introduction . . .

by DeWayne Townsend

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 the ***Newsletter***; help us to update the Job Listings, Calendar of Events, Meeting Reports, Abstracts in press and other items of general membership interest. If you attend a scientific meeting at which you heard about 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 **<u>your</u>** ***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 any of the members of the Publications Committee.

The Publications Committee wants to make collaboration between members of the Society as easy as possible and toward that goal we are encouraging the use of E-mail and other forms of electronic communications. We encourage everyone who has an E-mail address to forward it to the Publications Committee. The Publications Committee is willing to help any member of the PASPCR get you in touch with the individuals who can set up your E-mail account and to some extent will help you get started.

The **PASPCR** has a Gopher server that can be found from your home Gopher under "International Organizations" as "PanAmerican Society for Pigment Cell Research (PASPCR)". Here you have access to past PASPCR Newsletters, the current ByLaws and membership list. We are currently working with the IFPCS to develop a list of resources available to PASPCR members. This list will include cell lines, antibodies, coat color mutants and other items of interest to pigment researchers. If you have any other ideas for items to be placed on Gopher, please contact someone on the Newsletter Publishing Committee.

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--- enclosure: IFPCS DataBase Form ---

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## Calendar of Events :

***Dec 9 - 10, 1994*** Annual Meeting of the Japanese Society for Pigment Cell Research, to be held in Tokyo, Japan (contact: Dept of Dermatology, Nihon University School of Medicine, FAX: 81/3/5995-9841)

**Dec 10 - 14, 1994** 34th Annual Meeting of the American Society for Cell Biology, to be held in San Francisco, CA (contact: ASCB National Office, phone: 301/530-7153)

**Feb 22 - 25, 1995** 2nd International Conference on Advances in the Biology and Clinical Management of Melanoma, to be held in Houston, TX (contact: MD Anderson Cancer Center, Conference Services, 1515 Holcombe Blvd, Houston, TX, 77030-4095, phone: 713/792-2222)

**Mar 18 - 22, 1995** Annual Meeting of the American Association for Cancer Research, to be held in Toronto, Canada (contact: AACR National Office, FAX: 215/440-9313)

**May - , 1995** Melanoma '95, to be held in Brighton, United Kingdom (contact: Dr. N. Kirkham, Histopathology, Royal Sussex County Hospital, Eastern Road, Brighton BN2 5BE, UK, phone: 44/273-696955)

**June 25 - 28, 1995** VIth PASPCR Annual Meeting, to be held in Kansas City, Kansas, (contact: Dr. Sally Frost-Mason, Department of Physiology, University of Kansas, 3038 Hayworth Hall, Lawrence, KS 66046-2106, FAX: 913/864-5321)

**Oct 29- Nov 3, 1996** XVIth International Pigment Cell Conference, to be held in Anaheim, California, (contact: MMC/UCI Center for Health Education, P.O. Box 1428, Long Beach, CA 90801-1428, FAX: 310/933-2012)

## Welcome to New Members

**by Richard A King**

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

Marcus Boehm
Robert M. Hoffman
Anthony J. Nappi

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

## Corporate Sponsors

**by Richard A King**

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.

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## 1994 Council Elections

The following members (listed below in alphabetical order) are candidates on the 1994 ballot for three 3 year Council positions open beginning January 1, 1995. You should have received your ballots in the mail by this time and we would encourage all members to vote in this election; ballots must be received in the PASPCR Secretary/Treasurer's office by December 15, 1994. The results of the election will be listed in the next issue of the PASPCR Newsletter (January, 1995).

Miles Chedekel
Magdalena Eisinger
Bryan Fuller
Ruth Halaban
Alan Houghton
William Oetting
Walter Quevedo

## Letter from the President :

**by Vincent J Hearing**

As of the end of 1994, my term as President will be already 2/3 over and the time has flown by (at least for me - it may seem like I have been here forever to many of you)! I would like to take this opportunity to thank all of you in the Society for your outstanding support, especially to thank the Officer and Council Members of the **PASPCR**, who have worked extremely hard over the past couple of years to get our various programs underway. We have established a lot of new initiatives (including this Newsletter) that require a lot of work, and as any of them will readily tell you, I have no problem in delegating such work to others.

The **PASPCR** has a lot to be proud of and thankful for. Our numbers have now increased to about 140 and continued growth seems inevitable. I would encourage each of you to actively recruit more researchers in the field to get involved in the **PASPCR**. You will notice from our list of members (an updated list will be published in the next issue of the Newsletter) that there are still many in the field who should belong but as yet do not. A simple contact is usually all that is needed to make them aware of the **PASPCR**, our activities, and the dates and times of our Annual Meetings. We will all certainly benefit from the addition of new members and there can be no doubt that new recruits will also certainly benefit from interaction with us. It only takes attendance at one of our Annual Meetings to see the enthusiasm, support, collegial atmosphere and scientific interactions that are generated among our members.

We can also be very proud of our Society's encouragement of young investigators in the field. To date, the **PASPCR** has spent over $17,000 in travel stipends to allow students and young investigators to attend our meetings - this is a dramatic achievement for such a small Society to accomplish within a half-dozen years. The foresight and goals of our founding Officers and Council Members (especially Jim Nordlund and Dick King), who set realistic but noble directions for the **PASPCR,** have continued to encourage the development of young researchers in the field. To this end, the **PASPCR** has concurrently already awarded 14 Young Investigator Awards, along with almost another $3,500 in prizes, to outstanding young scientists who present their work at our Annual Meetings. This investment in pigment cell research will be paid back to us many-fold in the future.

During this same time frame, the **IFPCS** has surfaced to become a functional entity; there are a number of new programs that the **IFPCS** is initiating that you will be hearing about in the coming year and I would encourage everyone to support those as much as possible. Along with Pat Riley and Takuji Takeuchi, I have been involved in establishing a DataBase for Pigment Cell Research that should prove to be highly useful to all of us within the next year or so. Please take a few moments to fill out the form (cf the copy within this Newsletter) and send it in so that all Pigment Cell Research resources will be included in that DataBase. Information will be forthcoming on how you will be able to access that DataBase (on the Internet as one example), but it will only be useful if everyone takes the time to contribute relevant information.

I feel that the road ahead of us as a Society is relatively smooth. So far we have had 5 annual meetings - each better than the last. Our most recent meeting in Philadelphia was an outstanding one from scientific and social viewpoints, and next June in Kansas City should continue that trend - please plan to attend. The year after that is the IPCC in Anaheim, and it is already shaping up to be the best IPCC yet; you can rest assured that the **PASPCR** is playing an active role in ensuring the financial and scientifice success of such meetings and we hope to see you and hear about your research at both of them.

Finally, although I have but a single year left before turning the reins over to the very capable hands of Sally Frost-Mason, I would like to encourage all of you to become even more interactive in your Society. If you have new ideas about other ways the **PASPCR** can help each of us further our research potentials, please let me know. I welcome your input - there is still a year left for me to actually accomplish something, and I am sure that Sally will be anxious to take the **PASPCR** to even new heights beginning in 1996. Let me take this opportunity to wish all of you a very happy and safe holiday season, and a prosperous and successful New Year.

## 1995 PASPCR VI$^{th}$ Annual Meeting Site : **by Sally Frost-Mason**

Update - Sixth Meeting of the PASPCR, June 25-28, 1995, Kansas City, MO

Plans continue to evolve for the Sixth Meeting of the PASPCR. First announcements were mailed out in October, and response thus far has been strong, with many requests for additional information having been received by the planning committee. If you did not receive a first announcement and

would like more information about these meetings please contact Sally Frost-Mason at (913)864-3661, FAX (913)864-5331, or email: sfm@clasmain.clas.ukans.edu.

The scientific program for these meetings will be highlighted by keynote talks by Roger Cone, Garth Nicholson, and Shirley Tilghman. Symposia complementing each of the research areas addressed by the keynote speakers are being organized, and minisymposia on a variety of subjects are also planned. There will be posters with ample time for display and discussion and many opportunities for informal interactions at these meetings.

The meetings will be held at the Ritz-Carlton Hotel on the Country Club Plaza in Kansas City, Missouri. This elegant hotel is within walking distance of many fine restaurants, shops, and museums, so participants should be encouraged to bring family and friends to enjoy the festivities.

Planned activities will begin Sunday evening with a poolside reception at the Ritz. On Monday evening come prepared to join the fun as we will be heading out to the Benjamin Ranch on the outskirts of KC. There we will be treated to a meal including barbecue chicken, pork ribs, and beef brisket with a selection of KC's finest barbecue sauces. After dinner we can all unwind to country western and contemporary music and dancing and, for those who are not experienced at this, a dance instructor will be on hand to help us all line dance. Not a dancer? Not to worry! You can try your hand at steer roping on the steel horse or the cow chip toss (using the "real thing"). A gypsy fortune teller will be on hand to predict you chances on that next grant renewal! The bar will be open all evening. The atmosphere at the ranch is relaxed and casual, and if you own cowboy boots don't forget to bring them along.

Tuesday evening you may wish to go on a Kansas City Jazz Pub Crawl and experience jazz at its finest at three of the local establishments famous for their live entertainment. Or perhaps you would like to spend an evening on a riverboat gambling. Or maybe at the end of two long days you'll choose a relaxing evening in one of Kansas City's fine restaurants and bars located on the Plaza near the Ritz.

Whatever your preference, we hope you will join us in Kansas City in June. The science should be superb and the activities are bound to be fun!

## XVI IPCC (International Pigment Cell Conference) by Roger Bowers, Frank Meyskens

The XVI$^{th}$ International Pigment Cell Conference will be held from October 29th to November 3, 1996 at the Disneyland Hotel in Anaheim, California. Frank Meyskens is the Organizer of this meeting with Roger Bowers and Alistair Cochran serving as co-chairs of the Organizing Committee. More information regarding this meeting (and its interesting venue) will be forthcoming in future Newsletters and in separate mailings. Dr. Meyskens has asked that the following announcements be included in our Newsletter.

**Satellite Conferences**: No satellite conferences will be supported by the local organizing committee that are held within the time frame of the XVIth International Pigment Cell Conference, Tuesday, October 29, 1996; 6:00 pm to Sunday, November 3, 1996; 8:00 am. There are a wide number of venues possible to hold small or large satellite conferences either before or after the main pigment cell meeting. Our Memorial/UCI Educational Foundation will be happy to work with you in planning, for a small fee, and we request that we be notified of the intent of any satellite conference no later than June 1, 1995. If we are notified later than this date, accommodations and planning availability cannot be guaranteed.

**Competitive Stipend for Travel Support**: The Organizing Committee will provide funds in a competitive manner for graduate students, post-doctoral fellows and those within five years of formal academic appointment. The number of stipends will depend on the availability of funds and further information will become available during the second and subsequent informational mailings.

## Future PASPCR Meeting Sites ?

**by Vincent Hearing / Richard King**

The VIth Annual Meeting of the **PASPCR** is set to be held in Kansas City in June, 1995 (cf above) and the following year the XVIth International Pigment Cell Conference will be held in Sept, 1996 in Anaheim. We will soon be considering sites for our 1997 and 1998 PASPCR annual meetings (1999 will be another IPCC). The **PASPCR** Council would like to receive applications from those interested in hosting future meetings, and all such applications must be received in the **PASPCR** Secretary/Treasurer's office by January 1, 1995. That application should state the proposed time for the meeting (we traditionally have them in June), the proposed location for where it would be held, what type of funding support could be, or has been, obtained, points of scientific emphasis for the meeting and any other information you think relevant. Please contact Dr. Richard King (Secretary/Treasurer) for more information. The **PASPCR** Council will discuss and potentially approve 1 or more future meeting sites early next year, so all interested parties should be sure the relevant paperwork is complete in his office by the first of the year.

## PASPCR Secretary / Treasurer's Report :

**by Richard A King**

Following is a synopsis of the PASPCR Council Meeting held at the Wyndham Franklin Plaza Hotel in Philadelphia on June 26, 1994. . . .

Hearing opened the meeting and a quorum was declared present. The minutes of the telephone Council meeting on May 5, 1994, were approved. King, Treasurer, reported that the total revenue for 1993 was $14,211.54; total expenses for 1993 were $12,099.87, and the balance for the Society on December 31, 1993, was $26,335.04. The treasurer's report was accepted.

Frost-Mason, chair of the the Nominating Committee, requested suggestions for future honorary members and for the Career Achievement Award for the next annual meeting. She also noted that the 1995 elections will include the offices of President-elect, Secretary-Treasurer and three council positions. The issue of having the Secretary-Treasurer term longer than two consecutive three-year terms was raised and it was noted that the bylaws explicitly state a limitation of two consecutive three-year terms for this position. Townsend, chair of the Publications Committee, reviewed the mechanism for publishing the Newsletter and suggested that a post card could be sent to the membership requesting information for the newsletter. It was also suggested that the Newsletter indicate all awards, honorary members and nominations for Council positions. Pawelek, chair of the Membership Committee, circulated a draft membership brochure. Frost-Mason discussed the next PASPCR meeting to be held in Kansas City on June 25-28, 1995. Hotel costs will be $115/night plus tax per room. The theme of the meeting will be Cell and Developmental Biology, and the plans include three major symposia and eight smaller symposia. The local organizing committee consists of Frost-Mason, N. Mason and two University of Kansas faculty and a program committee will be organized in the near future. It was noted that a representative of the Lawrence Gelb Research Foundation should be involved in the selection of the Gelb Lectureship speaker.

Cochran reviewed the plans for the Anaheim IPCC meeting on October 29-November 2, 1996. The two themes of the meetings are (1) Living with the Sun, Melanin and Society and (2) Molecular Biology of the Melanocyte. The scientific advisory board consists of F Meyskens, R Bowers, A Cochran and additional members from the PASPCR, ESPCR and JSPCR. R Boissy and S Orlow were nominated for the PASPCR. A special feature of the IPCC meeting will be the availability of competitive stipends for the graduate students and post-docs. The meeting will start on Tuesday evening, October 29 with a theme of applied photobiology. Wednesday, October 30 and Thursday, October 31, will have meetings through the day. Friday, November 1, will have meetings in the morning and social activities in the

afternoon. The conference banquet will be held on Friday night. Saturday, November 2, will have meetings in the morning and an afternoon multi-disciplinary educational forum. Other related meetings will follow on Sunday. An early deadline for abstracts is planned (March, 1996). Financial support for the meeting to date includes $10,000 from the PASPCR and $12,000 from the IFPCS. It was decided that it should be a goal to publish the proceedings and that the expenses for the publication of the proceedings be included in the registration fee for the meeting.

Under old business reviewed, King reviewed the request to establish an Emeritus or Senior membership category and agreed to draft a proposal for discussion at the next council meeting.

Under new business, Hearing reviewed the need for guidelines for PASPCR sponsorship of various meetings, and he and King agreed to draft a set of guidelines for review at the next council meeting.

The minutes have been prepared by R. King, Secretary-Treasurer

## Meeting Report : by George J Hill, Helene Z Hill, Seth J Orlow

**5th Annual Meeting of the European Society for Pigment Cell Research**

**Vienna, Austria October 19-22, 1994**

The 5th ESPCR meeting was held in the historic Hofburg Palace in Vienna. Participants came not only from all over Europe but from Asia and America as well. The program was divided into three themes: I. melanin and melanogenesis, II. benign and malignant melanocytes, and III. melanoma and its treatment. The abstracts of the meeting were published in Vol 4 Suppl 3 of Melanoma Research (September 1994).

**Symposium I. Melanins and Melanogenesis**

B Larsson (Sweden) discussed the classical interactions between melanins and various drugs and metals. Although most binding is electrostatic, for some molecules hydrophobic and van der Waal's forces also play a role. The chemistry of extracutaneous melanins (specifically neuromelanin) was reviewed by M D'Ischia (Italy). G Prota (Italy) summarized the state of investigations concerning melanin's photoprotective effects. Although clearly photoprotective, under some circumstances certain melanins themselves appear to pose a risk. A plea for studies comparing the epidemiologic effects not only of melanin quantity but also of melanin quality was made. Such studies are made possible by modern techniques of melanin chemical analysis.

Studies involving the transfection of genes encoding members of the TRP family, alone or in combination, into nonmelanocytic cells (fibroblasts) were reviewed by H Rorsman (Sweden). By allowing the study of each TRP in isolation, individual enzymatic activities and inter-TRP interactions can be addressed. The (controversial) findings attributing dopachrome tautomerase activity to TRP-1 were reviewed. SJ Orlow (USA) summarized the current state of knowledge regarding the melanosome's biogenesis and structure. New melanosomal membrane proteins (*p* locus) and matrix constituents (*silver* locus) have now been identified. The bipartite theory of melanosome biogenesis deduced from EM studies is supported by modern cell biologic investigation. Melanosomes appear to be specialized lysosomes; their acidic interior pH may be critical for proper melanin synthesis and deposition. An overview of growth factors which act upon melanocytes and the signed transduction pathways they activate was presented by S MacNeil (UK). The combination of reduced intracellular calcium and elevated cyclic AMP lead to increased pigmentation. Nonetheless, it has been difficult to explore the effects of MSH *in vitro*. It was emphasized that the extracellular matrix likely is critical to controlling the cell's state of responsiveness, and that we need to better recreate the melanocyte's natural environment *in vitro*. Continuing in the same vein, B Gilchrest (USA) analyzed the central role of the protein-kinase C pathway. Paracrine pathways linking melanocytes and keratinocytes continue to unfold. The interaction between melanocyte and extracellular matrix (ECM) was again picked up by J Smolle (Austria), who emphasized the importance of stromal interactions in melanoma invasion.

**Symposium II. "Benign and Malignant Melanocytes"**

The first session was chaired by H Kerl of the University of Graz, Austria. In his Introductory Lecture on "Moles -- Typical and Atypical," Kerl pointed out that it is more important to understand the biological behavior of melanocytes and melanoma tumor cells than to be concerned about terminology.

However, standardized language is important. He argued that the NIH Consensus Development Conference in 1992, which proposed to abandon the term "dysplastic nevus" in favor of such terms as "atypical mole" and "nevus with architectural disorder," did not produce an improvement in language. In fact, the designations of the NIH Consensus Development Conference are "not precise and lack any meaning." The discussants of Kerl's paper agreed with him. H Luther, et al, from the Ruhr-University, Bochum, Germany, studied 866 children aged 1-7 years and restudied 377 of them five years later, evaluating skin type, environment, life style, and nevus development. Children with skin types I and II who had repeated holidays in Mediterranean climates had a significant increase in the number of melanocytic nevi. HP Soyer, et al, of the University of Graz, reported on the diagnostic reliability of dermatoscopic criteria for detecting melanoma. They studied 159 pigmented skin tumors, including 65 melanomas, 100% of which were diagnosed correctly with their dermoscope. "Whitish veil," irregular pigment network, and irregular extensions were important criteria which were not readily apparent to the unaided eye. U Mossbacher reported for the University of Vienna's Department of Dermatology on the computer assisted estimation of volume weighted nuclear mean volume (Vv) to discriminate Spitz's nevus from melanoma. Her co-authors were A Steiner and M Binder; and the organizers of this conference, K Wolff and H Pehamberger. The mean Vv of melanoma was about twice that of the Spitz nevus, a highly significant difference. J Bhawan of Boston University, USA, spoke about MEL-5, a novel antibody, in the differential diagnosis of pigmented skin lesions. MEL- 5 is available from Signet Laboratories, Dedham, Massachusetts. In his experience, "This antibody is consistent in detecting normal or atypical melanocytes in the epidermis." Sensitivity, specificity and accuracy were not discussed. G Ghanem reported on the experience in his laboratory at the Free University of Brussels, Belgium, on modulation by cAMP of adhesion molecules expressed on human umbilical vein endothelial cells (HUVEC) and melanomas. cAMP stimulated ICAM-1 expression on HUVEC cells, but it reduced the constitutive expression of ICAM-1 and its stimulation by tumor necrosis factor-α (TNF-α) on melanoma cells. Kerl's group at Graz reported that both benign and malignant melanocytic lesions reacted selectively with a secretogranin IV (HISL- 19) monoclonal antibody, providing additional evidence for the neuro- endocrine origin of melanocytes, and possible clinical implications of this from a functional point of view. ML Stracke of the National Cancer Institute, Bethesda, USA, reported on the discovery, purification, and activity of a new autocrine mobility factor, antotaxin (ATX). Her colleagues were J Muratta, S Aznavoorian and LA Liotta. ATX is a 102 kD protein that is sensitive to pertussis toxin, indicative of a G-protein-linked cell surface receptor. ATX has 45% amino acid identity with PC-1, a pyrophosphatase/Type I phosphodiesterase expressed on the surface of activated B cells and plasma cells. She made a convincing argument that ATX represents a new class of ectokinases that play an important role in tumor cell motility, and thus in the growth and metastasis of tumors. There are profound therapeutic implications from this work.

The second session of the morning program was chaired by W Westerhof of the University of Amsterdam, The Netherlands. In his introductory lecture, he described four phases of melanin pigmentation of the skin: (1) pigment metabolism; (2) melanosome transfer to keratinocytes; (3) distribution of melanocytes per $mm^2$; and (4) occurrence of dermal pigment. PD Das from Westerhof's group at the University of Amsterdam discussed the involvement of T-cells in vitiligo. He showed immunohistochemical evidence for a "hit and run" mechanism to explain the disappearance of T-cells after reacting with local melanocytes. This is consistent with the hypothesis that autoimmunity is the cause of destruction of melanocytes in vitiligo. A Norris of AJ Thody's group at the University of Newcastle upon Tyne, UK, showed that expression of the tyrosine kinase receptor, c-kit, by melanocytes may be downregulated in vitiligo. They used MEL-5 antibody, described above. Their studies of MGF and TRP-1 suggest that this approach may be a useful way to unravel the mystery of vitiligo. M Picardo, et al, of the University "La Sapienze," Rome, Italy, studied free radical scavenger levels in melanocyte cultures, because of the current belief that oxygen radical species (ROS) may play an important role in various pigmentary disorders. They studied superoxide dismutase (SOD) and catalase (CAT) activity, intracellular vitamin E, and membrane fatty acids. Their results indeed suggest that an imbalance of antioxidant defenses may be related to the occurrence of some clinical pigment cell disorders. In a second paper these authors found reduced glutathione (GSH) and ubiquinone levels, associated with UVB-induced oxidation of skin lipids, and important effects of generated toxic byproducts on normal human melanocytes in culture. EB Bröcker, W Dummer, and JC Becker, of the University of Wurtzburg, Germany, studied immune escape mechanisms in human melanoma, and found (1) antigenic heterogeneity in melanoma; (2) downregulation of MHC Class I antigens during progression of melanoma; (3) ICAM-1 shedding by melanoma cells that blocks NK and T-cell killing; (4) cytokines from melanoma cells that downmodulate MHC expression; and (5) failure of melanoma cells to express the B7 signal that activates CD4+ T clones in response to their MHC-Class II antigens. JF Dore reported for AJ Cochran's group at the University of California at Los Angeles, USA, and Lyon, France, that human melanoma cells with high metastatic potential bind the lectin peanut agglutinin. This is a potentially important biological marker of poor prognosis, and may provide a therapeutic opportunity as well. A group of investigators at the University of Uppsala, Sweden (A Platz, E Grafström, B Lagerlöf, B Mannervik, and U Ringborg) showed a correlation between glutathione-S-

transferase and N-ras mutation and expression in melanoma metastases. Elevated GST-Pi expression was coincident with altered N-ras expression, suggesting co-regulation *in vivo*, which may have important prognostic and therapeutic implications.

**Symposium III. "Melanoma and Its Treatment"**

The first session was chaired by the Secretary General of the 5th Meeting of the ESPCR, H Pehamberger. Pehamberger spoke about epiluminescence microscopy (ELM) and showed many beautiful slides to illustrate the value of ELM and the difficulty that may be encountered when non-experts, or non-trained clinicians, attempt to use ELM. In an accompanying lecture, his colleague, M Binder, showed a sensitivity of 98% for the detection of melanoma with ELM by trained dermatologists. R Böni, et al, from the University of Zurich, Switzerland, showed an impressive 100% sensitivity for the detection of metastases of melanoma of 5mm or greater using a ($^{18}$F)FDG wholebody PET scanner. V Vormwald-Dugan and her colleagues at the University of Heidelberg, Germany, found melanoma cells in the blood of 95.4% of 51 patients with Stage IV melanoma, using PCR technology. They also found positive PCR results in the blood of less advanced patients who had various poor prognostic signs, which suggests that this technique may be useful to identify patients who should be entered onto adjuvant therapy protocols. From the University of Glasgow, Scotland, MK Lingam reported for himself and RM MacKie and AJ McKay, that 0.5-1.0 ml of intradermal patent Blue V dye injected near a melanoma or excision scar is rapidly picked up in the primary draining lymph node (sentinel node), which is a great help to the surgeon and pathologist, for staging and for therapy. They found the sentinel node in 100% (33/33) of patients; 8 were found to contain previously unsuspected micrometastases. B Partsch reported for the University of Vienna group that ultrasound measurement of the thickness of cutaneous melanoma differed from histologic measurement in many cases, by 37% above to 48% below in 95% of cases, and they concluded that sonometry lacks the accuracy reported by others. K Wolff, President of the 5th ESPCR Meeting, and H Pehamberger, Secretary General of the meeting, were co- authors of this report. IH Wolf, et al, from the University of Graz, reported a surprising finding when they studied sensitivity in the clinical diagnosis of melanoma. Sensitivity for diagnosis was best in some groups, e.g. older patients, males, and intermediate thickness melanomas, up to 90.2%. But sensitivity was lower for melanomas thicker than 4 mm (64.8), suggesting that large melanomas may be misdiagnosed clinically, even by experts. G Stingl of the University of Vienna reviewed immunotherapeutic strategies for melanoma and presented his very interesting work with a vaccine produced with IL-2-transduced clone M-3 of Cloudman S91 melanoma cells. His work is nearly ready for clinical trials and generated considerable excitement.

The second session was chaired by M Santinami and C Garbe. The University of Milan experience with systemic therapy of melanoma was reviewed by M Santinami, who reported that they are now seeing a 40% response rate with CVD (cisplatin, vindesine, and dacarbazine). They are optimistic about adding αIFN plus IL-2 to this combination, for patients with metastatic melanoma. C Garbe of the Free University of Berlin, Germany, reviewed their very extensive experience in patients with disseminated metastases of melanoma. They followed 261 patients from 1970 to 1993 and analyzed the outcome from the perspective of treatments used and various prognostic factors. They found a significant prolongation of survival for each of three treatment protocols in 88 patients compared with no treatment in 173 patients ($p<0.01$). Two of the treatment protocols were DTIC-based chemotherapy, and one was IFN-α plus Vindesine. They reported that although treatment is beneficial in improving the length of survival, only 2/261 patients survived longer than 5 years, and curability of disseminated melanoma has not yet been achieved. Dr. A. Davis-Daneshfar, et al, from the University of Zurich, Switzerland, found a surprisingly high (36%) rate of antibodies against recombinant interferon-α (rIFN-α) during immunotherapy for melanoma, which may be an explanation for the failure of rIFN-α therapy in some cases. MK Lingman reported on the experience of the University of Glasgow, Scotland, with isolated limb perfusion in recurrent or poor- prognosis melanoma confined to an extremity. Their experience with 103 patients treated since 1983 showed excellent short term success (no limb loss and no mortality due to perfusion). 75% and 48% had CR to the first and second perfusions, respectively. Unfortunately, only 14/103 of their patients are alive and disease free at this time. E Link from the University College Medical School, London, UK, reported her experience with $^{211}$At-methylene blue (MTB) for therapy of murine melanoma. Her paper showed that methylene blue binds well to melanin, and that, in mice, $^{211}$AT-MTB can have a profound beneficial effect. Fortunately, radio-labelled MTB does not appear to be toxic for the eye and other melanin-containing tissues. The Glasgow group reported their work with $^{125}$I-radiolabelled MTB treatment of B16/F10 melanoma in mice in a poster presentation. They reported a delay in tumor growth, and they speculated that this may be a "clinically possible" approach to therapy. T Myer, et al, from the University of Regensberg, Germany, presented a new and potentially valuable model system for evaluating new agents for therapy of melanoma, using a crystal violet microassay *in vitro* followed, for favorable agents, by testing on human xenografts in NMRI nude mice. MJ Wagner, et al, from the University of Sheffield, UK, reported that tamoxifen inhibited the adhesion of human uveal melanoma cells to extracellular matrices. This extends their previous observation with the B16 melanoma. It provides additional

support for the use of tamoxifen in therapy of melanoma, consistent with observations reported recently by several other groups.

**PhotoProtection**

The photoprotection session was preceded by an enlightening talk by B Gilchrest of Boston University School of Medicine. She has shown that pigment synthesis in melanocytes *in vitro* and in guinea pigs in vivo is activated by the β-isoform of protein kinase C. Expression of this enzyme in humans is related to skin type. Furthermore, pigmented melanocytes and a non-pigmented derivative express high and low PKC-β respectively. The activity of tyrosinase and its phosphorylation increase in parallel with PKC-β after exposure of the cells to phorbol ester. Electron microscopy of differentially tagged tyrosinase and PKC-β reveals their co-localization on the melanosome membrane. Gilchrest's research has also shown that melanogenesis is stimulated by DNA repair. Incubation of UV-irradiated melanocytes with T4 endonuclease, an enzyme that catalyzes the first step in excision repair, increases survival and enhances melanogenesis. Furthermore, cells exposed to pTpT encapsulated in liposomes showed enhanced tyrosinase activity and pigmentation when compared to controls or similarly encapsulated pdApdA dimers. Since pTpT also caused guinea pig skin to tan, she speculates it might be useful in the future in photoprotection of human skin. A Young introduced the topic of photoprotection with a discussion of its various aspects. These include genetic: i.e. light skin versus dark skin; repair capacity; immunocompetence; morphological changes e.g. stratum corneum thickening; and behavior. His experiments clearly demonstrate histologically pigmentary increases in solar simulator irradiated type I and type II skin but this affords little protection. Repeated daily exposures of sub- erythema doses to types III and IV skin is only protective by a factor of 2. Young cautioned that sunscreens may protect against erythema but they are less effective at protection of damage to DNA and their effectiveness against human skin cancers is still not known. Furthermore, the false sense of security they impart encourages people to spend more time in the sun than they would without screens. A direction for the future might be photochemo-protection. Experiments with human volunteers treated chronically with suberythemal solar simulated light demonstrate that application of 5-MOP and sunscreen was more protective than sun screen alone. With such a regimen, skin types I through IV were protected as opposed to skin types I through III with sun screen alone. 5-MOP and sunscreen are more effective at reducing DNA damage. During the discussion that followed, Young acknowledged that, in a randomized study in Australia, sunscreens reduced the number of solar keratoses in volunteers. This study suggests that sunscreens may be effective at reducing solar-induced skin cancer. The co-chairman of this session with Young was H Honigsmann of the University of Vienna. His goal is to reduce solar induced skin reactions in such conditions as polymorphous light eruption. To accomplish this, his patients are treated with PUVA which uses UVA doses that are considerably lower than those that elicit blistering. The treatment is effective for several months. The pigmentation induced by PUVA appears to be the key in the therapy. PUVA is also effective in some cases of vitiligo. The mechanism is not known but several models are proposed: activation of dormant melanocytes, stimulation of melanocytes to migrate into the depigmented area, alteration of immune responses and/or release of cytokines in neighboring areas. H Hill reported on the effects of near-monochromatic UVC, UVB, UVA and polychromatic FS20 lamps on survival (colony forming ability) of two Cloudman S91 mouse melanoma cell lines that differ in constitutive pigment. The more pigmented line was more sensitive to killing by all three monochromatic lamps, but was less sensitive to killing by the FS20 lamp than the less pigmented cells. Hill cautioned that, when dealing with effects in pigmented cells, extrapolations from monochromatic effects to polychromatic and solar expectations must be done with caution. A Thody and his group have examined the effects of reactive oxygen species (ROS) on survival of pigmented and non-pigmented cells evaluated using the MTT assay. Xanthine/xanthine oxidase was used to generate superoxide anion radical in tyrosinase$^+$ and tyrosinase$^-$ variants of B16 melanoma. The tyrosinase+ variant was less sensitive to killing. Inducing tyrosinase with an αMSH analog enhanced survival even further in the tyrosinase$^+$ line but had no effect on the tyrosinase$^-$ line. The protective nature of tyrosinase may be due to detoxification of superoxide anion radical by using it as a substrate to oxidize tyrosine and DOPA in the synthesis of melanin. During the discussion, T Sarna questioned whether superoxide anion radical could enter cells. Since hydrogen peroxide does not have an effect in this system, it was agreed that a mechanism for translocation of superoxide anion radical into the cells must exist. In the next paper, S Frank et al. from Padua and Leiden studied the effect of psoralen-fatty acid adducts on tyrosinase activity and melanin synthesis in human melanocytes. Their results suggest that PUVA induces hyperpigmentation by forming adducts between psoralens and unsaturated membrane fatty acids which in turn activate protein kinase C. Besson et al. from Bordeaux cultured keratinocytes and melanocytes and then reconstituted pigmented epidermis by cocultivation of these cells in dead deepidermized dermis. The reconstituted epidermis had a normal looking histology. The melanocytes were stimulated upon irradiation and transferred melanosomes to the keratinocytes. There were a number in interesting posters dealing with extra-cutaneous melanocytes. AM Meyer zum Gottesberge has cultured melanocytes from guinea pig ears and shown that melanosomes are associated with cytokeratin- 19

filaments. The group from Mucia had 3 interesting posters. In one they demonstrated that rodent eye melanocytes are similar to those in the epidermis. In a second, they reported the finding of an unusual tyrosine hydroxylase activity in gerbil melanocytes. Western blots were negative for TRP1, tyrosinase and DCT but positive for a 70 kD protein consistent with the MW of a melanoma tyrosinase. In their third paper, they demonstrated that gerbil inner ear melanocytes respond to injections of αMSH by increasing melanogenesis and by transferring melanosomes to neighboring cells.

## Members in the News

**Zalfa Abdel-Malek,** University of Cincinnati, has received funding from the NIEHS for her proposal entitled "Response of Melanocytes to UV Light is Mediated by MSH".

**Lisa Austin**, has graduated with a Ph.D. in Anatomy and Cell Biology from the laboratory of RE Boissy at the University of Cincinnati; she is currently obtaining her postdoctoral training in R Steinman's Laboratory of Cell Physiology and Immunology at the Rockefeller University.

**Diane Barker**, has graduated with a Master's Degree in Genetic Counseling from the laboratory of Z Abdel-Malek at the University of Cincinnati; she has recently married and will soon travel with her husband to St. Petersburg, Russia, where she will work in a molecular biology laboratory.

**Karen Bijwaard**, received her Master's Degree from the Department of Pathology, Georgetown University; she can be contacted by E-mail at: kbijwa02@gumedlib.dml.georgetown.edu.

**Ana Maria de Lauro Castrucci**, at the Dept. Fisiologica, Inst. Biociencias, can be contacted by E-mail at amdlcast@cce.usp.br

**Jamal Farooqui,** has received funding from the NIH for his proposal entitled "Proopiomelanocortin Expression in Human Epidermis".

**Estela Medrano**, has accepted a tenured position as Associate Professor of Cell Biology at the Huffington Center on Aging, with a joint appointment in the Department of Dermatology at Baylor College of Medicine.

**Seth Orlow**, presented an invited lecture entitled "The Biogenesis of Melanosomes: Implications for the Biologic Basis of Melanization" at the Fifth ESPCR meeting held in Vienna

**William Pavan,** has moved from Princeton University to the National Institutes of Health; his address is Bldg 49 Rm 4A66, NIH, Bethesda, MD 20892 USA, FAX: 301/402-2170; phone 301/402-2036

**Susan Porter**, at the University of British Columbia, can be contacted by E-mail at susan_porter@academic.pathology.ubc.ca

## Positions - Wanted and Available :

Opportunity available to do graduate studies towards a doctoral degree at the University of Cincinnati College of Medicine. Graduate program is through the Department of Cell Biology, Neurobiology, & Anatomy. Dissertation project would focus on molecular biology of the melanocyte physiology and pigmentary diseases. For information contact: Raymond E. Boissy, Ph.D., Department of Dermatology, University of Cincinnati College of Medicine, 231 Bethesda Avenue ML-592, Cincinnati, Ohio 45267-0592; (513)558-6242 [TEL]; (513)558-0198 [FAX]; boissyre@ucbeh.san.uc.edu [eMAIL].

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The Bibliography published in this issue covers the period August through October, 1994. 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.

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