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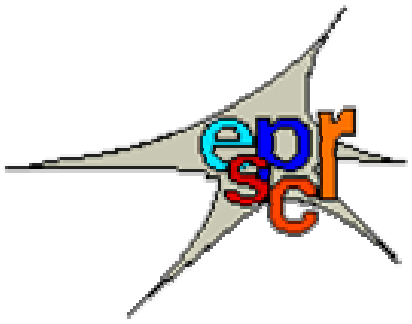

EUROPEAN SOCIETY FOR PIGMENT CELL RESEARCH *BULLETIN*

N° 46 - Aug 2003

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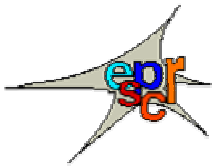

LETTER TO THE EDITOR
DISCUSSION, REVIEW,
SHORT COMMUNICATION, ...

ESPCR GENERAL ASSEMBLY

Tuesday, September 10, 2002
Egmond aan Zee, The Netherlands

A General Assembly of the ESPCR took place on Tuesday, September 10, at the Hotel Zuiderduin, in Egmond aan Zee, Holland.

1- Opening of the General Assembly
The Assembly was opened by Prof. Bennett. Agendas and the Minutes of the previous General Assembly, held in Rome, Italy, were distributed to all the members attending the Assembly (18 in total).

2- Approval of the minutes of ESPCR General Assembly in Rome
The Minutes of the previous General Assembly were read and unanimously approved without changes. They were signed by Prof. Bennett.

3- Secretary's report
The Secretary commented on the main activities during 2002. A report on the Xth ESPCR Meeting held in Rome was coordinated by the Secretary and published in the ESPCR Bulletin (December 2001), with a general introduction by Dr. M. Picardo. Chair persons were contacted, who kindly agreed to write a short summary of the relevant aspects of their session. These contributors were Drs. M. d'Ischia, E. Healy, L. Larue, N. Smit, F. Solano, G. Ghanem, J.-M. Naeyaert and A. Taïeb. For future ESPCR Meetings, the Meeting Organizer and the Secretary will coordinate efforts to ensure that the collaboration of chair persons is engaged in time to cover all the relevant activities.
During 2002, the existing ESPCR databases have been finally merged. The database run by the Treasurer and the one presented in the Web page are regularly updated, compared, and completed with new information. Complete contact information including email addresses is available for more than 95 % of the membership. Research interests are available for more than 50% of the membership.
The term of four Council members, Drs. F. Beermann, M. Picardo, A. Thody and W. Westerhof expired this year, making it necessary to proceed to an election. Drs. Beermann, Picardo and Westerhof were eligible for re-election. A call for nominations was issued on May 15, with June 15 as deadline. Seven candidates were duly nominated and a ballot was launched on July 4. Three procedures for voting were set up: by regular mail, fax, or email. In this case, a secret email vote was made possible. A large majority of the members that voted did so by direct email. The elected candidates were:
- Dr. Friedo Beermann, from the ISREC, Lausanne (Switzerland)
- Dr. Mauro Picardo, from the Dermatological Institute San Gallicano, Rome (Italy)
- Dr. Nico Smit, from the University of Leiden (The Netherlands)
- Prof. Alain Taïeb, from the University of Bordeaux (France)

On the other hand, the term of the current Officers, elected on 2000, will expire next year. The ESPCR Council decided that elections should be held one year in advance, to ensure a reasonable overlap between acting and elected Officers, aiming at an efficient transfer of duties. A call for nominations was issued simultaneously to the one for ESPCR Council. Only one nomination per Office was received, and it was not necessary to proceed to a formal election. The names of the nominees, whose

term will begin in September 2003, was announced by our President in a letter distributed to the membership on July 4. These names are:

- President: Prof. José Carlos García-Borrón (Spain)
- Secretary: Prof. Jean-Marie Naeyaert (Belgium)
- Treasurer: Dr. Patrick Verrando (France)

During this year ESPCR needed to select candidates for two awards. The H.S. Raper Medal was established by the ESPCR, to recognize "outstanding contributions to the biochemistry and molecular biology of pigmentation". The Takeuchi Medal is awarded by the JSPCR as an international recognition of "outstanding contributions to the molecular biology of pigmentation". Nominations from the membership were requested by mail on January 8 (deadline for reception February 8). Nominations were forwarded to the Council for voting, and then communicated by the President to the corresponding Awards Committees, who selected the following awardees:

- HS Raper Medal: Prof. Anthony Thody
- Takeuchi Medal: Drs. Shigeki Shibahara and Masayoshi Tachibana.

There were no further questions or comments from the audience. Prof. Bennett thanked the Secretary and moved to the next item.

4- Treasurer's report

This report included detailed data on the membership, and was delivered by Dr. Larue. As of September, the Society comprises 195 members, with 19 new members in 2002 and 14 student members. Therefore, the number of members has remained approximately stable for the last few years. Dr Larue described the incomes and outgoings, as follows (data given in euros):

Balance carried over from 2001:	**3,855.05**
Income 10/2001-09/2002	
Member subscriptions	6,520.00
Pigment Cell Research subscriptions	3,280.00
Donations	0,138.00
Total income	9,938.00
Outgoings 9/2001-9/2002	
International Federation of Pigment Cell Societies, subscriptions for 2001	3,062.65
Bulletin and web costs (Prof. Ghanem)	0,600.00
Bank charges CCF	0,323.42
Bank charges Natwest	0,048.23
ESPCR Travel Awards	1,580.00
Pigment Cell Research Subscriptions	3,280.00
Two plaques for honorary members	0,629.81
HS Raper medal	0,031.35
Credit card machine (running budget)	0,206.05
Stamps (gift from the treasurer)	
Total outgoings	9,761.51
Balance at 09/02	**4,031.54**

Dr. Larue noted that the positive balance is stable as compared to last year. Prof. Bennett thanked the Treasurer for this summary, and the report was unanimously accepted.
Before moving on to the next item, Prof. Bennett summarized the discussion in the Council Meeting concerning the need to find corporate sponsors, and informed on the appointment of an ad-hoc Committee formed by Drs. C. Goding and M. Picardo.

5- ESPCR Bulletin and Web site report
This was delivered by Prof. Ghanem, who commented on the large number of hard copies of the ESPCR Bulletin that are still printed and mailed, and on the decision of the Council to discontinue the preparation of a printed Bulletin. A computer printout or a photocopy will be mailed to those requesting a hard copy. Access to the Bulletin will remain protected, restricted to members in good standing, and denied to those members that did not pay for the last two years.
Prof. Ghanem then moved to the Web site report. He acknowledged the help and numerous suggestions from the Officers, notably D. Bennett and L. Larue. He reviewed recent improvements, including online registration forms, a list of related sites of interest, and frequently updated membership lists. The site registered between 1000 and 2000 hits per month, but the exact number of hits is impossible to determine owing to differences in the routes to access the Web page. The issues of security and confidentiality discussed by the Council were then considered, with the decision that the membership list including contact information will remain password-protected.
After some discussion on the pertinence of minor layout changes on the Web page, Prof. Bennett thanked G. Ghanem, and moved on to the next item.

6- Election of Officers, Council Members and new Council composition
This was very briefly summarized by Profs. Bennett and García-Borrón, since most of the relevant information had already been given under item 3. The Assembly was reminded of the new composition of the Council, effective after approval by the General Assembly, which is: F. Beermann (Lausanne), D. Bennett (London), G. Ghanem (Brussels), J.-C. García-Borrón (Murcia), C. Goding (Oxted), L. Larue (Paris), J.-M. Naeyaert (Ghent), S. Pavel (Leiden), M. Picardo (Rome), N. Smit (Leiden) and A. Taïeb (Bordeaux).

7- Number of voting members in the ESPCR Council
Prof. Bennett explained the situation arising from the fact that Prof. Ghanem, in his capacity of Web Master and Bulletin Editor, has become an *ex officio,* non-voting Council member. She summarized the discussion during the Council Meeting, and the decision that the total number of Council members should remain 11, according to the current Constitution, with 10 voting members. Prof. Bennett asked for approval by the General Assembly for this change in the rule governing Council composition. This was unanimously approved by the General Assembly.

8- Any other business
No further business was raised.

9- Close of Assembly
With no other matters to discuss, the General Assembly was then closed by Prof. Bennett.

CURRENT LITERATURE

1. Chemistry of Melanins and other pigments

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NOT AVAILABLE

2. Biology of pigment cells and pigmentary disorders

(Dr. M. Picardo)

Hoogduijin et al examined haw the concentration of Ca^{2+}in the medium can regulate the homeostasis of normal human melanocytes. They hypothesize that melanin plays a pivotal role in or the maintenance of Ca^{2+} intracellular content inside melanocytes. Using fluorescent microscopy they were able to measure intracellular content of Ca^{2+} in both melanocyte cultures and individual melanocytes from subjects with different phototype. High content of Ca^{2+} and fragmentation of cytoplasm were observed in a culture from a subject with phototype I. By adding Ca^{2+} to melanocytes grew in Ca^{2+} free buffer, an increase in cytoplasmic Ca^{2+} more pronounced in melanocytes from skin types I-II than in those from darker pigmented skin was observed. The authors suggested that in Negroid melanocytes the high content of melanosomal melanin is able to bind Ca^{2+} from cytoplasm. This mechanism could regulate the homeostasis of Ca^{2+} in the epidermis and, subsequently, the keratinocyte proliferation and differentiation. The folding and maturation of human tyrosinase was described by **Francis et al.** They employed an in vitro translation system coupled with ER-derived microsomes or with semipermeabilized cells. Tyrosinase produced in ER-derived microsomes or in nonmelanocytic semipermeabilized cells remained misfolded, but a tyrosinase homodimer was formed when tyrosinase was tranlocated into semipermeabilized melanocytes. The oligomerization process was found to be strictly related to functionality of tyrosinase and other melanocyte specific proteins, such as tyrosinase related protein 1. **Marles and co-workers** identified the expression of tyrosine hydroxylase isoenzyme I inside human epidermal melanosomes. The localization of the enzyme in the melanosomal membrane by side with tyrosinase was demonstrated by using immunohistochemistry and immunofluorescence double staining and HPLC analyses assayed the production of L-dopa in melanosomal extracts. Considering that L-dopa acts as catalytic intermediate for tyrosinase, the presence of tyrosine hydroxylase in the melanosomal membrane could facilitate tyrosinase activation in loco providing L-dopa. The possible contribution of tyrosinase to production of dopamine was studied by **Eisenhofer et al.** Their data revealed a correlation between tyrosine hydroxylase deficit and norepinephrine reduction in both pigmented and albino mice, whereas the peripheral content of dopamine is higher in wild-type mice compared to albino mice even in the presence of tyrosine hydroxilase. The analysis of age-related changes in peripheral dopamine level and tyrosinase activity showed that with advancing age dopamine content become similar in wild-type and albino mice and a switch to tyrosinase-dependent production of melanin, with enzyme localization around hair follicoles and enhanced synthesis of melanin was observed. **Kauser et al** examined the functional role of β-endorphin and its interaction with the class μ membrane-bound receptor in the regulation of epidermal melanocyte biology. The most relevant data were the detection both in vitro and in vivo of β- endorphin/μ-opiate receptor system in epidermal melanocytes, the localization of the complex peptide-receptor inside the melanosomes, the ability of the activation of this pathway to upregulate melanocyte dendricity, proliferation pigmentation. The author suggested that β-endorphin could act via activation of protein kinase C-β-isoform inducing a stimulation of melanogenesis through a direct eliciting of tyrosinase activity or affecting MITF expression, and leading to an increase of tyrosinase expression. These results showed that β-endorphin, in costrast to other melanocortins, is capable of modulating skin pigmentation via an MC1-R independent mechanism. **Scott and co-workers** studied the mechanism by which the activation the c-AMP signalling pathway can stimulate dendrite extension in melanocytes. Considering that they previously reported that dendrite formation is mediated by activation of Rac and inhibition of Rho, they examined the effect of c-AMP on Rac and Rho activity through microinjection of activated mutant proteins or toxin inhibitors. Elevation of c-AMP, through treatment with forskolin, dcbAMP, and NDP-MSH, was capable of inducing opposing effects in both murine melanoma cell lines and human melanocytes, with inhibition of Rho and stimulation of Rac. Moreover the effects of agents that specifically inhibit Rho, inactivate all Rho proteins or activate Rac were investigated and a major role of Rho inhibition in the mechanism of dendrite formation has been suggested. In an in vivo study, **Stefanato et al** reported the appearance of NGF in melanocytes and the modulation of NGF and Bcl-2 in melanocytes, following UV exposure. The simultaneous presence of high levels of bcl-2 and NGF, which is also able to up-regulate bcl-2 expression, might explain the strong resistence of melanocytes to apoptosis. The comparison between skin biopsies from irradiated and non-irradiated sites revealed no significant difference in the number of Bcl-2 positive melanocytes, whereas a relevant decrement of NGF positive melanocytes was observed in UV-irradiated skin. **Sviderskaya et al** investigated the role of p6 in melanocytes, focusing on its effect on senescence and genetic requirement for melanocyte immortalization. Analysing two strains from subjects with

mutation of both copies of CDKN2A locus, they provided evidence that normal human melanocyte senescence is p16-dependent and does not involve p53 and p21. Moreover, only in p16-deficient melanocytes immortalization can be induced through expression of exogenous human telomerase reverse transcriptase. The characterization of serotoninergic and melatoninergic system in both whole skin and cultured skin cells was performed by **Slominski et al.** The cutaneous expression of genes codifying for serotonin and melatonin receptors was detected. Moreover a functional role for serotonin and melatonin in the regulation of proliferation of skin cells, including melanocytes, was demonstrated even if, at least in vitro these effects are strictly dependent on cell type and culture conditions. A strong synergic action of stress and UV in inducing pigmentary response was observed by **Inoue and co-workers.** An increase in adrenocorticitropic hormone and tyrosinase activity was detected in stressed animals compared to non stressed mice. After UVB exposure a strong increment of the number of dihydroxyphenylalanine- positive melanocyte was observed, and this effect was reduced through pre-treatment with an adrenocorticotropic hormone inhibitor, such as corticostatin. Thus, the release of adrenocorticotropic hormone seems to be involved, at least in part in the enhancement of UV-mediated pigmentation under stressful conditions. **Widlund and Fisher** reviewed the transcriptional networks in which MITF play a pivotal role, focusing on its involvement in survival pathways during normal development as well as during neoplastic growth of melanoma. **Saito and co-workers** identified dual roles of MITF isoform M. MTF-M was found to act as both nuclear target and nuclear mediator of Wnt signalling pathway. Moreover MITF, through a cooperation with LEF-1, regulated the transcription of genes codifying for MITF and DCT, thus ensuring a propagation inside melanocytes of signals elicited from the binding of Wnt to its receptor. A direct correlation between mRNA expression of melanocyte-lineage genes SILV and MLANA and MITF was found in melanoma cell lines and clinical tumor specimens from **Du et al.** The effects of sphingosine-1-phosphate on melanogenesis were investigated from **Kim et al.** Sphingosine-1-phosphate was found to determine an inhibition of melanin synthesis in a dose-dependent manner in of an immortalized mouse cell line. Moreover a sustained ERK activation and, subsequently, a degradation of MITF, were observed. MITF phosphorylation and degradation and tyrosinase and TRP-1 down-regulation were completely abrogated by a specific ERK inhibitor strongly supporting an implication of ERK pathway in the depigmenting action of sphingosine-1-phosphate. **Ahn et al** evaluated the possible role of NF-kappaB on the synthesis of melanotropic factors from keratinocytes. The treatment of HaCaT keratinocytes transfected with pNF-kappaB-SEAP-NPT plasmid with melanogenic inhibitors, such as kojic acid, niacinamide, hydroquinone, arbutin or glycolic acid, followed by UVB exposure remarkably reduced NF-kappaB binding and IL-6 secretion. Thus the melanogenesis inhibitors could act at lest in part by modulating the synthesis melanotrophic factors in keratinocytes. The effect of androgen on human melanocytes is a topic under investigation. **Tadokoro and co-workers** reported that androgen supplementation induce a suppression of tyrosinase activity in human melanocytes through a mechanism which involve the activation of the cell membrane transduction pathway of androgen via the binding between sex-hormone-binding globulin (SHBG) and its receptor R_{SHBG}, and the subsequent regulation of intracellular cAMP. They suggested that strong androgens might act as antagonists in this pathway leading to the inhibition of cAMP accumulation and to the posttranscriptional and/or posttranslational control of tyrosinase activity.

Hall and al investigated the effect of U1866A, an androstenone derivative, on tyrosinase translocation from the endoplasmic reticulum to endolysosomal compartment. They found that U1866A is able to decrease pigmentation of melanocytes without inhibiting tyrosinase activity. Immunofluorescence studies showed that U1866A can affect the translocation of tyrosinase by a mechanism not related to its effect on cholesterol trafficking, but likely dependent on alteration of proteins necessary for endolysosomal transport. **Mollaaghababa R and Pavan WJ** described the relevance of SOX10, a member of the high-mobility group-domain SOX family of transcription factors, in development and functionality of both melanocytes and glia. The consequences of SOX10 mutations and biologic relevance of genes regulated by SOX10 activity are extensively reported. Human and mouse abnormalities of melanocyte development, function or survival have been summarized by **Spritz et al.** The function of β-catenin, a protein involved in cell-cell adhesion, in melanocyte genesis, development, migration and transformation is reviewed from **Larue and co-workers.** Several papers focused on vitiligo. **Schallreuter et al** confirmed previous published data reporting an over-expression of p53 in epidermis of vitiligo patients. They found that the functionality of p53 in vitiligo is not altered and did not observe any variation in its expression after UVB phototherapy. The authors speculated that the over-production of p53 is due to the constant oxidative stress determined by H_2O_2 accumulation in vitiligo skin and that the protective role of p53 could partially explain the low incidence of actinic keratosis in vitiligo patients. **Wankowicz-Kalinska and co-workers** reviewed the current literature on the immune response in melanoma and vitiligo, focusing on the role of depigmentation in anti-melanoma response. Moreover, they reported that in the same patient, the depigmenting skin was characterized from the high local content of TNF-α and INF-γ, produced from the interaction between T-cells and melanocytes and able to mediate the maturation of dendritic cells in DC1 and their translocation in the lymph node, whereas in melanoma skin the tumor cell produced mainly immunosuppressive factors that induced the production DC2/3 cells. The same group investigate the mechanisms involved in the destruction of melanocytes in human autoimmune vitiligo. They demonstrated the presence of melanocyte-specific T cells in depigmenting skin of patient affected by autoimmune vitiligo and both CD4+ and CD8+ T cells showed a Type-I-like pattern, directly correlated with the depigmenting process. **Mulekar** described a method for transplanting epidermal cells in patients with stable vitiligo. A suspension of melanocytes and keratinocytes was applied to depigmenting skin areas and covered with collagen to keep it in place. He reported that this surgical treatment gives a good repigmentation in the majority of patients affected by segmental and focal vitiligo and in at least the 50% of subjects with generalized vitiligo. **Yoon and Hearing** established optimal conditions for murine keratinocyte-melanocyte co-colture. Their model culture system involves the employment of immortalized mouse melan-a melanocytes, as suitable substitute of primary mouse melanocytes, and SP-1 keratinocytes, which are able to proliferate in the absence or grow factors, and the induction of differentiation of melanocytes, through supplementation with α-MSH or UV, and of

keratinocyte, through treatment with calcium. They evaluated the effect of arbutin, a depigmenting agent, on tyrosinase activity, melanin content and distribution, and cell proliferation in the presence or absence of keratinocyte. Their results provide further evidence for a synergic interaction between keratinocyte and melanocyte in the melanogenic response and suggested the availability of the co-colture model for the evaluation of the effects of new agents that are able to influence both keratinocyte and melanocyte functions.
In another paper, same authors tested commercial skin equivalents made with epidermal cells obtained from donors with different ethnic origins. Using melanogenesis enhancers or inhibitors, they showed that these reconstituided skin analogues are an useful and low-cost alternative to animals for evaluating the effects of new molecules on regulation of pigmentation.
The issue of June of **Annales of New York Academy Science** focused on pigmentation and several papers examined the current literature data on the mechanisms regulating melanogenic response. The correlation between genetic background, MC1R mutation, accessory proteins in melanocortin signalling, melanin composition and melanocyte function were extensively illustrated from **Sturm et al, Ancans et al, He et al and Kadekaro et al.**

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3. MSH, MCH, other hormones, differentiation

(Dr. R. Morandini)

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(Dr. E. Wenczl)

NOT AVAILABLE

5. Neuromelanins

(Prof. M. d'Ischia)

NOT AVAILABLE

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Shortened abstract: The retina pigment epithelium (RPE) is fundamental for the development and function of the vertebrate eye. Molecularly, the presumptive RPE can be identified by the early expression of two transcription factors, Mitf and Otx. Here we show that Otx2 induces a pigmented phenotype when overexpressed in avian neural retina cells. OTX2 binds specifically to a bicoid motif present in the promoter regions of three Mitf target genes, QNR71, TRP-1, and tyrosinase, leading to their transactivation. OTX2 and MITF co-localize in the nuclei of RPE cells and physically interact, and their co-expression results in a cooperative activation of QNR71 and tyrosinase promoters. These data suggest that both transcription factors operate at the same hierarchical level to establish the identity of the RPE.

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Loss of Kindlin-1, a Human Homolog of the Caenorhabditis elegans Actin-Extracellular-Matrix Linker Protein UNC-112, Causes Kindler Syndrome. Am J Hum Genet 73(1):174-187, 2003.
Abstract: Kindler syndrome is an autosomal recessive disorder characterized by neonatal blistering, sun sensitivity, atrophy, abnormal pigmentation, and fragility of the skin. Linkage and homozygosity analysis in an isolated Panamanian cohort and in additional inbred families mapped the gene to 20p12.3. Loss-of-function mutations were identified in the FLJ20116 gene (renamed "KIND1" [encoding kindlin-1]). Kindlin-1 is a human homolog of the Caenorhabditis elegans protein UNC-112, a membrane-associated structural/signaling protein that has been implicated in linking the actin cytoskeleton to the extracellular matrix (ECM). Thus, Kindler syndrome is, to our knowledge, the first skin fragility disorder caused by a defect in actin-ECM linkage, rather than keratin-ECM linkage.

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7. Tyrosinase, TRPs, other enzymes

(Prof. J.C. Garcia-Borron)

The number of papers dealing with natural or synthetic tyrosinase inhibitors is increasing steadily. This certainly reflects the interest of the cosmetic industry for safe and effective depigmenting agents. It remains to be seen how many of the compounds found to inhibit tyrosinase in different types of *in vitro* assays are actually effective *in vivo* and are able to make their way to the cosmetic market. It will also be interesting to see if these studies identify new tools for the study of tyrosinase active site and reaction mechanisms.

Relevant information on the processing of tyrosinase and its related proteins continues to flow at a high pace. One of the manuscripts referenced in this issue describes new data demonstrating that Tyrp-2 has a distinct maturation pathway from tyrosinase and Tyrp-1 (Negroiu G, Dwek RA, Petrescu SM., J Biol Chem. 2003 Jul 18;278(29):27035-42). Information on the maturation of Tyrp-2 is particularly welcome, since data on this enzyme were scarce. In another paper (Francis E, Wang N, Parag H, Halaban R, Hebert DN. J Biol Chem. 2003 Jul 11;278(28):25607-17), an elegant approach based in the use of semipermeabilized melanocytic and nonmelanocytic cells is used to propose the occurrence of melanocyte-specific factors assisting tyrosinase maturation. Interestingly, this paper provides evidence for an oligomerization step that might take place early during the processing of the enzyme. Another paper deals with tyrosinase processing in a mouse model for oculocutaneous albinism (OCA) type 4, a newly identified human autosomal recessive hypopigmentary disorder that disrupts pigmentation in the skin, hair and eyes (Costin GE, Valencia JC, Vieira WD, Lamoreux ML, Hearing VJ., J Cell Sci. 2003 Aug 1;116(Pt 15):3203-12). This condition appears associated to defects of tyrosinase traffic, as was previously shown for other forms of albinism.

A most interesting study describes a developmentally regulated role of tyrosinase as a major source of peripheral dopamine (Eisenhofer G, Tian H, Holmes C, Matsunaga J, Roffler-Tarlov S, Hearing VJ. FASEB J. 2003 Jul;17(10):1248-55). According to this study, tyrosinase provides a tyrosine-hydroxylase independent major pathway of peripheral dopamine synthesis in young, but not adult, mice. It will be fascinating to see whether this new role of tyrosinase is somehow related to any of the various non-pigmentary defects in tyrosinase-negative albino animals.

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8. Melanosomes

(Dr. J. Borovansky)

In recent period the research effort has focused as usually to melanosome transport (*Andersson et al., Bahadoran et al., Menasche et al.)* and to melanosome biogenesis *(Berson et al., Chiang et al.)* Four reviews have appeared describing melanosome disintegration/degradation *(Borovanský&Elleder)*, melanosome concept, biogenesis and its regulation and melanosome proteomics *(Kushimoto et al.)*, diseases of pigmentation *(Spritz et al)* and a general melanocyte biology (including melanosomes) *(Sulaimon&Kitchell).* Tyrosine hydroxylase was detected in melanosomes *(Marles et al.).* A relationship between melanocortin-1 receptor genotype and melanosome maturation was shown *(Leonard et al).* Another report demonstrating the presence of melanosomes in a schwannoma has appeared *(Goasguen et al).* Selective destruction of pigmented porcine RPE by an argon laser beam was achieved *(Brinkmann et al.).* Increased loss of melanosomes by autophagocytosis was a typical feature of liver melanomacrophages in *Rana esculenta* in the posthibernation period *(Barni et al.).*

- Andersson TPM, Svensson SPS, Karlsson AM.
  Regulation of melanosome movement by MAP kinase. Pigment Cell Res 16(3): 215-221, 2003.
  Comments: MAPK (mitogen-activated protein kinase) was activated during melatonin induced melanosome aggregation in *Xenopus* melanophores. Activation was decreased by an inhibitor of MAPK – PD98059 and by forskolin. The authors suppose that in addition to cAMP/PKA signalling pathway the MAPK cascade might be engaged in organelle transport also in other eukaryotic cells.

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  Characterization of the molecular defects in Rab27a, caused by RAB27A missense mutations found in patients with Griscelli syndrome. J Biol Chem 278(13): 11386 – 11389, 2003.
  Comments: The effect of overexpression of three single homozygote missense mutations in RAB27A, found in patients with Griscelli syndrome leading to W73G, L130P, and A152P transitions, on melanosome, melanophilin and myosin Va localization and interaction in B16 melanoma cells was evaluated and function of Rab27a was studied. Different changes in interactions for each mutated Rab27a studied were found, all impairing the melanosome transport.

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  Mechanisms of changes to the liver pigmentary component during the annual cycle (activity and hibernation) of *Rana esculenta* L. J Anat 200: 185-194, 2002.
  Comments: Liver melanomacrophages (Kupffer cells) represent cell population engaged in melanin synthesis and degradation with changes in metabolic activity during the annual cycle of the frog. Many melanosomes and dopa-oxidase activity are observed in the prehibernation period unlike the posthibernation period when melanosome loss by autophagocytosis is a prevailing phenomenon. No attempt to explain the melanosome demolition in molecular terms has been done.

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  Proprotein convertase cleavage liberates a fibrillogenic fragment of a resident glycoprotein to initiate melanosome biogenesis. J Cell Biol 161(3): 521-533, 2003.
  Comments: Formation of intralumenal fibrils requires cleavage of PMel17 by a furin-like proprotein convertase to initiate melanosome biogenesis; longer PMel17 fragments are unable to form organized fibrils. In an accompanying editorial *Kelly & Balch (J Cell Biol 161(3):461-462,2003)* suggest that fibril formation (similarly to amyloid fibril formation) is an evolutionary conserved pathway used to generate natural product nanostructures.

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  Melanosome degradation: Fact or fiction. Pigment Cell Res 16(3): 280-287, 2003.
  Comments: A minireview summarizing for the first time what has been known about melanosome disintegration and melanin degradation. Histochemical and biochemical studies suggest the participation of acid hydrolases in the process melanosome degradation except the melanin moiety which seems to be sensitive to oxidative breakdown which can be often induced by photochemical processes.

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  Targeting of the retinal pigment epithelium (RPE) by means of a rapidly scanned continuous wave laser beam. Lasers in Surgery and Med 32(4): 252-264, 2003.
  Comments: Melanosomes act as an energy-converting device, e.g.they can convert light energy into heat. This ability was exploited to damage selectively the porcine RPE *in vitro* by an argon laser beam (514nm).

- Chiang PW, Oiso N, Gautam R, Suzuki T, Swank RT, Spritz RA.

The Hermansky-Pudlak syndrome 1 (HPS1) and HPS4 proteins are components of two complexes, BLOC-3 and BLOC-4, involved in the biogenesis of lysosome-related organelles. J Biol Chem 278(22): 20332-20337, 2003.
Comments: HPS1 and HPS4 proteins are shown to be components of a novel protein complex associated with vesicles and organelles, termed BLOC-3 (biogenesis of lysosome-related organelles complex 3), from which a smaller HPS1-HPS4 complex can be split off as discrete module – BLOC4. Their role in trafficking cargo proteins to newly formed cytoplasmic organelles is anticipated but details remain to be determined.

- Goasguen O, Boucher E, Pouit B, Soulard R, Le Charpentier M, Pernot P.
Melanotic schwannoma, a tumour with a unpredictable prognosis: case report and review of the literature. [*In French*] Neurochirurgie 49(1): 31-38, 2003.
Comments: A case report of melanotic schwannoma with a literature review on the topic. Pigmented schwannomas typically contain HMB45-positive pigment cells with melanosomes in various maturation steps.

- Kushimoto T, Valencia JC, Costin GE, Toyofuku K, Watabe H, Yasumoto K, Rouzaud F, Vieira WD, Hearing VJ.
The melanosome: An ideal model to study cellular differentiation. Pigment Cell Res 16(3): 237-244, 2003.
Comments: A review based on the Seiji Memorial Lecture presented by V.J. Hearing at the XVIIIth IPCC. Main areas: Evolution of the melanosome concept. Impact of molecular biology and genetics on the melanosome. Physiological regulation of melanosome biogenesis. Melanosomes as a model for organelle biogenesis. Disruption of tyrosinase trafficking in OCA. Proteomics of the melanosome.

- Leonard JH, Marks LH, Chen W, Cook AL, Boyle GM, Smit DJ, Brown DL, Stow JL, Parsons PG, Sturm RA.
Screening of human primary melanocytes of defined melanocortin-1 receptor genotype: Pigmentation marker, ultrastructural and UV-survival studies. Pigment Cell Res 16(3): 198-207.
Comments: The title perfectly reflects the article content. As for melanosomes, the ultrastructural analysis demonstrated that while consensus strains contained stage IV melanosomes in their terminal dendrites, Arg151Cys and Arg160Trp homozygote strains contained only stage II melanosomes.

- Marles LK, Peters EM, Tobin DJ, Hibberts NA, Schallreuter KU.
Tyrosine hydroxylase isoenzyme I is present in human melanosomes: A possible novel function in pigmentation. Exptl Dermatology 12(1): 61-70, 2003.
Comments: The presence of tyrosine hydroxylase isoenzyme I was demonstrated in melanosomes (and cytosol) of human epidermal melanocytes. The melanosome membrane location of both tyrosine hydroxylase and tyrosinase implies a coupled interaction, where L-DOPA production facilitates the activation of tyrosinase.

- Menasche G, Feldmann J, Houdusse A, Desaymard C, Fischer A, Goud B, de Saint Basile G.
Biochemical and functional characterization of Rab27a mutations occurring in Griscelli syndrome patients. Blood 101(7): 2736-2742, 2003.
Comments: Mutations in RAB27A are responsible for Griscelli syndrome 1 (*see also Spritz et al - below).* Residues critical for the structure and function of Rab proteins have been searched for. Introduction of a proline residue to position 52 or 130 dramatically affected GTP and GDP binding activity of Rab27a probably by disrupting protein folding. Trp73Gly mutant construct neither interacted with the Rab27a effector - melanophilin nor modified melanosome distribution.

- Spritz RA, Chiang PW, Oiso N, Alkhateeb A.
Human and mouse disorders of pigmentation. Curr Opin Genet Dev 13(3): 284-289, 2003.
Comments: A review divided into three basic sections: 1) Diseases of melanocyte development; 2) Diseases of melanocyte function (focused to diseases of melanosome biogenesis, maturation and function); 3) Diaseases of melanocyte survival. The review emphasizes remarkable progress in understanding human and mouse pigmention disorders.
As well as the fundamental biology that underlies these diseases.

- Sulaimon SS, Kitchell BE.
The biology of melanocytes. Veterinary Dermatol 14(2): 57-65, 2003.
Comments: A wide general review.

9. Melanoma experimental, Cell culture

(Dr. N. Smit)

Melanocytes and other culture systems

Interesting special issues appeared of the Ann NY Acad Sci (issue 994) and Oncogene (issue 203) which both contain several review papers about regulation of pigmentation (see e.g Ancans et al) and melanoma. Bennett DC gives a nice review in Oncogene about the possible importance of senescence in melanocytes and progression to melanoma. In the more detailed paper by Sviderskaya, Bennett et al in JNCI melanocyte cultures are described of two melanoma patients who both had two inactive p16 alleles and functional ARF. These cultures showed impaired senescence and could both be immortalized by telomerase reverse transcriptase which was not the case for melanocytes with normal p16.
Pigment Cell Res. issue 230 (3) contains 12 contributions of (special and invited) lectures from the different sessions of the 18th IPCC meeting in Holland last year.
In the study by Dooley et al melanocyte cultures were used for comparison with non-melanocytic cells (fibroblasts and keratinocytes) and two melanoma cultures. The melanocytic cells were maintained in Clonetics melanocyte media. DNA microarrays gave "distal"and "proximal" melanocyte biomarkers for the comparisons with the non melanocytic cells and the melanoma cells, respectively. These experiments may be a first step towards the discovery of important differences between normal melanocytes and other cell types, especially when varying conditions of culture media with relevant growth factors or other stimuli (UV irradiation) are investigated.
Sturm et al have prepared more than 300 melanocyte cultures with known MC1R genotype. In one of the original research articles in the PCR issue 230 (3) by Leonard et al some of these cultures and their pigmentation characteristics are described. All cells with wild type concensus showed dark pigmentation under the used culture conditions (RPMI1640/FCS + TPA and cholera toxin). Cultures grouped of the variant genotypes, homozygous Arg151Cys -/- and Arg160Trp-/- showed much less pigmented cell pellets. Influences of MSH on such cultures may have to be studied in different culture media since melanocytes have been described to be unresponsive to MSH in TPA, cholera toxin containing media. Kadekaroo et al already present some results of MSH influences on their MC1R genotyped cultures.
Yoon and Hearing report about the co-culture of murine melanocytes and keratinocytes. In another paper they also describe the MelanoDerm skin equivalent model commercially available from MatTek. In this model melanocytes of different skin types are shown to respond to MSH in the L-NMM medium supplied by the manufacturer by increasing melanin content and tyrosinase activity in the skin equivalent. Ponec et al (Int J Pharmaceuticals 2000, 203: 211-225) have described the different commercially available reconstructed skin models. Despite the fact that still clear differences were observed in comparison with native skin these models are considered to provide a promising means for studying the effects of various agents. Thus, despite the differences with native skin the MelanoDerm model system also seems useful for studying regulation of pigmentation in an air-exposed skin equivalent model.

- Ancans J, Flanagan N, Hoogduijn MJ, Thody AJ.
  P-locus is a target for the melanogenic effects of MC-1R signaling: a possible control point for facultative pigmentation. Ann.N.Y.Acad.Sci. 994:373-7.:373-377, 2003.

- Bennett DC.
  Human melanocyte senescence and melanoma susceptibility genes. Oncogene 22:3063-3069, 2003.

- Conner SR, Scott G, Aplin AE.
  Adhesion-dependent activation of the ERK1/2 cascade is by-passed in melanoma cells. J.Biol.Chem. 2003, **.**. Basal ERK1/2 activity was low and growth-factor activation was adhesion-dependent in normal human melanocytes. By contrast in mutant B-Raf expressing melanoma cells (SK-MEL-24 and SK-MEL-28), the ERK1/2 pathway was constitutively active and adhesion-dependent regulation of ERK1/2 activity was by-passed. Expression of mutant V599E B-Raf in normal melanocytes was sufficient to promote adhesion-independent ERK1/2 signaling. These results indicate that alterations in the adhesion requirement for ERK1/2 signaling in melanocytes are associated with the acquisition of malignant cell behavior

- Dooley TP, Curto EV, Davis RL, Grammatico P, Robinson ES, Wilborn TW.
  DNA microarrays and likelihood ratio bioinformatic methods: discovery of human melanocyte biomarkers. Pigment Cell Res. 16:245-253, 2003.

- Dupin E, Real C, Glavieux-Pardanaud C, Vaigot P, Le Douarin NM.
  Reversal of developmental restrictions in neural crest lineages: transition from Schwann cells to glial-melanocytic precursors in vitro. Proc.Natl.Acad.Sci.U.S.A 100:5229-5233, 2003.

- Girnita L, Girnita A, Larsson O.
  Mdm2-dependent ubiquitination and degradation of the insulin-like growth factor 1 receptor. Proc.Natl.Acad.Sci.U.S.A 100:8247-8252, 2003.

- He L, Eldridge AG, Jackson PK, Gunn TM, Barsh GS.
Accessory proteins for melanocortin signaling: attractin and mahogunin. Ann.N.Y.Acad.Sci. 994:288-98, 2003.

- Inoue K, Hosoi J, Ideta R, Ohta N, Ifuku O, Tsuchiya T.
Stress Augmented Ultraviolet-Irradiation-Induced Pigmentation. J.Invest Dermatol. 121:165-171, 2003.

- Jule S, Bosse P, Egidy G, Panthier JJ.
Establishment and characterization of a normal melanocyte cell line derived from pig skin. Pigment Cell Res. 16:407-410, 2003.

- Kadekaro AL, Kanto H, Kavanagh R, Abdel-Malek ZA.
Significance of the melanocortin 1 receptor in regulating human melanocyte pigmentation, proliferation, and survival. Ann.N.Y.Acad.Sci. 994:359-65.:359-365, 2003.
We characterized the MC1R genotype in a panel of human melanocyte cultures and identified three cultures that were homozygous for Arg160Trp, heterozygous for Arg151Cys and Asp294His, and heterozygous for Arg160Trp and Asp294His substitutions, respectively. Those cultures failed to respond to alpha-MSH with increase in cAMP levels, tyrosinase activity, or proliferation and had an exaggerated response to the cytotoxic effect of ultraviolet (UV) radiation.

- Kauser S, Schallreuter KU, Thody AJ, Gummer C, Tobin DJ
Regulation of human epidermal melanocyte biology by beta-endorphin. J.Invest Dermatol. 120:1073-1080, 2003.

- Kim DS, Hwang ES, Lee JE, Kim SY, Park KC
Sphingosine-1-phosphate promotes mouse melanocyte survival via ERK and Akt activation. Cell Signal. 15:919-926, 2003.

- Kuroda TS, Ariga H, Fukuda M
The Actin-Binding Domain of Slac2-a/Melanophilin Is Required for Melanosome Distribution in Melanocytes. Mol.Cell Biol. 23:5245-5255, 2003.

- Leonard JH, Marks LH, Chen W, Cook AL, Boyle GM, Smit DJ, Brown DL, Stow JL, Parsons PG, Sturm RA
Screening of human primary melanocytes of defined melanocortin-1 receptor genotype: pigmentation marker, ultrastructural and UV-survival studies. Pigment Cell Res. 16:198-207, 2003.

- Li HY, Li WX, Sun LG.
Influence of prostaglandin E2 on proliferation of melanocytes in full-thickness skin graft]. Zhonghua Zheng.Xing.Wai Ke.Za Zhi. 19:54-56, 2003.

- Meier F, Caroli U, Satyamoorthy K, Schittek B, Bauer J, Berking C, Moller H, Maczey E, Rassner G, Herlyn M, Garbe C.
Fibroblast growth factor-2 but not Mel-CAM and/or beta3 integrin promotes progression of melanocytes to melanoma. Exp.Dermatol12:296-306, 2003.

- Norgauer J, Dichmann S, Peters F, Mockenhaupt M, Schraufst t, I, Herouy Y.
Tumor necrosis factor alpha induces upregulation of CXC-chemokine receptor type II expression and magnifies the proliferative activity of CXC-chemokines in human melanocytes. Eur.J.Dermatol. 13:124-129, 2003.

- Runger TM, Kotas M, Poot M, Leverkus M, Epe B, Jeggo PA, Hellfritsch D.
Reduced joining of DNA ends correlates with chromosomal instability in three melanoma cell lines. Tumour.Biol. 24:100-108, 2003.

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Antiapoptotic action of 1alpha,25-dihydroxyvitamin D3 in primary human melanocytes. Melanoma Res. 13:339-347, 2003.

- Sturm RA, Duffy DL, Box NF, Newton RA, Shepherd AG, Chen W, Marks LH, Leonard JH, Martin NG.
Genetic association and cellular function of MC1R variant alleles in human pigmentation. Ann.N.Y.Acad.Sci. 994:348-58.:348-358, 2003.

- Sviderskaya EV, Gray-Schopfer VC, Hill SP, Smit NP, Evans-Whipp TJ, Bond J, Hill L, Bataille V, Peters G, Kipling D, Wynford-Thomas D, Bennett DC.
p16/cyclin-dependent kinase inhibitor 2A deficiency in human melanocyte senescence, apoptosis, and immortalization: possible implications for melanoma progression. J.Natl.Cancer Inst. 95**:**723-732, 2003.

- Tadokoro T, Rouzaud F, Itami S, Hearing VJ, Yoshikawa K.
  The inhibitory effect of androgen and sex-hormone-binding globulin on the intracellular cAMP level and tyrosinase activity of normal human melanocytes. Pigment Cell Res. 16:190-197, 2003.

- Yoon TJ, Hearing VJ.
  Co-culture of mouse epidermal cells for studies of pigmentation. Pigment Cell Res16:159-163, 2003.
  We have now optimized co-culture conditions for murine melanocytes and keratinocytes so that pigmentation and the effects of specific mutations can be studied in a more physiologically relevant context

- Yoon TJ, Lei TC, Yamaguchi Y, Batzer J, Wolber R, Hearing VJ.
  Reconstituted 3-dimensional human skin of various ethnic origins as an in vitro model for studies of pigmentation. Anal.Biochem. 318:260-269, 2003.

Melanotoxicity

Farmer et al have used melanosomal melanin in melanoma cells for chemical targeting. Metal and oxygen induced stress were more toxic for melanoma cells than for melanocytes. The authors hypothesize that disorganization of the melanosomes in the melanoma cells makes them more sensitive to the treatments.
Pearson et al have tested some more lipophilic analogues of N-Acetyl-4-S-cysteaminylphenol, a well known tyrosinase dependent antimelanoma compound. High toxicity was found for some of the compounds comparable to cisplatin and their activity does not seem to be completely tyrosinase dependent. Quinone formation of these agents can result in the reaction with glutathione and may lead to cytotoxicity and depigmentation as is the case for hydroquinone and 4-hydroxyanisole (Kasraee et al). Tretinoin may enhance the depigmenting effects of these agents by further interference with glutathione meabolism and inhibition of glutathione S-transferase.
Next to the possibility of using tyrosinase to induce toxicity via quinone products the inhibition of tyrosinase may also result in increased toxicity of certain chemicals like the tetrahydroisoquinolines used in the study by Perluigi et al, probably resulting from insufficient removal of ROS by tyrosinase and other antioxidant enzymes.
Solano et al describe other mechanisms of detoxification in neurons and melanocytes that may be of interest. Indeed the action of TRP-2, D-dopachrome tautomerase, macrophage migration inhibitory factor and DT-diaphorase may be important enzymes preventing quinone damage.

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  Melanin as a Target for Melanoma Chemotherapy: Pro-oxidant Effect of Oxygen and Metals on Melanoma Viability. Pigment Cell Res. 16**:**273-279, 2003.

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  Enhancement of the Depigmenting Effect of Hydroquinone and 4-Hydroxyanisole by All-TRANS-Retinoic Acid (Tretinoin): The Impairment of Glutathione-Dependent Cytoprotection? Dermatology 206:289-291, 2003.

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  Synthesis and antimelanoma activity of tertiary amide analogues of N-acetyl-4-S-cysteaminylphenol. Oncol.Res. 13:503-512, 2003.

- Perluigi M, De Marco F, Foppoli C, Coccia R, Blarzino C, Marcante ML, Cini C.
  Tyrosinase protects human melanocytes from ROS-generating compounds. Biochem.Biophys.Res.Commun. 305**:**250-256, 2003.

- Solano F, Hearing VJ, Garcia-Borron JC.
  Neurotoxicity due to o-quinones: neuromelanin formation and possible mechanisms for o-quinone detoxification. Neurotox.Res. 1:153-169, 2000.

ANNOUNCEMENTS & RELATED ACTIVITIES

Calendar of events

2003 XIth Annual Meeting of the PASPCR

Wood's Hole, Cape Cod, MA, USA MA, September 3-7

Contact: Dr. Jean BOLOGNIA
Tel : +1 513 558 0198
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Web site: www.cbc.umn.edu/ifpcs

2003 10th Congress of the European Society of Photobiology (ESP)

Vienna, Austria, September 6 - 11

Tel : +43 67 16 2500
Fax : +43 22 46 1304
E-mail : office@esp2003.org
Web site : www.esp2003.org

2003 XIth Meeting of the ESPCR

Gent, Belgium, 17-20 September

Contact: MEDISCON
P.O. Box 113
5660 AC Geldrop
The Netherlands
Tel: +31 (0)40-2852212
Fax: +31 (0)40-2851966
E-mail: mediscon@iae.nl
Web site: www.espcrgent2003.org

2003 24th Symposium of the International Society of Dermatopathology

Istanbul, Turkey, 17-21 September

Tel : +90 312 324 5724
Fax : +90 312 310 5800
E-mail : rana@isdp2003.org
Web site : www.ilds.org

2003 Australasian College of Dermatologists and the Japanese Dermatological Association Combined Conference

Ayers Rock, Australia, 18-21 September

Tel : +61 2 9879 6177
Fax : +61 2 9816 1174
E-mail : admin@dermcoll.asn.au
Web site : www.dermcoll.asn.au

2003 14th European Study Group of Lysosomal Diseases - (ESGLD) Workshop

Podebrady, Czech Republic, September 18-21

PLANNED TOPICS OF THE WORKSHOP

Contact: Ms. Barbora VINSOVA
GUARANT Ltd.,
Opletalova 22,
CZ - 110 00 Praha 1
Tel: +420 2 8400 1444 Fax: +420 2 8400 1448
E-mail: esgld@guarant.cz
Web : http://www.ESGLD2003.CZ/

2003 12th Congress of the European Academy of Dermatology and Venereology (EADV)

Barcelona, Spain, October 15-18

Tel : +34 93 200 7083
Fax : +34 93 209 3152
E-mail : congresos@atlantaviajes.es
Web site : www.eadv.org

2003 3rd european Symposium on Teledermatology, Chirurgie Dermatologique

Las Vegas, USA, September 18-21

Tel : +1 312 998 7700
Fax : +1 312 988 7759
E-mail : sdef@idt.net
Web site : www.sdefderm.com

2004 14th International Congress on Photobiology

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

2004 XIIth Annual Meeting of the PanAmerican Society for Pigment Cell Research

June, Orange County, California, USA

Organizers:Dr. Frank MEYSKENS (UC-Irvine) and Dr. Rogers BOWERS (Cal State-LA)
Contact: Dr Frank MEYSKENS
E-mail: flmeyske@uci.edu

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

NEW MEMBERS

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

DA SILVA N.
MRC Human Gen Unit
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GALLONE A.
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YAZDI A.
Ludwig Maximilians Uni
Dermatology
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D - 80337 MÜNCHEN

To: All ESPCR Members
Election of ESPCR Officers, 2003-2006

Dear Colleagues,

As you know, an election of ESPCR Officers for the 2003-2006 term took place recently. The elected Treasurer, Dr. Patrick Verrando, expressed his wish to resign to the Office, and it was necessary to proceed to a new election. Following the call for nominations, issued on February 20 with a deadline on April 28, only one candidate has been nominated. There was therefore no need to proceed to a formal election.

It is a great pleasure to announce that the new ESPCR Treasurer will be Dr. Jo Lambert (Belgium). No doubt, her high talent and outstanding dedication to the Society will allow her to fulfil this post effectively.

Therefore the new Officers, whose term will begin in September 2003, are:

President: Prof. José-Carlos García-Borrón (Spain)

Secretary: Prof. Jean-Marie Naeyaert (Belgium)

Treasurer: Dr. Jo Lambert (Belgium)

We look forward to seeing you all at the Ghent ESPCR Meeting.

Prof. José-Carlos García-Borrón
Secretary

Join ESPCR in October – 3 months' free membership!

Did you know that if you are a new member joining ESPCR between October and December, after our annual meeting, your subscription will cover membership until December 2003, instead of December 2002? So, to all members, if you have colleagues who would benefit from joining ESPCR (surely you do?), please encourage them to join soon, and get the most out of their subscription. They can read about the benefits and find an application form at:

Http://www.ulb.ac.be/medecine/loce/espcr/gen_inf.htm

Alternatively, please contact our Treasurer for information and application forms:

Dr. Lionel Larue (Treasurer, ESPCR), Institut Curie – Section Recherche,
UMR146 CNRS, Bât 110, Centre Universitaire, 91405 Orsay, France
E-mail: Lionel.Larue@curie.u-psud.fr

New Treasurer, from late September,
Dr Jo Lambert (Treasurer, ESPCR), Dept. of Dermatology
University Hospital, De Pintelaan 185, B - 9000 GENT, Belgium
E-mail: jo.lambert@rug.ac.be

Announcement from Dr Lynn Lamoreux, Wellcome Trust Mouse Pigmentary Mutants Facility, Texas

Following our cryopreservation program, and our current policy not to breed mice that are available elsewhere, in about two weeks I will discontinue the following stocks. All these stocks are congenic or co-isogenic with C57BL/6J. Stocks marked (*) will be available through MMRRC (see next paragraph). Others will not be saved unless users require them. We have additional stocks and will announce their demise when the time comes. **Please contact me immediately if you would like to acquire any of the stocks listed here, and therefore wish me not to discontinue them.**
Lynn Lamoreux <mllamoreux@hotmail.com>

The **Mutant Mouse Regional Resource Centers** (MMRRC) Web site is found at **WWW.MMRRC.org** . The MMRRC program is sponsored by the National Center for Research Resources (NCRR) at the National Institutes of Health (NIH). The purpose of the program is to ensure the continued availability of scientifically valuable, genetically engineered mice and to distribute these mice to qualified researchers studying human and animal biology and disease.
JAX: The Jackson Laboratory, Bar Harbor, Maine, USA.

*$Mitf^{Mi\text{-}B}$	Brownish
*$Mitf^{mi\text{-}ce}$	Cloudy Eye
*$Mitf^{mi\text{-}bw}$	Black eyed white
*$Mitf^{mi\text{-}di}$	Defective Iris
$Mitf^{mi\text{-}wh}$	White – Available at JAX
$Mitf^{mi\text{-}rw}$	Red eyed white, available at JAX
*$Mitf^{Mi\text{-}OR}$	Oak Ridge
$Mitf^{mi\text{-}vit}$	Vitiligo, available at JAX
*YS	George Wolff's classic stock
*$Ednrb^{s}$	piebald
*$Mc1r^{E\text{-}so}$	Sombre
A^{y}/a	lethal yellow, available at JAX
A^{y}/a in strain JU/CtLL	
$Tyr^{c\text{-}2J}$	Albino, available at JAX
$Tyr^{c\text{-}h}$	Himalayan, available at JAX
Dct^{slt}	slaty, available at JAX
*$Dct^{slt\text{-}lt}$	slaty light
$Rab38^{cht}$	chocolate, available at JAX
$Tyrp1^{b}$	brown, available at JAX
$Tyrp1^{cJ}$	cordovan, available at JAX
cordovan with slaty	
albino and cordovan	
albino and slaty	
albino and brown	
albino and black	
$Tyr^{c\text{-}p}$	platinum, available at JAX
platinum and brown	
platinum and cordovan	
$Tyr^{c\text{-}ch}$	chinchilla
chinchilla and brown	