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E S P C R B U L L E T I N

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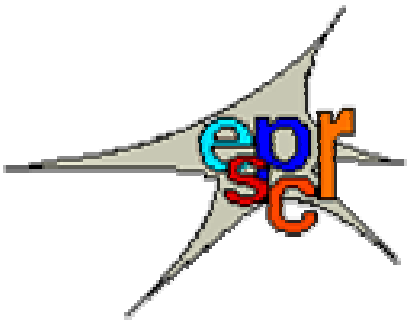

EUROPEAN SOCIETY FOR PIGMENT CELL RESEARCH *BULLETIN*

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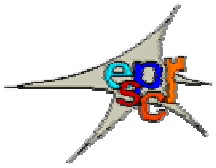
CONTENTS

Discussion, Letters to the editor, Reviews, Short communications, ...

Review of the literature

1. Chemistry of Melanins and other pigments (Dr A. Napolitano)
2. Biology of pigment cells and pigmentary disorders (Dr M. Picardo)
3. MSH, MCH, other hormones (Dr R. Morandini)
4. Photobiology (Dr N. Smit)
5. Neuromelanins (Prof M. d'Ischia)
6. Genetics, molecular and developmental biology (Dr F. Beermann)
7. Tyrosinase, TRPs, other enzymes (Prof JC. Garcia-Borron)
8. Melanosomes (Prof J. Borovansky)
9. Melanoma experimental, cell culture

Announcements and related activities



LETTER TO THE EDITOR
DISCUSSION, REVIEW,
SHORT COMMUNICATION, ...

MESSAGE FROM THE PRESIDENT OF THE ESPCR

Dear ESPCR member,

I am writing you to pass on an important notice concerning the 2005 ESPCR Officers elections.

As you may remember, a call for nominations was issued and the Officers elections were planned for this month. However, I recently learned that Jean Marie Naeyaert has suddenly fallen ill for an undetermined time, and will not be able to fulfil his work as ESPCR Secretary and conduct the elections process. Moreover, Prof. Naeyaert has been nominated as a candidate for the ESPCR Presidency and is in fact the only nominee. He also asked to withdraw his nomination, and a new call is therefore needed.

Under these circumstances and given the dates and the proximity of the summer vacations, the ESPCR Council has decided to postpone the elections until late September, after the next IPCC. Accordingly, a new call for nominations will be issued in due time and the elections will be completed before the end of the year.

We will give you further information on this issue, and hopefully some better news on Prof. Naeyaert's health, during the next ESPCR General Assembly that will take place in Reston, on September 21, from 10:30 to 11:00.

I take this occasion to wish you good and relaxing summer vacations.

Looking forward to meeting you in Reston,

Jose Carlos García-Borrón
President to the ESPCR

Meeting Report

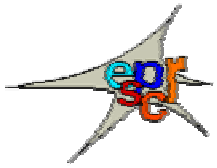
First Meeting of the Asian Society for Pigment Cell Research (ASPCR)
Feb. 1- 2, 2005 - New Delhi, India
www.aspcr.org

Editor's Selection

Mechanisms of skin tanning in different racial/ethnic groups in response to ultraviolet radiation

Tadokoro T, Yamaguchi Y, Batzer J, Coelho SG, Zmudzka BZ, Miller SA, Wolber R, Beer JZ, Hearing VJ.
J Invest Dermatol. 2005 Jun;124(6):1326-32.

Abstract : Ultraviolet radiation stimulates pigmentation in human skin, but the mechanism(s) whereby this increase in melanin production (commonly known as tanning) occurs is not well understood. Few studies have examined the molecular consequences of UV on human skin of various racial backgrounds in situ. We investigated the effects of UV on human skin of various races before and at different times after a single 1 minimal erythemal dose UV exposure. We measured the distribution of DNA damage that results, as well as the melanin content/distribution and the expression of various melanocyte-specific genes. The density of melanocytes at the epidermal:dermal junction in different types of human skin are remarkably similar and do not change significantly within 1 wk after UV exposure. The expression of melanocyte-specific proteins (including TYR (tyrosinase), TYRP1 (tyrosinase-related protein 1), DCT (tyrosinase-related protein 2), MART1 (melanoma antigens recognized by T-cells) gp100 (Pmel17/silver), and MITF (micropthalmia transcription factor)) increased from 0 to 7 d after UV exposure, but the melanin content of the skin increased only slightly. The most significant change, however, was a change in the distribution of melanin from the lower layer upwards to the middle layer of the skin, which was more dramatic in the darker skin. These results provide a basis for understanding the origin of different skin colors and responses to UV within different races.



CURRENT LITERATURE

1. Chemistry of Melanins and other Pigments

(Dr. A. Napolitano)

The structural features of natural and synthetic melanins were intensively investigated by several research groups using theoretical approaches and spectroscopic techniques. A map of steady state fluorescence as a function of excitation and emission wavelengths, and significantly, a three-dimensional map of the "specific quantum yield" i.e the fraction of photons absorbed at each wavelength that are subsequently radiated at each emission wavelength was presented by the group of Paul Meredith at the Queensland University (Nighswander-Rempel et al). An interpretation for the red shifting and broadening of the absorption spectrum observed during 5,6-dihydroxyindole-2-carboxylic acid polymerization as followed by UV spectroscopy was provided by first principles density functional theory calcns. (Tran et al.). The group of J. Simon examined bovine iris and choroid melanosomes at two ages by inductively coupled plasma mass spectrometry, elemental analysis, IR spectrometry, and X-ray photoelectron spectrometry (Hong et al). The results suggest some differences in the content of carboxylate-containing monomer between iris and choroid melanosomes and loss of carboxylic functions with ageing.
The possible effects of the peroxidase/H_2O_2 system in melanogenesis is considered in a paper by Garcia Molina et al. Of relevance in this connection is a study by Mastore et al establishing by electrochemical methods the endogenous production of H_2O_2 during melanogenesis and confirming previous reports that tyrosinase can manifest both catalase and peroxidase activities.
Current analytical methodologies were used to measure eumelanin and pheomelanin in human skin, before and following irradation, thus providing evidence that both pheomelanin and eumelanin are positively related to skin color. (Hennessy, A. et al) The ratio of melanin classes was found similar in people with widely different cancer rates and UVR sensitivity, suggesting that factors other than the amount of pheomelanin may be important in determining UVR susceptibility in persons with red hair. Finally, a review by Napppi and Christensen offers an interpretation of the insect innate immunity in terms of melanogenesis and associated cytotoxic reactions.

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3. MSH, MCH, other hormones, differentiation

(Dr. R. Morandini)

Si-multi-electrode arrays implanted into brain tissue for long-term recording lose electrical connectivity due to the post-implantation inflammatory reaction. This inflammatory reaction creates a physical and electrical gap between the electrode and the surrounding neurons. Zhong (2005) uses nitrocellulose-based, bioactive coatings that release alpha-MSH. The alpha-MSH released on day 21 was still bioactive, and successfully inhibited nitric oxide (NO) production by LPS-stimulated microglia. In the same way, Schultz (2005) shows that Polyelectrolyte multilayer films made of poly-(L-lysine) (PLL) and poly-(L-glutamic acid) (PGA) have been functionalized by covalent binding of a synthetic analogue of the anti-inflammatory peptide, alpha-MSH to PGA to create biologically active coatings for tracheal prostheses. For prostheses modified by PGA ending multilayer films, a more regular and less obstructive cell layer was observed on the endoluminal side compared to those modified by PLL ending films. Systemic anti-inflammatory IL-10 production was only detected in rats implanted with prostheses functionalized by alpha-MSH, demonstrating, in vivo, the anti-inflammatory activity of the embedded peptide into multilayer architectures.
These data are in accordance and confirm the anti-inflammatory action of alpha-MSH.

alpha-MSH acts through the stimulation of cAMP pathway. Busca (2005) has shown that cAMP transcriptionally activates Hifla gene in a melanocyte cell-specific manner resulting in stimulation of VEGF expression. alpha-MSH is a potent anti-inflammatory hormone.

The mammalian melanocortin system has been established as a crucial regulatory component in an extraordinarily diverse number of physiological functions. In contrast, comparatively little is known about the avian melanocortin system. The data reviewed by Boswell (2005) indicate that the melanocortin system has been strongly conserved during vertebrate evolution and that alpha-MSH is produced locally in birds to act as an autocrine/paracrine hormone.

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4. Photobiology

(Dr. N. Smit)

A role of IFN-γ in activation of melanocytes is suggested for the development of pigmented spots in a mouse model (Aoki eta l). The paper describes that genes of various chemokines are upregulated by IFN-γ. An interactive network of keratinocytes, T lymphocytes, mast cells and macrophages would provide a suitable local environment for the activation of melanocytes. Importance of the local environment may also be implicated from the work of Tadokoro et al. In skin of different racial/ethnic groups the effects of UV was examined in situ. Expression of various melanocyte-specific proteins was increased after UV exposure but the most significant change was the shift of melanin distribution from the lower layer upwards to the middle layer, especially in the darker skin types. The study by Landi et al confirms earlier studies demonstrating the association of MC1R variant alleles and increased risk of sporadic and familial melanoma.

In individuals with fewer additional risk factors (darker skin type and few nevi) this association is even stronger. In the previous bulletin already the work of Bohm was described that showed influence of MSH on nucleotide excision repair, improved survival and reduced apoptosis. Also in the paper by Kadekaro et al positive effects of αMSH and endothelin-1 on prevention of UV induced apoptosis is reported. Melanocyte cultures with loss of function MC1R mutations did not show the same protection against apoptosis for the cells treated with αMSH. The increase in apoptosis for the loss of function MC1R melanocytes by the control UV treatment was however also lower than in the cells with functional MC1R .

A possible difference in the apoptotic response between cells with functional and non-functional MC1R might explain why certain cancer prone individuals develop malignant melanoma. Runger et al describe that such differences in apoptotic responses between keratinocytes and melanocytes may give an explanation why mutations in the cell cycle regulating genes INK4a/ARF ultimately lead to melanoma and not to the non-melanoma UV induced skin cancers. The paper by Assefa et al gives a nice review about factors involved in the apoptotic response to UV in keratinocytes and gives some more insight in the complex mechanisms involved in UV induced signaling. The role of reactive oxygen species, lysosomal proteases and many cytosolic signaling proteins as described in this review could be differently regulated in melanocytes but will also be of great relevance for the situation in the pigment cells.

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Malignant melanoma -- a medical students' viewpoint. J Dtsch Dermatol Ges 421-430, 2005.
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5. Neuromelanins

(Prof. M. d'Ischia)

Among the papers that appeared from March to July 2005, two reviewing articles are deserving of mention. One, due to Fedorow et al. (2005), provides a comparative perspective of neuromelanin and the melanins found in other body tissues. After surveying the basic differences concerning biogenesis and cellular localization, the authors examined possible mechanisms in common relating to the biological functions, and emphasized the possible role of neuromelanin in the intracellular oxidative processes leading to neuronal cell death.

The other review, by Mendez-Alvarez and Soto-Otero (2005), surveys the potentially dangerous role of dopamine for dopaminergic neurones in an oxidative stress setting and the relationship with the pathogenesis of Parkinson's disease. In the authors' view, main damaging processes mediated by the catecholamine include i) autoxidation of the catechol ring to form a range of reactive oxygen species via sequential electron transfer to oxygen and concomitant deposition of neuromelanin acting as an iron sink; and ii) oxidative conversion to neurotoxins which may interfere with mitochondrial respiration thus leading to cell death.

Finally, Morawski et al. (2005) investigated the intra- and extraneuronal concentrations of iron and other elements of the human substantia nigra pars compacta vs. pars reticulata using a sophisticated methodology based on a scanning proton beam focussed down to below 1 m that induces characteristic X-rays in the specimen. This technique allowed subcellular spatial resolution and yielded unprecedented insight into the intra- and extraneuronal iron concentrations and distribution. The data provided corroborating evidence that the increased intraneuronal iron content is linked to neuromelanin.

- Fedorow H., Tribl F., Halliday G., Gerlach M., Riederer P., Double K. L.
  Neuromelanin in human dopamine neurons: Comparison with peripheral melanins and relevance to Parkinson's disease. Progress in Neurobiology 75(2):109-124, 2005.
  Abstract : Neuromelanin (NM) is a dark polymer pigment produced in specific populations of catecholaminergic neurons in the brain. It appears in greatest quantities in the human brain, in lesser amts. in some other non-human primates, but is absent from the brain in many lower species. Interest in this pigment has seen a resurgence in recent years because of a hypothesised link between neuromelanin and the especial vulnerability of neuromelanin-contg. neurons to cell death in Parkinson's disease (PD). Little is known regarding the biol. of neuromelanin. As neuromelanin appears to have characteristics in common with the better studied peripheral melanin pigments this review compares what is known about neuromelanin with melanins found in other body tissues. Unlike peripheral melanins, which are produced in specialised cells called melanocytes and may be transferred to other cell types, neuromelanin granules are believed to be stored in the cell in which they are produced. Neuromelanin granules display a unique, more heterogeneous appearance compared with peripheral melanins. Unlike melanin, neuromelanin is traditionally thought to result from a non-enzymic synthesis pathway with no known pathway for neuromelanin catabolism. More recent data, however, is indicative of some regulation of neuromelanin synthesis and turnover. By analogy with peripheral melanins, neuromelanin may function in vivo to attenuate the effects of damaging stimuli. Among several possible mechanisms suggested, the ability of neuromelanin to interact with transition metals, esp. iron, and to mediate intracellular oxidative mechanisms has received particular attention. Recent data from neuromelanin in the Parkinson's disease brain suggests that this proposed function may be compromised, thus rendering pigmented neurons vulnerable to oxidative damage in this disorder.

- Mendez-Alvarez Estefania, Soto-Otero, Ramon.
  Dopamine: a double-edged sword for the human brain. Recent Research Developments in Life Sciences 2:217-246, 2004.
  Abstract : Dopamine is a catecholamine that plays an important role in the human brain as an inhibitor neurotransmitter particularly involved in the modulation of the motor function. It is synthesized in the nerve terminals of dopaminergic neurons from the precursor amino acid tyrosine. The synthesis begins with the conversion of tyrosine to L-DOPA through the action of tyrosine hydroxylase, a rate-limiting step for dopamine synthesis, for which reason the activity of this enzyme is tightly controlled. The L-DOPA is then immediately metabolized to dopamine by L-arom. amino acid decarboxylase. In the nerve terminals, dopamine is stored in synaptic vesicles whose acidic content prevents the autoxidn. of the neurotransmitter, and from which is released by an exocytotic process triggered by a convenient physiol. stimuli. The action of dopamine is terminated by its re-uptake by a membrane-assocd. transporter protein and subsequent reutilization or catabolism by monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT). However, the major hazard with this neurotransmitter comes from the easier oxidn. of its catechol ring through a process which involves a single-electron transfer to oxygen (O2). Thus, the autoxidn. of dopamine results in the formation of anion superoxide (O2 -), hydrogen peroxide (H2O2), hydroxyl radical (OH) and other reactive oxygen species (ROS) capable of generating oxidative stress and consequently to initiate a neurodegenerative process.

The autoxidn. of dopamine is terminated with the formation of neuromelanin, a polymeric substance capable of accumulate iron, which enhances the vulnerability of dopaminergic neurons due the ability of this metal to promote the generation of ROS. The metab. of dopamine by MAO also involves the generation of H2O2, thus contributing to enhance the hazard of this neurotransmitter.
Furthermore, dopamine easily forms dopaminergic neurotoxins in the brain, which may cause depletion of ATP in dopaminergic neurons through inhibition of the mitochondrial respiratory chain with subsequent cell death. This review summarizes recent data supporting the danger dopamine holds for the brain, particularly for dopaminergic neurons, and its potential involvement in the pathogenesis and development of Parkinson's disease.

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Determination of trace elements in the human substantia nigra. Nuclear Instruments & Methods in Physics Research, Section B: Beam Interactions with Materials and Atoms 231:224-228, 2005.
Abstract : "The gain in brain is mainly in the stain" was long time a key sentence for research in neurodegenerative disease. However, for a quantification of the element concns. (esp. iron) in brain tissue, std. staining methods are insufficient. Advanced phys. methods allow a quant. elemental anal. of brain tissue. The sophisticated ion beam anal. provides a quant. detn. of elemental concns. with a subcellular spatial resoln. using a scanning proton beam focussed down to below 1 m that induces characteristic X-rays in the specimen (PIXE - particle induced X-ray emission). Histochem. and biochem. detns. of total iron content in brain regions from idiopathic Parkinson's disease have demonstrated an increase of iron in parkinsonian substantia nigra pars compacta but not in the pars reticulata, however without a clear cellular classification. For the first time, we have differentially investigated the intra- and extraneuronal elemental concns. (esp. iron) of the human substantia nigra pars compacta vs. pars reticulata with detection limits in the range of 50 mol/l. Thus, we could compare the neuronal iron concn. in human brain sections of healthy and parkinsonian brain tissue. Clear differences in the iron concn. and distribution could be disclosed. Addnl., we could show in situ that the increased intraneuronal iron content is linked to neuromelanin.

6. Genetics, molecular and developmental biology

(Dr. F. Beermann)

1: In the last few months, 3 papers were published which point to the existence of melanocytes and/or cells capable of producing pigment in heart (Mjaatvedt et al.), lens (Wang et al.) or thymus (Yamazaki et al.).

2: Mitf is one of the or the most important transcription factor involved in melanocyte-specific gene regulation. In the July 7 issue of Nature, Garraway et al. now report that Mitf is amplified in human metastatic melanoma and even more prevalent in metastasis. Additional experimental evidence furthermore suggests that Mitf can be regarded as a melanoma oncogene. For further comments, see also News and Views by Glen Merlino (Nature 436, 33-34).

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Metastasizing melanoma formation caused by expression of activated N-RasQ61K on an INK4a-deficient background. Cancer Res 65(10):4005-4011, 2005.

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Association of an Agouti allele with fawn or sable coat color in domestic dogs. Mamm Genome 16(4):262-272, 2005.

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A Tyrosinase missense mutation causes albinism in the Wistar rat. Pigment Cell Res 18(2):144-145., 2005.

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Hypoxia-inducible factor 1{alpha} is a new target of microphthalmia-associated transcription factor (MITF) in melanoma cells. J Cell Biol 170(1):49-59. Epub 2005 Jun 2027., 2005.
Shortened abstract: Our data demonstrate that Hif1a is a new MITF target gene and that MITF mediates the cAMP stimulation of Hif1a in melanocytes and melanoma cells. Importantly, we provide results demonstrating that HIF1 plays a pro-survival role in this cell system. We therefore conclude that the alpha-MSH/cAMP pathway, using MITF as a signal transducer and HIF1alpha as a target, might contribute to melanoma progression.

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Integrative genomic analyses identify MITF as a lineage survival oncogene amplified in malignant melanoma. Nature 436(7047):117-122, 2005.
Abstract: Systematic analyses of cancer genomes promise to unveil patterns of genetic alterations linked to the genesis and spread of human cancers. High-density single-nucleotide polymorphism (SNP) arrays enable detailed and genome-wide identification of both loss-of-heterozygosity events and copy-number alterations in cancer. Here, by integrating SNP array-based genetic maps with gene expression signatures derived from NCI60 cell lines, we identified the melanocyte master regulator MITF (microphthalmia-associated transcription factor) as the target of a novel melanoma amplification. We found that MITF amplification was more prevalent in metastatic disease and correlated with decreased overall patient survival. BRAF mutation and p16 inactivation accompanied MITF amplification in melanoma cell lines. Ectopic MITF expression in conjunction with the BRAF(V600E) mutant transformed primary human melanocytes, and thus MITF can function as a melanoma oncogene. Reduction of MITF activity sensitizes melanoma cells to chemotherapeutic agents. Targeting MITF in combination with BRAF or cyclin-dependent kinase inhibitors may offer a rational therapeutic avenue into melanoma, a highly chemotherapy-resistant neoplasm. Together, these data suggest that MITF represents a distinct class of 'lineage survival' or 'lineage addiction' oncogenes required for both tissue-specific cancer development and tumour progression.

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Allele variations in the OCA2 gene (pink-eyed-dilution locus) are associated with genetic susceptibility to melanoma. Eur J Hum Genet 27 Epub, 2005.

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Shortened abstract: Runx3 is expressed predominantly in the dermal compartment of the hair follicles as they form and during the hair cycle, as well as in the nail and sweat gland skin appendages. Distinct expression is also detected periodically in isolated cells of the epidermis and in melanocytes, populating the hair bulb. Runx3-deficient mice display a perturbation of the normal hair coat, which we show to be due to hair type and hair shape changes.

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beta-Catenin and Hedgehog Signal Strength Can Specify Number and Location of Hair Follicles in Adult Epidermis without Recruitment of Bulge Stem Cells. Dev Cell 9(1):121-131, 2005.
Comment: This paper mainly addresses (de novo) hair follicle formation, but also the role of ß-catenin induced hair-follicles to provide a niche for melanocytes.

- Steingrimsson E, Copeland NG, Jenkins NA.
Melanocyte stem cell maintenance and hair graying. Cell 121(1):9-12, 2005.

- Tadokoro T, Yamaguchi Y, Batzer J, Coelho SG, Zmudzka BZ, Miller SA, Wolber R, Beer JZ, Hearing VJ.
Mechanisms of skin tanning in different racial/ethnic groups in response to ultraviolet radiation. J Invest Dermatol 124(6):1326-1332, 2005.

- Thomas BB, Aramant RB, Sadda SR, Seiler MJ.
Light response differences in the superior colliculus of albino and pigmented rats. Neurosci Lett 9 Epub 2005.

- Wang L, Prescott AR, Spruce BA, Sanderson J, Duncan G.
Sigma receptor antagonists inhibit human lens cell growth and induce pigmentation. Invest Ophthalmol Vis Sci 46(4):1403-1408, 2005.

- Yamazaki H, Sakata E, Yamane T, Yanagisawa A, Abe K, Yamamura K, Hayashi S, Kunisada T.
Presence and distribution of neural crest-derived cells in the murine developing thymus and their potential for differentiation. Int Immunol 17(5):549-558. Epub 2005 Apr 2018, 2005.

- Zahed L, Zahreddine H, Noureddine B, Rebeiz N, Shakar N, Zalloua P, Haddad F.
Molecular basis of oculocutaneous albinism type 1 in Lebanese patients. J Hum Genet 4 Epub 2005.

7. Tyrosinase, TRPs, other enzymes

(Prof. J.C. Garcia-Borron)

- Boissy RE, Visscher M, Delong MA.
  DeoxyArbutin: a novel reversible tyrosinase inhibitor with effective in vivo skin lightening potency. Exp Dermatol. 14(8):601-8, 2005.

- Hall AM, Orlow SJ.
  Degradation of tyrosinase induced by phenylthiourea occurs following Golgi maturation. Pigment Cell Res. 18(2):122-9, 2005.

- Monji A, Inoue H, Oshima H, Aihara M, Tomioka M, Kumagai N.
  Tyrosinase induction and inactivation in normal cultured human melanocytes by endothelin-1. Int J Tissue React. 27(2):41-9, 2005.

- Schmidt-Kuntzel A, Eizirik E, O'brien SJ, Menotti-Raymond M.
  Tyrosinase and Tyrosinase Related Protein 1 Alleles Specify Domestic Cat Coat Color Phenotypes of the albino and brown Loci. J Hered. 96(4):289-301, 2005.

- Tadokoro T, Yamaguchi Y, Batzer J, Coelho SG, Zmudzka BZ, Miller SA, Wolber R, Beer JZ, Hearing VJ.
  Mechanisms of skin tanning in different racial/ethnic groups in response to ultraviolet radiation. J Invest Dermatol. 124(6):1326-32, 2005.

- Urosevic M, Braun B, Willers J, Burg G, Dummer R.
  Expression of melanoma-associated antigens in melanoma cell cultures. Exp Dermatol. 14(7):491-7, 2005.

- Wang N, Daniels R, Hebert DN.
  The Cotranslational Maturation of the Type I Membrane Glycoprotein Tyrosinase: The Hsp70 System Hands off to the Lectin-based Chaperone System. Mol Biol Cell. 2005 Jun 15

- Willers J, Lucchese A, Mittelman A, Dummer R, Kanduc D.
  Definition of anti-tyrosinase MAb T311 linear determinant by proteome-based similarity analysis. Exp Dermatol. 14(7):543-50, 2005.

8. Melanosomes

(Prof. J. Borovansky)

Various pathological pigment lesions (Dowling-Degos disease, melasma, PEComa) were ultrastructurally characterized (*Zhang&Zhu, Grimes et al, Koutlas et al*). Trafficking defects in Hermansky-Pudlak syndrome were both studied (*Boissy et al, Natsuga et al*) and explained in reviews (*Bonifacino, DiPietro&Dell´Angelica*). Oxidative changes of the melanin moiety of retinal pigment epithelium melanosomes were demonstrated (*Hong&Simon*) and discussed in relation to lipofuscin formation (*Sarangajaran &Apte*). MART-1 was shown to form a complex with Pmel17 which is important for melanosome maturation (*Hoashi et al*). An inverse relationship between MIA expression on the one hand and that of tyrosinase and TRP-1 on the other hand was observed (*Tatzel et al*). Lectins and niacinamide were reported to be able to inhibit melanosome transfer from melanocytes to keratinocytes *in vitro* with preliminary good results as for niacinamide also *in vivo* (*Greatens et al*). Threshold radiant exposures for bubble formation in water suspension of RPE melanosomes and nucleation temperatures were experimentally determined and used to calculate the absorption coefficient of a melanosome (*Neumann&Brinkmann*).

- Boissy RE, Richmond B, Huizing M, Helip-Wooley A, Zhao Y, Koshoffer A, Gahl WA.
  Melanocyte-specific proteins are aberrantly trafficked in melanocytes of Hermansky-Pudlak syndrome – type 3. Am J Pathol 166(1): 231-240, 2005.
  Comments: To assess the role of HPS3 protein in melanocytes, the cultured pigments cells developed from HPS3 patients were evaluated both histologically and biochemically. HPS3 melanocytes contained morphologically normal melanosomes, predominantly of stage I and II. DOPA reaction demonstrated an increase in melanization of melanosomes. Unique to HPS3 melanocytes were numerous DOPA-positive vesicles and tubular elements present throughout the cell body and dendrites. Tyrosinase, tyrosinase-related protein 1, DCT and LAMP1 and 3 localisation in HPS3 melanocytes demonstrated a fine flocular distribution in contrast to the coarse, granular distribution characteristic of control melanocytes. The localization profile of other proteins expressed by melanocytes appeared normal.

- Bonifacino JS.
  Insights into the biogenesis of lysosome-related organelles from the study of the Hermansky-Pudlak syndrome. Ann NY Acad Sci 1038: 103-114, 2004.
  Comment: A review.

- Di Pietro SM, Dell'Angelica EC.
  The cell biology of Hermansky-Pudlak syndrome: Recent advances. Traffic 6(7): 525 – 533, 2005.
  Comments: A review . Following the identification of a number of genes associated with HP syndrome the emerging picture is that HP syndrome can result from defects in the formation of, and cargo recruitment into, membrane-bounded transport carriers, in the tethering and regulation of fusion between endosomal compartments and/or derived transport carriers and the intracellular positioning and movement of late endocytic organelles.

- Fedorow H, Tribl F, Halliday G, Gerlach M, Riederer P, Double KL.
  Neuromelanin in human dopamine neurons: Comparison with peripheral melanins and relevance to Parkinson's disease. Progress in Neurobiol 75(2): 109-124, 2005.
  Comment: An extensive review comparing ultrastructural, biochemical, chemical properties and biological role of neuromelanin granules with those of melanosomes.

- Greatens A, Hakozaki T, Koshoffer A, Epstein H, Shwemberger S, Babcock G, Bisset D, Takiwaki H, Arase S, Wickett RR, Boissy RE.
  Effective inhibition of melanosome transfer to keratinocytes by lectins and niacinamide is reversible. Exp Dermatol 14(7): 498-508, 2005.
  Comments: Plasma membrane lectins and their glycoconjugates expressed by keratinocytes and melanocytes are critical molecules involved in the transport of melanosomes. Niacinamide is known to inhibit the transfer of melanosomes. The dosages of lectins and niacinamide not affecting cell viability were shown to exert an inhibitory effect on melanosome transfer when used either alone or together in cocultures of melanocytes-keratinocytes. Niacinamide was also tested in vivo – its topical application resulted in a dose-dependent and reversible pigment reduction in facial hyperpigmented spots.

- Grimes PE, Yamada N, Bhawan J.
  Light microscopic, immunohistochemical, and ultrastructural alterations in patients with melasma. Am J Dermatopathol 27(2): 96-101, 2005.

Comments: Having studied biopsies from 21 patients with melasma, the authors conclude that melasma is consequence of specific hyperfunctional melanocytes that cause excessive melanin deposition in the epidermis and dermis. Electron microscopy revealed more melanosomes in melanocytes, keratinocytes and dendrites in the involved skin in comparison to the uninvolved skin.

- Hoashi T, Watabe H, Muller J, Yamaguchi Y, Vieira WD, Hearing VJ
  MART-1 is required for the function of the melanosomal matrix protein PMel17/gp100 and maturation of melanosomes. J Biol Chem 280(14): 14006-140016, 2005.
  Comments: The role of MART1 (Melan A) in melanogenesis has remained unclear. Small interfering RNA technology and transfection of MART1 to MART1 negative melanoma cells were used to characterize the function(s) of MART1 in human melanocytes and human melanoma cells. MART-1 was shown to form a complex with protein Pmel17 which affects Pmel17 stability, its trafficking to early melanosomes and its processing to the Stage II form. Colour immunofluorescence microscopic pictures make the conclusions convincing.

- Hong L, Simon JD
  Physical and chemical characterization of iris and choroid melanosomes isolated from newborn and mature cows. Photochem. Photobiol. 81(3): 517-523, 2005.
  Comments: Bovine choroid and iris melanosomes were isolated from eyes of adult and newborn animals. Their physicochemical properties were studied by means of elemental analysis, infrared spectrometry, inductively coupled plasma mass spectrometry and X-ray photoelectron spectrometry. The article represents the most detailed study of the melanin moiety of isolated eye melanosomes and demonstrates not only tissue-related but particularly age-related chemical differences, namely oxidation-induced ring-opening of phenol rings and a decrease of carboxylate groups in the pigment.

- Koutlas IG, Pambuccian SE, Jessurun J, Manivel JC, Gopalakrishnan R
  Perivascular epitheloid cell tumor of the oral mucosa. Arch Pathol Lab Med 129(5): 690-693, 2005.
  Comments: A case report of perivascular epitheloid cell tumor (PEComa),. PEComas are a family of tumors defined by coexpression of melanocytic and muscle markers. Tumor cells were positive for melanocytic markers (HMB-45, MelanA/MART-1, MITF) and muscle markers (smooth muscle actin, desmin and calponin). Ultrastructural examination revealed stage I melanosomes. There are 2 hypotheses to explain the histogenesis of PEComas: 1) They are derived from undifferentiated cells of the neural crest that can express dual smooth muscle and melanocytic phenotype; 2) these tumors are of myoblastic origin but are molecularly altered and coexpress melanogenesis and melanocytic markers.

- Natsuga K, Akiyama M, Shimizu T, Suzuki T, Ito S, Tomita Y, Tanaka J, Shimizu H.
  Ultrastructural features of trafficking defects are pronounced in melanocytic nevus in Hermansky-Pudlak syndrome type 1. J Invest Dermatol 125(1): 154-158, 2005.
  Comments: Electron microscopic investigation of a melanocytic naevus seen in 17-y-old Japanese girl with HPS-1 revealed the presence of aberrant immature melanosomes , large membranous structures and giant melanosomes in the vicinity of trans Golgi network, i.e. the characteristic abnormalities because of protein trafficking defects. It is interesting that these ultrastructural features were far more clearly demonstrated in the naevus cells than in the epidermal melanocytes. The patient was a compound heterozygote of HPS-1 mutation with a novel mutation.

- Neumann J, Brinkmann R.
  Boiling nucleation on melanosomes and microbeads transiently heated by nanosecond and microsecond laser pulses. J Biomed Optics 10(2) , 2005, article 024001-*in press.*
  Comments: Melanosomes can act as devices converting energy, e.g. light into heat. Selective tissue damage on the cellular level can be achieved by microbubble formation around laser heated intracellular pigments. Aqueous suspension of porcine RPE melanosomes irradiated by short pulsed laser superheated the surrounding water to 150°C.

- Pashkova N, Catlett NL, Novak JL, Weisman LS.
  A point mutation in the cargo-binding domain of myosin V affects its interaction with multiple cargoes. Eukaryotic Cell 4(4): 787-798, 2005.
  Comments: Class V myosins move diverse intracellular cargoes which attach via interaction of cargo specific proteins to the myosin globular tail. The paper describes subdomains of the globular tails of yeast myosin V and their interactions. Transport of melanosomes is mentioned only marginally.

- Sarangajaran R, Apte SP.
  Melanin aggregation and polymerization: Possible implications in age-related macular degeneration. Ophthalmic Res 37(3): 136-141, 2005.
  Comments: Degradation processes in/of melanosomes and lysosomes in the retinal pigment epithelium appear to be intimately connected so that they may involve exchange of contents between these two organelles. It is speculated that age-related accumulation of low molecular weight phototoxic prooxidant melanin oligomers within

lysosomes of RPE may be responsible for decreasing the digestive rate of incorporated cellular components which may lead to lipofuscin formation.

- Tatzel J, Poser I, Schroeder J, Bosserhoff AK.
  Inhibition of melanoma inhibitory actvity (MIA) expression in melanoma cells leads to molecular and phenotypic changes. Pigment Cell Res 18(2): 92-101, 2005.
  Comments: Excellent report demonstrating an inverse correlation between melanoma inhibitory activity (MIA) expression and pigmentation. MIA-deficient cell clones (obtained via stable antisense MIA cDNA transfection) were distinctly pigmented and contained stage III and IV melanosomes. Molecular analyses revealed reexpression of tyrosinase and TRP-1 in MIA deficient cells. PAX3 mRNA and MITF protein were also expressed only in MIA deficient cells. (MITF and PAX3 are positive regulators of TRP-1 and tyrosinase transcription).

- Zhang RZ, Zhu WY.
  A study of immunohistochemical and electron microscopic changes in Dowling-Degos disease. J Dermatol 32(1): 12-18, 2005.
  Comments: Dowling-Degos disease is an autosomal dominant inherited pigmentary disorder characterized by reticulate pigmentation of the flexures, comedone-like lesions and pitted scars. Thorough ultrastructural and immunohistochemical analyses of the pigmentary lesions revealed elongated epidermal rete ridges with basilar hyperpigmentation. All pigmented cells in the basal layer were recognized by antiPEP-1, antiPEP-2, HMB-45 and NKI/beteb antibodies. Melanocytes contained regular melanosomes in all stages of their maturation. Supranuclear „ melanosome caps“ were present both in melanocytes and keratinocytes in the hyperpigmented area.

ANNOUNCEMENTS & RELATED ACTIVITIES

Calendar of events
PCR new enhanced website
IPCC Info Update

Calendar of events

2005 6th World Congress on Melanoma

September 6-10, Vancouver BC, Canada
Contact: Congress Secretariat
Venue West Conference Services Ltd.
645 - 375 Water Street
Vancouver BC,
V6B 5C6 - Canada
Tel : 1-604-681-5226
Fax: 1-604-681-2503
E-mail: congress@venuewest.com
Web site : www.ipcc.info/

2005 XIVth International Pigment Cell Conference (IPCC)

September 18-23, Reston, Virginia, USA
Contact: Dr. V. HEARING
E-mail: hearingv@nih.gov
Web: www.ipcc.info
Satellite Meetings : Friday, September 23, 2005
- "**Melanoma**", coordinated by Meenhard Herlyn
(co-sponsored by the Society for Melanoma Research)
- "**Photobiology**", co-chaired by Frances Noonan and Sharon Miller
(co-sponsored by the American Society for Photobiology)
- "**Vitiligo**", co-chaired by Mauro Picardo and Alain Taieb
(co-sponsored by the IFPCS Vitiligo Special Interest Group)

2005 35th Annual ESDR Meeting

September 22-24, Tübingen, Germany
Contact: E-mail: office@esdr.org
Web: www.esdr.ch

2005 14th Congress of the European Academy of Dermatology and Venereology

October 12-16, London, United Kingdom
Contact: CTS
Data House
Curriers Close, Tile Hill
UK - Coventry CV4 8AW
Tel: +44 (0)870 429 4612
Fax: +44 (0)870 429 4613
Email: eadv@ctsnet.co.uk
Web: www.eadv2005.com

2005 Perspectives in Melanoma IX

November 17-18, Tampa, Florida — Tampa Marriott Waterside
Chairmen: John M. Kirkwood, MD and Alexander M.M. Eggermont, MD, PhD
Contact: Coleson Chase
Tel: +1 (770) 751 7332
Email: meetings@imedex.com
Web: http://www.imedex.com or http://www.imedex.com/announcements/melanoma05.asp

2005 19th Annual Meeting of the Japanese Society for Pigment Cell Research (JSPCR)

December 3-4, Yokohama City, Japan
Chair: Prof. Toyoko Akiyama, Keio University
Contact: E-mail: hakiyama@hc.cc.keio.ac.jp

2006 4thEuropean Academy of Dermatology and Venereolog (EADV) Symposium

February 9-12, Saariselkä, Lapland, Finland
Contact : E-mail: lapland2006@congrex.fi
Web: www.eadv.org/lapland2006

2006 36th Annual ESDR Meeting

September 7-9, Paris, France
Contact: E-mail: office@esdr.org
Web: www.esdr.ch

2006 XIIIth Meeting of the ESPCR

September 24-27, Barcelona, Spain
Contact: Dr. L. Montoliu
E-mail: montoliu@cnb.uam.es
Web: www.cnb.uam.es/~espcr06/

2007 37th Annual ESDR Meeting

September 6-8, Zurich, Switzerland
Contact: E-mail: office@esdr.org
Web: www.esdr.ch

2007 XIVth Meeting of the ESPCR

September , Bari, Italy
Organizer: Prof. Rosa Cicero

2007 21st World Congress of Dermatology

October 1-5, Buenos Aires, Argentina
Contact: E-mail: info@dermato2007.org
Web: www.dermato2007.org

2008 International Investigative Dermatology (Joint Meeting of the ESDR, SID and JSID)

May 14-17 , Kyoto, Japan
Contact: E-mail: office@esdr.org Web: www.esdr.ch

2008 20th International Pigment Cell Conference (IPCC)

Sapporo, Japan

PIGMENT CELL Research new enhanced website at www.pcr.org

We are pleased to announce the launch of a new enhanced website for Pigment Cell Research with several new features, improved navigation and a modernized lay-out.

On this site, there is a specific Editor s page, where Colin Goding will be posting comments relevant to the journal, or to the pigment cell community. Right now, you will find a very valuable article on writing a scientific paper.

All reviews published in Pigment Cell Research since February 2005 are freely available, and can be accessed from the new website as well.

In addition, we have collated articles on vitiligo and melanoma respectively in two virtual issues. The virtual issues will be updated progressively as more papers are published on these topics in the journal. More virtual issues are planned to be launched within the next year.

Under the heading of Pigment Cell Resources we have designed a special area with society information as well as relevant meetings. Also, as an extra service to the pigment cell community we will have a special section with the results of key gene arrays on melanocytes. Data in this section will be freely available to the community and will be carefully selected for quality and usefulness by Colin Goding and Bill Pavan. The first array data included is from Keith Hoek (Zürich) and details expression of genes in normal human melanocytes in culture. This data should enable you to determine whether any gene of interest is expressed in this cell type.

Colin Goding
Editor-in-Chief

Pernille Hammelsø
Journal Publishing Manager

IPCC INFO UPDATE

Dear Colleagues,

There will be an Open Season for Late-Breaking Abstracts that can be submitted to the IPCC from July 24 - Aug 24.
The format requirements are the same as before and are noted on the web site. The rule remains that an individual can be a presenter of only 1 paper (oral or poster) at the IPCC, but can be a coauthor on any number of abstracts.

* Late-Breaking abstracts will be by poster only (with the possible exception that if a currently scheduled oral lecture is cancelled, all abstracts will be considered for that open spot).
* Late-Breaking abstracts will not be published in the PCR Supplement, but will be copied and distributed to all attendees of the meeting.
* All Late-Breaking abstracts must be submitted online by August 24.

The Scientific Program of the 19th IPCC is now finalized and can be accessed on the web site. Abstracts will be available for download on the web site as of August 1st (Late-Breaking abstracts will be added soon after the Aug 24th deadline).

The deadline for Registration and Hotel Reservations is August 24, 2005, after which time there is a late penalty fee for registration and hotel rooms will be available only at the standard rate.

IMPORTANT DATES

July 24, 2005	- Late-Breaking Abstract submission begins.
Aug 24, 2005	- Deadline for hotel reservations, normal registration and Late-Breaking Abstract submission.
Sept 18-22, 2005	- 19th Intl Pigment Cell Conference, Hyatt Regency Hotel, Reston, Virginia
Sept 23, 2005	- Melanoma, Photobiology and Vitiligo Satellite Symposia.

On behalf of the Local and the International Program Committees, we look forward to welcoming you to the Washington DC area for a very successful meeting.

Vince Hearing, Organizer, 19th IPCC
E-mail: hearingv@nih.gov

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Plan to attend the 19th International Pigment Cell Conference
http://www.ipcc.info

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