ESPCR and ESPCR Bulletin WEB site
http://www.ulb.ac.be/medecine/loce/esPCR.htm

HAPPY NEW YEAR 2000

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INTERNATIONAL FEDERATION OF PIGMENT CELL SOCIETIES

OFFICERS: Shouke Ito (JSPCR, President); Stan Pavel (ESPCR, Vice-President); Richard A. King (PASPCR, Secretary/Treasurer).

COUNCIL MEMBERS: Sally Frost-Mason (PASPCR); Sheila Mac Neil (ESPCR); Masako Mizoguchi (JSPCR); James J. Nordlund (PASPCR); Patrick A. Riley (ESPCR); Shigeki Shibahara (JSPCR); Vincent J. Hearing (Ex-Officio member as the Editor of Pigment Cell Research)

A Letter from the IFPCS President to the ESPCR members.

As the chair of the 17th International Pigment Cell Conference (IFCC) held in Nagoya this fall, I wish to express my sincere thanks to ESPCR and PASPCR members as well as other participants who came a long distance to attend the meeting. We were very pleased to welcome 69 participants from the European continent (13 countries), 71 from the North American continent (2 countries), and 28 from the Asian continent (4 countries), in addition to 139 from Japan. Interest and attendance at the symposia and satellite meetings were great and stimulating discussions were held during and between the formal sessions throughout the meeting. We do believe that most, if not all, of the participants learned new advances in pigment cell research and also enjoyed the social programs.

The outgoing and new members of the IFPCS Council held two official meetings during the Nagoya IFCC and elected, as Officers for the next 3 years, Shouke Ito (JSPCR) President, Stan Pavel (ESPCR) Vice-President and Richard A. King (PASPCR) Secretary/Treasurer. The election was based on the rotation cycle that began 9 years ago when the IFPCS was established at the Kobe IFCC. I am very honored to serve as the President following the successful completion of the terms of the previous 3 Presidents, Drs. Yutaka Mishima, Giuseppe Pozzoli, and Vincent J. Hearing. On behalf of the Officers, I wish to assure you that we will work hard with the Council to continue the growth and interactions initiated during the first 3 IFPCS administrations. We want to congratulate the departing Officers, President Vincent J. Hearing, Vice-President Yoshiaki Horii, and Secretary-Treasurer Patrick A. Riley for their outstanding work and achievements in the last 3 years. Their efforts greatly helped the IFPCS grow and initiate new activities that make the IFPCS more effective in fostering scientific exchange among members. We also would like to welcome new Council members, Drs. Patrick Riley (who served as the Secretary/Treasurer following the untimely death of Dr. Bengt S. Larsson), Richard A. King, and Shigeki Shibahara and express farewell to departing Council members, Drs. Yoshiaki Horii and Yutaka Mishima.

The IFPCS has established the following goals for the Federation (also available on the IFPCS Web page at https://www.cbc.umn.edu/ifpcs/)

1. To encourage the dissemination of knowledge related to pigment cells by the establishment, sponsorship and support for the publication of books, bulletins, newsletter, journal, reports or other means.

2. To organize a tri-annual international meeting, to honor outstanding contributions in the field by awarding the Myron Gordon award at that meeting, and to select a scientist who has made recent and significant advances in the field to present the Seiji Memorial lecture.

3. To foster and enhance research on pigment cells and pigmentation among the regional Societies and to foster scientific collaboration, cooperation and communication among the regional Societies.

Goal #1 was achieved by establishing an official IFPCS-sponsored journal, Pigment Cell Research (http://www.pigment.org). Thanks to the efforts of the founding Editor Dr. Joseph T. Bagnara (1987-1994) and the subsequent Editors Drs. Takoji Takeuchi (1995) and Jiro Matsumoto (1996-1999), the journal has grown steadily and shown continuous improvement to the point that it now has an Impact

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Factor score of 1.3. I wish to congratulate Dr. Jiro Matsumoto for his outstanding job in promoting the progress of the journal during his 4-year term as Editor. The journal will now enter a new era under the leadership of Editor Dr. Vincent J. Hearing (2000-2004) who will be supported by a new panel of 15 Associate Editors. To further promote the growth of the journal, it is essential that the numbers of subscribers and submitted papers be increased. I wish to urge all PASPCR members to subscribe to Pigment Cell Research, as this is the official journal of the Federation. With your help, I am confident that the 5-year editorship of Dr. Hearing will produce even further progress in the rank and value of Pigment Cell Research.

Goal #2 may be the most visible one among the several efforts that the IFPCS has been making. Starting with the Nagoya IPCC, the Federation has established the rule that the (International) Scientific Program Committee should include the IFPCS President and 3 Council members, allowing the Local Organizing Committee to work closely with representatives from the Federation in selecting speakers and Symposium topics. As the Chair of the 17th IPCC, I found this system to work very smoothly and effectively. Much of the credit for the scientific success of the Nagoya IPCC should be given to Dr. Hearing and other members of the International Program Committee. As the President of the Federation, I am now looking forward to working closely with the Chair of the 18th IPCC, Dr. Stan Pavel. I am happy to inform you that the venue of the 18th IPCC, to be held in September 2002, is a splendid, five-star hotel in Scheveningen on the North Sea coast of the Netherlands.

Goal #3 is being achieved through three related and important initiatives that the IFPCS has taken in the past several years. Special Interest Groups have been established and are providing substantial benefits to our scientific community, as shown on our Web page. We now have Special Interest Groups in the subdisciplines of Biology of Melanoma, Developmental Biology, Genetics of Pigmentation, Hypo/Hyperpigmentation, Ocular/Extracutaneous Pigmentation, and Vitiligo. As the Chair of the 17th IPCC, I was very pleased that three of those groups held Satellite meetings at the IPCC under the regimes of the Vienna: A Manifestation of Aggression? 2) Regulation and Genetics of Pigmentary Genes, and 3) Cellular and Molecular Control of Pigment Cell Development. All the Satellite meetings were well attended and appreciated. The Federation Council has decided to continue these Interest Groups as a mechanism to promote pigment cell research, another initiative to achieve Goal #3 was the establishment of the IFPCS Visiting Scientist Award. The grants, established in 1997, are intended to support investigators from one of the regional Societies who wish to visit the laboratory of an investigator in another regional Society to learn specialized techniques and/or to establish collaborations. You will find a full description of the program, the name of generous corporate donors, and the name of awardees on the IFPCS web page. The program was established with funding for 9 visiting scientist awards, with each regional Society being allotted 3 awards for the 3-years period beginning in 1997. To date 5 individuals have received an award of $3,000 each to cover expenses for their travel and accommodation. The initial 3-year period of the program will end next year, but we hope to continue this program with a renewal of corporate donations.

The third initiative is the establishment of the InterPig DataBase, which collects data on research reagents and resources available to the pigment cell community. The database is available to all researchers, especially to members of regional Societies. It includes 115 biochemicals, cell cultures, immunological and molecular biology reagents, and mouse mutants. I hope that ESPCR members will take advantages of the database and will consider adding their new and/or valuable reagents to the database so that these reagents are available to other investigators. This will make the database more useful and will promote pigment cell research collaborations among the scientific community.

Finally, I sincerely hope that we will see healthy and steady progress in our 3 regional Pigment Cell Societies, ESPCR, JSPCR, and PASPCR as our term on the IFPCS Council extends to the 21st century. I urge each of you to contribute to your Society in any way you can: submitting your abstracts to the regional Society meetings, publishing your papers in the Pigment Cell Research, collaborating with other members, and recruiting other scientists and clinicians to join us.

Shouske Ito, President, IFPCS
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2. Biology of pigment cells and pigmented disorders

(Ree. M. Picaldo)

A special issue of the Journal of Investigative Dermatology was dedicated to the Proceeding of the Annual Symposium on the Biology of the skin dedicated to the molecular mechanisms of light-induced damage and the effect of light on human skin disease. Among the papers reported, some reviews are focused on the mechanisms of control of pigmentation and other on the disease of the pigimentary system. V. Hearing summarized the current knowledge on the regulation of mammalian pigmentation at the genetic and biochemical level. Almost half of mammalian pigmentation regulatory genes encode proteins that localize, either specifically or area specifically, to melanosomes; mutation in these genes generally lead to phenotypic changes in pigmentation as well as in other pleiotropic changes. The expression and function of these proteins affects both the phenotypic appearance and the melanin properties, especially in their photoprotective characteristics. I. Suzuki et al have reported data on the participation of the melanocortin-1 receptor (MC1R) in the mechanism of UV-induced pigmentation trough the stimulation of cAMP formation, which is a principal mechanism for inducing melanogenesis. B. Gilchrest and M. Elfer reviewed the data on the role of DNA photoproteins in stimulating pigmentation. R. Setlow, in considering the UV spectral regions contributing to melanoma, reported the possible role of UV. K. Schallreuter and co-workers reviewed the literature and present new data on oxidative stress in the epidermal compartment during vitiligo. They reported that high H2O2 levels can be demonstrated in vivo in the skin of patients with active disease by utilizing Fourier-Transform Raman spectroscopy and that H2O2 accumulation was associated with low epidermal catalase levels. The authors conclude that there are several lines of evidence that the entire epidermis of patients with vitiligo is involved in the disease process and that correction of the epidermal redox status is mandatory for repigmentation.

It has recently been shown that cutaneous axon terminals and epidermal melanocytes make contact via chemical synapses in human skin and that calcitonin gene-related peptide (CGRP) reduces melanocyte proliferation. To further clarify the effect of neuropeptides on the biology and morphology of melanocytes, especially with respect to melanogenesis and melanocyte dendricity, Toyoda et al have exposed organ cultures of normal human skin and cultured melanocytes to various neuropeptides present in intradermal nerve endings. Among the neuropeptides examined, CGRP showed to increase melanocyte number, epidermal melanin content, melanosome number and degree of melanization. Their findings suggest that keratinocytes produce and secrete some melanotrophic factors following stimulation with CGRP, which modulate growth, melanin synthesis, and dendricity of melanocytes. For the authors, these data demonstrate intimate interaction between the cutaneous nervous system and melanocytes within the epidermal environment.

Alpha-melanocyte stimulating hormone (alpha-MSH) is produced by several different type including neural cells, entodermal cells, monocytes, and keratinocytes. A biologic role in melanocyte pigmentation is widely recognized, but several recent studies described an role in anti-inflammatory and immunomodulating responses. J. Maresco et al, investigate the mechanism by which alpha-MSH was effective in opposing TNFa-stimulated increase in NF-kB DNA binding activity in normal ocular melanocytes; cell cultured from ocular melanoma tumors; and cutaneous melanoma cell lines. The authors showed that alpha-MSH significantly reduced NF-kB DNA binding activity in melanocytes and melanoma cells. Their increasing results suggest that this can be a key pathway by which immunomodulation anti-inflammation may operate.

Funakata et al have previously reported that advanced melanoma cells generally produce higher amounts of proopiomelanocortin (POMC) peptides than normal melanocytes and that the production correlates with tumor progression. In this study, to elucidate the mechanism of this upregulation, they evaluated the expression of genes encoding corticotropin-releasing hormone (CRH) and its receptor, CRH-R, as well as POMC and the MSH receptor (MC1-R), using cultured human melanoma cells, mouse cells and normal melanocytes. Their results show that all melanocytic cells express CRH, CRH-R, POMC and MC1-R, with higher intensities in melanoma cells. Furthermore, immunohistochemistry showed that CRH as well as POMC was strongly expressed in advanced melanoma such as vertically growing lesions of acral lentigenous, nodular and metastatic melanosomas, in contrast to negative expression in nveous cells. Those results indicate tumor progression accelerate CRH, CRH-R, and POMC expression by melanoma cells.

Vitamin A is an intrinsic modulator of proliferation and differentiation in human epidermis, and may be destroyed by ultraviolet radiation (UV). Impinging on the skin. To identify the deleterious effects of a perturbed cellular vitamin A status, Anderson and co-worker have investigated the endogenous retinoid concentration and the metabolism of [3H]retinol and all-trans [3H]retinoic acid in cultured human keratinocytes and melanocytes exposed to UVR. Before UVR the study of cells cultured in keratinocytes and melanocytes, but in both cell types, UVR instantaneously reduced the concentration of retinol and of 3,4-dihydroxyretinol. The retinoid concentration reduced to normal within 1-2 days post-irradiation. However, in both types of irradiated cells, the accumulation of the biologically most active metabolite, all-trans [3H]retinoic acid, was higher than in control cells. Furthermore the metabolism of authentically supplied [3H]retinoic acid was reduced, especially in irradiated keratinocytes, which probably contributed to the restoration of retinoid levels after

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K. Schallreuter and J. Wood reported, in cultured melanocytes, a significantly more rapid active transport and autocrine turnover of L-phenylalanine than of L-tyrosine. Moreover, the transport of extracellular L-phenylalanine and its metabolism to L-tyrosine was via phenylalanine hydroxylase and coupled to a calcium-dependent active uptake/storage, whereas L-tyrosine uptake was calcium independent. According to the authors, these results suggest the importance of an autocrine calcium-dependent active L-phenylalanine uptake/turover in melanocytes as a major pathway for melanogenesis.

Exposure to phenolic agents contributes to the development of occupational vitiligo. Proposed as a causative factor for leukodermia in vivo, the para-substituted phenol 4-tertiary butyl phenol was chosen by Le Poole and co-workers to investigate early cellular events responsible for selective disappearance of melanocytes from epidermis of individuals sensitive to such agents. To this end, differential display of melanocyte mRNA isolated from three separate cultures was performed following a 12 h exposure of cells to 4-tertiary butyl phenol or vehicle. A total of 130 genes were identified. The L30 ribosomal protein was upregulated by the treatment, potentially reflecting altered levels of protein synthesis in response to stress. In addition, a gene sequence upregulated following exposure to 4-tertiary butyl phenol was identified as the Arf receptor (a PI-receptor for adenosine). Flow cytometry confirmed differential expression in melanocytes and fibroblasts. Interestingly, it has been reported that PI3-puriﬁcation stimulation can induce apoptosis. This is in concordance with results reported demonstrating induction of apoptosis by 4-tertiary butyl phenol in human melanocytes, as well as with morphologic changes observed in this study in cells exposed to 4-tertiary butyl phenol for 72h.

Yang and co-workers have determined that 4-TBP competitively inhibited both tyrosine hydroxylase and dihydroxyphenylalanine (DOPA) oxidation activities of tyrosinase, i.e., the mRNA, the first two catalytic steps in the biochemical conversion of tyrosine to melanin in cultured human melanocytes. This inhibition occurred at concentrations that did not influence the viability of melanocytes. Since depigmentation occurred without a cytotoxic response it is unclear whether the interaction between 4-TBP and tyrosinase leads to the destruction of melanocytes in contact/occupational vitiligo.

Sulfur-containing tyrosine analogs such as 4-S-cysteaminyldopanol (4-S-CAP) and its N-earcyll derivative, N-earcyll-4-S-CAP, are tyrosinase inhibitors and are known to cause selective cytotoxicity and cell death of melanocytes and melanoma cells. It is not clear, however, if the cytotoxicity derives from a cytostatic or cytotoxic effect. The latter can also be either apototic or necrotic. Misamguji and co-workers summarize their attempts to clarify the nature of melanocyte toxicity and cell death by using a new derivative of 4-S-CAP, N-earcyll-4-S-CAP (NFCAP). The tyrosinase-mediated cytotoxicity of NFCAP was further confirmed by the decreased viability of COS-7 monkey kidney cells, transfected with human tyrosinase cDNA. NFCAP, however, also transiently inhibited the proliferation of melan cells, a control tyrosinase-negative albino melanocyte line, and vector-transfected COS-7 cells. Thus, the major process of NFCAP-mediated melanocytoxicity involves cytoplasmic apoptosis associated with active tyrosinase. In addition, there was a transient, non-tyrosinase-mediated cytotoxicity.

Microphthalmia (mi) is a transcription factor that plays a major role in the regulation of growth and function in melan cells and melanocytes. Association of mi with other proteins is in the critical step of mi-mediated transcriptional activation. Razi et al have found potential protein kinase C-dependent protein (PKC) associated with mi in yeast two-hybrid screening. PKC by itself, although localized in the cytoplasm and nucleus of the cell, has no known physiological function and did not demonstrate transcriptional activity. Its ability to suppress mi transcriptional activity in the transient transfected fibroblast cell system suggests that it can function in vivo as a negative regulator of mi-induced transcriptional activation.

In order to study whether mechanical stretching plays a role in human melanocytes, Klempnerberger et al have established a culture technique to mimic the physical stretching. Primary cultures of human melanocytes were plated on silicon supports which undergo a stretching of about 10% of the initial length. After application of stretched stretching and relaxation for 4 days, cell count was significantly enhanced. In addition, they found 2-fold increase in heat shock protein (HSP) 90, both at the protein and mRNA level. The stretch-mediated up-regulation of HSP90 expression in melanocytes appeared to be independent of stretch-mediated growth stimulation. For the authors, these findings have strong implications for the design and cultivation of melanocytes for transplantation purposes.

In mice a motor neuron of the myosin V class (designated myosin Va) is known to be the product of distinct locus, where a mutation prevents melanosome transport in melanocytes. There is conflicting evidence about whether it has a role in dendritic outgrowth. Edgar and Bennett have demonstrated its role by transiently transfecting antisense oligonucleotides to inhibit its expression in a melanocyte cell line. Myosin Va protein levels were similar in 3 melanocyte cell lines with differing amounts of pigmentation, indicating that expression of myosin Va is not tightly coupled to expression of melanin. Immunocytochemistry showed 2 types of myosin Va localization. A punctate pattern of staining concentrated in the perinuclear region was indicative of endosomal association, and the observation of occasional punctate staining aligned with F-actin bundles supported the idea that myosin Va has a role in transporting melanosomes along actin filaments. Staining was also intense at tips of dendrites and at sites of dendrite-cell contact, consistent with a possible role in dendrite growth. The authors conclude that in addition to its role in transporting melanosomes through myosin Va has a role in the extension of new dendrites by melanocytes but not in maintenance of pre-existing dendrites.

Rogers et al demonstrate that myosin V is the actin-based motor responsible for melanosomes transport. Mobility of melanosomes treated with mitotic extract was found to decrease dramatically, as compared with untreated or interphase

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extracted melanosome. This mitotic inhibition of mobility correlated with the disorganization of myosin V from melanosome, whereas the activity of soluble motor remained unaffected. The authors conclude that organelle transport by myosin V is controlled by a cell cycle-regulated association of this motor to organelles, and that this binding is likely regulated by phosphorylation of myosin V during mitosis.

Melanosocytes (Mc) and their progenitors melanoblasts (Mb) are derived from the neural crest and migrate along the dorsolateral pathway to colonize the dermis, the epidermis, and finally the hair matrix. To examine the involvement of cadherin in the migration of Mc lineage cells, Nishimura et al combined flow cytometric analysis of dissociated live cells with immunohistochemical staining of tissue sections to quantify the level of cadherin expression on the surface of Mc/Mb. While most of the normal Mc/Mb disappear after the neocellular stage in normal mice, forced expression of cadherin in the epidermis of transgenic mice promotes survival of epidermal Mc/Mb, maintaining epidermal-type cadherin expression pattern (E-cad(high)P-cad(low)) throughout the postnatal life. These finding indicate the involvement of extrinsic cues in coordinating the cadherin expression pattern and suggest a role for E- and P-cadherin in guiding Mc progenitors to their final destinations.

Solinmori et al reported that cultured melanoma cells can synthesize steroid such as corticosterone from progesterone or deoxycorticosterone. Corticosterone production was strongly responsive to deoxycorticosterone substrate addition (12-fold increase), but unresponsive to the adrenal stimulating factors ACTH and angiotensin II.

Francis and co-worker described the occurrence of 4 transcripts differentially displayed between syngenic murine B16F10 (metastatic melanoma) and melan-a (immortalized melanocytes) cell line. They report that one of such transcript, which is B16F10-specific, represent a protein phosphatase-2A B' regulatory subunit. In situ hybridization studies on human clinical samples detected high expression of this gene in a number of malignant melanomas. For the authors these results imply strongly that this protein phosphatase-2A regulatory subunit may have a role in melanoma tumor progression.

Clotti et al have investigated the expression of intercellular adhesion molecule-1 (ICAM-1) and granulocyte-macrophage colony stimulating factor (GM-CSF) in melanoma patients by evaluating fresh biopsy specimens by in situ hybridization and immunocytochemistry. Most of their metastatic melanoma samples and a few of the primary melanoma lesions showed ICAM-1 expression. The expression of ICAM-1 was significantly (P<0.01) higher in metastatic lesions than in primary tumours. GM-CSF mRNA and protein were higher detected in 10 of the 18 metastatic samples and in two of the 15 primary lesions. These findings, if confirmed by a wider number of patients, could suggest the prognostic value of the simultaneous, and probably co-ordinated, expression of ICAM-1 and GM-CSF. They also highlight the importance of these molecules in the metastasis process of melanoma. In particular, the particular cytokine to be used as anticancer therapy and/or as adjuvant to chemotheraphy.

Growth hormone (GH) exerts its regulatory functions in controlling metabolism, balanced growth and differentiation cell expression by acting on specific receptors, which trigger a phosphorylation cascade resulting in the modulation of numerous signalling pathways, and dictate gene expression. Lincoln and co-worker use immunohistochemical techniques to demonstrate the presence of GH receptors in 126 formalin-fixed, paraffin-embedded melanocytic tumours comprising melanocytic naevi, superficial spreading melanoma, nodular melanoma, lentigo melanoma and metastatic melanomas. The relative proportion of positive cells and intensity of staining was higher in neoplastic cells, compared to normal cutaneous cells. In the primary lesions, dermal tumour cells tended to be more immunoreactive relative to those seen in dermal region. Metastatic lesions in various organs also expressed GH receptors in secondary tumour cells and all of the metastatic cases were positive. The expression of GH-receptors in human melanoma cells means that these cells are directly responsive to GH action and that GH may stimulate local production of IGF-1, which then acts in an autocrine mechanism.

Grawcm et al assess the expression patterns of vascular endothelial growth factor (VEGF) and its two receptors, flt-1 and KDR, in normal human melanocytes, transformed melanocytes expressing the simian virus 40 Teges (SV40T), and melanoma cells derived from primary and metastatic lesions. Constitutive expression of VEGF, flt-1 and KDR mRNA and protein was observed in the majority of primary and metastatic melanoma cell lines, and in SV40T-transformed melanocytes. In summary, co-expression of VEGF and its receptors seems to be a tumor-associated phenomenon in melanoma development. However VEGF production did not support autocrine proliferation of the melanoma cell line studied.

Dipetidyl peptidase IV (DPPIV) is a cell surface peptidase expressed by normal melanocytes, epithelial cells, and other cells. Malignant cells, including melanomas and carcinomas, frequently lose or alter DPPIV cell surface expression. Loss of DPPIV expression occurring during melanoma progression at a stage when they transformed melanocytes become independent of exogenous growth factors for survival. Welley and co-worker suggest that rescue of fibroblast activation protein a receptor with DPPIV could provide a role in regulating growth and survival of melanoma cells. These results support the view that down-regulation of DPPIV is an important early event in the pathogenesis of melanoma.

Macrophage migration inhibitory factor (MIF) is known to function as a cytokine, hormone, and procoagulant-inducided immunoregulator. Shimizu et al have reported for the first time that human melanocytes and melanoma cells express MIF mRNA and produce MIF proteins. To assess the role of MIF overexpression in melanoma cells, G361 cells, a widely available human melanoma cell line, were transfected with an antisense human MIF plasmid. Their results demonstrate that the cell growth rate of the transfected cells was markedly suppressed, suggesting that MIF participates in the
mechanism of proliferation of melanoma cells. Further more, the administration of anti-MIF antibody significantly suppressed tumor-induced angiogenesis. The authors suggest that MIF may function as a novel growth factor that stimulates incessant growth and invasion of melanomas concomitant with neovascularization.

Ephrin-A1, a new melanoma growth factor, is angiogenic and chemotactic for endothelial cells. EPH-A2, or ECaK (a receptor for ephrin-A1), is ectopically expressed in most melanoma cell lines; the possible role of the receptor in tumor progression is unknown. Raj et al have studied the expression of this ligand and receptor in biopsies of benign and malignant melanocytic lesions. Their findings are consistent with 2 possible roles for ephrin-A1 in melanoma development: it may promote melanocytic growth or survival and induce vascularization in advanced melanomas. Both effects may be potentiated by inflammatory responses.

Activation of the endothelial receptor B (ETRB) in cultured melanocytic progenitors promotes cell proliferation while inhibiting differentiation, two hallmarks of malignant transformation. Lahav et al have tested whether ETRB has a similar role in malignant transformation of melanoma. When tested in culture, they find that the selective ETRB antagonist BQ788 can inhibit the growth of seven human melanoma cell lines. Extending these study in vivo, they find that administration of BQ788 significantly slows human melanoma tumor growth in nude mice. Thus, the authors suggest that ETRB inhibitors may be beneficial for the treatment of melanoma.

Sauder reports the expression of p53, p16, and Bcl in malignant melanomas resulting in benign nevi. P53 immunoreactivity was found only in the malignant component, with no expression being seen in the benign component of the lesions. In opinion of the author, this suggests that this tumor suppressor gene is involved in the pathogenesis of melanomas.

Pavey et al have demonstrated the existence of a UV-induced response pathway involving up-regulated p16 expression may provide a mechanism linking the loss of p16 and UV exposure with the development of melanomas.

The Cdc25C locus encoding the PTTSLR protein kinase maps to chromosome band 1p36 and consists of 2 duplicated and tandemly linked genes. Ariza and co-worker have determined whether dimethylination of PTTSLR kinase leads to deregulation of apoptosis. The authors suggest that alterations in PTTSLR gene expression and protein localization may result in the loss of apoptotic signaling.

It is not known if immune response to T cell-defined human histocompatibility leukocyte antigen (HLA) class I-restricted melanoma antigens leads to an expanded peripheral pool of T cells in all patients, affects cytotoxic T lymphocyte (CTL) generation, and correlates with anti-tumor response in metastatic lesions. To this end, Anichini and co-worker have developed a limiting dilution analysis technique that allowed to evaluate the same frequency of peptide-specific T cells as by staining T cells with HLA-A peptide tetrameric complexes. They demonstrate that expansion of peripheral immune repertoire is melan-A/Mel-1. They take place in some metastatic patients and leads to enhanced CTL induction after antigen-presenting cell-mediated selection, but, in most metastatic lesions, it does not overcome tumor escape from immune surveillance.

Picardo et al have tested the existence of a correlation between antioxidant and phototypes in melanocytes cultures. Their results suggest that the different patterns of antioxidants and of membrane fatty acids of melanocytes are correlated with their physiologic response to UV light. The decreased antioxidant enzyme activities and the increased percentage of polyunsaturated fatty acids in the membranes can be considered as adjunctive risk factors for people with low phototype who exposed to a level of UV light higher than in their original region.

Blasi et al investigate the antioxidant status of cultured uveal melanocytes from patients with uveal melanoma and uveal melanoma cells to characterize some of the biochemical properties of these cells in respect to the normal uveal melanocytes. Their results show a different pattern of antioxidants in uveal melanoma cells with respect to normal ones, possibly related to their anatomic distribution. However two subgroups were identified on the basis of the antioxidant pattern that could be the expression of a constitutional increased susceptibility to oxidative stress in some subjects. Moreover, an imbalance of the antioxidants was observed in melanoma cells, possibly related to the disease status and progression.

The melanocytes in the mammalian eye have been thought to produce melanin only during fetal development and in the very young individual; recent discovery that melanocytes are able to produce melanin analogues used in the treatment of glaucoma, causes increased pigmentation of the iris in monkeys and humans indicates that the tridial melanocytes can produce melanin in adult individuals. Lindquist et al have observed that in the iris of the treated eye the only difference from the untreated eye was an increased amount of melanin in these cells. Thus it seem likely that treatment with latanoprost in some individuals cause an increase of the low normal melanin synthesis in tridial melanocytes.

Greenblatt et al have demonstrate that a subset of melanocytic proliferations of the conjunctiva exists that cannot be reproducibly classified by pathologists as benign, malignant, or indeterminate.

Ishimizu et al report that a sex steroid-thyroid hormone (Mechano-F; MIF) was a potent drug for treatment of vitiligo. The efficacy of MIF treatment of vitiligo was proven to be due to the stimulatory effect of melanocytic proliferation and melanin production via alpha-MSH.

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- Andersen S E et al.  

- Asschimi A et al.  

- Ariza ME et al.  

- Baranda L et al.  

- Blau MA et al.  

- Ciotti P et al.  

- Eary DJ et al.  

- Edgar AJ, Bennett JP.  

- Francis G et al.  

- Fushanaka Y et al.  

- Gilchrist B, Eller M.  

- Graeven U et al.  

- Grossniklaus HE et al.  

- Haycock JW et al.  

- Hearing VJ.  

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- Kippenberger S et al.  
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- Le Poole IC et al.  

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- Schallermeier KU, Wood JM.  

- Schallermeier KU et al.  

- Setlow RB.  

- Shinmin T et al. 
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3. MSH, MCH, other hormones, differentiation

(Editors, L. Be.)

- Dannin JW, Grancewsy M, Warren CE. Glycoprotein glycosylation and cancer progression. Biochim. Biophys. Acta 1475(1):31-34, 1999. Shortened abstract: The authors review evidence that beta1,6GlCNAc-branching of N-glycans contributes directly to cancer progression, and they consider possible functions for the glycan. Mapt5 encodes N-acetylglucosaminyltransferase V (GlcNAc-TV), the Golgi enzyme required in the biosynthesis of beta1,6GlCNAc-branchol N-glycans. Mapt5 expression is regulated by RAS-RAP-ARF, a signaling pathway constitutively activated in tumor cells. Eradicative expression of GlcNAc-TII, an enzyme that accepts GlcNAc-TV for acceptor, suppresses metastasis in B16 melanoma cells*.

- Funasaki Y, Sato H, Chakraborty AK, Ohishi A, Chrousos GP, Ichihashi M. Expression of proopiomelanocortin, corticotropin-releasing hormone (CRH), and CRH receptor in melanoma cells, nevus cells, and normal human melanocytes. J Invest. Dermatol. Symp. Proc. 4(2):105-9, 1999. Shortened abstract: The authors have previously showed that normal human melanocytes produce and secrete alpha-MSH and ACTH, and furthermore, that advanced melanoma cells generally produce higher amounts of POMC peptides that correlate with tumor progression. Using reverse transcriptase-polymerase chain reaction, they show in this paper that all melanocytic cells (cultured human melanoma cells, nevus cells, and normal melanocytes) express CRH, CRH-R, POMC, and MSH receptor (MC1-R), with highest intensities in melanoma cells. Furthermore, immunohistochemistry shows that CRH as well as POMC is strongly expressed in advanced melanomas, such as vertically growing lesions of acral lentigious, nodular and metastatic melanomas, in contrast to negative expression in nevus cells. These results indicate that tumor progression accentuates CRH, CRH-R, and POMC expression by melanoma cells*.


- Haylock JW, Wagner M, Morindini R., Ghanem O, Ronass IG, Mac Neil S. Alpha-melanocyte-stimulating hormone inhibits NF-kappaB activation in human melanocytes and melanoma cells. J. Invest. Dermatol. 113(4):560-6, 1999. Commentary: The authors have showed that "a-MSH has a pronounced effect on NF-kappaB activity in melanocytes and melanoma cells, identifying a specific dimeric complex, and suggest this to be a key pathway by which immunomodulation/inflammation may operate". A complementary paper about the central action of a-MSH to inhibit peripheral NF-kappaB activation was published on the same month (October 1999), in the following reference: Ichihaya S, Saka T., Catanas A, Barsh GS, Purukawa S, Lipton JM.

- Ichimiya M.


Summary: This immunohistochemical analysis was performed on samples from five patients with generalized vitiligo successfully treated with oral administration of Methyl-17 alpha (M). Immuneactivity to alpha-MSH in melanocytes became much stronger after the treatment, than before the treatment. However, the immuneactivity to ACTH in melanocytes (both before and after the treatment) was minimal and there was little significant difference in these immuneactivities in keratinocytes between the depigmented lesions before treatment and the repigmented lesion after treatment. The efficacy of MP in treatment of vitiligo was proven to be due to the stimulatory effect of melanocyte proliferation and melanin production via alpha-MSH.


- Rakchovsky M., Pawelek J.


Shortened abstract: "Fusion of Cloudman S91 melanoma cells with macrophages results in hybrids with increased metastatic potential". The authors report that such hybrids acquire new pathways for motility, including an acquired melanocyte-stimulating hormone-inducible motility, perhaps reflecting the FN fragment chemotaxis of macrophages. Their "results support a long-standing hypothesis that metastasis is initiated following hybridization between tumor-invasive macrophages and cells of the primary tumor".


4. Photobiology

(Dr. E. Wencel)

- Bacharak-Biblia M., Lubowski M., Altmyer P.

Dose-dependent shift of apoptotic and unaltered melanocytes into the dermis after irradiation with UVA I. Dermatology. 198:5-10, 1999.

- Besou-Touya S., Morinou F., Surleve-Bazille J.E., Boulou-Sage P., Pugn C., Taeib A.


Summary: The authors have demonstrated that it was possible to maintain ex vivo nevus cells from congenital pigmented nevi and to produce their 3-dimensional in vivo organization. In the described model UVB exposure induced an upwards migration of nevus cells in the suprabasal layers of the epidermis.

- Eves P., Smith-Thomas L., Hedley S., Wagner M., Balasa C., Mac Neil S.


Summary: Three drugs known to induce toxicity in the eye, tamoxifen, chloroquine and thallidomide, were used to assess the sensitivity of cells to xenobiotic drugs. UVB irradiation was used to achieve an increase in the pigment content of the cells. Retinal pigment epithelial cell were shown to be much more resistant to the effects of all three drugs than the choroidal melanocytes and this resistance appeared to be largely independent of the presence of pigment. Further the results illustrated that it is infeasible to generalize about drug binding to melanin.

- Gelladen FM, Moir I., Meyer M., Michaelidiz TM.


Summary: The findings of this in vivo and in vitro study suggest that effects of UVB irradiation on epidermal cell death and cell cycle progression are influenced by survival-promoting Bel-2.

- Glichrist BA, Elser MS, Geller AC, Yasar M.


Summary: It is an interesting review that hypothesizes the photoprotective role of melanocytes in the UV-induced pathomechanism of melanoma.

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Summary: UV radiation-induced mutation of the p53 gene is suggested as a causative event in skin cancer, including melanoma. The results of this study performed on different melanoma cell lines suggest that in melanoma several p53 regulatory steps are dislodged; its basal expression is high, its activation in response to UVC damage is diminished and the regulation of its target genes p21Cip1/Waf1 and GADD45 are dissociated from p53 regulation.


Summary: The induction of DNA breaks by UVA in the nucleus of normal cultured human melanocytes was investigated using the comet assay. Endogenous pigment and/or melanin-related molecules were found to enhance DNA breaks. After UVA doses where strong comets were observed, neither cytotoxicity nor stimulation of tyrosinase activity were detected. However, the accumulation of p53 protein suggested that cells reacted to genotoxic stress under these genotoxic conditions. The same approach was used to compare two sunscreens with identical sun protection factors but different UVA protection factors.


Summary: The authors have shown retinoic acid (RA) to augment both constitutive and UVR induced pigmentation in the lightly pigmented HRA:Shh-2 murine model. The modes of action of RA in this system is unknown, but RA and UVR needed to be applied on the same site and UVR was effective whereas UVA was not. It is probable that complex synergistic interactions are occurring between UVR, RA and keratinocyte-derived paracrine factors to enhance tyrosinase activity and cell division in these quiescent melanocytes.

5. Neuramelines

(Prof. M. D'Arcia)

The binding of metal ions to neurameline as a possible underlying cause of neurotoxicity and neuronal degeneration continues to be an active focus of research during the last months of 1999. The role of iron and its pathophysiological relevance to neurameline is addressed by Briddell et al. who revisited the structure of neurameline and synthetic analogues and succeed in demonstrating by IR techniques that iron binding involves phenolic OH groups in human neurameline and both phenolic OH and NH imidazole groups in synthetic neurameline. The presence of an aliphatic component specific to neurameline was also confirmed, in accord with the heterogeneous nature of the pigment. Along the same line of thought, Kienzl et al., used energy dispersive X-ray electron microscopy analysis to confirm an abnormal iron accumulation in the melanized neurons of the substantia nigra pars compacta in patients with Parkinson's disease. A mechanism of iron-neurameline-dependent cytotoxicity via continuous production of reactive oxygen species was proposed. In another paper, Meglio et al. reported the levels of lipid peroxidation in liposomes and caudate putamen homogenates induced by A5+ ions. The encouraging effect was shown to depend on interaction with superoxide ions produced by autooxidation of melanin, and is therefore consistent with a predominant mechanism basically different from that of Fe and other redox active metals.

Two related studies from the group on the role of catecholamine metabolism in major depression (Zhu et al., Oqulway et al.) indicated that tyrosine hydroxylase, but not monoamine oxidase, was overexpressed in the locus coeruleus of depressive patients. The distribution of tyrosine hydroxylase-like immunoreactivity in the locus coeruleus was uneven and was paralleled by a similar distribution of neurameline-containing cells in normal and depressive subjects. It was suggested that in major depressive patients there is either an overactivation of locus coeruleus neuron or a deficiency in noradrenergic levels. Using in situ hybridization histochemistry Muller et al. demonstrated, inter alia, that there is a significant increase in the percentage of neurameline-pigmented cells in the coexistence galanin, an inhibitory modulator of cholinergic and noradrenergic neurotransmission, in patients with Alzheimer's disease. The role of galanin in Alzheimer's disease is discussed.


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6. Genetics, molecular biology (Dr. F. Biermann)


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7. Tyrosinase, TRP1, TRP2 and other enzymes

(Prov. J.C. Garcia-Borro)
8. Melanosomes (New Topic)

(Dr. J. Borovansky)

This newly introduced section will be devoted to melanosomes. Melanosomes are a term commonly used in geology (where it refers to the darker-coloured portions of migmatic rocks - see e.g. Muhlen K.R.; Migmatic and the origin of granitic rocks, Elsevier, Amsterdam 1968 or Berger A. Kalt A. J. Petrology 40(1): 1659-1719, 1999) and in life sciences. Our attention will be, of course, focused on melanosomes in the latter sense. These melanoblast particles have an interesting biogenesis, fate so far unexplained in terms of molecular events, typical ultrastructure and specific chemical composition. They represent the site of melanogenesis including production of potentially cytotoxic species. Melanosomes play multiple physiological and pathological roles (absorption and conversion of energy, involvement in redox and free radical reactions, ion exchange capacity, affinity to various compounds) and they display unique antigens. All these properties can be exploited in practice, particularly in the diagnosis and treatment of malignant melanoma. The demonstration of melanosomal presence is also important in differential diagnostic modifications in human and veterinary pathology.


- Lindquist NG, Larsson BS, Stenmoehnert J, Sjosquist B. Age-related melanogenesis in the eye of mice, studied by microautoradiography or H-3-methionine, a specific marker of melanin synthesis. Experimental Eye Res 67(5):254-264, 1998

**Comments:** Evidence that new melanomas are formed in iridial pigment cells in adult mice.


**Comments:** In 3 human melanoma cell lines HMB45 reacted with melanomas, whereas in pulmonary lymphangiogranulomatosis cells the binding sites for HMB45 were located in cytoplasmic granules resembling immature melanomas.


**Comments:** Mutations at the p locus affect the size, number, shape and content of melanosomes.


**Comments:** Case report of a disease characterized by churning of macrophages.


**Comments:** PKC-beta is closely associated with tyrosinase on the outer surface of melanomas.


**Comments:** Demonstration of cysteine transport by a carrier-mediated process into melanosomal fraction.


**Comments:** Tumor consists of neuroblast-like cells admixed with large epithelioid cells containing melanomas.


**Comments:** Melanomas aggregates were consistently observed in macroglobules and in Schwann cells.


**Comments:** Review summarizing clinical manifestations of syndromes associated with defects of melanomas, lymphomes and cytoplasmic granular elements with an effort to explain the molecular basis of these disorders and with emphasis on the AP-3-mediated pathway of organelle-specific protein biogenesis and trafficking.

- Stout PR, Rub JA. Deposition of [H]-tyrosine, [H]-3-nitrotyrosine, and [H]-3-fluorotyrosine in mouse hair melanomas after systemic administration. Drug Metabolism and Disposition 27(5):731-736, 1999.

**Comments:** Transmethurgical study exploiting melanosomal affinity and aiming at a better basis for using hair for analyses of drug and environmental toxin exposure.


**Comments:** Concise but highly didactic overview in an excellent graphic arrangement covering all the aspects of melanomas.


**Comments:** Bidirectional, microtubule-dependent melanosome movement coupled with actomyosin Va dependent capture of melanosomes in the periphery is the predominant mechanism responsible for the centrilocul transport and peripheral accumulation of melanosomes in melanocytes.
9. Melanoma experimental, Cell culture
(Dr. N. Smit)

A: Drug toxicity

The paper by Glass-Marmor et al shows the effects of the Ca^{2+} ionophore A23187 and the importance of the levels of free Ca^{2+} in melanoma cells. Accumulation of intracellular-free Ca^{2+} was considered to cause a reduction in the energy-producing systems of the cell, leading to melanoma cell death. This could be an indication that a proper regulation of the energy production may be of great importance for the viability of melanoma cells but also for melanocytes in general.

Plant indole alkaloids have been tested by Krupadpudi et al for their toxicity towards different cancer cell lines and fibroblasts. No discernible cell-type specificity among the cancer cell lines (including SfM1 1a melanoma) was found. Davol et al have used the FGF receptor on melanoma cells for targeting NGF-agonists and used this in combination with suramin resulting in 68% tumour growth inhibition compared to controls in a model of beige mice bearing SK-Mel-5 human melanoma xenografts. In the study by Lahav et al the presence of the endothelin receptor E (ETRB) on melanoma cell lines was utilized and the ETRB antagonist BQ-788 was found to inhibit growth of seven melanoma lines.

Masinjani et al describe that the cytotoxic effects of tyrphostins analogs such as 4,6-diamino-4,4' diaminodiphenyl (4,4'-DAP) and its derivative N-propyl-4,6-DAP (NPA)-DAP are tyrosine mediated. Differences between the toxicities towards the (tyrosinase +) mel-a and (tyrosinase-) melan-c melanocyte cultures and tyrosinase transfected COS cells and the controls are shown. Haegawa et al have shown already in 1997 (Bioch. Pharmacol. 53, 1433-44) that the dihydro-1,4-benzoxazine-1,6-dione (BO) is the ultimate toxic product of 4,4'-DAP. The importance of GSH adduct formation and free radical mediated toxicity of these compounds is indicated in both the papers. The present paper by Masinjani et al now shows that this may even trigger apoptosis in these cells. In the paper by Fervais et al it is described that the apoptotic induced in e.g. M14 melanoma cells by two different monocarboxylic 540 photoproduts is mediated by caspase 8. Different mechanisms for the release of mitochondrial cytochrome C by the two products were found.

Wang et al show that the enzyme DT-diaphorase may be an interesting target enzyme in melanoma and other tumours since it has been shown to be elevated in different tumour tissues. The bioactivation of anti-tumour agents such as mitomycin-C by this enzyme and possibilities to further increase its activity may be utilized for specific induction of cytotoxicity in various tumour cells.

- Broadhead AS.
- Comenzo: We have examined the heterogeneity of chemosensitivity in metastatic cutaneous melanoma specimens using an ex vivo ATP-based chemosensitivity assay (ATP-TCA). The degree of heterogeneity observed suggests that the ATP-TCA could be used to select patients who might benefit from specific chemotherapeutic agents alone or in combination.
- Davol PA, Garza S, Prakash A.
  Coupling suramin and a chimeric toxin directed to basic fibroblast growth factor receptors increases therapeutic efficacy against human melanoma in an animal model. Cancer. 86(9):1733-41, 1999.
- Glass-Marmor L, Pesaro J, Beinser B.
- Hanaszaka H, Misztani H, Asahig K, Shimizu M.
- Jackson TL, Lubkin SR, Siemens NO, Kerr DB, Seader PD, Murray JD.
- Jackson TL, Lubkin SR, Murray JD.
- Comments: A promising two-step approach that is designed to minimize systemic drug toxicity while maximizing activity in tumours employs monoclonal antibody (mAb)-enzyme conjugation for the activation of anticancer prodrugs.
- Kuswandad N, Eno-Amooquaye E, Burke PJ, Houghton PJ.
- Klein JL, Roberts JD, George MD, Kurtzberg J, Bean P, Chornom JC, Olsen K.
  Swainsonine protects both murine and human haematoipetic systems from chemotherapeutic toxicity. Br. J.
  Cancer. 80(1-2):87-95, 1999.

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Comments: We demonstrate that swainsonine protects C57BL/6 mice bearing melanoma-derived tumours from cyclophosphamide-induced toxicity without interfering with the drug's ability to inhibit tumour growth.

- Lahan R, Hoffstetter G, Paterson PH.


Comments: The effect of dietary supplementation with secoisolariciresinol diglycoside (SDG), a lignan precursor isolated from flaxseed, on experimental metastasis of B16BL6 murine melanoma cells in C57BL/6 mice was investigated.

- McDevitt TC, Nelson KE, Stayton PS.

- Misamitori Y, Toyofuku K, Sugiyama S, Yamada K, Jimbow K.


- Poirier S, Seyed MA, Hirpara JL, Clement MV, Loh KW.

- Qin L, Kelso MJ, Hasson C, West ML, Partridge DP, Parsons PG.

Comments: A series of hydroxamates, which are not metalloprotease inhibitors, have been found to be selectively toxic to a range of transformed and human tumour cells without killing normal cells (fibroblasts, melanocytes) at the same concentrations. Two hydroxamates inhibited growth of xenografts of human melanoma cells in nude mice; resistance did not develop in vivo or in vitro.

- Rosenthal MG, Marks JW, Cheung L.H.


- Wang X, Doherty GP, Leith MK, Curphey TJ, Begleiter A.

- Yang F, Boinay RE.

- Zagendron R, Gobal J, Mucha K, Frenszewicz B, Jakobiak M.

R: Gene and immunotherapy
- Aarnoudse CA, van den Doel PB, Heemskerk B, Schrier PI.
Interleukin-2-induced, melanoma-specific T cells recognize CAMEL, an unexpected translation product of LAGE.


do in summary, CTL induction with IL-2 transfected melanoma cells has revealed a new tumor antigen that may serve as a target for immunotherapy.


	Comments: We demonstrated increased transgene expression after mixing adenosine preparations with polyplexes, cationic lipids, and CaCl2 prior to transduction in vitro. Further studies will determine whether polyplexes can improve intratumoral gene transfer.


	Comments: We transfected human A375F melanoma cells that do not express IL-10 with the murine IL-10 gene and subsequently analyzed for changes in tumor growth and metastasis in nude mice. Surprisingly, IL-10 gene transfer resulted in a loss of metastatic and significant inhibition of tumor growth.


C. Melanoma culture

The paper by Edgar and Bennett describes the effects of transfectant transfection of antisense phosphorothioate oligodeoxynucleotides targeted against myosin Va mRNA. In melan-A mouse melanocytes this resulted in a reduced expression of the myosin Va protein. Replacing the cells after transfection showed that the capacity to regain the normal morphology was reduced in the cells containing the specific antisense oligodeoxynucleotide but unaffected by the control oligodeoxynucleotide. This work shows the importance of myosin Va in normal cell formation in cultured melanocytes in addition to its involvement in melanosome transport. Katsagia et al describe the presence of keratin subunits in neonatal epidermal melanocytes from a commercially available cell kit. As the authors mention it was not expected to find keratin - 1003 -
expression in melanocytes. The submitis do not form any keratin filaments and the question about their possible role in melanocyte (development)remains to be answered. In the papers by Kaufmann et al at differences in the half-life of neurofibromin is studied in melanocytes of NF1 patients. Melanocyte growth factors bFGF and TPA increased the half life of neurofibromin which seems to be dependent on lysosomal (or melanosomal) degradation. The paper by Schallreuter and Wood nicely demonstrates that phenylalanine may be an important precursor for melanin formation in cultured melanocytes since it can be converted to L-tyrosine by phenylalanine hydroxylase. Since the phenylalanine uptake seems to be an active transport which is calcium dependent the levels of phenylalanine and calcium in culture medium may be important for the final melanin production in the melanocyte cultures. Suzuki et al describe the use of melanocyte cultures of skin type V or VI first responded to MSH at an effective dose of 0.1 nM. One culture of skin type I or II was much less responsive. Genetic analysis of the MCI receptor variants are being used to study these responses to MSH as it has also been presented by Abdel-Malek at the XVIII IPCC meeting in Nagoya (Pigment Cell Res suppl 7, p.44). These studies may be of major benefit for our understanding of different responsiveness of melanocytes cultures to stimulation of melanogenesis.

- Alazko T, Roseberg M, Sakurai O.

FGF expression allows neuro cells to survive in three-dimensional collagen gel under conditions that induce apoptosis in normal human melanocytes. J Invest. Dermatol. 113(1);111-6, 1999. Partial abstract: Here we report growth characteristics of in vitro cultured normal human melanocytes and dermal neuro-derived melanocytes. As previously reported, neuro cells have a moderate to high FGF-2 expression level. Here we demonstrate that dermal neuro cells are able to survive in three-dimensional type I collagen culture, while normal human melanocytes rapidly undergo apoptosis.

- Basou-Touya S, Moriconi P, Surleve-Bazelle JL, Blouduc-Sage P, Pain C, Tajeb A. An in vivo study of congenital pigmented nevi in epidermal reconstituents. Pigment Cell Res. 12(3);164-74, 1999. Partial abstract: Typical nesting of neural cells was observed in the dermal-epidermal junction or in the superficial dermis. UVB exposure induced an upward migration of neural cells in the suprabasal layers of the epidermis. This tissue model can be considered as an excellent system for the ex vivo reproduction of pigmented nevi and as an assay of the sensitivity of neural cells towards UVB irradiation.


- Lin ZX, Hough JR, Raman A. Sulphorhodamine B assay for measuring proliferation of a pigmented melanocyte cell line and its application to the evaluation of crude drugs used in the treatment of vitiligo. J. Ethnopharmacol. 66(2);141-50, 1999.

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Partial abstract: Hyaluronic acid is, in fact, considered to be an optimal biomaterial allowing proliferation of both keratinocytes and melanocytes, and it is already used for clinical aims.


Partial abstract: To clarify the effect of neuropeptides on the biology and morphology of melanocytes, organ cultures of dorsal human skin and cultured melanocytes were exposed to various neuropeptides. The findings suggest that keratinocytes produce and secrete some melanotrophic factors following stimulation with calcitonin gene-related peptide (CGRP), which modulate growth, melanin synthesis, and dendriticy of melanocytes.

Calendar of events

Also available from address: http://www.ulb.ac.be/medecine/loce/espcr.htm

2000 Melanoma: Basic Biology and Immunological Approaches to Therapy
May 3-7 The Woodlands Resort, The Woodlands (near Houston), TX
Contact: American Association for Cancer Research
Public Ledger Building, Suite 826
150 S. Independence Mall West
Philadelphia, PA 19106-3483
Phone: 215-440-9300
Fax: 215-351-9165
E-Mail: meetings@aacr.org
Website: http://www.aacr.org

2000 1Xth Annual Meeting of the Pan American Society for Pigment Cell Research (PASPCR)
June 25-28 College Station, TX
Contact: Dr. Lynn LAMOREUX
Dept. of Veterinary Pathobiology
The Texas Veterinary Medical Center
Texas A & M University, College Station
TX 77843-4467
Phone: (409)845-6084
Fax: (409)845-9972
E-mail: llamoreux@cvrm.tamu.edu

2000 9th ESPCR Meeting: Ulm, Germany
Sept 28-Oct 1 University of Ulm (BWK)
Dept of Dermatology
Oberer Eselsberg 40
D - 89081 ULM
Tel: 49-731 502-3770
Fax: 49-731 502-3772
E-mail: ralf.peter@medizin.uni-ulm.de

2001 5th World Conference on Melanoma: Venice
Feb 28-Mar 3 Secretory General
5th World Conference on Melanoma
Casa di Culta S. Pio X
Via F. Nava 31
I- 20159 Milano
Phone/Fax: 39-02-69516449
E-Mail: info@melanoma2001.org
Website: www.melanoma2001.org
2001 Xth Annual Meeting of the Pan American Society for Pigment Cell Research, Minneapolis, MN
Contact: Dr. Richard KING
E-Mail: king@mail.abc.umn.edu

Contact: Dr. Stan PAVEL
University Hospital Leiden
Dept of Dermatology
PO Box 9600
NL - 2300 RC LEIDEN
Tel: 31-(71) 526 1952
Fax: 31-(71) 524 8106
E-mail: SPavel@algemeen.aaz.nl

2002 European School of Oncology
European School of Pathology
Courses on Melanoma
Skin Cancer Awareness Training (For Health Professionals)
The course aims to enable health professionals to promote awareness and understanding of the issues surrounding skin cancer and its prevention.
For Information contact: Suzanne Cooper
Education Department
Marie Curie Cancer Care
Belgrave Square 28
London SW1X 8QG
Phone: 0171 201 2320

SAD NEWS OF THE DEATH OF A COLLEAGUE

With much sadness, we must tell the membership of the death in September 1999 of Giovanna Prota (wife of Professor Giuseppe Prota). Giovanna was well known within the Society and much admired as a gentle, lovely lady. She will be sadly missed by all who knew her. We offer our condolences to Giuseppe and their family.

Sheila Mac Neil and Stan Pavel