



# PASPCR

## Newsletter

Volume 5 Number 1

March, 1997

### Introduction . . .

by the Publications Committee

The PASPCR Newsletter is published quarterly and is intended to serve as a means of communication for members of our Society. As such, we invite our members to contribute to the Newsletter; help us to update the Job Listings, Calendar of Events, Meeting Reports, Abstracts in press and other items of general interest. If you attend a scientific meeting at which you heard presentations of interest to PASPCR members, 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 any of the members of the Publications Committee.

: : : : REMINDER : : : : Providence PASPCR Meeting Abstract Deadline - - - MARCH 12th : : :

WorldWideWeb Pages for the PASPCR. The PASPCR now has its own WWW home page. We plan this to be a major source of information for the PASPCR membership. The address is: <http://lenti.med.umn.edu/paspcr>. This site contains information on the goals of the society, future meetings, council information, past issues of the PASPCR newsletter as well as links to other sites including the InterPig DataBase, past and future International Pigment Cell Conferences (IPCC) and the International Federation of Pigment Cell Societies (IFPCS).

We have now included the membership directory on that page; please notify us if you wish any or all of your information to be deleted or modified on that site.

Please check out the PASPCR web site and send any comments and/or suggestions to either the PASPCR WebMaster Bill Oetting at [bill@lenti.med.umn.edu](mailto:bill@lenti.med.umn.edu) or to Vince Hearing at [hearingv@dc37a.nci.nih.gov](mailto:hearingv@dc37a.nci.nih.gov).

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**Calendar of Events :**

**Apr 23 - 26, 1997**

Society for Investigative Dermatology Annual meeting, Washington, DC (contact: the SID, Suite 500A, 1101 Cedar Ave., Cleveland, OH 44106, FAX: 216: 844-6859)

**Jun 10 - 14, 1997**

4th World Conference on Melanoma to be held in Sydney, Australia (contact: The Melanoma Foundation, PO Box M123, Camperdown, NSW 2050 Australia; FAX: +61 2/550-6316)

**Jun 15- 18, 1997**

VIIth PASPCR Annual Meeting, to be held in Providence, RI (contact: Dr. Walter C Quevedo, Jr., Brown University, Division of Biology and Medicine, Providence, RI 02912; FAX: 401/863-1971)

**Jun 22 - 24, 1997**

International Meeting "Pigmentary Disorders from a Global Perspective" to be held in Bali, Indonesia (contact: Bureau PAOG, Tafelbergweg 25, 1105 BC Amsterdam, The Netherlands; FAX: +31 20/696-3229)

**Aug 24 - 29, 1997**

International Congress of Biochem & Mol Biology with the Amer Soc for Biochem & Mol Biology, to be held in San Francisco, CA (contact: FASEB, 9650 Rockville Pike, Bethesda, MD 20814, USA; FAX: +1 301/530-7014)

**Oct 9- 11, 1997**

7th ESPCR Annual Meeting, to be held in Bordeaux, France (contact: 7th ESPCR Meeting Bordeaux, c/o Congres Seminaires Organisation, 81, Boulevard, Pierre 1er, 33110 Le Bouscat, Bordeaux, France)

**Dec 13 - 17, 1997**

American Society for Cell Biology Annual Meeting, to be held in Washington DC (contact: FASEB, 9650 Rockville Pike, Bethesda, MD 20814, USA; FAX: +1 301/530-7014)

**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)

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## Welcome to New Members

by James J Nordlund

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

**Jun-ichiro Hiraoka      Dan-Ning Hu      Toshihiro Shioda**

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.

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## Corporate Sponsors

by James J Nordlund

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***

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### ***Corporate Patrons***

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## PASPCR Council Election Results

by James J Nordlund

Congratulations to the new Council Members elected to 3 year terms . . .

**Gregory Barsh      Lynn Lamoreux      John Pawelek**

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## VIIth Annual Meeting of the PASPCR

by Walter Quevedo/ Hal Swartz

June 15th - 18th, 1997      The Westin Hotel      Providence, RI

The Organizing Committee for the 7th Meeting of the PanAmerican Society for Pigment Cell Research enthusiastically invites you to attend the Society's annual meeting this June 15th - 18th in Providence. The Westin Hotel is attractive to the eye and brought to life by a staff that is friendly, professional and efficient. Alistair Cooke has said that Spring in New England is one of America's great attractions. Come and enjoy it with us! We have attempted to supplement Mother Nature's visceral pleasure by providing challenge for the intellect as entertainment and refreshment for periodic relaxation of the mind and body. To get things started, the keynote speakers will provide the foundations for four important themes of the meeting: 1) The molecular biology of melanosome synthesis and function, 2) Novel approaches to the development of anti-melanoma vaccines and other treatments, 3) The origin, distribution and functional significance of ocular melanin, and 4) The nature and significance of programmed death (apoptosis) of normal melanocytes and melanoma cells. Symposia, mini-symposia

and workshops will reflect not only these themes but also those inclusive of the broadest interests of the Society's members. The Sunrise Teaching Sessions will permit individuals specialized in one approach to pigment cell research to gain basic access to the vocabulary, methods and concepts of fellow members taking other approaches. The Program Committee has emphasized the importance of providing opportunities for social interaction throughout the scientific sessions. Social activity beyond the Westin Hotel will include the Annual Reception/Banquet at the Brown Faculty Club noted for its architecture and kitchen. An optional outing to the Haffenreffer Grant of Mt. Hope for a "clambake" will provide an opportunity for a glimpse of the historic buildings of Providence and Bristol, Rhode Island. You might consider lingering in the area for a few days, for historic Newport, Rhode Island and Boston and Cape Cod, Massachusetts are within an hour's drive. The weather should be pleasant, neither too warm or too cool. So help to make the annual meeting a success by attending and actively participating in all of its functions.

For the Organizing Committee, Best Regards /s/ Walter Quevedo and Harold Swartz

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## **PASPCR 7th Annual Meeting**

June 15th - 18th, 1997      Westin Hotel      Providence, Rhode Island

Calling all members! Time is passing rapidly! In less than 4 short months the Annual Meeting will be in session. It is time to prepare to attend and to participate in all of its scientific and social activities. New features for this year's meeting include "sunrise teaching sessions" and NO parallel sessions! Please note the following important dates:

**March 12:** Deadline for submitting abstracts.(needed from all speakers, including invited and keynote speakers)

**March 12:** Deadline for voting for the course subjects of the "Sunrise Sessions"

**March 12:** Deadline for "Clambake/Steakfry" reservation (a good time at a modest price)

**May 14:** Deadlines for registration without "late payment charge" and for registration cancellation

**May 15:** Westin Hotel deadline for making room reservations at the special meeting rate

### **TENTATIVE PROGRAM**

#### **Sunday:**

12:00 - 2:00 pm Setup and First Formal Poster Viewing Session

2:00 - 6:00 pm Molecular aspects of Malignant Melanoma; (includes keynote talk): "Identification of Human Melanoma Antigens Recognized by Tumor Infiltrating Lymphocytes - Their Use for Immunotherapy"

6:00 - 7:30 pm Reception

7:30 pm - ??? Dinner (on your own)

#### **Monday:**

7:00 - 8:15 am Sunrise session #1 and continental breakfast

8:30 - 11:15 am Pigment Cell Genetics & Molecular Biology

11:15 - 12:00 am Keynote talk: Occurrence and Significance of Apoptosis among Melanocytes and Melanoma Cells

12:00 - 1:15 pm Poster Session #2 & Lunch (on your own)

1:15 - 3:45 pm Role of Melanocyte Death During Development and Adaptive Responses of Skin to Damaging Agents

4:00 - 6:00 pm Signaling Pathways in Pigment Regulation

7:00 - 10:00 pm "Clambake/Steak fry" (optional)

#### **Tuesday:**

7:00 - 8:15 am Sunrise session #2 and continental breakfast  
8:30 - 12:00 am Melanosomes: Biogenesis and Structure (includes Gelb Lecture)  
12:00 - 1:15 pm Poster Session #3 & Lunch (on your own)  
1:15 - 3:15 pm Comparative Aspects of Non-Mammalian Pigmentation  
3:30 - 6:00 pm Photobiology and Biophysics of Melanin and Melanocytes  
7:00 - 10:00 pm Banquet, Brown University Club

**Wednesday:**

7:00 - 8:15 am Sunrise session #3 and continental breakfast  
8:30 - 11:45 am Development, Regulation and Significance of Ocular Pigmentation (includes Keynote Lecture)  
12:00 - 1:00 pm Business meeting and presentation of awards

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**PASPCR Travel Stipend / Young Investigator Award Information**

**by James J Nordlund**

The next meeting of the PASPCR is not so far away, a little over 3 months. The ABSTRACT DEADLINE is March 12th for this meeting. Requests for travel support are due in the PASPCR Secretary/Treasurer's office by March 15th. Candidates to receive the Young Investigator Awards must be nominated and those nomination letters must accompany the submitted abstract.

· **Travel Awards:** Travel awards up to \$300 are given for students and new faculty needing assistance to attend the annual meeting of the PASPCR. The criteria require that the individual be a student, post-doctoral fellow or member of the faculty for less than 5 years. The candidates must be a coauthor on an abstract and preference is given to those presenting the abstract. A candidate can receive no more than three travel awards. Applications for Travel Stipends must be received in Dr. Jim Nordlund's office by March 15th to be considered.

· **Young Investigator Awards:** There are three young investigator awards, one for students, one for post-docs and one for young faculty (less than 3 years total as a member of a faculty). The award is given both for the work being presented at the PASPCR annual meeting and for other accomplishments. Nominations are made by preceptors and mentors or other individuals. The nomination form with criteria is included in your meeting announcement package. The nomination form must be completed and returned by March 12th with the submitted abstract to Dr. Walter Quevedo's office. An anonymous committee will select the winner who will be named at the meeting in Providence. All awards are not necessarily given each year.

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**Pigment Cell Research Wants YOU!**

**by James J Nordlund**

THE PRICE OF THE JOURNAL PIGMENT CELL RESEARCH COMES TUMBLING DOWN. Hope that the stock markets don't crash like the cost of our pigment journal. Your subscription to Pigment Cell Research will be about 45% less than in previous years. The real price was over \$200 but most were getting it at discount for about \$160. At the recent meeting in Anaheim, Munksgaard agreed to revise its pricing schedule for the journal Pigment Cell Research for Society members only. For an annual fee of \$95 total you can have your own copy of Pigment Cell Research, the official journal of the International Federation of Pigment Cell Societies.

You get a lot for this small price. For example, you will get the bimonthly issues of the latest and best of pigment biology. In addition you will get the proceedings of the meeting of the European Society for Pigment Cell Research to be held in France later this year. You will get the proceedings of the upcoming PASPCR meeting in Providence, RI under the chairmanship of Walt Quevedo. You will get the proceedings of the XVIth meeting including the abstracts and the published manuscripts.

We need everyone's support. We need to get most of the members subscribing to keep this journal flourishing. Joe Bagnara did a yeoman's job getting it up and started and Dr. Jiro Matsumoto is doing a great job making the issues bigger and better.

An application for the journal will be included with your dues statement for 1997.

**SUPPORT YOUR JOURNAL AND SOCIETY. SUBSCRIBE TO THE JOURNAL WHEN YOU  
RENEW YOUR MEMBERSHIP TO PASPCR.**

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**Meeting Report - XIth JSPCR Annual Meeting**

**by Yasuo Kubota / Jiro Matsumoto**

The XIth Annual Meeting of the JSPCR was held in Kawasaki, Japan from December 6th-7th, 1996. This meeting was organized by the Department of Dermatology, St. Marianna University School of Medicine with Prof Masako Mizoguchi as Chairman and Dr Yasuo Kubota as Secretary/General. The scientific program was composed of two Invited Lectures, one Special Lecture, five Research Seminars and 33 oral presentations. One of the major themes of this meeting was "Melanocyte differentiation and development" and most of the invited and special lectures were arranged along this line of thought.

**Invited Lecture 1** "Segregation of melanocyte precursors and regulation of their fate during neural crest development" **Dr James A Weston**, Univ Oregon, addressed that mouse melanocyte precursors (MPs) segregate from the neural crest as that subpopulation enters a migration staging area, takes the dorsal pathway to distribute in the dermal mesenchyme and then reaches the epidermal layer. During their development, MPs transiently require the function of c-kit and its ligand SCF. He presented data relating the expression of SCF mRNA in vivo by means of in situ hybridization.

**Special Lecture** "Life styles of pigment cells during embryogenesis and postnatal life" **Dr Nishikawa**, Kyoto Univ, presented data on the cellular and molecular basis controlling the proliferation and differentiation of mouse melanocyte precursors. Based on his own and other groups' studies, he addressed that a number of molecules have been expressed from the very early phase of melanocyte differentiation, and that using such molecules as probes, melanocyte precursors have been easily distinguished from other cells of neural crest origin. He concluded that the life styles of melanocytes were essentially determined by the microenvironment where they resided. In this connection, Dr Kunisada, a member of Nishikawa's group, reported in his oral presentation that in transgenic mice bearing mouse SCF-DNAs fused with the human cytokeratin 14 promoter, epidermal melanocytes consecutively proliferate and the whole skin is heavily pigmented, suggesting the importance of SCF for growth, differentiation and motility of melanocytes. They also discussed the accumulation of mast cells in the dermis and epidermis of these hyperpigmented transgenic mice.

**Invited Lecture 2** "Regulation of transcription in melanocyte differentiation and development" **Dr Colin Goding**, Marie Curie Research Inst, discussed the role of transcription factors in melanocyte development and differentiation based on his studies regarding identification and characterization of the sequences required for melanocyte-specific expression of the mouse TRP-1 and human tyrosinase promoters. He also discussed Brn-2 (POU domain transcription factor) and a bHLH-LZ protein associated with microphthalmia (Mi). The involvement of Brn-2 in melanocyte development was shown by deterioration of its function upon introduction of a double amino acid substitution to it. The ability of Mi for transcription activation was suggested to be regulated negatively by phosphorylation.

**In a Research Seminar**, **Dr Tomohisa Hirobe**, National Inst Radiological Sciences, summarized his recent findings on the proliferation and differentiation of mouse epidermal melanocytes following skin wound healing, indicating the combined roles of genetic and local tissue environmental factors. In combination with this seminar, Dr Rikako Furuya, Shiseido Research Center, reported her recent results on skin hyperpigmentation caused by UV irradiation as chronic effects, using melanocytes cultured from disaggregated epidermal cell suspensions of hairless mice (HR-1 x HR/De). Her conclusion was that the

chronic effects of repeated UV exposures on melanocyte proliferation and differentiation were associated largely with changes in the nature of keratinocytes.

**In another Research Seminar, Dr Saida**, Shinshu Univ, presented his concept on "Malignant melanoma (MM) in situ" and emphasized its significance in clinical and basic oncology. He reported several cases of MM in situ appearing in the sole and the nail apparatus and proposed that the concept of MM in situ and the theory of its de novo origin should have great impact on the early correct diagnosis of MM and the design of basic research on human carcinogenesis.

With regard to new melanogenic inhibitors, several papers were read before this meeting; **Dr Funasaka** from Kobe Univ reported the inhibitory effects of DL- $\alpha$ -tocopherol having an antioxidant activity on melanogenesis. Dr Eiichiro Yagi, Pharmaco Science Research Lab, reported that an extract of Cola de caballo, a plant grown in the Andes district, has dual inhibitory effects for melanogenesis and inflammation induced by UVB irradiation. Dr Tomohiro Yokota, Kanebo Cosmetics Lab, reported that glabridin in hydrophobic licorice extracts showed an inhibitory effect on melanogenesis and inflammation. He also mentioned the relationship between the structure of glabridin and these two different inhibitory functions.

As to the intracellular localization of post-DOPAchrome melanogenesis, **Dr Shinkichi Hatae**, Mishima Research Inst for Dermatology, suggested that melanin polymer by DOPAchrome reaction at GERL and coated vesicles is produced by tyrosinase via DHI and that premelanosomes could polymerize melanin monomer, DHI, independently from tyrosinase.

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## **XVIth IPCC (International Pigment Cell Conference) Program Summaries**

The XVIth International Pigment Cell Conference was held from October 29th to November 3rd, 1996 at the Disneyland Hotel in Anaheim, California. Frank Meyskens was the Organizer of this meeting with Roger Bowers and Alistair Cochran serving as co-chairs of the Organizing Committee. Following are synopses of the various remaining Symposia, Workshops and Poster Discussions written by Chairs of those sessions that arrived after the publication of the last Newsletter (all of these reviews are also now posted on our Web Site). The Editor conveys a special thank you to all contributors of these summaries.

### ***Symposium IV Photobiology of Melanocytes: Etiology and Prevention***

*by Lisa Zeise*

This session had six well-presented papers; however, the presentations would be greatly enhanced if attributes of the light sources used were mentioned.

**Nik Kollias:** "Photobiology of Human Pigmentation"- The keynote speaker presented a clear, concise review of the literature published on human pigmentation and its regulation. A technique known as laser scanning confocal microscopy (LSCM), was described. Melanin is a good contrast agent and has an index of refraction of 1.7. LSCM utilizes this information for application in viewing actively pigmenting cells. This technique is exciting and will aid in the study of human pigmentation formation in vivo.

**Yoko Funasaka:** "The effect of ultraviolet B induced adult T cell leukemia-derived factor on survival and growth of human melanocytes"- Adult T cell Leukemia-Derived Factor (ADF), a human homolog of thioredoxin, is induced by hydrogen peroxide and ultraviolet (UV) light, regulates gene expression, and scavenges reactive oxygen species to aid in protecting cells. This paper analyzed the effect of recombinant ADF (rADF) on normal human melanocytes and co-culture melanocytes and keratinocytes after UVB irradiation. ADF release was observed in keratinocytes but not melanocytes or fibroblasts after UVB irradiation. ADF was found to upregulate  $\alpha$ -MSH induced DNA synthesis, to strongly induce melanocortin 1 receptor after 24 h, and to sustain survival of both keratinocytes and melanocytes.

**Frank L. Meyskens Jr.:** "Expression of NK-kB/IkB/c-Rel in human melanocytes and melanoma cells: changes in association and dissociation"- Redox control in melanocytes and melanoma cells was studied by quantifying the presence of NF-kB (p50), IkB, and c-Rel (p75) in basal cells and UVB

stimulated systems. I $\kappa$ B and p50 were expressed more at the basal level in melanoma cells compared to melanocytes. UVB suppressed I $\kappa$ B levels but did not affect p50 levels in melanoma cells. In melanocytes, UVB increased both I $\kappa$ B and p50 levels. In contrast, basal p75 was increased in melanocytes and very low in melanoma cells. UVB also enhanced p75 in melanocytes; melanoma cells showed no difference. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), was generated with a glucose/glucose oxidase system and detected by chemiluminescence of luminal. Melanocytes and melanoma cells handled H<sub>2</sub>O<sub>2</sub> differently as evidenced by time course measurements. The closing question posed was, "Is this difference in the handling of H<sub>2</sub>O<sub>2</sub> due to the antioxidant ability of melanin?"

**Mauro Picardo:** "Alteration of antioxidants in normal melanocytes from patients with melanoma"- The role of free radicals in melanoma production was examined by the activities of superoxide dismutase (SOD) and catalase (CAT), the levels of vitamin E and ubiquinone, and the fatty acid pattern of cell membranes. Normal melanocytes and melanoma cells from the same patient were compared. CAT and SOD activities were higher in melanocytes. Melanoma cells exhibited lower CAT activity and a wide range of SOD activity. Melanoma cells had a higher concentration of arachidonic acid with respect to normal melanocytes. Levels of vitamin E were found to be inversely proportional to CAT activity. The ratio of vitamin E level to CAT activity was felt to correlate with antioxidant activity in cells. In melanoma patients, normal melanocytes were thought to exhibit an alteration in antioxidant pool, and thus, to exhibit increased sensitivity to oxidative stress.

**Mayumi Fujita:** "Activation of p53 is required for ultraviolet radiation-induced cell cycle arrest, apoptosis and BCL-2 regulation in melanoma cells"- Transcription of the p53 gene is involved in cell cycle arrest. To determine whether UV is involved in this gene mechanism both blocking and induction of p53 were examined. The former was studied using WM 35, the primary melanoma with functional p53, and transfection with the viable gene. Induction was studied by observing how UVB affected the cell cycle. UVB induced p53 expression and lead to cell cycle arrest. UVB also was observed to yield apoptosis in WM35 clones but not in p53 clones. By incorporating a temperature shift (38°C to 32°C), the conformation of p53 protein was changed from mutant to wild-type. Studies using WM 1617 and TS clones of p53 showed that UVB induced cell cycle arrest and apoptosis. Also, wild-type p53 was induced, p21 expression was increased which induced cell arrest. Thus, p53 is crucial for UVR induced cell cycle arrest and apoptosis in melanoma cells.

**Ashok K Chakraborty:** "Production and release of proopiomelanocortin (POMC) derived peptides by human melanocytes and keratinocytes in culture: regulation by UVB"- It is demonstrated that UVB radiation stimulates increased expression of the proopiomelanocortin (POMC) gene which is accompanied by production and release of a  $\alpha$ -melanocyte stimulating hormone and adrenocorticotropin by both normal and malignant human melanocytes and keratinocytes. The production and release of both peptides are also stimulated by dibutyryl cAMP and interleukin 1 $\alpha$  but not by endothelin-1 or tumor necrosis factor- $\alpha$ . N-acetyl-cysteine, a precursor of glutathione, an intracellular free radical scavenger, abolishes the UVB-stimulated POMC peptide production and secretion. The conclusions were described and may be found in the following paper: AK Chakraborty et al. (1996) Same title, *Biochim Biophys Acta* 1313, pp. 130-138.

#### **Workshop D *Biophysics and Chemistry of Melanin***

*by Hal Swartz*

This workshop was organized by **T Sarna**. It brought together presentations and discussions of a wide spectrum of physical and chemical techniques which are helping to elucidate the nature of melanins. This is a most complex and difficult task because of the nature of the melanin molecule: it is a multi-functional polymer with many different and potentially important physical properties and chemical reactivities. The presentation by J Menter on electron transfer and photoprotective properties of melanins in solution focused on the polyquinoid nature of melanin which enables them to couple oxidation of electron donors with the reduction of electron acceptors. The presentation, as did many of the other



presentations, emphasized the importance of the structure of the melanin and the particular conditions in determining the physical and chemical effect that are observed. In looking at a prototypic reduction, i.e., the reduction of ferricyanide, it was shown that melanin could either retard or accelerate the rate of reduction depending on the conditions. An important general principle that was noted is the importance and nature and extent of binding by melanin. The presentation also emphasized the important capability of melanin to affect electron transfer. These properties lead to some important photo chemical interactions as well as dark chemistry.

The presentation by **K Wakamatsu** summarized some of the extensive work done by him in collaboration with S Ito. He reported on their microanalytical methods which make it possible to quantitate the amount of eumelanin and pheomelanin by means of analysis of partial degradation products. The presentation included a demonstration of the validity of their approach by methodology which enabled them to dissolve some melanins completely. The presentation by **R Peter** focused on the redox state of enzymatically generated tyrosine melanin. He showed how very elegant results could be obtained using carbon 13 NMR and isotopic label precursors. With this technique he was able to quantitate the amount of oxidized and reduced subunits. **M Eisner** reported on EXAFS studies of chelated iron sites in natural and synthetic neuromelanins which have been carried out by an international group, including Drs Zecca and Crippa from Italy. It was pointed out that neuromelanins may have an important role in the understanding of Parkinson's Disease. The elegant EXAFS technique was demonstrated to be able to characterize the chelated iron sites in both synthetic neuromelanins and genuine substantia nigra. The results indicated some of the potential problems involved in the use of synthetic neuromelanins, especially if these do not fully reflect the chemical nature of neuromelanin as it is found in the human brain.

The last presentation was by **H Swartz**, who summarized results on the implications of the interactions of melanin with reactive species, based on extensive work done in collaboration with Drs Sarna, Nilges, and Pilas over a number of years. The capabilities of melanin to affect reactions by several different mechanisms was emphasized. Depending on the type of melanin and the conditions, melanin can play an important role by binding and changing the activity of both metal ions and organic molecules and thereby affect the amount of reactive species that are produced. It was emphasized here, as in the other presentations, of the need to take into account the effects of different types of melanin on the particular reaction or biological effect that is being assayed.

Overall, this workshop presented an excellent overview of the nature of melanin and indicated some of the remarkable progress that is occurring in understanding it.

### **Workshop E Vitiligo**

*by David Norris*

This workshop of vitiligo covered topics related to the pathomechanisms of the development of vitiligo, and better approaches to repigmentation in vitiligo. **D Norris** (Univ Colorado) discussed the resistance of epidermal melanocytes to cytotoxic damage, proposing that intrinsic anti-apoptotic defenses mediated by proteins such as bcl-2 protect melanocytes from cytotoxicity induced by immunologic and inflammatory mediators and ultraviolet radiation. The environment of the epidermis is continually exposed to oxidative stress, ultraviolet radiation, cytokines, cytotoxic lymphocytes, and biochemical triggers of cell damage, and melanocyte survival is determined by a balance of survival signals and death signals.

**J Nordlund** (Univ Cincinnati) discussed proposed etiologies for melanocyte destruction in vitiligo, and alleged that no current proposed mechanism was completely convincing, except for the hypothesis of intrinsic melanocyte defect. This inspired considerable discussion, with a common accord that the multiple possible mechanisms proposed in vitiligo might indeed be involved differentially in distinct subsets of patients. The problems in linking particular mechanisms to melanocyte damage in individual patients were acknowledged.

**A Taieb** (Bordeaux Univ) demonstrated the usefulness of studying mechanisms of vitiligo in vitro in complex organotypic epidermal cultures, reporting that an intrinsic defect in melanocytes from vitiligo patients is not demonstrated in the absence of external stimuli, and concluding that an external trigger is needed for vitiligo.

**R van den Wingaard** (Amsterdam Univ) reported that no differences in susceptibility to apoptosis were observed between melanocytes from normals compared to vitiligo subjects. Their work suggested that immunologic cell death of vitiligo melanocytes may be enhanced by changes in bcl-2 levels, which will be better defined in further investigation. They also confirmed reports that melanocytes resist induction of apoptosis triggered by binding the Fas receptor on the melanocyte plasma membrane.

**RK Tripathi** (Univ Cincinnati) reported on genetic studies to determine whether the MITF (microphthalmia) genetic locus was linked to the development of human vitiligo. Even though this candidate gene is linked to other depigmentary problems, it was found to not be a genetic locus determining human vitiligo.

**W Westerhof** (Amsterdam Univ) reported on the advantages of narrow-band UVR (311 nm) over typical PUVA therapy. In a large clinical trial, narrow band UVR was found to be more effective than PUVA and offered a number of advantages (safety, ease of treatment, fewer collateral changes). Neither treatment was good for hand and foot vitiligo. Although there is continued progress on understanding basic mechanisms of melanocyte damage in vitiligo and although effective (although slow) treatments are available, we are not yet able to link breakthroughs in understanding the mechanism of this common disease with matched breakthroughs in treatment that are safe, rapid, and effective in all patients. Approaches to repigment hands and feet from endogenous melanocytes are still largely unsuccessful.

#### *Workshop F Control of Melanogenesis*

*by John Pawelek*

**Dr J Pawelek** presented a summary of his work with Dr A Chakraborty in which it was shown that the Pmel17/Silver gene product has the ability to catalyze the polymerization of DHICA into DHICA-melanin, suggesting a potential role for this protein in vivo. He cautioned, however, that in the case of melanogenesis in vitro and in vivo enzymatic activities might not necessarily correspond, particularly since melanin intermediates are often a) unstable in vitro, spontaneously creating new potential substrates for the melanogenic factor in question, and b) recognized as substrates by more than one melanogenic protein in vitro.

**Dr H Kondoh** presented his work with Dr Y Mishima on the role of TRPs in the control of eumelanogenesis. They showed that TRP-2 plays an important role on the content of DHICA-melanin in both eumelanin and mixed melanins, as well as preventing cell death by converting DOPACHrome to DHICA, which has less cytotoxicity than DHI.

**Dr F Solano** presented work from his laboratory comparing TRP's from murine and human melanoma cells. They found that the three human melanoma lines had less DOPACHrome tautomerase activity than mouse B16 melanoma cells, and that the mouse enzyme appeared to contain Zn at its metal binding sites. Tyrosinase and TRP1 from all cell lines both showed DOPA oxidase activity.

**Dr M Miranda** presented a spirited and fascinating overview of melanogenesis, tyrosinase expression, and reproductive differentiation in black and white truffles (Ascomycotina). His observations underscored the wide-spread uses that melanins have been put through by various life forms. Of particular interest was the observation that white truffles do not produce black melanins, yet they are tyrosinase positive.

**Dr H Chen** summarized his work with Dr K Jimbow demonstrating, for the first time, the potential involvement of phosphatidylinositol 3-kinase activity in the sorting and transport of newly synthesized TRP-1 in melanogenesis.

#### *Poster Session #2 Melanogenesis*

*by John Pawelek*

**Dr B Fuller** discussed work from his laboratory on the regulation of tyrosinase in mouse melanoma cells and human melanocytes by PKC and PKA pathways. Using protein kinase inhibitors, evidence was obtained that PKC activity is not associated with stimulation of tyrosinase, rather it seemed to be a negative regulator of the melanogenesis pathway.

**Dr K Yasumoto** presented his work with Drs Fuse and Shibahara on pigment cell-specific transcription of the tyrosinase family and MITF genes. Their results suggested that transcription of the TRP-2 gene is regulated in a different manner from that of the tyrosinase and TRP-1 genes. Further, they identified a melanocyte-type promoter of the MITF gene and are currently searching for the regulatory elements required for its pigment-specific expression.

**Dr Y Xu** presented work on sorting of a melanosome membrane protein to both the endosomal and secretory pathways. They found that a major portion of the TRP-1 produced by melanocytic cells is secreted. Cell surface expression of TRP-1 was also detected.

**Dr M Furumura** and co-workers used the technique of differential display to identify novel genes modulated during pheomelanogenesis. Several clones of cells were isolated that appeared to express genes that were regulated by agouti signalling protein, potentially opening new directions in the understanding of genetic regulation of pheomelanogenesis.

### ***Poster Session #3 Biophysics and Chemistry of Melanin***

*by Hal Swartz*

This interesting session was organized by **P Riley**. The session was well attended, indicating the attractiveness of such poster sessions. It consisted of oral presentations of the highlights of some of the posters of most general interest that were included in the poster session on biophysics and chemistry of melanin.

**Z Abdel-Malek** summarized the very interesting and important results on understanding the molecular mechanism of the effect of aMSH on UVB induced growth arrest. It was shown that the aMSH has an important effect on the kinetics but not the extent of apoptosis.

The presentation by **P Autier** highlighted the complex interactions that occur between physical effects such as exposure to sunlight and human behavior. As a consequence of the increased reaction of individuals with certain skin types to UV, the subjects reduced the amount of exposure to sunlight and thereby their risk for malignant disease. Failure to take into account such behavioral changes could lead to erroneous interpretations of the relationship between exposure, practice predisposed to the induction of malignancy, and the amount of malignancy that is observed.

**N Kobayashi** reported on the phenomenon of photoprotection by supranuclear melanin caps against DNA damage in normal human epidermis. This result suggested that appropriate positioning of melanin over the nucleus could account for the observed differences of sun induced skin cancer in highly pigment races.

The final presentation was given by **T Sarna** on behalf of the groups from Krakow and Medical College of Wisconsin. He summarized the complex and very important properties of melanin in both promoting and inhibiting autooxidation. In aggregate, the presentations at this poster session provided a stimulating and informative insight into the wide spectrum of effective approaches being used to relate the biophysical and chemical properties of melanin to human disease.

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***Invitation to the XVIIth IPCC (International Pigment Cell Conference)***

*by Shosuke Ito*

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

Nagoya Congress Center

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.

Kazumasa Wakamatsu, Ph.D.

Chair, IPCC Nagoya

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](mailto:sito@fujita-hu.ac.jp)

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### **Positions - Wanted and Available :**

**Postdoctoral Position - Postdoctoral Research Associate position** available to conduct research on the structure/function analysis of melanogenic proteins, particularly tyrosinase related protein-1 (TRP1). The primary goal of the project is to assess how TRP1 regulates melanin synthesis, interacts with tyrosinase, and is associated with oculocutaneous albinism type 3 (OCA3). Candidate must have a PhD with experience in routine molecular biology procedures and transfection/site directed mutagenesis technology. Salary will be commensurate with training and experience. Interested individuals should send curriculum vitae to and/or contact: Raymond E. Boissy, Department of Dermatology, University of Cincinnati College of Medicine, 231 Bethesda Avenue - ML0592, Cincinnati, OH, 45267-0592. 513-558-6242 (TEL), 513-558-0198 (FAX), [boissyre@uc.edu](mailto:boissyre@uc.edu) (E-MAIL).

**Cell Biologists - Unilever's Research and Engineering Division** has two openings for the following position description. Changes in pigmentation of the skin are part of the adaptation response to a variety of conditions. These changes are caused and characterized by very marked changes in skin cell biology and biochemistry. We wish to recruit two scientists to be part of a new project team researching mechanisms of pigmentation and mode of action of certain skin lightening agents in vivo. The project will require the establishment and investigation of appropriate in vitro and in vivo models for pigmentation research. Expertise required: Candidates must have a good honours degree and PhD in a

biochemical or cell biology subject with at least 3 years of research training in a good laboratory. The candidate must have a proven research record. Postdoctoral experience would be advantageous. Please send your CV quoting the Reference number MM960604 to: Bryony Leleux, Personnel Department, Unilever Research, Colworth Laboratory, Sharnbrook, Bedfordshire, MK44 1LQ; Email [bryony.leleux@urcgb.sprint.com](mailto:bryony.leleux@urcgb.sprint.com).

**Predoctoral and Postdoctoral Positions** - available for molecular biologists in the areas of drug discovery and metabolism research. Requires experience in gene cloning, DNA sequencing, recombinant protein expression and cell culture methods. Prior experience in dermatology research is desirable. Southern Research Institute is a diversified research and development organization. Our Life Sciences Division provides comprehensive preclinical drug development and testing capabilities as well as basic research in drug design and synthesis, pharmaceutical formulations, toxicology, virology, microbiology, and pharmacology. To apply, send resume or curriculum vitae to: Southern Research Institute, Attention: Suzann Allen, Human Resources, Department 118, P.O. Box 55305, Birmingham, AL, 35255-5305.

**Faculty Position - Massachusetts General Hospital, Harvard Medical School, Cutaneous Biology Research Center.** The Cutaneous Biology Research Center (CBRC) seeks a molecular, cellular or developmental biologist to establish a program in fundamental research relevant to skin pigmentation. Areas of reseearch can include but are not limited to pigment synthesis and transfer in melanocytes, genetics of mouse coat color and development/migration of neural crest cells. Applicants must have a Ph.D. and/or M.D. degree and relevant postdoctoral experience. Only applicants with a strong research record and the potential to develop extramurally supported research programs will be considered. Individuals with a demonstrated ability to develop imaginative approaches to important biological questions are particularly encouraged to apply. Rank/salary/start-up funds and space are negotiable depending on experience and qualifications. The CBRC occupies 45,000 square feet of fully equipped laboratory space in a new multidisciplinary research facility. Interested individuals should send curriculum vitae, reprints, a statement of research and future directions, along with the names, addresses and telephone numbers of three references to: Dr. Paul F. Goetinck, Chair, Faculty Search Committee, Cutaneous Biology Research Center, Massachusetts General Hospital - East, Building 149, 13th Street, Charlestown, MA 02129

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## **INTERPIG DataBase**

**by Vincent Hearing**

The INTERPIG database is on the InterNet! You can now access the InterPig DataBase at the following address: <http://lenti.med.umn.edu/paspcr/interpig.html>. Please note that as of this time, less than 5% of the various IFPCS members have contributed entries. Think of how useful and complete this list would be if everyone took the time to supply their information. Please take a moment to fill out the database data entry form (either online through the Web page or via Email) and send it back to Dr. Hearing. Please contact Vince Hearing or Bill Oetting if you need more information about these mechanisms of submission.

## **Bibliography :**

The Bibliography published in this issue covers the period November, 1996 through January, 1997. 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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### **MSH, POMC, GROWTH FACTORS & RECEPTORS**

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