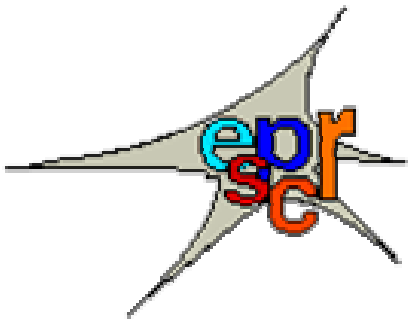
N° 42 - April 2002

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

PUBLISHED BY THE EUROPEAN SOCIETY FOR PIGMENT CELL RESEARCH



EUROPEAN SOCIETY FOR PIGMENT CELL RESEARCH *BULLETIN*

N° 42 - April 2002

Editorial Office: *G. Ghanem (Editor), C. Meunier, R. Morandini (Production Team), Laboratory of Oncology and Experimental Surgery (L.O.C.E.), Université Libre de Bruxelles, Institut J. Bordet, Rue Héger-Bordet 1, B – 1000 Brussels, Belgium.*
Phone: 32-2-541.32.96 Fax: 32-2-534.95.50 E-Mail:gghanem@ulb.ac.be

IPCC Abstract deadline: May 1st 2002
Travel Awards available for IPCC: deadline May 15th 2002

CONTENTS

IPCC 2002: http://users.raketnet.nl/ipcc/
Mirror site: http://ulb.ac.be/medecine/loce/espcr/ipcc/Default.htm

DISCUSSION

Animal Models

by Lynn Lamoreux

Let's talk pigs

The well known but under utilized Sinclair Swine herd developed by Max Amoss is characterized by a high incidence of melanomas that are present at birth or soon thereafter. In these pigs, the relationship between melanoma and vitiligo is potentially illuminating of both phenomena., If the melanoma stimulates accompanying vitiligo, then commonly the melanoma regresses over the course of the first few months of the pig's life, and the vitiligo progresses to the eventual destruction of most of the skin pigmentation so that the black pigs become white by the time they are a year or two old. Interestingly, pheomelanic piglets rarely are born with the melanoma, if they are, the melanomas quickly regress, and also these pheomelanic pigs do not exhibit vitiligo.

Work with these pigs suggests three genetic loci share major responsibility for the formation of the melanoma.

The only large herd of Sinclair swine selected for melanoma is housed at Texas A&M University, where it has most recently been used to map genes related to melanoma incidence. And of course has also been used by our member John Pawelek to test some of his esoteric theories relaavent to melanoma. Many of you had a chance to admire these pigs while attending the PASPCR meeting in College Station.

The Sinclair pig is one of our best models for both melanoma and vitiligo, and the Texas A&M colony is threatened with extinction. Also it is true that Texas A&M has been able to clone several litters of pigs (other kinds of pigs) using fibroblast cells. Therefore several members of the pigment cell community have offered to obtain tissues from this herd of pigs, grow up fibroblast cells, and store them for the future. We also hope to preserve the melanoma cell lines. References below represent some of the work of Dr. Max Amoss, who has maintained these pigs for many years.

REFERENCES

Review

1. Spontaneous Regression of Sinclair Swine Cutaneous Malignant Melanoma Amoss, MS, Fadok, VA, Multani, AS, Pathak, S, Greene, JF, Jr., Measel, JW, Jr., Morgan, CD. In “Advances in Swine Biomedical Research eds Tumbleson and Schook Plenum Press, NY 1996.

Editorial

1. What is Inherited in Neoplastic systems? Animal Models of Cutaneous malignant Melanoma. Clark, WH, Jr., Laboratory Investigation 711, 1994

Manuscripts

1. Histopathology of Regression in Sinclair Swine Model of Melanoma.
   Greene, JF, Jr., Townsend, JS, IV, Amoss, MS, Jr. Laboratory Investigation 7117, 1994.

2. Regression by Differentiation in the Sinclair Swine Model of Cutaneous Melanoma. Greene, JF, Jr., Morgan, CD, Rao, Amoss, MS, Jr., Arguello, F.
   Melanoma Research 7471, 1997.

3. Genetic Determinants of Cutaneous malignant Melanoma in Sinclair Swine.
   Blangero, J, Tissot, RG, Beattie, Amoss, MS, Jr. British Journal of Cancer 73667, 1996.

4. Genetic Predisposition and Specific Chromosomal Defects Associated with Sinclair Swine Malignant Melanomas, Pathak, S, Amoss, MS, Jr. International Journal of Oncology 1153, 1997.

5. Spontaneous Regression of Cutaneous Melanomas in Sinclair Swine is Associated with Defective Telomerase Activity and Extensive Telomere Erosion. Pathak, S, Multani, AS, McConkey DJ, Amoss, MS, Jr. International Journal of Oncology 171219, 2000.

6. Immunophenotypic Characterization of Tumor Infiltrating Lymphocytes and peripheral Blood Lymphocytes Isolated from Melanomatous and non-Melanomatous Sinclair Miniature Swine. Morgan, CD, Measel, JW, Jr., Amoss, MS, Jr., Rao, A, Greene, JF, Jr. Veterinary Immunology and Immunopathology 55189, 1996.

7. Cycloheximide-induced Apoptosis in Melanoma Cells Derived from Regressing Cutaneous Tumors of Sinclair Swine. Gossett, R, Kier, AB, Schroeder, F, McConkey, D, Fadok, V, Amoss, MS, Jr. Journal of Comparative Pathology 115353, 1996.

1. Biology of pigment cells and pigmentary disorders

(Dr. M. Picardo)

Sanchez Mas et al studied on the regulation of ornithine decarboxylase (ODC), the rate-limiting enzyme in the biosynthesis of polyamines, which are been suggested might be involved in various aspects of skin biology. They examined the regulatory mechanism at the gene expression, protein and enzyme activity levels and moreover they analysed the possible involvement of ODC in the regulation of melanogenesis in B16 cells. Their results show that ODC mRNA and protein levels are up-regulated by 12-O-tetradecanoylphorbol 13-acetate, whereas α-MSH moderately and transiently down-regulate ODC mRNA and triggers a modest activation of its enzymatic activity. Moreover, polyamine depletion increase tyr activity by a post-translational mechanism that synergistically potentiates the stimulatory action of α-MSH. **Hirobe** investigated the role of endothelins (ET-1, ET-2 and ET-3) in the regulation of the proliferation and differentiation of neonatal mouse epidermal melanoblasts and melanocytes by adding ET to culture media in the presence or absence of keratinocytes. He found that ET induced the differentiation of melanocytes in the presence of α-MSH, suggesting that these two factors could interact synergistically. Moreover he reported that ET-1, ET-2 and ET-3 are equally involved in regulating the proliferation and differentiation of mouse epidermal melanocytes; these results suggest the possibility that neonatal mouse epidermal melanocytes express ETRB, the receptor which binds ET-1, ET-2 and ET-2 equally, at the newborn stage. These findings propose that ET are one member of the keratinocyte-derived factors involved in regulating proliferation and differentiation of melanoblasts and melanocytes in the presence of cAMP elevator and/or bFGF. **Watabe et al** reported findings providing some important viewpoints to understand the roles and working mechanisms of retinoic acid (RA) in melanocyte development and melanogenesis. They employed NCC-melb4 cells, which are thought to be immature melanocyte precursors, as they expressed several melanocyte specific markers, but were negative for tyrosinase and did not produce melanin. They showed that NCC-melb4 cells treated with all-trans retinoic acid (ATRA) became tyrosinase and DOPA reaction positive, changed in shape from polygonal to dendritic, and contained melanosomes at advanced stages. These findings indicate that ATRA promotes the differentiation of melanocyte precursors, and also suggest a possible role for RA in melanocyte development *in vivo*. Furthermore, RT-PCR analyses revealed that PKC-α and microphtalmia-associated transcription factor (MITF) mRNA expression was markedly increased by ATRA treatment, suggesting that MITF, as well as PKC-α, may be the key factor in ATRA-induced melanocyte differentiation. Moreover they demonstrated that apoptosis was increased following treatment with ATRA using electron microscopy, the TUNEL method, DNA fragmentation assay, and flow cytometry. The apoptotic pathway activate by ATRA involved the activation of caspase 3 and the down-regulation of bcl-2. Using the same NCC-melb4 cell line **Kawakami and co-workers** investigated the effect of TGF-β1 on the differentiation and proliferation of immature melanocyte precursors. They detected that neuronal crest cells (NCC) and NCC-melb4 cells *in vitro* secrete TGF-β1. Furthermore the anti-TGF-β1 antibody inhibits KIT expression by autocrine/paracrine regulation. The authors hypothesised that intrinsic TGF-β1 combined with SCF/KIT plays an important part in vertebrate neural development. These findings provide important clues towards understanding the roles and working mechanisms of TGF-β1 in melanocyte development and melanogenesis. **Hedley et al** investigated to what extend melanocytes within a reconstructed skin model are sensitive to regulation by dermal fibroblasts, basement membrane (BM) proteins and the addition of α-MSH. Their data showed that the presence of BM antigens was found to be necessary for the positional orientation of the melanocytes. Moreover addition of fibroblasts suppressed theextent of spontaneous pigmentation of melanocytes within this model. **Buchli et al** reported that normal human skin melanocytes express the m1, m2, m3, m4, and m5 subtypes of classic muscarinic acetylcholine receptors on their cell membrane and that these receptors regulate the concentration of intracellular free Ca2+, which may play an important physiologic role in melanocyte behaviour and skin pigmentation. **Sviderskaya and co-workers** used cultured melanocytes from littermate Ink4a-Arf (locus which encodes for two potent inhibitors of cellular growth $p16^{INK4a}$ and ARF) nullizygous, hemizigous and wild-type mice to investigate the roles of p16 and Arf in the control of senescence and possibly pigmentation in melanocytes. Their data showed that normal mouse melanocyte senescence and associated pigmentation require both copies of Ink4a-Arf and appear to depend more on p16 than on Arf function. Moreover mutations of the INK4a-ARF locus may favour tumorigenesis from melanocytes by impairing senescence, cell differentiation and (where ARF is disrupted) cell death. These findings provide some potential reasons for specific melanoma susceptibility in humans with INK4a (and ARF) alterations. **Pavey and Gabrielli** demonstrated that the increased expression p16 after suberythemal doses of UVR is potentiated by α-MSH and this effect is mimicked by cAMP. They suggested that this link between p16 and MC1R may providea molecular basis for the increased skin cancer risk associated with MC1R polymorphisms. **Suzuki and co-workers,** employing an *in situ* hybridization technique for mRNA

of various gene products critical for pigmentation, demonstrated for the first time that mRNA levels of POMC, tyrosinase, TYRP-1, DCT, P-protein, P-mel 17 and MITF increase in the human epidermis in response to UVB exposure. Their results suggest that the tanning response of human skin is regulated at mRNA level, and that POMC-derived melanocortins, such as α-MSH and ACTH, may be key factors in the transcriptional regulation of these genes *in vivo*. **Yoshida et al** reconfirmed that histamine has a melanogenic effect on human cultured melanocytes via H_2 receptors. In their study, they further demonstrated that two types of H_2 antagonists, famotidine and ranitidine, inhibited the increase in tyrosinase activity by histamine in a concentration-dependent manner. They found that a topically applied H_2 antagonist suppressed pigmentation by reducing the increase of activated melanocytes by UVB irradiation. They eliminated the possibility that the H_2 antagonist suppressed the pigmentation only via a shielding ability against UVB by showing that it was also effective when the treatment was initiated after irradiation. The authors concluded that histamine is involved in UVB-induced pigmentation by an H_2 receptor-mediated activation of melanocytes. However, it must consider that this pathway plays a limitated pert in the pigmentation induced by UVB, as the H_2 antagonist was only able to reduce the increased number of DOPA-positive melanocytes by 30%. **Zhao et al** investigated the formation UV photoproducts in melanocytic nevi *in situ* and surronding skin after exposure to solar-stimulating radiation (SSR). Using a recent developed ^{32}P-postlabeling technique, they have measured four types of photoproducts, including cyclobutane pyrimidine dimers (CPD) and 6-4 photoproducts.Their findings showed that the levels of both CPD and 6-4 photoproducts in nevi were significantly lower than those in surrounding skin, the difference being 3-5 fold. The evidence that the lowest photoproduct levels were induced in the darkest color of nevi suggests that melanin protected human skin against UV-induced DNA damage. **Tada and co-workers** reported on the role of ET-1, bFGF and α-MSH and of UVB radiation in the activation of various MAP kinases, $p90^{rsk}$, and CREB in huamn melanocytes. Their results suggest that, whereas the signaling pathways that are mediated by PKC, tyrosine kinase, and intracellular Ca^{2+} mobilization converge on the activation of $p90^{rsk}$ and CREB, the cAMP-mediated pathway modulates different downstream effectors that are yet to be identified. Interestingly, CREB phosphorylation is also induced by exposure of melanocytes to UVB in the absence of ERK1/2 or $p90^{rsk}$ phosphorylation. Irradiation with UVB induces robust phosphorylation of p38 as well as JNK/SAPK. These data suggest that mitogens and stress induce CREB phosphorylation by activating at least two distinct pathways. **Khlgatian and co-workers** tried to elucidate the impact of p53 protein level and activity on tyrosinase expression. Regardless of the precise molecular mechanisms, their data established that p53 protein negatively regulates tyrosinase gene transcription, whereas activation of p53 increases tyrosinase mRNA level. These results could demonstrate the essential role of p53 even in intact skin in the induction of pigmentation by thymidine dinucleotides (pTpT), selected as the test agents because it appears to act mimicking DNA damage specifically. These results suggest that tanning should be included in the broad array of DNA damage-induced p53-mediated adaptative differentiation responses that protect mammalian cells during subsequent exposure to DNA-damaging agents such as UV irradiation. **Miyashita et al** examined the expression of rhodopsin gene in mouse tissues. RT-PCR analyses revealed that eye and skin expressed rhodopsin mRNA, whereas liver did not express it. The authors hypothesised that the absence of expression in non sun-exposed tissues such as the liver could suggest that rhodopsin in melanocytes may have some role in photoprotection. **van der Wijngaard and co-workers** studied the expression of membrane cofactor protein, decay accelerating factor and CD59 in non-lesional, perilesional and lesional vitiligo skin compared to those of control specimens. Immunohistochemical data showed that expression of membrane cofactor protein and decay accelerating factor in whole epidermis was lower in lesional and peri-lesional skin in comparison with non-lesional skin. Further flow cytometric analyses of cultured melanocytes demonstrated that non-lesional vitiligo and control melanocytes have comparable regulatory proteins expression levels. Their data suggest that both keratinocytes and melanocytes in the involved vitiliginous whole epidermis express lower levels of decay accelerating factor and membrane cofactor protein compared with controls that could render them more vulnerable to autologous complement attack

Le Gal et al examined the role of cellular immunity in melanoma-associated vitiligo by expanding infiltrating lymphocytes from fresh biopsy specimens of vitiligo patches in melanoma patients**.** They therefore determined the phenotype and antigenic specificity of vitiligo infiltrating lymphocytes expanded from depigmented skin samples of patients with melanoma. Their data suggest that vitiligo in melanoma patients could be the visible consequence of a cellular antitumoral response, although not predictive of the clinical outcome of this immune reaction.

- An HT, Yoo JY, Lee MK, Shin MH, Rhie GE, Seo JY, Chung JH, Eun HC, Cho KH
  Single dose radiation is more effective for the UV-induced activation and proliferation of melanocytes than fractionated dose radiation. Photodermatol Photoimmunol Photomed 17(6): 266-271, 2002.

- Buchli R, Ndoye A, Arredondo J, Webber RJ, and Grando SA
  Identification and characterization of muscarinic actylcholine receptor subtypes expressed in human skin melanocytes. Mol Cell Biochem 228(1-2): 57-72, 2001.

- Chwirot BW, Chwirot S, Sypniewska N, Michniewicz Z, Redzinski J, Kurzawski G, and Ruka W
  Fluorescence in situ detection of human cutaneous melanoma: study of diagnostic parameters of the method. J Invest Dermatol 117: 1449-1451, 2001.

- Fujita H, Sasano E, Yasunaga K, Furuta K, Yodoka S, Wada I and Himeno M
Evidence for distinct membrane traffic pathways to melanosomes and lysosomes in melanocytes. J Invest Dermatol Symposium Proceedings 6: 19-24, 2001.

- Funasaka Y, Chakraborty AK, Yodoi J and Ichihashi M,
The effect of thioredoxin on the expression of proopiomelanocortin-derived peptides, the melanocortin receptor and cell survival of normal human keratinocytes. J Invest Dermatol Symposium Proceedings 6: 32-37, 2001.

- Giambernardi TA, Sakaguchi AY, Gluhak J, Pavlin D, Troyer DA, Das G, Rodeck U, and Klebe RJ.
Neutrophil collagenase (MMP-8) is expressed during early development in neural crest cells as well as in adult melanoma cells. Matrix Biol 20(8): 577-587, 2002.

- Hedley SJ, Layton C, Heaton M, Chakrabarty KH, Dawson RA, Gawkrodger DJ, MacNeil S.
Fibroblasts play a regulatory role in the control of pigmentation in reconstructed huamn skin from skin types I and II. Pigment Cell Res 15(1): 49-56, 2002.

- Hirobe T.
Endothelins are involved in regulating the proliferation and differentiation of mouse epidermal melanocytes in serum-free primary culture. J Invest Dermatol Symposium Proc 6: 25-31, 2001.

- Im S, Kim J, On WY, Kang WH.
Increased expression of alpha-melanocyte-stimulating hormone in the lesional skin of melasma.
Br J Dermatol 146(1): 165-167, 2002.

- Jean S, Bideau C, Bellon L, Halimi G, De Meo M, Orsiere T, Dumenil G, Berge-Lefranc JL, and Botta A.
The expression of genes induced in melanocytes by exposure to 365nm UVA: study by cDNA arrays and real-time quantitative RT-PCR. Biocim Biophys Acta 1522(2): 89-96, 2002.

- Kato M, Takeda K, Kawamoto Y, Tsuzuki T, Dai Y, Nakayama S, Toriyama K, Tamada Y, Takahashi M, and Nakashima I.
RET tyrosinase kinase enhances hair grwth in association with promotion of melanogenesis.
Oncogene 20(51): 7536-7541, 2002.

- Kawakami T, Soma Y, Kawa Y, Yamasaki E, Watabe H, Hosaka E, Yajima K, Oshumi K, and Mizoguchi M.
Transforming growth factor β1 regulates melanocyte proliferation and differentiation in mouse neural crest cells via stem cell factor/KIT signaling. J Invest Dermatol 118: 471-478, 2002.

- Khlagatian MK, Hadshiew IM, Asawanonda P, Yaar M, Eller MS, Fujita M, Norris DA, and Gilchrest BA.
Tyrosinase gene expression is regulated by p53. J Invest Dermatol 118: 126-132, 2002.

- Le Gal FA, Avril MF, Bosq J, and Lefebvre P.
Direct evidence to support the role of antigen-specific CD8+ T cells in melanoma-associated vitiligo. J Invest Dermatol 117: 1464-1470, 2001.

- Miyashita Y, Moriya T, Kubota T, Yamada K, and Asami K
Expression of opsin molecule in cultured murine melanocytes. J Invest Dermatol Symposium Proceedings 6: 54-57, 2001.

- Olie RA, Hafner C, Kuttel R, Sigrist B, Willers J, Dummer R, Hall J, Stahel RA, and Zangemeister-Wittke.
Bcl-2 and bcl-xl antisense oligonucleotides induce apoptosis in melanoma cells of different clinical stages. J Invest Dermatol 118: 505-512, 2002.

- Pavey S and Gabrielli B.
Alpha-melanocyte stimulating hormone potentiate p16/CDKN2A expression in human skin after ultraviolet irradiation. Cancer Res 62(3): 875-880, 2002.

- Sanchez Mas J, Martinez-Esparza M, Bastida CM, Solano F, Penafiel R, and Garcia-Borron JC
Regulation of ornithine decarboxylase in B16 mouse melanoma cells: synergistic activation of melanogenesis by a α-MSH and ornithine decarboxylase inhibition. Biochim Biophys Acta 1542(1-3): 57-65, 2002.

- Suzuki I, Kato T, Motokawa Y, Tomita Y, Nakamura E, and Katagiri T
Increase of Pro-opiomelanocortin mRNA prior to tyrosinase, tyrosinase-related protein 1, dopachrome

tautomerase, Pmel-17/gp 100, and P-protein mRNA in human skin after ultraviolet B irradiation. J Invest Dermatol 118: 73-78, 2002.

- Sviderskaya EV, Hill SP, Evans-Whipp TJ, Chin L, Orlow SJ, Easty DJ, Cheong SC, Beach D, DePinho RA, and Bennett DC.
p16^{INK4a} in melanocyte senescence and differentiation. J Natl Cancer Inst 94(6): 446-454, 2002.

- Tada A, Pereira E, Beitner-Johnson D, Kavanagh R, and Abdel-Malek ZA.
Mitogen- and ultraviolet-B-induced signaling pathways in normal human melanocytes. J Invest Dermatol 118: 316-322, 2002.

- Tsatmali M, Ancans J, Thody AJ
Melanocyte function and its control by melanocortin peptides. J Histochem Cytochem 50(2): 125-133, 2002.

- Vachtenheim J, Novotna H, and Ghanem G.
Transcriptional repression of the microphtalmia gene in melanoma cells correlates with the unresponsiveness of target genes to ectopic micropthalmia-associated transcription factor.
J Invest Dermatol 117: 1505-1511, 2001.

- Valery C, Grob J, and Verrando P.
Identification by cDNA microarray technology of genes madulated by artificial ultraviolet radiation in normal human melanocytes: relation to melanocarcinogenesis. J Invest Dermatol 117: 1471-1482, 2001.

- van der Gaag EJ, Leccia MT, Dekker SK, Jalbert NL, Amodeo DM, and Byers HR.
Role of zyxin in differential cell spreading and proliferation of melanoma and melanocytes. J Invest Dermatol 118: 246-254, 2002.

- van der Wijngaard RM, Asghar SS, Pijnenborg AC, Tigges AJ, Westerhof W, Das PK.
Aberrant expression of complement regulatory proteins, membrane cofactor protein and decay accelerating factor, in the involved epidermis of patients with vitiligo. Br J Dermatol 146(1): 80-87, 2002.

- Yoshida M, Hirotsu S, Nakahara M, Uchiwa H, and Tomita Y.
Histamine is involved in ultraviolet B-induced pigmentation of guinea pig skin. J Invest Dermatol 118: 255-260, 2002.

- Watabe H, Soma Y, Ito M, Kawa Y, and Mizoguchi M.
All-trans retinoic acid induces differentiation and apoptosis of murine melanocyte precursors with induction of the microphtalmia-associated transcription factor. J Invest Dermatol 118: 35-42, 2002.

- Zhao C, Snellman E, Jansen CT, and Hemminki K.
Ultraviolet photoproduct levels in melanocytic nevi and surrounding epidermis in human skin in situ. J Invest Dermatol 118: 180-184, 2002.

- Zonios G, Bykowski J, and Kollias N.
Skin melanin, haemoglobin, and light scattering properties can be quantitatively assessed in vivo using diffuse reflectance spectroscopy. J Invest Dermatol 117: 1452-1457, 2001.

2. MSH, MCH, other hormones, differentiation

(Dr. B. Loir)

- Chen J, Cheng Z, Miao Y, Jurisson SS, Quinn TP.
Alpha-melanocyte-stimulating hormone peptide analogs labeled with technetium-99m and indium-111 for malignant melanoma targeting. Cancer 94(4 Suppl):1196-201, 2002.
Comments: The authors developed "an excellent candidate for radiodetection and radiotherapy": the labeled DOTA-Re-CCMSH. This melanoma-targeting peptide was produced by conjugaison of the metal chelate 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) to the N-terminus of a rhenium-cyclized alpha-MSH peptide analog [Cys3410,D-Phe7]alpha-MSH(3--13) (Re-CCMSH).

- Funasaka Y, Chakraborty AK, Yodoi J, Ichihashi M.
The effect of thioredoxin on the expression of proopiomelanocortin-derived peptides, the melanocortin 1 receptor and cell survival of normal human keratinocytes. J Investig Dermatol Symp Proc. 6(1):32-7, 2001.

- Griffond B, Baker BI.
Cell and molecular cell biology of melanin-concentrating hormone. Int Rev Cytol. 213:233-77, 2002. Review.

- Healy E, Jordan SA, Budd PS, Suffolk R, Rees JL, Jackson IJ.
Functional variation of MC1R alleles from red-haired individuals. Hum Mol Genet.10(21):2397-402, 2001.

- Kanetsky PA, Swoyer J, Panossian S, Holmes R, Guerry D, Rebbeck TR.
A polymorphism in the agouti signaling protein gene is associated with human pigmentation. Am J Hum Genet. 70(3):770-5, 2002.

- Pavey S, Gabrielli B.
Alpha-melanocyte stimulating hormone potentiates p16/CDKN2A expression in human skin after ultraviolet irradiation. Cancer Res. 62(3):875-80, 2002.
Summary: The authors "demonstrate that the increased expression of p16 after exposure to suberythemal doses of UVR is potentiated by alpha-MSH, a ligand for MC1R, and this effect is mimicked by cAMP, the intracellular mediator of alpha-MSH signaling via the MC1 receptor." They propose that "this link between p16 and MC1R may provide a molecular basis for the increased skin cancer risk associated with MC1R polymorphisms."

- Saito Y, Wang Z, Hagino-Yamagishi K, Civelli O, Kawashima S, Maruyama K. **Endogenous melanin-concentrating hormone receptor SLC-1 in human melanoma SK-MEL-37 cells.** Biochem Biophys Res Commun. 289(1):44-50, 2001.

- Sanchez Mas J, Martinez-Esparza M, Bastida CM, Solano F, Penafiel R, Garcia-Borron JC.
Regulation of ornithine decarboxylase in B16 mouse melanoma cells: synergistic activation of melanogenesis by alphaMSH and ornithine decarboxylase inhibition. Biochim Biophys Acta 1542(1-3):57-65, 2002.

- Sviderskaya EV, Hill SP, Evans-Whipp TJ, Chin L, Orlow SJ, Easty DJ, Cheong SC, Beach D, DePinho RA, Bennett DC.
p16(Ink4a) in melanocyte senescence and differentiation. J Natl Cancer Inst. 94(6):446-54, 2002.

- Tsatmali M, Ancans J, Thody AJ.
Melanocyte function and its control by melanocortin peptides. J Histochem Cytochem. 50(2):125-34, 2002.

- Virador VM, Muller J, Wu X, Abdel-Malek ZA, Yu ZX, Ferrans VJ, Kobayashi N, Wakamatsu K, Ito S, Hammer JA, Hearing VJ.
Influence of alpha-melanocyte-stimulating hormone and ultraviolet radiation on the transfer of melanosomes to keratinocytes. FASEB J. 16(1):105-7, 2002.
Summary: UV radiation induced an accumulation of melanosomes in murine melanocytes, whereas treatment with a-MSH induced exocytosis of melanosomes accompanied by ruffling of the cell membrane. In the other hand, phagocytosis of melanosomes by murine keratinocytes was increased by exposure of these cells to UV radiation or to MSH. Moreover, "coculture of melanocytes and keratinocytes resulted in an increase in MSH released to the medium". Accordingly, "a combination of signals that increase melanosome production and release by melanocytes and that stimulate phagocytosis by keratinocytes are" proposed as "the most relevant mechanisms involved in skin tanning".

- Voisey J, van DA.
Agouti: from mouse to man, from skin to fat. Pigment Cell Res. 15(1):10-8, 2002.

The two following references are related to the expression of MC1R in non-melanocyte cell types. However, they concern human sebocytes of normal skin and human peripheral lymphocyte subsets. So, the melanocortic system could be also involved in the modulation of inflammatory responses in the pilosebaceous unit and in the modulation of immune responses.

- Bohm M, Schiller M, Stander S, Seltmann H, Li Z, Brzoska T, Metze D, Schioth HB, Skottner A, Seiffert K, Zouboulis CC, Luger TA.
Evidence for expression of melanocortin-1 receptor in human sebocytes in vitro and in situ. J Invest Dermatol. 118(3):533-539, 2002.

- Neumann Andersen G, Nagaeva O, Mandrika I, Petrovska R, Muceniece R, Mincheva-Nilsson L, Wikberg JE.
MC(1) receptors are constitutively expressed on leucocyte subpopulations with antigen presenting and cytotoxic functions. Clin Exp Immunol. 126(3):441-6, 2001.

3. Photobiology

(Dr. E. Wenczl)

- Berking C, Takemoto R, Binder RL.
  Photocarcinogenesis in human adult skin grafs. Carcinogenesis 23:181-187, 2002.

- Deng J, Zhang H, Kloosterboer F et al.
  Ceramide does not act as a general second messenger for ultraviolet-induced apoptosis. Oncogene 21:44-52, 2002.

- Landi MT, Baccarelli A, Tarone RE et al.
  DNA repair, dysplastic nevi, and sunlight sensitivity in the development of cutaneous maignant melanoma. J Natl Cancer Inst 94:94-101, 2002.

- Mehta RR, Bratescu L, Graves JM et al.
  In vitro transformation of human congenital naevus to malignant melanoma. Melanoma Res 12:27-33, 2002.

- Pavey S, Gabrielli B.
  Alpha-melanocyte stimulating hormone potentiates p16/CDKN2A expression in human skin after ultraviolet irradiation. Cancer Res 62:875-880, 2002.

- Shyong EQ, Lu Y, Lazinsky A et al.
  Effects of the isoflavone 4,5,7-trihydroxyisoflavone (genistein) on psoralen plus ultraviolet A radiation (PUVA)-induced photodamage. Carcinogenesis 23:317-321, 2002.

- Suzuki I, Kato T, Motokowa T et al.
  Increase of pro-opiomelanocortin mRNA prior to tyrosinase, tyrosinase-related protein 1, dopachrome tautomerase, Pmel-17/gp100, and P-protein mRNA in human skin after UVB irradiation. J Invest Dermatol 118:73-78, 2002.

- Tada A, Pereira E, Beitner-Johnson D et al.
  Mitogen- and UVB-induced signaling pathways in normal human melanocytes. J Invest Dermatol 118:316-322.

- Tsao H, Kwitkiwski K, Sober AJ.
  A single-institution case series of patients with cutaneous melanoma and non-Hodgkin's lymphoma. J Am Acad Dermatol 46:55-61, 2002.

- Ullrich SE.
  Photoimmune suppression and photocarcinogenesis. Front Biosci 7:D684-703, 2002.

- Virador VM, Muller J, Wu X et al.
  Influence of alpha-melanocyte stimulating hormone and ultraviolet radiation on the transfer of melanosomes to keratinocytes. FASEB 16:105-107, 2002.

- Yoshida M, Hirotsu S, Nakahara M et al.
  Histamine is involved in UVB-induced pigmentation of guinea pig skin. J Invest Dermatol 118:255-260, 2002.

- Zhao C, Snellman E, Jansen CT et al.
  Ultraviolet photoproduct levels in melanocytic nevi and surrounding epidermis in human skin in situ. J Invest Dermatol 118:180-184, 2002.

4. Neuromelanins

(Prof. M. d'Ischia)

Neuromelanin (March 2002)

Most of the papers on neuromelanin that appeared during the last months of 2001 and the beginning of 2002 centred on two main issues concerning neuromelanin detection and the mechanisms of oxidative stress dependent catecholamine neurotoxicity. Zecca et al. (2002) reported a new sensitive method for quantitation of nigral neuromelanin and demonstrated continuous pigment accumulation in nigral neurons during aging, the presence of large amounts of

neuromelanin in substantia nigra pars compacta and severe depletion of neuromelanin in Parkinson's disease. Elleder and Borovanski (2001) described a novel type of fluorogen in autofluorescent pigment histochem mechanisms involving UV irradiation. Dzierzega-Lecznar et al. (2002) investigated the potential of pyrolysis-gas chromatog.-mass spectrometry methods for identification of 5-S-cysteinyldopamine-derived units in synthetic melanin copolymers, and the possible application to structural analysis of natural neuromelanin.
The development of rational neuroprotection strategies is a main goal in research on neurodegenerative diseases. In a reviewing article Drukarch et al. (2001) focused on the process of dopamine oxidation leading to the formation of neuromelanin, as an often overlooked pathogenetic factor, and addressed the option of drug-mediated stimulation of detoxification mechanisms of dopamine auto-oxidation products as a novel means of neuroprotection in Parkinson's disease. Barzilai et al (2001) described the effects of neuromelanin and iron on neuronal survival and addressed in detail the molecular mechanisms of dopamine-induced apoptosis.
The potential neurotoxicity of apomorphine (El-Bacha et al., 2001), the chemical state imaging of iron in nerve cells from a patient with Parkinsonism-dementia complex (Ide-Ektessabi et al., 2002) and an improved methodology for detection of substantia nigra pathology in Alzheimer's disease (Schneider et al., 2002) figure among other central topics in a series of relevant papers.

- Barzilai Ari, Melamed Eldad, Shirvan.
  Is there a rationale for neuroprotection against dopamine toxicity in Parkinson's disease? Anat. Cell. Mol. Neurobiol. 21(3), 215-235, 2001.

- Drukarch Benjamin, Van Muiswinkel Freek L.
  Neuroprotection for Parkinson's disease: a new approach for a new millennium. Expert Opinion on Investigational Drugs 10(10), 1855-1868, 2001.

- Dzierzega-Lecznar A., Chodurek E., Stepien K., Wilczok T.
  Pyrolysis-gas chromatography-mass spectrometry of synthetic neuromelanins. Journal of Analytical and Applied Pyrolysis 62(2), 239-248, 2002.

- El-Bacha R. D. S., Daval J. L., Netter P., Minn, A.
  Is apomorphine neurotoxic? Biogenic Amines 16(4-5), 463-471, 2001.

- Elleder, Milan; Borovansky, Jan.
  Autofluorescence of melanins induced by ultraviolet radiation and near ultraviolet light. A histochemical and biochemical study. Histochem. J.33(5), 273-281, 2001.

- Ide-Ektessabi Ari, Fujisawa Shigeyoshi, Yoshida Sohei.
  Chemical state imaging of iron in nerve cells from a patient with Parkinsonism-dementia complex. Journal of Applied Physics 91(3),1613-1617, 2002.

- Schneider Julie A., Bienias Julia L., Gilley David W., Kvarnberg David E., Mufson Elliott J., Bennett David A.
  Improved detection of substantia nigra pathology in Alzheimer's disease. Journal of Histochemistry and Cytochemistry 50(1), 99-106, 2002.

- Zecca Luigi, Fariello Ruggero, Riederer Peter, Sulzer David, Gatti Alberto, Tampellini Davide.
  The absolute concentration of nigral neuromelanin, assayed by a new sensitive method, increases throughout the life and is dramatically decreased in Parkinson's disease. FEBS Letters 510(3), 216-220, 2002.

5. Genetics, molecular and developmental biology

(Dr. F. Beermann)

- Anderson MG, Smith RS, Hawes NL, Zabaleta A, Chang B, Wiggs JL, John SW.
  Mutations in genes encoding melanosomal proteins cause pigmentary glaucoma in DBA/2J mice. Nat Genet 30(1):81-85, 2002.

- de Wit NJ, Burtscher HJ, Weidle UH, Ruiter DJ, van Muijen GN.
  Differentially expressed genes identified in human melanoma cell lines with different metastatic behaviour using high density oligonucleotide arrays. Melanoma Res 12(1):57-69, 2002.

- Dorsky RI, Sheldahl LC, Moon RT.
  A transgenic Lef1/beta-catenin-dependent reporter is expressed in spatially restricted domains throughout zebrafish development. Dev Biol 241(2):229-237, 2002.

- Du J, Fisher DE.
Identification of Aim-1 as the underwhite mouse mutant and its transcriptional regulation by MITF. J Biol Chem 277(1):402-406, 2002.

- Fryer JP, Oetting WS, Brott MJ, King RA.
Alternative splicing of the tyrosinase gene transcript in normal human melanocytes and lymphocytes. J Invest Dermatol 117(5):1261-1265, 2001.

- Kamaraju AK, Bertolotto C, Chebath J, Revel M.
PAX3 down-regulation and shut-off of melanogenesis in melanoma B16/F10.9 by interleukin-6 receptor signaling. J Biol Chem 5:5, 2002.

- Kanetsky PA, Swoyer J, Panossian S, Holmes R, Guerry D, Rebbeck TR.
A polymorphism in the agouti signaling protein gene is associated with human pigmentation. Am J Hum Genet 70(3):770-775, 2002.

- Karim MA, Suzuki K, Fukai K, Oh J, Nagle DL, Moore KJ, Barbosa E, Falik-Borenstein T, Filipovich A, Ishida Y, Kivrikko S, Klein C, Kreuz F, Levin A, Miyajima H, Regueiro J, Russo C, Uyama E, Vierimaa O, Spritz RA.
Apparent genotype-phenotype correlation in childhood, adolescent, and adult Chediak-Higashi syndrome. Am J Med Genet 108(1):16-22, 2002.

- Kawakami T, Soma Y, Kawa Y, Ito M, Yamasaki E, Watabe H, Hosaka E, Yajima K, Ohsumi K, Mizoguchi M.
Transforming Growth Factor beta1 Regulates Melanocyte Proliferation and Differentiation in Mouse Neural Crest Cells Via Stem Cell Factor/KIT Signaling. J Invest Dermatol 118(3):471-478, 2002.

- Khlgatian MK, Hadshiew IM, Asawanonda P, Yaar M, Eller MS, Fujita M, Norris DA, Gilchrest BA.
Tyrosinase Gene Expression is Regulated by p53. J Invest Dermatol 118(1):126-132, 2002.

- Kunisada T, Yamazaki H, Hayashi SI.
Review: ligands for receptor tyrosine kinases expressed in the skin as environmental factors for melanocyte development. J Investig Dermatol Symp Proc 6(1):6-9, 2001.

- Le Poole IC, Sarangarajan R, Zhao Y, Stennett LS, Brown TL, Sheth P, Miki T, Boissy RE.
'VIT1', a novel gene associated with vitiligo. Pigment Cell Res 14(6):475-484, 2001.

- Levy C, Nechushtan H, Razin E.
A new role for the STAT3 inhibitor, PIAS3: a repressor of microphthalmia transcription factor. J Biol Chem 277(3):1962-1966, 2002.

- Li G, Schaider H, Satyamoorthy K, Hanakawa Y, Hashimoto K, Herlyn M.
Downregulation of E-cadherin and Desmoglein 1 by autocrine hepatocyte growth factor during melanoma development. Oncogene 20(56):8125-8135, 2001.

- Locke MM, Ruth LS, Millon LV, Penedo MC, Murray JD, Bowling AT.
The cream dilution gene, responsible for the palomino and buckskin coat colours, maps to horse chromosome 21. Anim Genet 32(6):340-343, 2001.

- Mansky KC, Marfatia K, Purdom GH, Luchin A, Hume DA, Ostrowski MC.
The microphthalmia transcription factor (MITF) contains two N-terminal domains required for transactivation of osteoclast target promoters and rescue of mi mutant osteoclasts. J Leukoc Biol 71(2):295-303, 2002.

- Mansky KC, Sulzbacher S, Purdom G, Nelsen L, Hume DA, Rehli M, Ostrowski MC.
The microphthalmia transcription factor and the related helix-loop-helix zipper factors TFE-3 and TFE-C collaborate to activate the tartrate-resistant acid phosphatase promoter. J Leukoc Biol 71(2):304-310, 2002.

- McArdle L, Rafferty M, Maelandsmo GM, Bergin O, Farr CJ, Dervan PA, O'Loughlin S, Herlyn M, Easty DJ.
Protein tyrosine phosphatase genes downregulated in melanoma. J Invest Dermatol 117(5):1255-1260, 2001.

- Mellgren EM, Johnson SL.
The evolution of morphological complexity in zebrafish stripes. Trends Genet 18(3):128-134, 2002.

- Morii E, Oboki K, Kataoka TR, Igarashi K, Kitamura Y.

Interaction and Cooperation of mi Transcription Factor (MITF) and Myc-associated Zinc-finger Protein-related Factor (MAZR) for Transcription of Mouse Mast Cell Protease 6 Gene. J Biol Chem 277(10):8566-8571, 2002.

- Nakamura E, Miyamura Y, Matsunaga J, Kano Y, Dakeishi-Hara M, Tanita M, Kono M, Tomita Y.
A novel mutation of the tyrosinase gene causing oculocutaneous albinism type 1 (OCA1). J Dermatol Sci 28(2):102-105, 2002.

- Rawls JF, Mellgren EM, Johnson SL.
How the zebrafish gets its stripes. Dev Biol 240(2):301-314, 2001.

- Sarangarajan R, Boissy RE.
Tyrp1 and oculocutaneous albinism type 3. Pigment Cell Res 14(6):437-444, 2001.

- Sato S, Tanaka M, Miura H, Ikeo K, Gojobori T, Takeuchi T, Yamamoto H.
Functional conservation of the promoter regions of vertebrate tyrosinase genes. J Investig Dermatol Symp Proc 6(1):10-18, 2001.

- Sato S, Yamamoto H.
Development of pigment cells in the brain of ascidian tadpole larvae: insights into the origins of vertebrate pigment cells. Pigment Cell Res 14(6):428-436, 2001.

- Scott G, Leopardi S, Printup S, Madden BC.
Filopodia are conduits for melanosome transfer to keratinocytes. J Cell Sci 115(Pt 7):1441-1451, 2002.

- Selicorni A, Guerneri S, Ratti A, Pizzuti A.
Cytogenetic mapping of a novel locus for type II Waardenburg syndrome. Hum Genet 110(1):64-67, 2002.

- Shi CX, Hitt M, Ng P, Graham FL.
Superior tissue-specific expression from tyrosinase and prostate-specific antigen promoters/enhancers in helper-dependent compared with first-generation adenoviral vectors. Hum Gene Ther 13(2):211-224, 2002.

- Shibahara S, Takeda K, Yasumoto K, Udono T, Watanabe K, Saito H, Takahashi K.
Microphthalmia-associated transcription factor (MITF): multiplicity in structure, function, and regulation. J Investig Dermatol Symp Proc 6(1):99-104, 2001.

- Suzuki T, Li W, Zhang Q, Novak EK, Sviderskaya EV, Wilson A, Bennett DC, Roe BA, Swank RT, Spritz RA.
The gene mutated in cocoa mice, carrying a defect of organelle biogenesis, is a homologue of the human Hermansky-Pudlak syndrome-3 gene. Genomics 78(1-2):30-37, 2001.

- Tachibana M.
Cochlear melanocytes and MITF signaling. J Investig Dermatol Symp Proc 6(1):95-98, 2001.

- Tanita M, Matsunaga J, Miyamura Y, Dakeishi M, Nakamura E, Kono M, Shimizu H, Tagami H, Tomita Y.
Polymorphic sequences of the tyrosinase gene: allele analysis on 16 OCA1 patients in Japan indicate that three polymorphic sequences in the tyrosinase gene promoter could be powerful markers for indirect gene diagnosis. J Hum Genet 47(1):1-6, 2002.

- Terry RB, Bailey E, Lear T, Cothran EG.
Rejection of MITF and MGF as the genes responsible for appaloosa coat colour patterns in horses. Anim Genet 33(1):82-84, 2002.

- Toyofuku K, Wada I, Valencia JC, Kushimoto T, Ferrans VJ, Hearing VJ.
Oculocutaneous albinism types 1 and 3 are ER retention diseases: mutation of tyrosinase or Tyrp1 can affect the processing of both mutant and wild-type proteins. Faseb J 15(12):2149-2161, 2001.

- Vachtenheim J, Novotna H, Ghanem G.
Transcriptional repression of the microphthalmia gene in melanoma cells correlates with the unresponsiveness of target genes to ectopic microphthalmia-associated transcription factor. J Invest Dermatol 117(6):1505-1511, 2001.

- Watabe H, Soma Y, Ito M, Kawa Y, Mizoguchi M.
All-trans retinoic acid induces differentiation and apoptosis of murine melanocyte precursors with induction

of the microphthalmia-associated transcription factor. J Invest Dermatol 118(1):35-42, 2002.

- Yamane T, Hayashi S, Kunisada T.
Embryonic stem cells as a model for studying melanocyte development. Methods Mol Biol 185:261-268, 2002.

- Yoshida H, Kunisada T, Grimm T, Nishimura EK, Nishioka E, Nishikawa SI.
Review: melanocyte migration and survival controlled by SCF/c-kit expression. J Investig Dermatol Symp Proc 6(1):1-5, 2001.

- Zhao S, Overbeek PA.
Regulation of choroid development by the retinal pigment epithelium. Mol Vis 7:277-282, 2001.

6. Tyrosinase, TRPs, other enzymes

(Prof. J.C. Garcia-Borron)

- Fang J, Han Q, Johnson JK, Christensen BM, Li J.
Functional expression and characterization of Aedes aegypti dopachrome conversion enzyme. Biochem Biophys Res Commun 290(1):287-93, 2002.

- Fenoll LG, Rodrijguez-Lopez JN, Garcija-Molina F, Garcija-Canovas F, Tudela J.
Michaelis constants of mushroom tyrosinase with respect to oxygen in the presence of monophenols and diphenols. Int J Biochem Cell Biol 34(4):332-6, 2002.

- Gerdemann C, Eicken C, Krebs B.
The crystal structure of catechol oxidase: new insight into the function of type-3 copper proteins. Acc Chem Res 35(3):183-91, 2002.

- Khlgatian M, Hadshiew IM, Asawanonda P, Yaar M, Eller MS, Fujita M, Norris DA, Gilchrest BA.
Tyrosinase Gene Expression is Regulated by p53. J Invest Dermatol 118(1):126-32, 2002.

- Loftus SK, Larson DM, Baxter LL, Antonellis A, Chen Y, Wu X, Jiang Y, Bittner M, Hammer JA 3rd, Pavan WJ.
Mutation of melanosome protein RAB38 in chocolate mice. Proc Natl Acad Sci U S A 99(7):4471-4476, 2002.

- Nakamura E, Miyamura Y, Matsunaga J, Kano Y, Dakeishi-Hara M, Tanita M, Kono M, Tomita Y.
A novel mutation of the tyrosinase gene causing oculocutaneous albinism type 1 (OCA1). J Dermatol Sci 28(2):102-5, 2002.

- Olivares C, Garcia-Borron JC, Solano F.
Identification of active site residues involved in metal cofactor binding and stereospecific substrate recognition in Mammalian tyrosinase. Implications to the catalytic cycle. Biochemistry 41(2):679-86, 2002.

- Sanchez Mas J, Martijnez-Esparza M, Bastida CM, Solano F, Penafiel R, Garcia-Borron JC.
Regulation of ornithine decarboxylase in B16 mouse melanoma cells: synergistic activation of melanogenesis by alphaMSH and ornithine decarboxylase inhibition. Biochim Biophys Acta 1542(1-3):57-65, 2002.

- Sarangarajan R, Boissy RE.
Tyrp1 and oculocutaneous albinism type 3. Pigment Cell Res 14(6):437-44, 2001.

- Sugumaran M.
Comparative biochemistry of eumelanogenesis and the protective roles of phenoloxidase and melanin in insects. Pigment Cell Res 15(1):2-9, 2002.

- Suzuki I, Kato T, Motokawa T, Tomita Y, Nakamura E, Katagiri T.
Increase of pro-opiomelanocortin mRNA prior to tyrosinase, tyrosinase-related protein 1, dopachrome tautomerase, Pmel-17/gp100, and P-protein mRNA in human skin after ultraviolet B irradiation. J Invest Dermatol 118(1):73-8, 2002.

- Vachtenheim J, Novotna H, Ghanem G.
Transcriptional repression of the microphthalmia gene in melanoma cells correlates with the unresponsiveness of target genes to ectopic microphthalmia-associated transcription factor. J Invest Dermatol 117(6):1505-11, 2001.

7. Melanosomes

(Dr. J. Borovansky)

Three papers deserve a special mention: 1) Review by *Seabra et al.* can be regarded as a chapter from a textbook of membrane and protein traffic in the secretory and endocytic pathways accompanied by beautiful colour schemes. 2) After *Raposo et al* (J Cell Biol 152: 809-823, 2001), *Fujita et al* bring the second demonstration of a distinction between melanosome and lysosome traffic pathways. 3) An observation (*Corcuff et al*) of melanosome behaviour *in vivo:* Instead of expected absorption, melanosomes reflected light as mirrors (probably due to an abrupt mismatch in the refractive index between the cytoplasm and melanosome membrane). There are two another papers on the interaction of light with melanosomes (*Brinkmann et al, Procaccini et al*)., two papers on the transfer of melanosomes from melanocytes to keratinocytes (*Scott et al, Virador et al*), two papers on the function of melanosomes (*Mackintosh, Peters & Schraermeyer*), two papers deal with melanosome biogenesis (*Chen et al, Suzuki et al*) and two papers describing melanosomes in tumours (*Banerjee et al, Tunev & Wells*). *Testorf et al* described changes in melanosome volumes in relation to their aggregation/dispersion in melanophores. *LePoole et al* demonstrated that γ-interferon reduced melanosomal antigen expression and hampered the recognition of melanoma cells by cytotoxic T cells.

- Banerjee SS, Eyden B, Trenholm PW, Sheikh MY, Wakamatsu K, Ancans J, Rosai J.
  Monotypic angiomyolipoma of the nasal cavity: A heretofore undescribed occurrence. Int J Surg Pathol 9(4): 309-315, 2001.
  Comments: A typical angiomyolipoma (AML) is composed of smooth muscle cells, fatty tissue, thick walled blood vessels and a distinctive population of perivascular epitheloid cells (PECs), which characteristically coexpress smooth muscle and melanocyte markers. In monotypic AML ("PEComa") the latter cell type is prevailing. A case of PEComa localized in nasal cavity is decribed: cells were strongly positive for HMB45, Melan A was detected focally; staining for S100 and tyrosinase were negative. EM revealed large number of rounded electron-dense granules, 250-400nm in diameter with homogenous and finely textured granule content. The Warthin-Starry technique for melanin gave negative reaction but chemical detection of eu- and phaeomelanin indicated that the granules might be atypical melanosomes (see also *Barnard M & Lajoie G* - Ultrastruct Pathol 25(1): 21-29, 2001).

- Brinkmann R, Hüttmann G, Rögener J, Roider J, Birngruber R, Lin CP.
  Origin of retinal pigment epithelium cell damage by pulsed laser irradiance in the nanosecond to microsecond time regimen. Lasers Surg .Med . 27:451-464, 2000.
  Comments: Melanosomes behave as a device converting one type of energy into another. This ability can be exploited in a new approach aiming at a selective photodamage of RPE to treat a variety of retinal diseases without causing adverse effects to surrounding tissues. Porcine RPE melanosomes and RPE cells were irradiated with a Nd:YLF laser or a Nd:YAG laser. The origin of RPE cell damage can be described by a mechanism in which microbubbles around melanosomes (heated to 150ºC by laser irradiation) cause rupture of the cell structure. Calculations of threshold radiant exposure were in agreement with the experimental findings when a melanosome absorption coefficient 13 000cm^{-1} was used.

- Chen H, Salopek TG, Jimbow K.
  The role of phosphoinositide-3-kinase in the sorting and transport of newly synthesized tyrosinase-related protein-1 (TRP-1). J Invest Dermatol Symp Proc 6(1): 1205-114, 2001.
  Comments: It is postulated that TRP-1 is sorted from the trans-Golgi network to a compartment in the vicinity of late endosomes, trafficking from which to the melanosome appears to be dependent on PI 3-kinase as it can be blocked by wortmannin.

- Corcuff P, Chaussepied C, Madry G, Hadjur C.
  Skin optics revisited by *in vivo* confocal microscopy: Melanin and sun exposure. J Cosmet Sci 52: 91-102, 2001.
  Comments: A new confocal prototype dedicated to the exploration of *in vivo* skin has been constructed around a laser confocal module and a skin contact device, assuring perfect stability of skin images. Melanosomes (with diameter of 200nm and length of 800nm) in keratinocytes acted as myriads of nanomirrors reflecting beams (instead of expected absorption) protecting the nuclei against injury. A hypothesis was suggested that the wavelength-independent reflection process would be effective in the whole spectrum and that melanosomes would absorb only the residual part of the light. Another striking observation turned out to be the total lasck of melanosome caps in basal keratinocytes for a period of three weeks following sun exposure.

- Fujita H, Sasano E, Yasunaga K, Furuta K, Yokota S, Wada I, Himeno M.
  Evidence for distinct membrane traffic pathways to melanosomes and lysosomes in melanocytes. J Invest Dermatol Symp Proc 6: 19-24, 2001.

Comments: Melan-a cells served as a model to study the membrane traffic to melanosomes and lysosomes. In biosynthetic pathways, the traffic route of melanosome membrane protein TRP-1 partially overlapped but was distinct from that of endo/lysosomal one (LAMP1, LGP85). The melanosome pathway is separated from the lysosomal one after the AP3-dependent sorting steps, probably at late endosome and/or prelysosomal compartment. The melanosome pathway was found to be segregated also from the endocytic pathway.

- LePoole IC, Riker AI, Quevedo ME, Stennett LS, Wang E, Marincola FM, Kast WM, Robinson JK, Nickoloff BJ. **Interferon-gamma reduces melanosomal antigen expression and recognition of melanoma cells by cytotoxic T cells.** Am J Pathol 160(2): 521-528, 2002.
  Comments: In melanoma tumour-infiltrating lymphocytes are frequently reactive with melanosomal antigens (see also *Overwijk&Restifo* /Crit Rev in Immunol 20:433-450, 2000). Interferon-gamma suppressed expression of antigens MART-1, TRP-1 and gp100 in M14 melanoma cells as demonstrated by immunohistology and FACS analysis. Hence, interferon-gamma may enhance inflammatory responses but hamper effective recognition of melanoma cells.

- Mackintosh JA.
  The antimicrobial properties of melanocytes, melanosomes and melanin and the evolution of black skin. J Theor Biol 211(2): 101-113, 2001.
  Comments: A hypothesis is outlined that melanocytes, melanosomes and melanin in melanocytes and keratinocytes have evolved and function as an integral part of innate immune system against invading microorganisms and fungi. This includes the lysosomal nature of melanosomes, the phagocytic and antigen-presenting role of melanocytes and the upregulation and modulation of melanogenesis and NO synthesis in melanocytes by modulators of inflammation and immunity.

- Peters S, Schraermeyer U.
  Features and functions of melanin in the retinal pigment epithelium. Ophthalmologe 98(12): 1181-1185.
  Comments: Functions of melanin in RPE are summarized. Melanosomes are involved in the lysosomal degradation pathways and possibly take part in the degradation of rod outer segments in the RPE.

- Procaccini EM, Riccio G, Bellocci M, Di Martino C., Monfrecola G.
  The effects of a diode laser (810nm) on pigmented guinea-pig skin. Lasers Med Sci 16: 171-175, 2001.
  Comments: The effects of diode laser at wavelength of 810nm on pigmented guinea pig skin were evaluated: a) the cellular target of laser radiation was the melanosome; b) the threshold radiant exposure at which melanosomes showed initial damage was 0.15J/cm²; c) at 0.3J/ cm² some melanosomes appeared slightly granular particularly near the melanosomal membrane, damage was restricted to melanosomes; d) at 0.5J/ cm² complete disruption of melanosomes was seen with the disarray of their internal substructure and some keratinocytes became necrotic; e) albino skin showed no alteration even at the highest exposure of 1.5J/ cm²; f) the diode laser specificity for melanin structures may provide a biological basis for the treatment of pigmented superficial cutaneous lesions.

- Scott G,Deng A, Rodriguez-Burford C, Sieberg M, Han RJ, Babiarz L, Grizzle W, Bell W, Pentland A.
  Protease-activated receptor 2, a receptor involved in melanosome transfer, is upregulated in human skin by ultraviolet irradiation. J Invest Dermatol 117(6): 1412-1420, 2001.
  Comments: Protease-activated receptor 2 (PAR-2) is involved in skin pigmentation through increased phagocytosios of melanosomes by keratinocytes. The authors show that PAR-2 expression in human skin is upregulated by UV irradiation. In nonirradiated skin, PAR-2 expression was confined to keratinocytes in the lower one third of the epidermis, whereas after UV irradiation PAR-2 expression was observed in keratinocytes in the entire epidermis. There were differences in PAR-2 upregulation between type I and skin types II, III.

- Seabra MC, Mules EH, Hume AN.
  Rab GTPases, intracellular traffic and disease. Trends in Molecular Med. 8(1): 23-30, 2002.
  Comments: Review focusing on recent advances in understanding human diseases (and corresponding mouse models) through the study of a family of crucial regulators of vesicular transport – Rab proteins. As for the pigment system a special attention is paid to melanosome transport defects such as Rab27a mutations in type 1 Griscelli syndrome, mutations of myosin Va in type 2 Griscelli syndrome and to Rab geranylgeranyl transferase mutations in a mouse model *(gunmetal)* of Hermanský-Pudlák syndrome.

- Suzuki T, Li W, Zhang Q, Novak EK, Sviderskaya EV, Wilson A, Bennett DC, Roe BA, Swank RT, Spritz RA.
  The gene mutated in cocoa mice, carrying a defect of organelle biogenesis, is a homologue of the human Hermansky-Pudlak syndrome-3 gene. Genomics 78(1-2): 30-37, 2001.
  Comments: The gene mutated in cocoa mice, which is associated with a HPS-like mutant phenotype, represents a candidate for human HPS. Analysis of of cocoa-mutant mice and cultured mutant melanocytes indicated that the normal cocoa gene product is involved in early stages of melanosome biogenesis and maturation.

- Testorf MF, Roback K, Lundström I, Svensson SPS.
  Volume changes of individual melanosomes measured by scanning force microscopy. Pigment Cell Res 14(6): 445-449.
  Comments: Scanning force microscopy was used to generate three-dimensional images of melanosomes from melanophores of Xenopus laevis to measure melanosomal height, width and length. The volumes of melanosomes isolated from aggregated and dispersed states were significantly different. The average ellipsoidal volume of aggregated melanosomes was by 18% smaller compared to that of dispersed melanosomes. This finding is surprising taking into account the rigidity of melanin biopolymer; *Nicolaus* (Melanins, Hermann, Paris 1968) compared mature melanosomes to fossils.

- Tunev SS, Wells MG.
  Cutaneous melanoma in a ferret (Mustela putorius furo). Veterinary Pathology 39(1): 141-143, 2002.
  Comments: The first described case of spontaneous cutaneous melanoma in the ferret. Ultrastructurally tumour cells contained intracytoplasmic melanosomes in different stages of development. Compound melanosomes were not identified. Also Warthin-Starry and Fontana-Masson silver stains demonstrated variable numbers of fine black intracytoplasmic granules in most cells.

- Virador VM, Muller J, Wu XF, Abdel-Malek ZXA, Yu ZX, Ferrans VJ, Kobayashi N, Wakamatsu K, Ito S, Hammer JA, Hearing VJ.
  Influence of alpha-melanocyte-stimulating hormone and of ultraviolet radiation on the transfer of melanosomes to keratinocytes. FASEB J 15(13): U135-U161, 2001.
  Comments: Murine melanocytes and keratinocytes alone and in coculture were used to characterize the processes involved in melanosome transfer. UV radiation induced an accumulation of melanosomes in melanocytes, whereas treatment with ∝-MSH induced exocytosis of melanosomes. Keratinocytes phagocytosed melanosomes and the phagocytic process was increased by exposure of keratinocytes to UV radiation or to MSH. Gene array analysis of MSH treated melanocytes showed upregulation of many genes associated with exocytosis. Cytophagocytosis of melanosome-filled processes was never observed. A combination of signals that increase melanosome production and release by melanocytes and that stimulate phagocytosis by keratinocytes seem to be the most relevant mechanis,ms involved in skin tanning.

8. Melanoma experimental, Cell culture

(Dr. N. Smit)

Melanocyte culture

Melanocytes showed a five fold higher uptake of beta-Carotene than keratinocytes after a 2 days incubation period. Beta-carotene was converted to retinol in both skin cells and may function as a local supply of vitamin A in the skin (Anderson et al).

Buchli et al show that calcium can be mobilized in melanocytes via the muscarinic acetylcholine receptor which is expressed with approximately 9,000 high affinity binding sites/cell. Influences on free calcium in the cell can be influenced by muscarine and carbachol binding to the receptor and may play an important physiological role in melanocytes.

Much information will arise about expression of a large number of genes in different pigment cell types exposed to various treatments. Using DermArray (Curto et al) a survey of 4405 human cDNAs was performed for the three major skin cell types, melanocytes, keratinocytes and fibroblasts. A total of 158 signature biomarker genes were identified for the three cell types. Jean et al and Valery et al used cDNA arrays of 588 and approximately 9000 genes to study the influence of UVA and UVB, respectively. A large number of genes were found to be modulated by the UV treatments and may provide a basis for further studies on the role of UV in melanoma induction. Schallreuter and Wood have described recently the role of thioredoxin (TRX) and thioredoxin reductase in the epidermal redox status (J Photochem. Photobiol B 2001, 64: 179). Funasaka et al showed that TRX increases expression of the MC1-receptor on keratinocytes but suppresses POMC mRNA expression in these cells. Next to a general antioxidant defence role of TRX also influences expression of MSH and its receptor which has implications for both keratinocytes and melanocytes.

Interesting reports appeared about melanosome transport from melanocytes to keratinocytes in coculture systems. Scott et al used time lapse digital movies and electron microscopy and suggest a unique role for filopodia as conduits for melanosome transfer to keratinocytes. Virador et al used cocultures of murine melanocytes and keratinocytes and suggest that a combination of signals leads to an increase in melanosome production and release by melanocytes and stimulation of phagocytosis by keratinocytes are the mechanisms that are most relevant for melanosome transfer and skin tanning.

The work of Tada et al shows important results that gives information about the signaling pathways as they are regulated in the **normal human melanocytes** by mitogens and UV-B-radiation. Sviderskaya et al have used mouse melanocytes with zero, one or no functional copies of the Ink4A-Arf locus. The effects of the defects in the two growth inhibitors, p16 and Arf, encoded by the Ink4A-Arf locus were studied in relation to melanocyte senescence and cancerogenesis.

- Andersson E, Vahlquist A, Rosdahl I.
Beta-carotene uptake and bioconversion to retinol differ between human melanocytes and keratinocytes. Nutr.Cancer 39:300-306, 2001.

- Buchli R, Ndoye A, Arredondo J, Webber RJ, Grando SA.
Identification and characterization of muscarinic acetylcholine receptor subtypes expressed in human skin melanocytes. Mol.Cell Biochem. 228:57-72, 2001.

- Curto EV, Lambert GW, Davis RL, Wilborn TW, Dooley TP.
Biomarkers of Human Skin Cells Identified Using DermArray DNA Arrays and New Bioinformatics Methods. Biochem.Biophys.Res.Commun. 291:1052-1064, 2002.

- Funasaka Y, Chakraborty AK, Yodoi J, Ichihashi M.
The effect of thioredoxin on the expression of proopiomelanocortin-derived peptides, the melanocortin 1 receptor and cell survival of normal human keratinocytes. J.Investig.Dermatol.Symp.Proc. 6:32-37, 2001.

- Gontier E, Cario-Andre M, Lepreux S, Vergnes P, Bizik J, Surleve-Bazeille JE, Taieb A.
Dermal nevus cells from congenital nevi cannot penetrate the dermis in skin reconstructs. Pigment Cell Res. 15:41-48, 2002.

- Gordon-Thomson C, Mason RS, Moore GP.
Regulation of epidermal growth factor receptor expression in human melanocytes. Exp.Dermatol. 10:321-328, 2001.

- Hachiya A, Kobayashi T, Takema Y, Imokawa G.
Biochemical characterization of endothelin-converting enzyme-1alpha in cultured skin-derived cells and its postulated role in the stimulation of melanogenesis in human epidermis. J.Biol.Chem. **277:**5395-5403, 2002.

- Hirobe T.
Endothelins are involved in regulating the proliferation and differentiation of mouse epidermal melanocytes in serum-free primary culture. J.Investig.Dermatol.Symp.Proc. 6:25-31, 2001.

- Hirobe T, Kawa Y, Mizoguchi M, Ito S, Wakamatsu K.
Effects of genic substitution at the pink-eyed dilution locus on the proliferation and differentiation of mouse epidermal melanocytes in vivo and in vitro. J.Exp.Zool. 292:351-366, 2002.

- Hume AN, Collinson LM, Hopkins CR, Strom M, Barral DC, Bossi G, Griffiths GM, Seabra MC.
The leaden Gene Product Is Required with Rab27a to Recruit Myosin Va to Melanosomes in Melanocytes. Traffic. 3:193-202, 2002.

- Ideta R, Soma T, Tsunenaga M, Ifuku O.
Cultured human dermal papilla cells secrete a chemotactic factor for melanocytes. J.Dermatol.Sci. 28:48-59, 2002.

- Im S, Lee ES, Kim W, On W, Kim J, Lee M, Kang WH.
Donor specific response of estrogen and progesterone on cultured human melanocytes. J.Korean Med.Sci. 17:58-64, 2002.

- Jean S, Bideau C, Bellon L, Halimi G, De Meo M, Orsiere T, Dumenil G, Berge-Lefranc JL, Botta A.
The expression of genes induced in melanocytes by exposure to 365-nm UVA: study by cDNA arrays and real-time quantitative RT-PCR. Biochim.Biophys.Acta 1522:89-96, 2001.

- Jean S, De Meo M, Sabatier AS, Laget M, Hubaud JC, Verrando P, Dumenil G.
Evaluation of sunscreen protection in human melanocytes exposed to UVA or UVB irradiation using the alkaline comet assay. Photochem.Photobiol. 74:417-423, 2001.

- Kashiwagi K, Tsukamoto K, Suzuki M, Tsukahara S.
Effects of isopropyl unoprostone and latanoprost on melanogenesis in mouse epidermal melanocytes. J.Glaucoma. 11:57-64, 2002.

- Kawakami T, Soma Y, Kawa Y, Ito M, Yamasaki E, Watabe H, Hosaka E, Yajima K, Ohsumi K, Mizoguchi M.
Transforming Growth Factor beta1 Regulates Melanocyte Proliferation and Differentiation in Mouse Neural Crest Cells Via Stem Cell Factor/KIT Signaling. J.Invest Dermatol. 118:471-478, 2002.

- Kobayashi A, Hachiya A, Ohuchi A, Kitahara T, Takema Y.
Inhibitory mechanism of an extract of Althaea officinalis L. on endothelin-1-induced melanocyte activation. Biol.Pharm.Bull. 25:229-234, 2002.

- Krasagakis K, Fimmel S, Genten D, Eberle J, Quas P, Ziegler W, Haller H, Orfanos CE.
Lack of protein kinase C (PKC)-beta and low PKC-alpha, -delta, -epsilon, and -zeta isozyme levels in proliferating human melanoma cells. Int.J.Oncol. 20:865-871, 2002.

- Kunisada T, Yamazaki H, Hayashi SI.
Review: ligands for receptor tyrosine kinases expressed in the skin as environmental factors for melanocyte development. J.Investig.Dermatol.Symp.Proc. 6:6-9, 2001.

- Mansvelder HD, Lodder JC, Sons MS, Kits KS.
Dopamine modulates exocytosis independent of Ca(2+) entry in melanotropic cells. J.Neurophysiol. 87:793-801, 2002.

- Meije CB, Hakvoort TB, Swart GW, Westerhof W, Lamers WH, Das PK.
Gene expression patterns in melanocytic cells: candidate markers for early stage and malignant transformation. J.Pathol. 196:51-58, 2002.

- Miyashita Y, Moriya T, Kubota T, Yamada K, Asami K.
Expression of opsin molecule in cultured murine melanocyte. J.Investig.Dermatol.Symp.Proc. 6:54-57, 2001.

- Paratore C, Goerich DE, Suter U, Wegner M, Sommer L.
Survival and glial fate acquisition of neural crest cells are regulated by an interplay between the transcription factor Sox10 and extrinsic combinatorial signaling. Development 128:3949-3961, 2001.

- Pavey S, Russell T, Gabrielli B.
G2 phase cell cycle arrest in human skin following UV irradiation. Oncogene **20:**6103-6110, 2001.

- Pavey S, Gabrielli B.
Alpha-melanocyte stimulating hormone potentiates p16/CDKN2A expression in human skin after ultraviolet irradiation. Cancer Res. 62:875-880, 2002.

- Scott G, Leopardi S, Printup S, Madden BC.
Filopodia are conduits for melanosome transfer to keratinocytes. J.Cell Sci. 115:1441-1451, 2002.

- Sviderskaya EV, Hill SP, Evans-Whipp TJ, Chin L, Orlow SJ, Easty DJ, Cheong SC, Beach D, DePinho RA, Bennett DC.
p16(Ink4a) in Melanocyte Senescence and Differentiation. J.Natl.Cancer Inst. 94:446-454, 2002.

- Tada A, Pereira E, Beitner-Johnson D, Kavanagh R, Abdel-Malek ZA. **Mitogen- and ultraviolet-B-induced signaling pathways in normal human melanocytes**. J.Invest Dermatol. 118:316-322, 2002.

- Toyofuku K, Wada I, Valencia JC, Kushimoto T, Ferrans VJ, Hearing VJ. **Oculocutaneous albinism types 1 and 3 are ER retention diseases: mutation of tyrosinase or Tyrp1 can affect the processing of both mutant and wild-type proteins**. FASEB J. 15:2149-2161, 2001.

- Valery C, Grob JJ, Verrando P.
Identification by cDNA microarray technology of genes modulated by artificial ultraviolet radiation in normal human melanocytes: relation to melanocarcinogenesis. J.Invest Dermatol. 117:1471-1482, 2001.

- van den Wijngaard RM, Asghar SS, Pijnenborg AC, Tigges AJ, Westerhof W, Das PK. **Aberrant expression of complement regulatory proteins, membrane cofactor protein and decay accelerating factor, in the involved epidermis of patients with vitiligo**. Br.J.Dermatol. 146:80-87, 2002.

- van der Gaag EJ, Leccia MT, Dekker SK, Jalbert NL, Amodeo DM, Byers HR.
Role of zyxin in differential cell spreading and proliferation of melanoma cells and melanocytes. J.Invest Dermatol. 118:246-254, 2002.

- Virador VM, Muller J, Wu X, Abdel-Malek ZA, Yu ZX, Ferrans VJ, Kobayashi N, Wakamatsu K, Ito S, Hammer JA, Hearing VJ.

Influence of alpha-melanocyte-stimulating hormone and ultraviolet radiation on the transfer of melanosomes to keratinocytes. FASEB J. 16:105-107, 2002.

- Watabe H, Soma Y, Ito M, Kawa Y, Mizoguchi M.
  All-trans retinoic acid induces differentiation and apoptosis of murine melanocyte precursors with induction of the microphthalmia-associated transcription factor. J.Invest Dermatol.118**:**35-42, 2002.

- Wellbrock C, Weisser C, Geissinger E, Troppmair J, Schartl M.
  Activation of p59Fyn Leads to Melanocyte Dedifferentiation by Influencing MKP-1-regulated Mitogen-activated Protein Kinase Signaling. J.Biol.Chem. 277:6443-6454, 2002.

Melanoma Experimental Treatment

Asai et al describe the isolation of new peptides which may cause tumor dormancy through inhibition of angiogenesis as it was tested in a mice model. Gude et al tested the effect of pentoxifylline (PTX) on the growth of B16-F10 melanoma tumors in C57BL/6J mice. The results indicate that PTX action is related to the antiproliferative effect on endothelial cells. Different recombinant versions of the type 1 repeats of thrombospondin (TSRs) were assayed for their ability to inhibit the growth of B16 F10 melanomas in mice in the study by Miao et al. The TSRs inhibit tumor growth by inhibition of angiogenesis. In the presence of a TGF-beta activating sequence the combination with TSR resulted in additional effects on B16F10 tumor cell apoptosis and proliferation.

Lant et al describe thirteen new analogues of N-acetyl-4-S-cysteaminylphenol which shows anti-melanoma activity which may depend on the presence of the enzyme tyrosinase that oxidizes the compound to the o-quinone product. Most of the new compounds displayed greater cytotoxicity towards different melanoma cell lines than the lead compound. Also in melanoma cells that contain no tyrosinase activity a moderate activity for some of the most cytotoxic compounds was observed suggesting that the compounds also have a tyrosinase independent mode of action.

Paolicchi et al describe clones of a melanoma metastasis Me665/2 that show differences in gamma-glutamyl transpeptidase (GGT) activity. The GGT poor melanoma cells accumulated more glutathione (GSH + GSSG) and GSH-cysteine disulfides than the GGT rich cells. This was accompanied with a stronger sensitivity of the GGT rich cells for a platinum compound or hydrogen peroxide.

- Asai T, Nagatsuka M, Kuromi K, Yamakawa S, Kurohane K, Ogino K, Tanaka M, Taki T, Oku N.
  Suppression of tumor growth by novel peptides homing to tumor-derived new blood vessels. FEBS Lett. 510:206-210, 2002.

- Ballas ZK, Krieg AM, Warren T, Rasmussen W, Davis HL, Waldschmidt M, Weiner GJ.
  Divergent therapeutic and immunologic effects of oligodeoxynucleotides with distinct CpG motifs. J.Immunol. 167:4878-4886, 2001.

- Bush JA, Cheung KJ, Jr., Li G.
  Curcumin induces apoptosis in human melanoma cells through a Fas receptor/caspase-8 pathway independent of p53. Exp.Cell Res. 271:305-314, 2001.

- Da Costa ML, Redmond HP, Bouchier-Hayes DJ.
  Taurolidine improves survival by abrogating the accelerated development and proliferation of solid tumors and development of organ metastases from circulating tumor cells released following surgery. J.Surg.Res. 101:111-119, 2001.

- Dabrowska A, Giermasz A, Golab J, Jakobisiak M.
  Potentiated antitumor effects of interleukin 12 and interferon alpha against B16F10 melanoma in mice. Neoplasma 48:358-361, 2001. Comments: It was shown in the study that combining IL-12 with IFN-alpha in a dose which alone does not show antitumor activity results in potentiated antitumor effects without inducing toxicity.

- Drewa T, Wozniak A, Olszewska D, Szlyk E, Lakomska I, Mila-Kierzenkowska C, Czajkowski R.
  The in vitro study of influence of four novel platinum compounds on rodent melanoma cells. Acta Pol.Pharm. 58:169-174, 2001.
  Comments: The purpose of this study was to assess cytotoxic effect of four new platinum compounds on B16 and CIS91 melanoma cells in vitro. It was concluded, that Pt-dmtp (2) represented the best cytotoxic properties in the group of four tested platinum compounds.

- Easmon J, Puerstinger G, Roth T, Fiebig HH, Jenny M, Jaeger W, Heinisch G, Hofmann J.
  2-benzoxazolyl and 2-benzimidazolyl hydrazones derived from 2-acetylpyridine: a novel class of antitumor agents. Int. J. Cancer 94:89-96, 2001.

Comments: Two compounds, EPH52 and EPH116 exhibited above-average inhibition of melanoma cells.

- Fulda S, Kufer MU, Meyer E, van Valen F, Dockhorn-Dworniczak B, Debatin KM.
Sensitization for death receptor- or drug-induced apoptosis by re-expression of caspase-8 through demethylation or gene transfer. Oncogene 20:5865-5877, 2001.

- Giermasz A, Makowski M, Nowis D, Jalili A, Maj M, Dabrowska A, Czajka A, Jakobisiak M, Golab J.
Potentiated antitumor effects of butyrate and actinomycin D in melanoma model in mice. Oncol.Rep. 9:199-203, 2002.

- Gruber BM, Anuszewska EL, Skierski JS.
Activation of programmed cell death (apoptosis) by adriamycin in human neoplastic cells. Mutat.Res. 484:87-93, 2001.

- Gude RP, Binda MM, Boquete AL, Bonfil RD.
Inhibition of endothelial cell proliferation and tumor-induced angiogenesis by pentoxifylline. J.Cancer Res.Clin.Oncol. 127:625-630, 2001

.
- Katunuma N, Tsuge H, Nukatsuka M, Asao T, Fukushima M.
Structure-based design of specific cathepsin inhibitors and their application to protection of bone metastases of cancer cells. Arch.Biochem.Biophys. 397:305-311, 2002.

- Kawarada Y, Ganss R, Garbi N, Sacher T, Arnold B, Hammerling GJ.
NK- and CD8(+) T cell-mediated eradication of established tumors by peritumoral injection of CpG-containing oligodeoxynucleotides. J.Immunol. 167: 5247-5253, 2001.

- Lant NJ, McKeown P, Timoney MC, Kelland LR, Rogers PM, Robins DJ. **Synthesis and anti-melanoma activity of analogues of N-acetyl-4-S-cysteaminylphenol substituted with two methyl groups alpha to the nitrogen**. Anticancer Drug Des 16:49-55, 2001.

- Liu JD, Chen SH, Lin CL, Tsai SH, Liang YC.
Inhibition of melanoma growth and metastasis by combination with (-)-epigallocatechin-3-gallate and dacarbazine in mice. J.Cell Biochem. 83:631-642, 2001.

- Mahboobi S, Pongratz H, Hufsky H, Hockemeyer J, Frieser M, Lyssenko A, Paper DH, Burgermeister J, Bohmer FD, Fiebig HH, Burger AM, Baasner S, Beckers T.
Synthetic 2-aroylindole derivatives as a new class of potent tubulin-inhibitory, antimitotic agents. J.Med.Chem. 44:4535-4553, 2001.

- Matthews NE, Adams MA, Maxwell LR, Gofton TE, Graham CH.
Nitric oxide-mediated regulation of chemosensitivity in cancer cells. J.Natl.Cancer Inst. 93:1879-1885, 2001.

- Miao WM, Seng WL, Duquette M, Lawler P, Laus C, Lawler J.
Thrombospondin-1 type 1 repeat recombinant proteins inhibit tumor growth through transforming growth factor-beta-dependent and -independent mechanisms. Cancer Res. 61:7830-7839, 2001.

- Nam NH, Kim Y, You YJ, Hong DH, Kim HM, Ahn BZ.
Combretoxazolones: synthesis, cytotoxicity and antitumor activity. Bioorg.Med.Chem.Lett. 11:3073-3076, 2001.
Comment: Compound 6g exhibited a significant antitumor activity in BDF1 mice bearing B16 murine melanoma cells with inhibition rates of 67 and 61% at 100 and 30 mg/kg/day, respectively.

- Nizard P, Gross DA, Chenal A, Beaumelle B, Kosmatopoulos K, Gillet D.
Anchoring cytokines to cancer cells using diphtheria toxin: better than immunotherapy by gene transfer? J.Soc.Biol. 195:229-234, 2001.

- Paolicchi A, Lorenzini E, Perego P, Supino R, Zunino F, Comporti M, Pompella A.
Extra-cellular thiol metabolism in clones of human metastatic melanoma with different gamma-glutamyl transpeptidase expression: implications for cell response to platinum-based drugs. Int.J.Cancer 97:740-745, 2002.

- Pattrick NG, Richardson SC, Casolaro M, Ferruti P, Duncan R.
Poly(amidoamine)-mediated intracytoplasmic delivery of ricin A-chain and gelonin. J.Control Release

77:225-232, 2001.

- Piantelli M, Tatone D, Castrilli G, Savini F, Maggiano N, Larocca LM, Ranelletti FO, Natali PG.
Quercetin and tamoxifen sensitize human melanoma cells to hyperthermia. Melanoma Res. 11:469-476, 2001.
Comments: The authors investigated whether quercetin and tamoxifen can sensitize M10, M14 and MNT1 human melanoma cells to hyperthermia. The results suggest that quercetin and tamoxifen can be usefully combined with hyperthermia in the therapy of recurrent and/or metastatic melanoma.

- Prendergast GC, Rane N.
Farnesyltransferase inhibitors: mechanism and applications. Expert.Opin.Investig.Drugs 10:2105-2116, 2001.
Comments: Farnesyltransferase (FT) inhibitors (FTIs) are among the first wave of signal transduction inhibitors. Still their action and specific targeting of tumor cells is not fully clear. FTI development was aimed at its inhibitory action on Ras. The antineoplastic properties of FTI are based on altering the function of other proteins than Ras, e.g. RhoB. On the basis of these mechanistic studies FTIs are considered useful not only for diseases like melanoma and breast cancer but also non-neoplastic diseases.

- Ruf P, Lindhofer H.
Induction of a long-lasting antitumor immunity by a trifunctional bispecific antibody. Blood 98:2526-2534, 2001.

- Saleh FH, Crotty KA, Hersey P, Menzies SW.
Primary melanoma tumour regression associated with an immune response to the tumour-associated antigen melan-A/MART-1. Int.J.Cancer 94:551-557, 2001.

- Shao J, Dai J, Ma JK.
- **A pilot study on anticancer activities of Chinese leek**. J.Altern.Complement Med. 7:517-522, 2001.

- Skibo EB, Xing C, Dorr RT.
Aziridinyl quinone antitumor agents based on indoles and cyclopent[b]indoles: structure-activity relationships for cytotoxicity and antitumor activity. J.Med.Chem. 44:3545-3562, 2001.

- Smith CN, Lindsay CD.
Kojic acid reduces the cytotoxic effects of sulfur mustard on cultures containing human melanoma cells in vitro. J.Appl.Toxicol.21:435-440, 2001.

- Smith CN, Lindsay CD, Hambrook JL.
An in vitro comparison of the cytotoxicity of sulphur mustard in melanoma and keratinocyte cell lines. Hum.Exp.Toxicol. 20:483-490, 2001.

- Tong Y, Song W, Crystal RG.
Combined intratumoral injection of bone marrow-derived dendritic cells and systemic chemotherapy to treat pre-existing murine tumors. Cancer Res. 61:7530-7535, 2001.
Comments: The novel findings of this study raise the possibility of using the potent strategy of combined intratumoral injections of dendritic cells and systemic chemotherapy for cancer treatment.

- Wang X, Fujimoto T, Zhang B, Mai M.
Streptococcal preparation OK-432 enhances the antitumor activity of CPT-11 by increasing Th1-cytokine production in mice. Anticancer Res. 21:2505-2510, 2001.
Comments: A combined therapy was tested on C57BL/6 mice inoculated with B16 melanoma. OK-432 is an immunomodulator and increases Th-1 cytokine production. OK-432 in combination with CPT-11 showed a stronger antitumor effect than CPT-11 alone.

- Yoshida M, Furumai R, Nishiyama M, Komatsu Y, Nishino N, Horinouchi S. **Histone deacetylase as a new target for cancer chemotherapy**. Cancer Chemother.Pharmacol. 48 Suppl 1:S20-6.:S20-S26, 2001.
Comments: Inhibitors of histone deacetylase (HDAC) have been shown to have antitumor activity. New HDAC inhibitors were synthesised and the strongest inhibitor CHAP31 exhibited anti tumor activity against B16/BL6 melanoma cells in BDF1mice. CHAP31 and other derivatives with HDAC inhibiting capacity may be useful therapeutic agents in cancer therapy.

- Zhang H, Feng Z, Zhang G.
The inhibitory effect of recombinant fibronectin polypeptide CH50 on the growth of B16 melanoma.
Zhonghua Zhong.Liu Za Zhi. 21:416-418, 1999.

ANNOUNCEMENTS & RELATED ACTIVITIES

Calendar of events

2002 Annual Meeting of the Society for Investigative Dermatology
Los Angeles, USA May 15-18

Tel: +(1) 216 579 9300
Fax: +(1) 216 579 9333
E-mail : cockburn@sidnet.org
Web-site: http://www.sidnet.org/

2002 Annual Swedish Meeting for Dermatology and Venereology
Eskilstuna, Sweden May 30-31

E-mail : mats.berg@mse.dll.se

2002 Forum "Peau Humaine"
Lyon, France June 5

Tel: +(33) 4 72 11 02 92
Fax: +(33) 4 72 11 02 90
E-mail : u346@lyon151.inserm.fr

2002 9th Meeting of the European Hair Research Society
Brussels, Belgium June 27-29

Tel: +(32) 69 22 07 40
Fax: +(32) 69 21 53 79
E-mail : skinterface@unicall.be
Web-site: http://www.ehrs.org

2002 Meeting of Bioengineering and Skin
Paris, France June 27-28

Tel: +(33) 1 53 35 82 34
Fax: +(33) 1 53 35 82 31
E-mail : m.keane@dermexpert.com

2002 Réunion de la Société française de Photodermatologie
Paris, France June 30

Tel: +(33) 3 20 44 59 62
Fax: +(33) 3 20 44 42 77

E-mail : pierthomas@chru-lille.fr

2002 20th World Congress of Dermatology

Paris, France July 1– 5

Contact: Philippe FOURNIER
12, rue de la Croix Faubin
75557 Paris cedex 11 - France
Tel: 33.(0).1.44.64.15.15
Fax: 33.(0).1.44.64.15.16
E-mail : p.fournier@colloquium.fr
Web-site: http://www.derm-wcd-2002.com/

2002 82nd Annual Meeting of the British Association of Dermatologists

Edinburgh, Scotland July 9-12

Tel: (44) 207 383 0266
Fax: (44) 207 383 5263
E-mail : admin@bod;org.uk
Web-site: http://wwww.bod.org.uk

2002 5th Teupitzer Colloquium

Teupitz, Germany July 12-14

Contact: Dept. of Dermatology
Univ. Medical Center Benjamin franklin
The Free University of Berlin
Fabeckstr. 60-62
G- 14195 Berlin-Dahlem
Germany
Tel: (49) 30-84456907
E-mail : ccgeilen@zedat.fu-berlin.de

2002 XIXth IUPAC Conference on Photochemistry

Budapest, July 14–19

Contact: Hungarian Chemical Society, (MKE)
Fu u. 68. Hungary
H - 1027 Budapest,
Tel: 36-1-201-6886
Fax: 36-1-201-8056
E-mail: mail.mke@mtesz.hu

2002 5th International Melanocortin Meeting

Sunriver Resort, OR, 25-28 August 2002

Contact: Dr. R Cone
Vollum Institute, OHSU, L-474
3181 S.W. Sam Jackson Park Rd.
Portland, OR 97201-3098
Tel: 503-494-4668
Fax: 503-494-4534
E-mail: cone@ohsu.edu
Website: www.ohsu.edu/melanocortin

2002 XVIIIth International Pigment Cell Conference

Egmond aan Zee, Holland 9 - 13 September 2002

Abstract deadline : May 1st, 2002

Deadline for Travel Awards: May 15th 2002

Contact: Dr. Stan PAVEL
E-mail: SPavel@algemeen.azl.nl
Boerhaave Congress Office
Congress manager Mrs Caroline M. van Battum
P.O. Box 2084, NL-2301 CB Leiden
Telephone:+31(0)715276434
Fax:+31(0)715275262
Email: C.M.van_Battum@lumc.nl
Web-site: http://users.raketnet.nl/ipcc/

2002 European Immunodermatology Society, Satellite Meeting

Geneva, Switzerland September 18 –19

Contact: Ms. A. Kuehn
Dept. of Dermatology
University of freiburg
Haupstrasse 7
D- 79104 Freiburg
Tel:+49/761-2706893
Fax:+49/761-2706655
Email: A_Kuehn@haut.ukl.uni-freiburg.de
Web-site: http://www.esdr.ch/ESDR_meeting_2002/Symposia/eis.htm

2002 5th International Congress on Cutaneous Adverse Drug Reactions Satellite congress of the 32nd ESDR annual meeting

PALEXPO Geneva, Switzerland September 18 –19

Contact: Luigi Naldi
Clinica Dermatologica – Ospedali Riuniti
Largo Barozzi 1
I- 24100 Bergamo
Tel:+0039-035-400625
Fax:+0039-035-253070
Email: gised@uninetcom.it

2002 32nd ESDR Annual Meeting

Geneva, Switzerland September 19 – 21

Tel:+(41) 22 839 84 84
Fax:+(41) 22 839 84 85
Email: esdr@symporg.ch
Web-site: http://www.esdr.org

2002 11th European Academy of Dermatology and Venereology Congress (EADV)

Prague, Czech Republic October 2-6

Tel:+(42) 0 284 00 1493
Fax:+(42) 0 284 00 1448
Email: eadv2002@guarant.cz
Web-site: http://www.eadv2002.cz

2002 Annual Meeting of the New Zealand Dermatological Society 2002

Wellington, New Zealand October 9-11

Tel:+(64) 04 5667 445
Fax:+(64) 04 5668 262
Email: btaylor@paradise.net.nz

2002 3rd European Symposium on Teledermatology

Graz, Austria November 8-9

Tel:+(43) 316 385 2423
Fax:+(43) 316 385 2466
Email: telederm.uni-graz.at

2002 7th Congress of the European Society for Paediatric Dermatology (ESPD)

Barcelona, Spain November 21-23

Tel:+(34) 322 75400 (ext 2422)
Fax:+(34) 322 75438
Email: rgmalt@medicina.ub.es
Web-site: http:www.espd2002.org/

2003 International Investigative Dermatology Meeting

South Miami Beach, Florida USA , April 30 - May 4

Joint Meeting of the ESDR, JSID, and SID

2003 XIth Annual Meeting of the PASPCR

Wood's Hole, MA, September 3-7

Contact: Dr. Jean BOLOGNIA
E-mail: jean_bolognia@qm.yale.edu

2003 XIth Meeting of the ESPCR

Gent, Belgium

Contact: Prof. JM NAEYAERT
E-mail: JeanMarie.Naeyaert@rug.ac.be

2004 14th International Congress on Photobiology

Jungmoon, Jeju (Cheju), Korea June 10-15

2004 XIIth Meeting of the ESPCR

Paris, France

Contact: Dr. Lionel LARUE
E-mail: Lionel.Larue@curie.fr

2005 XIVth International Pigment Cell Conference (IPCC)

Bethesda, USA

Contact: Dr. V. HEARING
E-mail: hearingv@nih.gov

International Federation of Pigment Cell Societies

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

COUNCIL MEMBERS: Zalfa Abdel-Malek (PASPCR); Dorothy C. Bennett (ESPCR); José C. García-Borrón (ESPCR); Masako Mizoguchi (JSPCR); James J. Nordlund (PASPCR); Shigeki Shibahara (JSPCR); Vincent J. Hearing (*Ex Officio* member as the Editor of Pigment Cell Research) and Stan Pavel (*Ex Officio* member as Organizer of the 18th IPCC)

A Letter from the IFPCS President to the members of three Regional Pigment Cell Societies

It is sad to remember the year 2001, the beginning of the 21th century, as the year of threats to peace in the world. I do believe that humans will eventually solve these difficult problems with their wisdom. When we talk about progress, however, I think that the past year has been remarkable one for pigment cell biologists. Scientists have made incredible advances in many areas of pigment cell biology, and these are now being disseminated to broader fields of biology and medicine. As the President of the IFPCS, I am glad that the annual meetings of the ESPCR (in Rome), the PASPCR (in Minneapolis), and the JSPCR (in Sendai) were successful and covered a broad range of topics in the pigment biology. I wish to congratulate the Chairs of those meetings: Drs. Mauro Picardo, Richard A. King, and Shigeki Shibahara for their successful meetings.

The IFPCS Council has established the following goals for the Federation (also available on the **IFPCS Web page** at http://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.

The first goal was achieved with the IFPCS becoming an official sponsor of ***Pigment Cell Research*** (**http://www.pigment.org**). The journal is now in the 15th year of publication and Dr. Vincent J. Hearing should be congratulated for his success in increasing the reputation of the journal in the last 2 years. I also want to thank Johnson & Johnson, L'Oreal, Shiseido, and Unilever for their generous support of the journal. This support has helped Dr. Hearing expand the color figures and other aspects of ***Pigment Cell Research***, and all regional society members are grateful for this continued corporate support. To further promote the growth of the journal, the numbers of subscribers and submitted papers need to be increased. I urge all members of the Regional Societies to subscribe to ***Pigment Cell Research,*** to encourage your Institution's library to subscribe, to submit papers, and to cite PCR's pertinent references in your publications. For more details, please look at the accompanying message from the Editor.

The second goal may be the most visible among the several efforts of the IFPCS. The ***International Pigment Cell Conference (IPCC)*** has been held every three years since 1946 when Dr. Myron Gordon held the first meeting in New York. Since the inauguration of the IFPCS in Kobe in 1990, the IFPCS with one of the regional Societies have co-organized the IPCC on a rotating basis among the ESPCR, PASPCR, and JSPCR. The 15th IPCC was held in London in 1993, the 16th IPCC in Anaheim in 1996, and the 17th IPCC in Nagoya in 1999. The 18th IPCC, will be held on September 9-13, 2002, in the Netherlands with Dr. Stan Pavel as Organizer. The meeting will be held at the Hotel Zuiderduin in Egmond aan Zee, originally a fisherman village in the north part of the Netherlands, only 30 km from Amsterdam. The hotel has excellent facilities including indoor swimming pool, sauna and squash, and is surrounded by fine restaurants and gift shops, and the IPCC will be the only occupants of the hotel during the meeting. The International Program Committee is completing plans for the scientific

program and you will receive the second announcement/call for abstracts in February. I urge each of you to plan to attend this exciting and stimulating Conference and to present your new findings. Please note that the deadline for submission of abstracts will be May 1, 2002.

The 19th IPCC in 2005 will be organized by the PASPCR. I am happy to inform you that the IFPCS Council at its recent meeting in Sendai, Japan approved the plans of Dr. Vincent J. Hearing to organize the 19th IPCC at NIH on September 18-23, 2005. The theme of this meeting will be human pigmentary diseases and this should be another opportunity for an outstanding international meeting.

The third goal is being achieved through several activities including the establishment of the ***IFPCS Visiting Scientist Award Program***. The grants from corporate support, established in 1997, are intended to allow investigators from one of the regional Societies to visit the laboratory of an investigator in another regional Society to learn specialized techniques and/or to establish inter-Society collaborations. This program has been supported by Beiersdorf, Clairol, Johnson and Johnson, Kanebo, L'Oreal, Shiseido, Nihon Surfactant, Procter and Gamble, Sunstar, Taisho, and Unilever, and has been quite successful. In 2001 Dr. Nico Smit of Leiden University, the Netherlands, was supported to visit Dr. Patrick A. Riley's laboratory in London and Dr. Olga Solovieva of Institut Curie, France, visited Dr. Takahiro Kunisada's laboratory at Gifu University, Japan. We hope to continue this program with a renewal of corporate contributions.

Another initiative for achieving this goal was the establishment of a standing committee of the IFPCS to maintain awareness of the animal resources used by members. Specific duties of this committee, chaired by Dr. Lynn Lamoreux, include an annual survey of animals of values to pigment cell research, a means of identifying threatened animal colonies, and the development of solution for problems with research animals. You should hear more about this new committee in 2002.

I sincerely hope that we will see healthy and steady progress in our 3 regional Pigment Cell Societies, ESPCR, JSPCR, and PASPCR in 2002. I wish to welcome new faces to the IFPCS Council: Dr. Zalfa Abdel-Malek (new President of the PASPCR). Finally, I urge each of you to contribute to your Society in any way you can: submitting your abstracts to the next IPCC, publishing your papers in ***Pigment Cell Research***, collaborating with other members, and recruiting others scientists and clinicians to join us. Let me take this opportunity to wish each of you and your colleagues a peaceful and successful year 2002.

January 1, 2002

Shosuke Ito

President, IFPCS

NEW MEMBERS

The ESPCR is delighted to welcome the following colleagues to membership and hope that they will play a full and active part in the Society.

BÖHM M.
Ldwig Boltzmann Institute
Dept of Dermatology
Esmarch str 58
D – 48149 MÜNSTER
Tel: 49-251 8358635
Fax: 49-251 8356522
E-mail : bohmm@uni-muenster.de

DEPASE A.
Via Brigata Lupi 3
I - 24122 BERGAMO
Tel: 39-335 5259330
Fax: 39-035 270181
E-mail : dr.depase@vitiligo-products.it

GAWKRODGER D.
Royal Hallamshire Hospital
UK - S102JF SHEFFIELD
Tel: 44-114 271 2203
Fax: 44-114 271 3763
E-mail : david.gawkrodger@sth.nhs.uk

SVIDERSKAYA E.
St Georges Hosp MS
Dept. of Anatomy and Developmental Biology
Cranmer Terrace
UK - LONDON SW17 ORE
Tel: 44-20 8725 5209
Fax: 44-20 8725 3326
E-mail : esviders@sghms.ac.uk

KOKOSCHKA E.-M.
University of Vienna
Dept of Dermatology
Waehringer Guertel 18-20
A - 1090 VIENNA
Tel: 43 1 406 12 54
Fax: 43 1 40400 7723
E-mail : Eva-Maria.Kokoschka@akh.wien.ac.at

ESPCR TRAVEL AWARDS FOR ATTENDANCE AT THE IPCC
CALL FOR APPLICATIONS

The European Society for Pigment Cell Research will provide a limited number of travel awards for attendance at the XVIII IPCC, to be held in Egmond aan Zee, September 2002. Depending on the number of applicants selected, awards may cover travel (economy return air, rail fare or car fuel costs), conference registration, and in some cases accommodation (economy class). Awards will be made by the ESPCR Travel Awards Committee on a competitive basis.

Applicants must:

- Be a PhD student or junior scientist (i.e. medical resident or postdoctoral).
- Be an ESPCR member in good standing (subscription paid).
- Make a contribution (oral or poster) to the conference.
- Have no other source of funds for this purpose. If funds from elsewhere are subsequently obtained, ESPCR should be informed immediately and the application for ESPCR funding withdrawn, or the ESPCR award declined/returned if already made, so that another applicant can be funded.

Deadline for applications: May 15, 2002

Please send an informal letter of application (e-mail or ordinary mail) to:

Dr Friedrich Beermann, Chair, ESPCR Travel Awards Committee
e-mail: Friedrich.Beermann@isrec.unil.ch

ISREC (Swiss Institute for Experimental Cancer Research)
Chemin des Boveresses 155
CH-1066 Epalinges
Switzerland

Enclosing:

- Proof of status (usually a short statement from the supervisor or Head of Department), including the date or expected date of completion of PhD or medical qualification.
- Evidence of non-availability of other funds (usually part of the statement from the supervisor or Head of Department). Please state if other applications for funding are being made (this has a positive effect on your application).
- Submitted abstract of the oral or poster contribution.
- Estimates of the costs of travel, accommodation and conference registration.
- Applicant's full address, phone and fax numbers, and e-mail address where available.

Financial report 2001 – ESPCR

(Given in Euros)

Number of members at 9/2001:	**183**
New members in 2001:	18
Members who paid subscription up to 9/2001: (including students)	106

	Eur
Balance carried over from 2000:	**11,579.29**
Income 2001-10/2001	
Member subscriptions	4,515.86
Pigment Cell Research subscriptions	1,565
Returned Visiting Scientist Award 2000	3,234.50
Donation, Integriderm ($500)	0,542.30
Total income	**9,857.66**
Outgoings 2001 –10/2001	
International Federation of Pigment Cell Societies, subscriptions for 2000	3,375
Bulletin and web costs (Prof. Ghanem)	0,900
Bank charges	0,151.40
Rome registration for Bulletin contributors	0,900
ESPCR Travel Awards	2,500
Pigment Cell Research Subscriptions	1,965
Contribution to Rome meeting	2,500
Fritz Anders Memorial Lecture	1,500
Credit card machine	0,556
Visiting Scientist Award	3,234.50
Total outgoings	**17,581.90**
Balance at 10/01	**3,855.05**

L. Larue
Treasurer