PANAMERICAN SOCIETY for PIGMENT CELL RESEARCH

PASPCR Newsletter

Volume 4 Number 2 June,1996

Introduction . . . by the Publications Committee

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 **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.

NEW! WorldWideWeb Pages for the PASPCR. The PASPCR now has its own **WWW** home page. We plan this to be a major source of current information for the PASPCR membership. The address for the page 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, the International Pigment Cell Conference in Anaheim 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.

The PASPCR WWW page system is still under construction and we want to know if there is any other information you would like located on this 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 or to Vince Hearing at hearingv@dc37a.nci.nih.gov.

IN THIS ISSUE . . . . .

PanAmerican Society for Pigment Cell Research

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Calendar of Events :

June 2 - 6, 1996 Annual Meeting of the American Society for Biochemistry and Molecular Biology and the American Association of Immunologists, to be held in New Orleans, LA (contact: FASEB Office, 9650 Rockville Pike, Bethesda, MD 20814-3998; FAX: 301/530-7014)

June 15 - 16, 1996 5th Melanoma Workshop, to be held in Hamburg, Germany (contact: Holger Voigt, Melanoma Research Project, 31 B Dammtorstrasse, Hamburg D-20354, Germany; FAX: +49 40/348-0525)

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

Dec 7 - 11, 1996 36th Annual Meeting of the American Society for Cell Biology and 6th International Congress on Cell Biology, to be held in San Francisco, CA, (contact: ASCB Secretariat, 9650 Rockville Pike, Bethesda, MD 20814-3992; FAX: 301/530-7139)

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 Perspectives" to be held in Bali, Indonesia (contact: Bureau PAOG, Tafelbergweg 25, 1105 BC Amsterdam, The Netherlands; FAX: +31 20/696-3229)

Welcome to New Members

by James J Nordlund

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

Dong Fang	Mei-Yu Hsu	Marcus D. Johansen
Luix Eduardo M. Nery	Tomasz W. Panz	Brinda K. Rana
Deepa Rungta	Fan Yang	

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

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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XVIth IPCC (International Pigment Cell Conference)

by Roger Bowers, Frank Meyskens

The XVIth International Pigment Cell Conference will be held from October 29th to November 3rd, 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. The PASPCR has established a Web page that contains relevant information for this meeting; take a look at: "**http://lenti.med.umn.edu/paspcr/ipcc.htm**".

Authors of abstracts will be notified of their place in the program by mid-July. All keynote and invited platform speakers will be asked to submit a manuscipt for publication in *Pigment Cell Research* in the upcoming year.

XVIth International Pigment Cell Conference - Tentative Conference Agenda

Tuesday, October 29, 1996

3:00 - 7:00 pm	Pre-registration/View Exhibits
7:00 - 10:00 pm	Welcome Reception: Fashion Show: "***Safe and Sexy in the Sun***"

Wednesday, October 30, 1996 Conference Attendees

7:00 - 8:00 am	Registration/Continental Breakfast/View Exhibits
8:00 - 8:05 am	Welcome: Chairman, Frank L. Meyskens, Jr. *Introduction*: Laurel Wilkening, Chancellor, Univ of California, Irvine
8:05 - 8:35 am	***Special Lecture***, R. Sherwood Rowland, Nobel Laureate, 1995, Chemistry "***Ozone Depletion, Ultraviolet Light, and the Pigment Cell***"

Symposium I: Economic and Societal Implications of Melanin amd Melanogenesis

8:35 - 9:00 am	Keynote Speaker
9:00 - 10:30 am	Invited and Competitive Abstract Speakers
10:30 - 11:00 am	Break

11:00 - 12:30 pm ***Workshop A: "Extracutaneous Melanin"***
Posters and Discussion #1 TBN* (11:00 - 12:00 Viewing; 12:00 - 12:30 Discussion)
12:30 - 2:00 pm Lunch on your own

Symposium II: Molecular Biology of Pigment Cells
2:00 - 2:30 pm Keynote Speaker
2:30 - 4:00 pm Invited and Competitive Abstract Speakers
4:00 - 4:05 pm IFPCS InterPig Database on the WorldWideWeb: Vincent Hearing
4:05 - 4:15 pm Break
4:15 - 6:15 pm ***Workshop B: "Regulating Mechanisms of Melanocyte Proliferation"***
4:15 - 6:00 pm Posters and Discussion #2 TBN* (4:15 - 5:30 Viewing; 5:30 - 6:00 Discussion)
5:30 - 7:00 pm ***Workshop C: "Biophysics of Melanin"***
6:15 pm Adjourn Free evening

Accompanying Guests (8:00 - 11:00 am) Welcome/Introduction: Buffet Breakfast;
(12:00 - 5:00 pm) Group Activity

Thursday, October 31, 1996
7:00 - 8:00 am Continental Breakfast/View Exhibits
8:00 - 8:30 am ***Seiji Lectureship:*** Introduction: Giuseppe Prota, President, IFPCS

Symposium III: Melanoma Research: Basic and Applied
8:30 - 9:00 am Keynote Speaker
9:00 - 10:30 am Invited and Competitive Abstract Speakers
10:30 - 11:00 am Break
11:00 - 12:30 pm ***Workshop D: "Control of Melanogenesis"***
11:00 - 12:30 pm Simultaneous Business Meetings of Regional Societies
12:30 - 2:00 pm Lunch on your own

Symposium IV: Photobiology of Melanocytes: Etiology and Prevention
2:00 - 2:30 pm Keynote Speaker
2:30 - 4:00 pm Invited and Competitive Abstract Speakers
4:00 - 7:00 pm ***Workshop E: The "Blues" Symposium***
4:00 - 7:00 pm Poster Viewing
Adjourn - Free evening

Friday, November 1, 1996
7:00 - 8:00 am Continental Breakfast/View Exhibits
8:00 - 8:30 am Introduction: Sally Frost-Mason, *President,* PASPCR
***Gelb Lectureship*:** Seth Orlow

Symposium V: Melanogenesis and Pigmentary Disorders
8:30 - 9:00 am Keynote Speaker
9:00 - 10:30 am Invited and Competitive Abstract Speakers
10:30 - 11:00 am Break
11:00 - 12:30 pm ***Workshop F: "Biology and Biochemistry of Melanosomes"***
11:00 - 12:30 pm Posters and Discussion #3 TBN* (11:00 - 12:00 Viewing; 12:00 - 12:30 Discussion)
12:30 -1:15 pm ***Controversy Session:*** "Semiquinone Radicals are <u>not</u> Important during Melanin Synthesis"
Pro: Patrick Riley Con: Stan Pavel
1:15 pm Adjourn Scientific Session
1:15 - 6:30 pm Break
6:30 - 7:30 pm Reception
7:30 - midnight Banquet, Awards and Dancing

Saturday, November 2, 1996
7:00 - 8:00 am Continental Breakfast/View Exhibits
8:00 - 8:30 am ***Presidential Address:*** Giuseppe Prota, President IFPCS

Symposium VI: Comparative Developmental Biology of Pigment Cells
8:30 - 9:00 am Keynote Speaker
9:00 - 10:30 am Invited and Competitive Abstract Speakers
10:30 - 11:00 am Break
11:00 - 12:30 pm ***Workshop G: "Genetic Aspects of Albinism"***
11:00 - 12:30 pm Posters and Discussion #4 TBN* (11:00 - 12:00 Viewing; 12:00 - 12:30 Discussion)
12:30 - 2:00 pm Lunch on your own
2:00 - 4:00 pm ***Educational Forum: "Living with the Sun"***
4:00 - 6:00 pm Family Farewell Reception and Wine Tasting

Sunday, November 3, 1996

8:00 - 5:00 pm
1. *Satellite Meeting (all day):* ***Classification of Cutaneous Melanoma***: Alistair Cochran
2. *Satellite Meeting (3 hours):* ***Safety of Sunscreens and Tanning Parlors***: J.P. Césarini, et al.
3. *Satellite Meeting* (*3 hours*): ***Ocular Melanin***: Giuseppe Prota

Workshops and poster and poster discussion sessions will be simultaneous. The poster sessions and discussions will feature areas that do not overlap with the workshop. The chairs of these sessions will be selected from submitted competitive abstracts and the Chairman in turn will organize this session with help from the Organizing Committee.

Positions - Wanted and Available :

Assistant Professor - The Department of Physiology at the University of Sao Paulo has an open position for assistant professor. Applications will be received until June 1st. A Ph.D. is required and post-doctoral experience is desirable. The selection will be held during the first week of July with the candidates' presence. The curriculum vitae including copies of the publications, the Ph.D. certificate and a research project on Human or Animal Physiology (including biochemical and biomolecular approaches) should accompany the application. A lecture (undergraduate level) on a picked out subject of one of three areas (Neurosensorial and Muscle Physiology; Cardiorespiratory and Excretory Physiology; Nutrition, Metabolism and Endocrine Physiology) chosen by the candidate should be given to the Selection Committee, that will also interview the candidates. Please contact: Ana Maria de L. Castrucci, Dep. Physiology, Inst. Biosciences, University of Sao Paulo, CP11176, CEP 05422-970, Sao Paulo, Brasil; Fax 5511 818-7422 phone 5511 818-7610 Email AMDLCAST@USP.BR

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

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, I estimate that 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 own 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.

Meeting Report

by Kazunori Urabe

International Symposium on "Melanogenesis and Malignant Melanoma: Biochemistry, Cell Biology, Molecular Biology, Pathophysiology, Diagnosis and Treatment". - Fukuoka, Japan December 5-6, 1995

This symposium was held by Yoshiaki Hori, M.D., Professor and Chairman, Department of Dermatology, Faculty of Medicine, Kyushu University, to discuss new findings about melanogenesis, biochemistry of melanin, genetics of pigmented disorders, immunology of pigmented disorders and malignant melanoma, clinical features of malignant melanoma, prevention of malignant melanoma and treatment of malignant melanoma. Sixteen investigators were invited from abroad to report their new data on their fields and thirty Japanese ones were also invited to attend the meeting and sixteen of them presented their findings. The symposium was opened in the international conference room in the new modern building which was built for the international congresses a half year ago. Exact respected schedule by the speakers gave opportunity to everyone to hear and discuss what they were interested.

There were five sessions in this symposium. The first session dealed with the biochemistry and molecular biology in benign and malignant pigment tissues. In this session, the relationship between genetic alterations in melanogenic proteins and the clinical pigment disorders were reported. And the biological characters of melanogenic cells affected by surrounding cells and the environmental stimulants were investigated. In the second session, immunological approaches for malignant melanoma were presented. Several specific antigens in melanoma were reported and the possibility for clinical application were discussed. In the third session, the characteristic nature of melanoma cell were analyzed intensively. In the fourth session, some of new techniques for the diagnosis of malignant melanoma were presented. And the last session included the several new therapeutic methods; biochemotherapy, isolated limb perfusion, hyperthermia, and new products targeting melanoma. All papers were summarized here. A full listing of abstract is available on request. However, papers reported in this meeting will be published in a book from Elsevier Science soon.

1) Biochemistry and Molecular Biology of Melanogenesis in Benign and Malignant Pigment Tissues

Matsunaga J from Akita University of Medicine reported the mutations in the tyrosinase gene causing tyrosinase-negative oculocutaneous albinism in Japanese. In these nine patients, mutations of the tyrosinase gene were found at codon 77, codon 278, codon 310 and codon 431 of the gene. He suggested that in these mutations, codon 77 and codon 310 might be major mutation sites in Japanese patients. King RA from University of Minnesota demonstrated eleven mutations (9 unique and 2 previous reported) of the P gene which is responsible for tyrosinase positive oculocutaneous albinism. Hermansky-Pudlak syndrome was also intensively studied by his group, which is a type of albinism associated with storage-pool deficient platelets and with the production of ceroid. Linkage analysis of the family revealed that the gene was located on chromosome 10q. Further studies were going on to clone the gene. I presented the data about the regulation of *microphthalmia* (*mi*) gene of which mutations induced white hair, microphthalmia and deafness in mice. The expression of *mi* gene was not affected by MSH stimulation. Using neural crest cells, Kubota Y from St. Marianna University in Kawasaki suggested that the stem cell factor might play a role in the development of c-kit positive cells from neural crest and that there was a critical time (Days 0-5) when the stem cell factor induce c-kit positive cells and that other factors such as cholera toxin might be necessary to induce further differentiation of the cells to melanocytes. Meyskens FL from University of California focused on the transcription factors of human melanocyte in response to ultraviolet radiation. His group demonstrated the high dose of 500 mJ of ultraviolet induced AP-1 and down regulated NFkβ and that normal human melanocytes required both the PKC and PKA signaling pathways for UVB induction of AP-1 and NFkβ. To elucidate the paracrine linkage of cytokines between human keratinocytes or fibroblasts and melanocytes for biological mechanisms of involved in cutaneous melanosis, Imokawa G from Kao Corporation characterized keratinocyte- and fibroblast-derived factors responsible for proliferation of melanocytes. They showed that IL-1α and endothelin(ET)-1, and GM-SCF were

predominantly produced by keratinocytes in response to UVB and UVA irradiation, respectively, whereas stem cell factor (SCF) was the major cytokines produced by fibroblasts, and that these factors were synergistic of additive stimulatory effects on DNA synthesis of cultured melanocytes. Prota G from University of Naples suggested that melanin-related metabolites might play a critical role of the well being of both melanocytes and the surrounding cells. He showed that DHI was capable of inhibiting lipoxygenase-induced oxidation of arachidonic acid, a primary event in inflammatory reactions, and that DHI and DHICA were also endowed of excellent antioxidant properties and were capable of scavenging oxygen radicals. Another study was also presented that DHICA was a potent enhancer of nitric oxide production by LPS stimulated murine macrophages. To characterize melanins in mouse and human hair of various colors, Ito S from Fujita Health University School of Health Science presented new findings in their methods; 1) solubilization of hair melanins in Soluene-350 was a convenient method to estimate the total amount of melanin. 2) chemical differences among melanins produced in the brown, slaty, and other colored mice could be elucidated by HPLC and spectrophotometric methods. 3) eumelanin to pheomelanin ratio could be estimated from the slope of absorption spectrum of melanin dissolved in Soluene-350. Demonstrating the effects of prostanoids, leukotrienes, lymphokines, cytokines, melanotropins, endothelins and other factors on melanocyte on various conditions, Nordlund JJ from University of Cincinnati concluded that the concepts about the melanocyte and its receptors must be updated to show the multiplicity of receptors that made the cell responsible to many cytokines, lymphokines and chemical mediators of inflammation, and that the melanocyte itself had the same capabilities for forming these various factors as other cells, and that the formation of these factors by the melanocytes suggested that melanocytes had both autocrine and paracrine roles for all epidermal cells including Langerhans cells. Kikuchi K from University of Tokyo examined the ET receptor subtypes involved in mitogenic signaling in human primary and metastatic melanoma, and suggested that the mitogenic effects of ET in human primary melanoma were mainly dedicated through ETB receptors, and that down-regulation of ETB receptors caused the decreased growth response of ET-1 in metastatic melanoma cells.

2) Immunological Approaches for Malignant Melanoma

Itoh K from Kurume University showed that the MAGE-1 and -4 proteins which were tumor-rejection antigens recognized by cytotoxic T lymphocytes, were expressed in many different cancers including melanoma, and in spermatogonia and primary spermatocytes. And he suggested that MAGE proteins might be appropriate target molecules for specific immunotherapy of cancer. Ferrone S from New York Medical College Valhalla presented the data of immunotherapy with the anti-idiotypic (anti-id) antibodies. He discussed the rationale underlying the selection of anti-id mAb as immunogens and of human high molecular weight-melanoma associated antigen as a target, and described the immunogenic and structural characteristics of the anti-id mAb MK2-23. He also presented the results of active specific immunotherapy with mAb MK2-23 in 50 patients with advanced melanoma. To reduce the immunogenicity of anti-id mAb MK2-23, Matsumoto K from Shinshu University School of Medicine evaluated the *in vitro* reactivity and immunogenicity of F(ab')2 fragments of mAb MK2-23 and of its chimeric form, and suggested that these might be useful immunogens to implement active specific immunotherapy in the patients with malignant melanoma. Hayashibe K from Kobe University School of Medicine analyzed a human melanoma-associated antigen D-1 which was identified by his group. They demonstrated that D-1 antigens were specifically expressed in melanoma cells and that HLA A33 might be associated with high expression group of D-1 antigen in patient with malignant melanoma. Taniguchi M from Chiba University investigated TCR repertoire in tumor-infiltrating lymphocytes in metastatic melanomas. He reported that only two TCR Vαs, such as Vα3+ and Vα4+ TCRs, dominated and comprised about 75% of total TIL TCR Vα repertoire, and that the majority of these two TCRs were extremely homogenous. And he also demonstrated that depletion of Vα3 T cells by anti-Vα3 resulted in protection against melanoma lung metastasis. Hearing VJ from National Institute of Health in Bethesda showed that many spontaneous autoimmune responses against melanocytes, including those directed against melanoma cells, reacted with epitopes derived from melanosomal proteins. He demonstrated that TRP2 was the most generally expressed of those potential antigens and thus might be the most appropriate target for vaccine strategies.

3) Biochemical Analysis on the Expression of Specific Proteins in Melanoma

Horikoshi T from Sapporo Medical University reported the serum 5-S-cysteinyldopa (5-S-CD) level reflects melanoma progression more sensitively than urinary 5-S-CD, serum or urinary DHICA, and

suggested that serum 5-S-CD might be the best biochemical marker for the detection of progression of melanotic melanoma. Melanin-producing cells are subject to a high risk of oxidative stress, particularly due to the presence of melanogenic machinery continuously producing o-quinones, the precursors of polymer melanin. Pavel S from Leiden University Hospital suggested that 0-methylation was one of the protective means decreasing redox cycling potential of melanin precursors and speeding up their transmembrane transport, and that L-cysteine and glutathione not only participated in the redox reactions but also controlled the quality and quantity of produced melanin. Taniguchi S from Shinshu University of Medicine found and cloned a variant actin (βm actin) which was responsible for the decrease of metastatic ability of mouse melanoma cell. When the βm actin cDNA expression vector was transfected into a highly metastatic cell lines, he observed the inhibitory effects on the cell motility, invasion, and metastatic ability depending on the expression of the exogenously transferred βm actin. He suggested that βm actin inhibits the dynamic conversion between the monomeric and polymerized form of actin, leading to both a decrease in cell motility and consequently the suppression of invasiveness and metastasis. Kageshita T from Kumamoto University School of Medicine examined 58 primary and 35 metastatic melanoma and 22 pigmented nevi using anti-vitronectin receptor (VN-R) chain antibody, and found that VN-R avb3 chains were expressed in 47, 34 and one samples, respectively. He suggested that the expression of VN-R avb3 chain in melanocytic tumors was correlated with development of deep invasion and metastatic process. Tsuchida T from Saitama Medical School demonstrated that among gangliosides, GM3 and GD3 was predominant in congenital pigmented nevi and primary malignant melanoma, respectively. And he also reported that moderate amounts of sulfatide were detected in congenital pigmented nevi and primary malignant melanomas, but not in metastatic melanomas.

4) Diagnosis of Malignant Melanoma

Malignant melanoma has a variable prognosis determined by several specific histologic features. As the histopathologic variables, Mihm MC from Albany Medical College listed these parameters; 1. tumor thickness, 2. level invasion, 3. mitotic rate (per millimeter square), 4. tumor infiltrating lymphocytes, 5. regression, 6. ulceration, 7. predominant cell type morphology, 8. microscopic satellites, 9. vascular invasion, 10. nodular growth (vertical growth phase). Of these parameters, he emphasized tumor infiltrating lymphocytes and discussed the predominant cell morphology, its cell biologic implications as well as its molecular characteristics and how they related to prognosis. Hara H from Nihon University School presented several methods for the detection of melanogenic and proliferative activities on malignant blue nevus; formaldehyde-induced fluorescence from formalin-fixed, paraffin-embedded materials, HPLC analysis of 5-S-cysteinyldopa from frozen specimen, argyophilic nucleolar organizer regions (AgNORs) and cytofluorometry. He concluded that the cells on malignant blue nevus showed a melanogenic activity and that cytofluorometric analysis could be regarded as a useful parameter for the determination of proliferative activity. Investigating the videomicroscopic features of 500 melanocytic nevi on the soles, Akasu R from Yamanashi Medical University indicated that the surface profile of benign melanocytic nevi was classified into 5 types, and that malignant melanoma *in situ* and acral lentiginous melanoma were exclusively compartmentalized in the miscellaneous type. And she suggested that epiluminescence microscopy might be a useful method for discrimination of plantar benign and malignant melanocytic lesions and might be useful for long-term follow-up of the melanocytic lesions. Sober AJ from Harvard Medical School presented several new techniques in the early diagnosis of melanoma; an epiluminescence microscopy, a computerized image analysis and a confocal laser microscopy. Confocal laser microscopy utilizes an argon, krypton, or Ti:sapphire laser into a confocal scanning microscope producing high resolution images. His group was investigating the use of this technique in the imaging of pigmented lesions and assessing the clinicopathologic correlation. McCarthy WH from Royal Prince Alfred Hospital in Sydney used lymphoscintigraphy to mark the surface location of the sentinel lymph node in each node field and to measure the depth of the node, and demonstrated that lymphoscintinography was accurate in 97% of patients in identifying potential sites of micrometastses of sentinel nodes.

5) Treatment of Malignant Melanoma

Jimbow K from University of Alberta in Canada investigated the anti-melanoma effect of the phenolic thioether amines for the development of a new targeted chemotherapy of radiochemotherapy for malignant melanoma. He evaluated the specificity and improved effectiveness of N-propionyl cysteaminylphenol (NPrCAP) and its prodrug dipropionyl CAP (DPrCAP) over N-acetyl CAP (NAcCAP) and its prodrug of diacetyl form (DPrCAP) as antimelanoma agents, and the mechanism of

drug action of NAcCAP and NPrCAP focusing on the production of quinone/semiquinone radicals mediated through interaction with tyrosinase and other oxidases. Cascinelli N from National Cancer Institute in Milano discussed three specific and actual subjects of high interest: adoption of a new technique for an earlier detection of nodal metastases, gene therapy of metastatic disease and interferon in the adjuvant therapy of patients with nodal metastases. Riley PA from University College London Medical School tested sixteen phenolic compounds for their ability to act as substrates for tyrosinase and their cytotoxic potentials. He revealed that protection of the hydroxy group by acetylation or glycosylation prevented *in vitro* oxidation by tyrosinase, and that both acetate and succinate esters were cytotoxic, and that protection of the phenolic OH group by sugars abolished *in vitro* cytotoxicity. Isolated limb perfusion (ILP) with melphalan produces a 50% complete remission rate in melanoma and a 6% in sarcoma of the limbs. In order to improve these results, Lejeune FJ from Universitaire Vandois in Switzerland added rTNFα to melphalan and rIFN-γ in ILP for in-transit melanoma metastases, irresectable soft-tissue sarcomas and carcinomas of the limbs. A 90% complete response rate was obtained for melanoma, a 36.4% complete response rate for sarcoma and a 57% complete response rate for squamous cell carcinoma. Thioureylenes such as 2-thiouracil are known to be selectively accumulated in nascent melanin. On animal experiments, Larsson BS from Uppsala University in Sweden showed that the thioureylenes might be used as vehicles of radionuclides for melanoma scanning or treatment, and of boron-10 for neutron capture therapy. He also indicated that radioiodinated 2-thiouracil might be useful in the diagnosis of disseminated malignant melanoma. Hyperthermic isolated limb perfusion with the infusion of chemotherapeutic agents and/or cytokines has been proven to be definitely effective for the treatment of malignant melanoma at least locoregionally. Nakayama J from Kyushu University studied the mechanism of cytotoxic effects of hyperthermia on melanoma cells, and indicated that hyperthermia caused activation of immune system of the host, probably through the upregulation of ICAM-1 expression in melanoma cell and/or immune competent cell of the host.

Bibliography :

The Bibliography published in this issue covers the period February, 1996 through April, 1996. 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.

MELANINS, MELANOGENS & MELANOGENESIS

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