N° 58 Aug 2007

ESPCR BULLETIN

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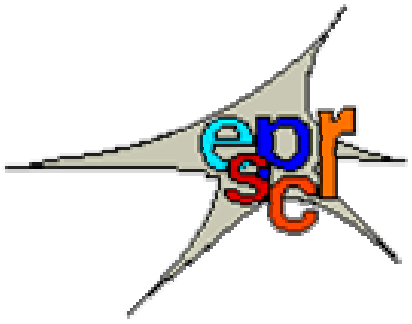

EUROPEAN SOCIETY FOR PIGMENT CELL RESEARCH *BULLETIN*

N° 58 - Aug 2007

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CONTENTS

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

MINUTES OF THE FIRST ESPCR COUNCIL MEETING

Sunday, September 24, 2006, 09:30

ESPCR meeting
Hotel ABBA Garden, Room Cervantes, Barcelona, SPAIN

1. Opening of the Meeting.

The meeting was opened by J-C. García-Borrón, who welcomed the following Council members: F. Beermann, D. Bennett, G. Ghanem, C. Goding, J. Lambert, L. Larue, M. Picardo, A. Taieb and N. Smit.

2. Apologies.

Apologies for absence were received from J. M. Naeyaert. The Council accepted them.

3. Minutes of the 2005 Council Meetings in Reston.

The Minutes of the Council and General assembly Meetings in Reston were approved without amendments and signed by the President.

4. Secretary's Report and matters arising.

Lionel Larue is acting as Secretary after the decision taken unanimously by the Council in Reston in 2005. The ESPCR secretary book is in the hand of the acting Secretary.

a) Meeting reports

- 2005 IPCC Meeting report: No ESPCR report is asked for IPCC meetings.
- 2006 ESPCR Meeting report: The chairmen and chairwomen were asked to provide a report of their session for the bulletin.

b) Raper Medal.

The new mould and two medals were given to the new ESPCR President. Nominations for the Raper medal will be sought in the beginning of 2008 for the IPCC meeting, which will be held in Sapporo in 2008.

c) Officer elections

Elections of new officers were conducted during the last trimester of 2005. After a call for nomination only one candidate has been nominated for each of the three ESPCR Offices. In consequence, no election was necessary. The new President is Mauro PICARDO, the new Secretary is Lionel LARUE and the new Treasurer is Jo LAMBERT. Their terms of office began at the end of this meeting and will end during the 2009 ESPCR meeting.

d) Council elections

Before the election, the situation of the Council members was as followed; F. Beermann, D. Bennett and M. Picardo are finishing their mission on Council. They could not be re-elected as Council members until 2010, but could be elected as Officer. The terms of J. Lambert, J. M.

Naeyaert, A. Taieb and N. Smit also expired in September 2006, but they could be re-elected in the council or as officer. J-C. García-Borrón (President), G. Ghanem (Web Master and Bulletin Editor), C. Goding (elected on 2005) and L. Larue (elected on 2004) remain on the board.

Five positions were available. Seven members were nominees. Elections were required. 58 members voted. The results are Lluis Montoliu (48 votes), Alessandra Napolitano (41 votes), Anja Bosserhoff (39 votes), Alain Taieb (37 votes), Miguel Seabra (35 votes), Corinne Bertolotto (33 votes), Nico Smit (28 votes). The new Council members are Lluis, Alessandra, Anja, Alain and Miguel.

After the Barcelona meeting the ESPCR Council members are

Anja Bosserhoff,
Jose Carlos Garcia-Borron as ex officio
Colin Goding
Ghanem Ghanem as non-voting permanent (Web site)
Jo Lambert as Treasurer
Lionel Larue as Secretary
Lluis Montoliu,
Alessandra Napolitano
Mauro Picardo as President
Miguel Seabra
Alain Taieb

The Council approved the report, and the President thanked Lionel Larue for his work.

5. Treasurer's Report.

- Statistics

The number of members in the ESPCR Web site list is 202. However, the actual number of members in good standing is 122 (8 honorary members, 92 regular members, 22 student members). We have 38 new members (12 students and 26 regulars).

This means that we slightly increase the number of members (122 for 121) and that the expected loss of members from the novel ASPCR society did not affect for the time being our Society.

- Finances

The finances are good over the year. For the 2006 year, we have a positive balance of 342,10 euros. On the account, we have a general positive balance of 12 690,67 euros.

The Treasurer, Jo Lambert, delivered the following report of incomes and outgoings (in Euros) during this 2006 year.

Number of members on 9/2006	122
Members who paid subscription up to 9/2006:	122
Regular members	92
Student members	22
Honorary members	8
View on new members in 2006:	38
Regular members	26

Student members	12

Income 10/2005-09/2006	
Member subscriptions 2006	6 250
Pigment Cell Research subscriptions	3 700
Donations by members	100
Total income	**10 050 euros**

Outgoings 10/2005-9/2006	
International Federation of Pigment Cell Societies	
Member dues for 2005 :	
92 x 28 USD = 2576 USD (1 USD = 0.78 EURO)	2 009
Bulletin and web costs	210
(Prof. Ghanem – equiv. 4 memberships)	
Bank charges Centea	248,09
ESPCR Travel Awards at Barcelona meeting	1 500
Fritz Anders Lecture Barcelona	1 500
Pigment Cell Research Subscriptions :	
37 x 128 USD = 4736 USD (1 USD = 0.78 EURO)	3 723,99
Credit card machine (running budget)	516,82
Total outgoings	**9 707,90 euros**

Balance on 15/09/06	**+ 342,10 euros**

This is an approximate amount, pending minor adjustments due to bank charges and exchange rates.

PS : The account balance on 19/09/06 is **12 690,67 euros**

Member statistics

	1998	1999	2000	2001	2002	2003	2004	2005	2006
Members				**106**	**113**	**121**	**99**	**121**	**122**
Regular				97	99	106	89	91	92
Student				9	9	15	10	22	22
Honorary				6	6	8	8	8	8
New members	**16**	**18**	**18**	**18**	**19**	**15**	**20**	**36**	**38**
Regular				14	13	10	16	22	26
Student				4	6	5	4	14	12
Resignations					6	4	13		
Out people					12	7	12		

- Bank account

ESPCR bank account remains in Belgium (Centea bank, account number 850-8169817-87).
The issue of the location of the bank account was discussed. The account was following the Treasurer, and travels from one European country to another every three years. This simplifies

the work of the Treasurer but causes expenses and is somewhat time consuming. Moreover, changing bank account and country means that a new VAT number should be obtained every three years, as the VAT number is associated with a country. The VAT issue is still not sorted out. (See point #11 Legal status of ESPCR).

- Increase our incomes
The President raised several issues on the financial aspects of ESPCR. Our society is a poor society and it has to fulfil his mission: promote research on pigment cells, attract young investigators, support meeting. In consequence three decisions were taken: stop sponsoring meetings, increase fees and attract members.

- *Support of ESPCR for ESPCR meeting*
A clear support of ESPCR is given to ESPCR meeting. However, the finance of ESPCR does not allow supporting financially ESPCR meetings. No financial support was given to the 2006 ESPCR meeting.

- *Fees for 2007*
As mentioned in 2006, a moderate increase was proposed to the Council meeting after six years of stability. The council approved an increased of 10 euros for regular members (60 to 70 euros) and 5 euros for students (30 to 35 euros). This increase will have to be approved by the General assembly.

- *Attract new members* during and after 2006 ESPCR meeting.
During the meeting: official announcement and make available printed forms for 2007.
After the meeting, action should be envisaged. One is by using the bulletin. Each contributor should high light one article in order that the authors of this article will be contacted by email if they are European and non-ESPCR members. These potential members will be contacted with an email sent by the ESPCR President to present the Society and to propose him to join.

The Council approved the report, and the President thanked Jo Lambert for her work.

6. ESPCR Bulletin and Web site report.

The ESPCR Web Master G. Ghanem delivered this.
- Web site: G. Ghanem reported that the Web site has been regularly updated and improved.
- ESPCR list: Everything is going smoothly
- Bulletin: Everything is going smoothly
The Council approved the report, and the President thanked G. Ghanem for his outstanding work.

7. Travel award committee report and related matters

F. Beermann informed on the activity of the Travel Awards Committee.
- ESPCR travel award. Sixteen applications were sent to the Committee but unfortunately two were sent after the deadline. From the fourteen applications, four were selected on their scientific merits. Two were PhD students and two were Post-doc fellows.
- Visiting scientist award. No grant was available from IFPCS.

Travel awards will be advertised in the Bulletin.

F. Beermann, L. Larue and N. Smit now compose the travel award committee. The chair of the committee is F. Beermann.
The status of the travel award committee will be proposed to the council meeting in 2007.

The Council approved the report, and the President thanked the member of the travel award committee.

8. Matters concerning the IFPCS

IFPCS officers were elected in 2005 at Reston. The Secretary-Treasurer of IFPCS is Jose-Carlos Garcia-Borron (ESPCR). Two other ESPCR members have to stand as IFPCS councillors. Jo Lambert and Mauro Picardo were designated as ESPCR representatives. Dot Bennett remains on the board as ex-officio.

Several matters concerning the future of IFPCS were discussed. The Federation has now 4 members. The way IFPCS is running should be reconsidered. Moreover, the rotation of PCR editor could be reconsider. Colin Goding (council member and PCR editor) reminds that IFPCS proposes an Editor and the Publisher (Blackwell) accepts it.

9. Matters concerning the Barcelona meeting

252 persons registered to the 2006 ESPCR meeting. This meeting is the biggest ever organized by ESPCR. It represents 26 countries from 5 continents. Twelve companies and six Spanish institutions supported this meeting. Sixty per cent of the income came from the attendees and 40% from sponsors. The budget is even. The 2004 ESPCR meeting broke already numbers of attendees (210). These results show that our Society is on the good track and it must stay like this.
The entire board for the scientific program, the number of program and the Venues congratulated Lluis Montoliu.

10. Venues for forthcoming Meetings.

The venue of the 2007 XIVth ESPCR Meeting is Bari, Italy, organized by R. Cicero. Rosa Cicero asked to change the date of the meeting. It will be from the 14-17th of October 2007. The council accepted this modification for 2007 and wish good luck to Rosa Cicero.
The next IPCC Meeting, 2008, will be held in Sapporo, Japan, organized by K. Jimbow.
One serious option was discussed for the venue of the 2009 XVth ESPCR Meeting. Organizer: Markus Böhm, Location: Münster, Germany.
For 2010, a possibility was considered. Organizer: Robert Kelsh, Location: Bath, UK.
For 2011, ESPCR has to organize IFPCS meeting.

11. Legal Status of the ESPCR.

The legal status of the Society was discussed. As of today, the ESPCR is not legally registered, because the original register in Italy is no longer valid.
Several options were considered. The goal is that ESPCR is to be official. Either ESPCR could be created as an international Charity Organization (French: ASBL; Dutch: VZW) or as another type of Organization (French: association loi 1901). Mauro Picardo will investigate some solution in Italy, Jo Lambert in Belgium and Alain Taieb in France.

- Incomes from Sponsors. Sponsors need a VAT number for donation. This issue is unfortunately not important to day because we do not have any sponsor. IFPCS could be used as intermediate.

- Outgoings to Companies. A VAT number is now absolutely required to pay invoices such as those from Blackwell corresponding to Pigment Cell Research subscriptions. IFPCS accepted to play intermediate in the matter. ESPCR thanks IFPCS for this help in this respect.

- Tax issue. This issue is not relevant because ESPCR income is too low to be taxable.

12. Any other business

No election should be conducted for 2007. The next election should be conducted for 2008.
Ghanem Ghanem pointed out the major issue concerning the animal experimentation problem, which is rising in Europe. The question remains ask. What our Society could do, if it would?

13. Close of the Meeting.

Jose-Carlos Garcia Borron thanked Ghanem Ghanem, Dot Bennett for their constant helps during these three years. The officers were thanked but Jose Carlos was sorry not to thank directly Jean-Marie Naeyaert directly.
With no other matters to discuss, the meeting was closed by J-C. García-Borrón.

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MINUTES OF THE ESPCR GENERAL ASSEMBLY

Tuesday, September 26th, 2006, 19:00

ESPCR meeting
Auditorium Sant Joan de Deu, Barcelona, SPAIN

1. Opening of the Meeting.

The meeting was opened by J-C. García-Borrón, who welcomed all ESPCR members.

2. Approval of the minutes of the ESPCR general assembly in Reston.

The Minutes of the General assembly Meeting in Reston were published in December 2005 ESPCR bulletin, issue number 53. The Minutes of the ESPCR General Assembly in Reston were unanimously approved.

3. Secretary's Report.

Lionel Larue is acting as Secretary.

a) Officer elections

After a call for nomination in 2005 only one candidate has been nominated for each of the three ESPCR Offices. The new President is Mauro PICARDO, the new Secretary is Lionel LARUE and the new Treasurer is Jo LAMBERT. Their terms of office began at the end of this meeting and will end during the 2009 ESPCR meeting.

b) Council elections

Five positions were available. Seven members were nominees. Elections were required. 58 members voted. Lluis Montoliu, Alessandra Napolitano, Anja Bosserhoff, Alain Taieb and Miguel Seabra were elected.

After the Barcelona meeting **the ESPCR Council members** are Anja Bosserhoff, Jose Carlos Garcia-Borron as ex officio, Colin Goding, Ghanem Ghanem as non-voting permanent (Web site), Jo Lambert as Treasurer, Lionel Larue as Secretary, Lluis Montoliu, Alessandra Napolitano, Mauro Picardo as President, Miguel Seabra and Alain Taieb.

After the last ESPCR Council Meeting, **the ESPCR representatives for IFPCS** are Dot Bennett (as ex-officio), Jose-Carlos Garcia-Borron (as Secretary-Treasurer), Jo Lambert and Mauro Picardo.

After the last ESPCR Council Meeting, **the ESPCR travel award committee** is composed of Friedrich Beermann (chair), Lionel Larue and Nico Smit.

The report was approved by the General Assembly and the President thanked Lionel Larue for his work.

4. Treasurer's Report.

- Statistics

The number of members in the ESPCR Web site list is 202. However, the actual number of members in good standing is 122 (8 honorary members, 92 regular members, 22 student members). We have 38 new members (12 students and 26 regulars).

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5. Financial matters

The President raised several issues on the financial aspects of ESPCR. Our society is a poor society and it has to fulfil his mission: promote research on pigment cells, attract young investigators, support meeting. In consequence three decisions were taken: stop sponsoring meetings, increase fees and attract members.

- Support of ESPCR for ESPCR meeting

A clear support of ESPCR is given to ESPCR meeting. However, the finance of ESPCR does not allow supporting financially ESPCR meetings. No financial support was given to the 2006 ESPCR meeting.

- Fees for 2007

The ESPCR council meeting propose to increase the fees after six years of stability. The General assembly approved unanimously an increased of 10 euros for regular members (60 to 70 euros) and 5 euros for students (30 to 35 euros).

- Bank account

ESPCR bank account remains in Belgium (Centea bank, account number 850-8169817-87). The bank should stay in Belgium to reduce the associated cost and the requirement to have a new VAT number.

6. ESPCR Bulletin and Web site report.

The ESPCR Web Master G. Ghanem delivered this.
- Web site: G. Ghanem reported that the Web site has been regularly updated and improved.
- ESPCR list: Everything is going smoothly, updated every month
- Bulletin: Everything is going smoothly

Lluis Montoliu proposed to simplify the web site address of our Society. A discussion between Ghanem and Lluis is on going to analyze this issue.

The next password for the web site was decided.
The report was approved by the General assembly, and the President thanked G. Ghanem for his outstanding work.

7. Venues for forthcoming Meetings.

The venue of the 2007 XIVth ESPCR Meeting is Bari, Italy, organized by R. Cicero. Rosa Cicero asked to change the date of the meeting. It will be from the 14-17th of October 2007. The council accepted this modification for 2007 and wish good luck to Rosa Cicero.
The next IPCC Meeting, 2008, will be held in Sapporo, Japan, organized by K. Jimbow.
The XVth ESPCR meeting will be held in Münster (Germany) and will be organized by Markus Böhm.

7. Any other business

Jose-Carlos Garcia-Borron thanked the officers, Ghanem Ghanem and Dot Bennett for their constant helps during these three years of Presidency.

8. Close of the Assembly.

With no other matters to discuss, the meeting was closed by J-C. García-Borrón.

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MINUTES OF THE SECOND ESPCR COUNCIL MEETING

Wednesday, September 27, 2006, 14:00

ESPCR meeting
Hotel ABBA Garden, Room Cervantes, Barcelona, SPAIN

1. Opening of the Meeting.

The meeting was opened by Mauro Picardo, who welcomed the following Council members: J.C. Garcia-Borron, G. Ghanem, J. Lambert, L. Larue, L. Montoliu, A. Napolitano and A. Taieb.

2. Apologies.

Apologies for absence were received from Anja Bosserhoff, Colin Goding and Miguel Seabra. They were accepted by the Council.

3. Presidential address and welcome to the new council members.

Mauro Picardo explains his general policy for the next three years and informs Council Members about the increase in membership fees which was approved at the General Assembly. The fee for membership has been increased from €60 to €70 for regular members and from €30 to €35 for students

4. ESPCR Website.

The ESPCR website should be the opportunity to increase news, exchange information, job opportunity, advertise special task forces of the Federation.

5. Exchange among board members

Mauro Picardo wishes that constant exchanges (email, telephone, etc.) among board members occur in order that we better accomplish the mission of ESPCR.

6. Bari ESPCR 2007 Meeting.

The frame of the scientific program was presented during this meeting.
A large number of comments were formulated by Lionel Larue, Mauro Picardo and Alain Taieb. An extensive work is required from the organizers to achieve this scientific program. Obviously, the scientific program must get the approval of the scientific committee.
Rosa Cicero has to present rapidly to the scientific committee the aim of this meeting, the number of days of the meeting, the clear schedule of the entire meeting including all the matters, the various sessions, the number of talks per session, the length of the different talks.
The Bari meeting is very important for the Society because the next ESPCR will be held in 2009 and we must not break the ESPCR positive stream; Ghent 160 participants, Paris 210 participants, Barcelona 250 participants. The constant rising of ESPCR meeting is due to the quality of the program, the novel themes presented aspects of our field (Developmental Biology, Cell biology, new visits of vitiligo). Other topics (molecular, cellular and physiological) are coming.
The exact venues, previsionnal budget and potential sponsors were not presented.

7. IPCC Meeting 2011

ESPCR will organize the IPCC meeting in 2011. Where should we organize the 2011 IPCC meeting? ESPCR secretary will formulate an email IPCC 2011 call for nomination in the beginning of 2008.
Mauro Picardo as preliminary reminded that the WCD (World Congress of Dermatology) will be held in Europe in 2011. From this, Mauro formulated the wish that IPCC and WCD meetings

could occur in the same place at the same time (one after the other one). The location of the WCD meeting is not yet determined; it could be in London or in Rome.

8. Any other business

During the Gala Dinner, the Board proposed Richard King as an honorary member of the ESPCR Society and it was approved at this meeting.
JC Garcìa-Borron, as secretary-treasurer of IFPCS, informed the members that the PCR subscription has been increased by Blackwell for 2007.

9. Close of the Meeting.

With no other matters to discuss, Mauro Picardo closed the meeting.

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CURRENT LITERATURE

1. Chemistry of Melanins and other Pigments

(Pr. A. Napolitano)

Several reports describing the binding properties of synthetic and natural melanins to different drugs including antibiotics (Buzman *et al, Pharmazie*), oligonucleotides and beta-adrenergic blocking agents (Pitkänen *et al Pharm Res*) have appeared. Of interest in this connection is a review article by Hong and Simon (*J Phys Chem B*) which summarizes recent data on the interactions between melanins and metals, providing a detailed insight into the nature of the binding sites, binding capacity, and relative affinity.
An interesting observation was reported by Olsen et al (*J. Am. Chem Soc*) regarding the absorption and emission spectra of the eumelanin precursor 5,6-dihydroxyindole-2-carboxylic acid (DHICA), which apparently subvert the mirror image symmetry rule. The dual features observed in the absorption spectra have been attributed to the excitation into the S1 and S2 states of a catecholate anion form of DHICA whereas emission were considered to arise from the S1 state of its proton-transfer conjugate following conversion via dual adiabatic and nonadiabatic reaction paths. The relevance of this observation to the absorption properties of melanins is also discussed considering the possibility that intramonomer proton transfer may function as an energy dissipation mechanism from high-lying photoexcited states of the macromolecule.
Characterization of the first tetramer arising from oxidation of a 5,6-dihyroxyindole (DHI) dimer (Panzella *et al Org Lett*) suggested a different positional reactivity of the DHI system when framed into a dimeric scaffold. This would imply that structural models of eumelanin should take into account not only the positional reactivity of the DHI monomer but also of its oligomers which accumulate in the early phases of the polymerization process.
An improved method has been presented (Nezirevic *et al, J. Chromatogr. A*) for analysis of the pheomelanin markers aminohydroxyphenylalanines based on the use of hydrophilic interaction liquid chromatography with mobile phases not including ion pairing reagents, conditions which are compatible with mass spectrometric detection and allow to perform a number of runs (up to 30) without reconditioning of the system.
Finally a new section has been introduced to put up the reports on applications of melanins which cover much different fields and are attracting increasing interest.

REACTIVITY AND PROPERTIES

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  Two-color excited-state absorption imaging of melanins. Proceedings of SPIE-The International Society for Optical Engineering 6424 (Photonic Therapeutics and Diagnostics III), 642402/1-642402/7, 2007.

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  Current Understanding of the Binding Sites, Capacity, Affinity, and Biological Significance of Metals in Melanin. J Phys Chem B. (2007) Jun 20; [Epub ahead of print]

- Olsen S, Riesz J, Mahadevan I, Coutts A, Bothma JP, Powell B J, McKenzie RH, Smith S C, Meredith P.
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  Binding of Betaxolol, Metoprolol and Oligonucleotides to Synthetic and Bovine Ocular Melanin, and Prediction of Drug Binding to Melanin in Human Choroid-Retinal Pigment Epithelium. Pharm. Res.

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- Choi SW, Lee SK, Kim EO, Oh JH, Yoon KS, Parris N, Hicks KB, Moreau RA. **Antioxidant and Antimelanogenic Activities of Polyamine Conjugates from Corn Bran and Related Hydroxycinnamic Acids**. J. Agric. Food Chemistry 55(10), 3920-3925, 2007.

- Liu SH, Pan IH, Chu IM. **Inhibitory effect of p-hydroxybenzyl alcohol on tyrosinase activity and melanogenesis**. Biol. Pharm. Bull.30(6):1135-11399, 2007.

- Kim YJ. **Antimelanogenic and antioxidant properties of gallic acid**. Biol. Pharm. Bull. 30(6):1052-1055, 2007.

- Kubo I, Nitoda T, Nihei K. **Effects of quercetin on mushroom tyrosinase and B16-F10 melanoma cells**. Molecules 12(5), 1045-1056, 2007.

- Maeda K, Naitou T, Umishio K, Fukuhara T, Motoyama A. **A novel melanin inhibitor: hydroperoxy traxastane-type triterpene from flowers of Arnica montana**. Biol. Pharm. Bull. 30(5):873-879, 2007.

- Nitoda T, Fan MD, Kubo I. **Anisaldehyde, a melanogenesis potentiator**. Z Naturforsch [C]. 62(1-2):143-149, 2007.

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MELANIN ANALYSIS

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2. Biology of pigment cells and pigmentary disorders

(Dr. M. Picardo)

Skin pigmentation and photoprotection are determined by the amount and type of melanin synthesized by the melanocytes in specialized membrane-bound organelles termed melanosomes, transferred to the neighboring keratinocytes. It is well known that racial differences in skin pigmentation are not due to the number of melanocytes, but they depend both on the amount and the type of melanin and also on the differences in size, number and distribution pattern of melanosomes within keratinocytes. Yoshida et al , using a human skin substitute (HSS) composed of cells derived from light and dark skin, strengthened the key role of the keratinocytes in modulating the skin pigmentation through differences in the release of melanogenic cytokines (bFGF, ET-1, □-MSH, SCF), the phagocytic activity and the distribution pattern of melanosomes. These mechanisms, in fact, appeared to be more effective in keratinocytes from dark skin, which are thus responsible for a darker coloration compared to that induced by light keratinocytes. The authors reported for the first time that in HSS the racial origin of the keratinocytes strictly influences the expression of melanogenic citokines, the melanogenesis and the distribution pattern of melanosomes in the epidermis. Recently it has been reported a new surprising genoprotective function of p53. As shown by Cui et al. p53 controls the sun tan response. As a transcription factor, p53 binds directly to the POMC gene promoter in keratinocytes and induces POMC transcription and □-MSH production. p53 exerts a crucial maintenance function in normal skin, protecting the genomes of epidermal keratinocytes and melanocytes against genotoxic damage and the risk of subsequent malignant transformation. Interestingly in some basal cell carcinomas, the tumors become pigmented due to the colonization of melanocytes. The authors found that this occurs only in tumors that retain wildtype p53, but not in those harboring p53 mutations. These data suggest that in subsets of basal cell carcinomas with wild-type p53, the constitutive activation of the p53-POMC mechanism leads to constitutive □-MSH production in the tumor, probably serving as a chemoattractant for colonizing melanocytes. Szabad et al described a novel culture system without chemical mitogens to obtain melanocytes from adult epidermis. In fact, most of culturing techniques use chemical mitogens to support melanocyte growth and to prevent contamination by keratinocytes and fibroblasts. They proposed a method to isolate and grow normal human adult melanocytes in a chemical free defined medium in which melanocytes proliferate already in the early passages, when they haven't already lost their pigmentation. Moreover, in this culture system, normal human adult melanocytes express EGFR both at the mRNA and at protein levels, and the treatment with EGF has a mitogenic effect. Due to conflicting results in the literature regarding the expression of EGFR in normal human melanocytes, the authors suggested that the reported results should help in solving this contradiction. The incidence of cutaneous melanoma is continously increasing and patients with advanced disease do not respond to conventional therapies mainly because of the acquired resistance to apoptosis of melanoma cells. Thomas et al investigated the role of the apoptosis inhibitor Survivin in in vivo melanocyte transformation and in tumor progression by the generation of a transgenic mouse with melanocyte-specific expression of Survivin (Dct-Survivin mouse). The authors showed in detail the capacity of Survivin to promote both early and late events of the UV-induced melanoma development. Survivin+/HGF+ mice generated from Dct-Survivin mice bred with melanoma prone MH19/HGF-B6 Tg mice showed: a) reduced susceptibility to UV-induced and spontaneous apoptosis; b) earlier tumor onset with an increased tumor density and c) higher tendency of lymph node and lung metastasis compared to Survivin-/HGF+ mice. These results showed the involvement of Survivin in both melanoma development and progression, also suggesting the potential role of Survivin as a target in the treatment of melanoma. Shc proteins are targets of activated tyrosine kinases and play a role in different cellular functions including survival, proliferation and apoptosis. Fagiani et al reported the identification and functional characterization of a new member of the Shc family termed RaLP. Among the different tissues analyzed, RaLP mRNA was detected in melanomas only. Its expression was low in nevi and radial growth phase (RGF) melanomas compared to the higher expression in vertical growth phase (VGP) and metastatic melanomas. This suggest a correlation between RaLP expression and the acquisition by the tumor cells of the ability to migrate and invade the underneath tissues. The authors showed that the down-regulation of RaLP expression in metastatic melanomas by siRNAs, reduced the migration of metastatic cells in vitro and the tumorigenesis in vivo, demonstrating the central function of RaLP in the tumorigenic potential of melanoma in vivo. Moreover, since IGF-1 and EGF are known a being involved in the survival, growth and migration of melanoma cells, the authors analyzed the role of RaLP in the signaling pathways of these two growth factors. When overexpressed in RGP or VGP RaLP-negative melanoma cells, RaLP acts as a downstream substrate of IGF-1R and EGFR, increases Ras/MAPK signaling and stimulates cell migration. RaLP silencing in RaLP-positive melanoma cells reduces their migratory potential without affecting MAPK signaling. These data suggest that RaLP activates the migratory pathways in both Ras dependent and independent manner. RaLP may represent a new and specific marker for metastatic melanoma and a potential target for novel anti-melanoma therapeutic approaches. Batistatou et al performed a histological and immunohistochemical analysis of common acquired nevi, excised from the same individual. They observed that multiple nevi from the same individual share similarities in the morphology and E-cadherin expression. The authors thus hypothesized the new concept that melanocytes of the all body are all genetically similar and changes predisposing to transformation can be a global melanocytic event for each person. The Authors suggest

genomic and proteomic-based approaches to verify this hypothesis. c-KIT, a receptor tyrosine kinase, once activated by binding to its specific ligand, the stem cell factor, leads to the activation of intracellular signaling pathways involved in the control of cellular proliferation and apoptosis. Hussein examined by immunohistochemical analysis, the expression of KIT protein in fifty specimens of healthy human skin, to better elucidate its expression in normal skin. The results showed a positive staining for KIT protein distributed on keratinocytes of the basal layer, mast cells, melanocytes, as well as on sebaceous and sweat glands. This report may be useful for studies which analyze KIT expression in cutaneous development and disorders. The study from Lee et al described the usefulness of artificial skin (AS) manufactured with both keratinocytes and melanocytes as an in vitro model to test the cutaneous biological changes induced by UV and provide a promising model closer to the in vivo skin in order to evaluate the phototoxicity of topical chemical agents. The heat shock proteins (Hsps), in addition to their chaperoning activities, are also involved in the regulation of apoptosis. Among them, Hsp70 has been reported to preserve various cell types from apoptosis induced by different stimuli such as oxidative stress, irradiation, TNF-□, heat shock. Bivik et al reported the role of Hsp70 in the protection of human melanocytes against UVB-induced apoptosis. Their findings demonstrated that melanocytes pre-heated before UVB exposure, show a significant increase of Hsp70 expression, a co-localization of Hsp70 signal with both lysosomes and mitochondria and a reduction in apoptosis. The authors showed the involvement of Hsp70 in preventing apoptosis through the reduction in the release of cathepsin D from lysosomes and cytochrome c from mitochondria, both events involved in the apoptotic process. Furthermore, the authors showed the protective role exerted by Hsp70 through the reduction in the translocation of the pro-apoptotic protein Bax from the cytosol to the mitochondria in cells expressing high levels of Hsp70. Finally, the authors reported on how these protective effects were abolished by Hsp70 siRNA transfection. On the other hand, the anti-apoptotic effect of Hsp70 may result in survival of melanocytes with DNA damaged by UV irradiation which constitute dangerous tumor precursors. Since overexpression of Hsp70 is a common feature of several types of tumor, targeting Hsp70 may thus represent a future anti-cancer therapeutic strategy. Due to the fact that agents that promote the pigmentation hold the potential to reduce UV-induced cell damage and that lightening agents have become increasingly important in the cosmetic and medical products used for the treatment of hyperpigmentation, several efforts have been devoted to screening for agents that regulate pigmentation. Ni-Komatsu et al discussed a chemical genetic approach to identify novel compounds and their targets involved in the regulation of mammalian pigmentation. By screening tagged triazine-based combinatorial libraries in immortalized murine melanocytes, albino melanocytes or zebrafish, 12 compounds were identified as either potent pigmentation enhancers or inhibitors in various systems. Target identification by affinity chromatography revealed prohibitin as a propigmentation effector and mitochondrial F1F0-adenotriphosphatase as the cellular binding targets for novel pigmentation enhancers. Newton and co-workers investigated the contribution of MITF to pigmentation regulation after treatment with the adenylate cyclase activator forskolin and/or resveratrol in normal human melanocytes. Resveratrol did not alterate MITF and its tyrosinase inhibitory effect was explained by both direct tyrosinase inhibition and a post-transcriptional effect that reduced the amount of fully processed tyrosinase. On the other hand, elevation of intracellular cAMP by forskolin markedly increased protein levels for MITF, tyrosinase and dopachrome tautomerase. However there was no concomitant increase in tyrosinase or dopachrome tautomerase mRNA. These data indicate that the increase of MITF protein abundance should be mediated through post-transcriptional processing events. Several studies have been focused on pathogenic mechanisms of pigmentation disorders. Schallreuter et al. showed that calmodulin expression is reduced in acute vitiligo. Due to their previous data reporting in vitiligo skin a low epidermal catalase activity and expression, leading to an over-accumulation of hydrogen peroxide, the authors hypothesised that calmodulin can be oxidased, loosing thus the capacity to activate calcium ATPase. This hypothesis was verified by measuring calcium ATPase activity in skin biopsies of lesional skin from patients with active vitiligo. The results showed a significant decrease of calcium ATPase activity in vitiligo skin, suggesting that hydrogen peroxide mediated oxidation of calmodulin strongly perturbs calcium homeostasis. The capacity for autocrine synthesis, transport and degradation of acetylcholine is severely affected in patients with depigmentation disorder vitiligo due to hydrogen peroxide accumulation as shown by in vivo FT-Raman spectroscopy. Schallreuter and Elwary investigated the possible regulatory effect of hydrogen peroxide over-accumulation in the cholinergic signal in vitiligo skin. Based on enzyme kinetics, in vitro FT-Raman, fluorescence spectroscopy and computer modelling the authors showed that oxidation of residues such as Met and Trp in the active site of both acetylcholinesterase and butyrylcholinesterase by hydrogen peroxide generates relevant structural changes, leading to the deactivation of both enzymes and the subsequent perturbation of cholinergic cascade. These evidence underline the involvement of cholinergic system in the pathogenesis of vitiligo. Furthermore, the authors suggested that pruritus present in patient with rapid progression of vitiligo can be caused by the accumulation of epidermal acetylcholine. Increased level of catecholamines and of their metabolites have been reported in plasma and urine of vitiligo patients as well as in lesional skin. The increase of these monoamines mainly occurs at the onset and progression phase, possibly contributing to the disappearance of melanocyte in vitiligo. Park et al investigated the toxic profile of dopamine and the molecular mechanism of dopamine-induced apoptosis in melanocytes. Moreover the authors tried to search for protective antioxidants against dopamine-induced toxicity in melanocytes. Especially, molecular mechanism of dopamine-induced apoptosis melanocytes was investigated by Western blotting for stress signalling pathways. The authors

demonstrated a selective dopamine toxicity in mouse and human melanocytes, while another major epidermal constituent, keratinocyte, was much more resistant to dopamine. Dopamine-induced apoptosis and JNK and p38 activation was shown by flow cytometry and Western blot analysis. Thiol-containing antioxidants, such as NAC or GSH, inhibited both stress-activated protein kinase activation and apoptosis, indicating the peculiar protective capacity of thiol compounds. The authors suggested that dopamine-induced cytotoxicity and cytoprotective effect of thiol compound reported could be a clue to understand pathogenesis of viltigo and to provide a new therapeutic strategy.

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3. MSH, MCH, other hormones, differentiation

( )

4. Photobiology

(Dr. N. Smit)

NOT AVAILABLE

5. Neuromelanins

(Pr. M. d'Ischia)

In this commentary two hypotheses relating to the etiopathogenesis of Parkinson's disease and three interesting biochemical aspects relevant to the catecholamine oxidation-neuromelanin-Parkinson's disease relationships will be addressed.
Sulzer (2007) reviewed possible causes or risk factors for Parkinson's disease and suggested that selective neuronal death may be due to multiple hits that combine a toxic response derived from dopamine oxidation or mitochondrial dysfunction with a failure of neuroprotective mechanisms, such as loss of function of parkin, a ubiquitin ligase that facilitates proteasomal protein degradation, or autophagic degradation.
Lang (2007) focused attention to the emerging view that Parkinson disease (PD) does not begin in the substantia nigra pars compacta but in other regions of the brain and proposed that once the original pathobiological process (for example, protein aggregation) is set in motion, additional processes more specific to dopaminergic neurones are triggered, resulting in acceleration of cell loss and nigrostriatal degeneration. This hypothesis would suggest a change in therapeutic strategy based on a combined treatment designed to address both the original mechanisms of the neurodegeneration and the processes specific to the dopaminergic substantia nigra.
Current views about the role of neuromelanin in Parkinson's disease implicate both the intracellular pigment in processes of free radical production and mitochondrial alteration, and the extracellular pigment, which may be liberated from degenerating melanized neurones, in the inflammatory response accompanying the disease. In an attempt to model neurone-glia interactions in Parkinson's disease, Depboylu et al. (2007) investigated the effects of extracellular purified neuromelanin on primary mesencephalic neurones in the presence and in the absence of glia. The results showed that extracellular neuromelanin may be toxic to surrounding neurones possibly via free radical production but not mitochondrial inhibition, and that glial cells have the potential to mitigate the neurotoxic effect of neuromelanin.
Bisaglia et al. (2007) carried out a detailed investigation of the oxidation products of dopamine to determine their relative abilities to interact with □-synuclein, a possible target protein in Parkinson's disease, and concluded that in the absence of thiol groups, 5,6-indolequinone is the reactive species. Finally, dolichoic acids containing 14-20 isoprene units were identified in neuromelanin by Ward et al. (2007).

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Kinetic and Structural Analysis of the Early Oxidation Products of Dopamine: analysis of the interactions with □ -synuclein. Journal of Biological Chemistry 282(21):15597-15605, 2007.
Abstract: Oxidative stress appears to be directly involved in the pathogenesis of several neurodegenerative disorders, including Alzheimer and Parkinson diseases. Nigral dopaminergic neurons are particularly exposed to oxidative stress because a pathol. accumulation of cytosolic dopamine gives rise to various toxic mols., including free radicals and reactive quinones. These latter species can react with proteins preventing them from exerting their physiol. functions. Among the possible targets of quinones, □-synuclein is of primary interest because of its direct involvement in dopamine metab. Contrary to the neurotoxic processes, neuromelanin synthesis seems to play a protective role by its ability to sequester a variety of potentially damaging substances. In this study, we carried out a kinetic and structural anal. of the early oxidn. products of dopamine. Specifically, considering the potential high toxicity of aminochrome for both cells and mitochondria, we focused our attention on its rearrangement to 5,6-dihydroxyindole. After the spectroscopic characterization of the products derived from the oxidn. of dopamine, the structural information obtained was used to analyze the reactivity of quinones toward □-synuclein. Our results suggest that indole-5,6-quinone, rather than dopamine-o-quinone or aminochrome, is the reactive species. We propose that the obsd. reactivity could represent a general reaction pathway whenever cysteinyl residues are absent in proteins or if they are sterically protected.

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Abstract: Background: Neuromelanin-contg. neurons of the substantia nigra are highly vulnerable to degenerate in Parkinson's disease. Inhibition of the respiratory chain or formation of reactive oxygen species (ROS) by intracellular neuromelanin and triggering of inflammatory processes by extracellular neuromelanin emanating from melanized neurons after their demise are thought to be causally implicated in the high vulnerability of melanized neurons. Objective: We addressed the direct effect of purified neuromelanin on mitochondrial complex I activity, and its influence on ROS prodn. and survival of primary mesencephalic neurons in the presence or absence of glia. Methods: Neuromelanin was isolated from midbrain of postmortem human brains. The content in iron and other elements was measured by inductively coupled mass spectrometry. The effect of neuromelanin on mitochondrial complex I activity was analyzed in post-nuclear exts. Primary neuronal enriched and neuron-glia mixed cultures from midbrain were treated with different concns. of neuromelanin.

The generation of ROS was detd. by fluorochrome detection. MAP2-pos. and TH-pos. neuronal viability was analyzed. Results: Neuromelanin did not affect complex I activity, but concn.-dependently increased ROS prodn. in neurons and reduced the no. of MAP2-pos. and TH-pos. cultured neurons. Glia protected neurons against the neuromelanin toxicity. Conclusion: Extracellular neuromelanin is detrimental to neurons implicating a mechanism of intracellular ROS prodn., but not complex I inhibition. ROS formation may be catalyzed by iron, which was sensitively identified in purified neuromelanin (3.3 mg/g). Importantly, we demonstrate that glial cells have the potential to mitigate the neurotoxic effect of neuromelanin.

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Abstract: Recent neuropathologic studies suggest that Parkinson disease (PD) does not begin in the substantia nigra compacta (SNc) but only involves this region later in the course of the disease. It is proposed that once the SNc is affected by the original pathobiological process (for example, protein aggregation), additional processes more specific to dopaminergic neurons are triggered (including sources of oxidative stress such as increased dopamine turnover, reduced levels of reduced glutathione, increased iron, and the presence of neuromelanin, as well as altered calcium homeostasis and excitotoxicity). This results in an acceleration of cell loss in the SNc, causing nigrostriatal degeneration to both reach a threshold for symptoms in advance of earlier affected brain areas and progress more rapidly than other aspects of the disease. Neuroprotective therapy directed solely at more general biologic processes may not have sufficient effects on this accelerated degeneration in the SNc, while neuroprotective therapy designed exclusively to slow the progression of dopaminergic cell loss will not alter the progression of the nondopaminergic symptoms that contribute the greatest disability in the later stages of the disease. Effective disease-modifying therapy may require a cocktail combining treatments designed to address the basic mechanisms of the neurodegeneration and the additional biologic processes specific to the dopaminergic SNc. This hypothesis has implications for the development of disease-modifying therapy and the interpretation of endpoints of clinical trials evaluating the efficacy of such treatments.

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High resolution quantitative element mapping of neuromelanin-containing neurons. Nuclear Instruments & Methods in Physics Research, Section B: Beam Interactions with Materials and Atoms 260(1):227-230, 2007.
Abstract: Neuromelanin is a dark colored intracellular pigment that appears in a specific population of neurons (dopaminergic and noradrenergic) predominantly in the substantia nigra and in the locus coeruleus. In recent years, there is increasing interest in the role of neuromelanin because of a hypothesised link between this pigment and the cell death of neuromelanin-contg. neurons in Parkinson's disease (PD). Therefore, the role of neuromelanin in the pathol. of PD is an actual focus in neuroscience. We have investigated the elemental contents and distributions of sulfur, calcium, iron, nickel and copper of neuromelanin in dopaminergic neurons for a Parkinson case and a control case (in situ, 6 □m brain sections). There was no difference in the iron concn. between the two cases. However, the calcium concn. was 3-fold higher in the Parkinson case, whereas the copper and nickel concns. decreased. An ultrastructural investigation of the concns. of calcium and iron within the neuromelanin suggests that these two elements are not necessarily co-localized.

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Abstract: We used a neuromelanin-magnetic resonance imaging technique to investigate abnormalities in the locus ceruleus in depression. We examined 20 patients with major depression and 43 age-matched controls using a 3 T scanner with a neuromelanin-sensitive sequence. The signal intensities of the areas corresponding to the rostral, middle, and caudal portions of the locus ceruleus were measured, and the contrast ratio relative to the adjacent pontine tegmentum was calculated. In controls, the contrast ratio in the middle portion was higher than in the rostral and caudal areas. In patients, contrast ratios in the rostral and middle portions were significantly decreased in comparison with controls, suggesting dysfunction of the ascending noradrenergic system. Neuromelanin-magnetic resonance imaging can be used to visualize abnormalities in the locus ceruleus of depressive patients.

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Multiple hit hypotheses for dopamine neuron loss in Parkinson's disease. Trends in Neurosciences 30(5), 244-250, 2007.
Abstract: Parkinson's disease arises from genetic and possibly neurotoxic causes that produce massive cell death of the neuromelanin-contg. dopaminergic neurons of the substantia nigra. Loss of these neurons is essential for the diagnostic parkinsonian features. Although many genetic mutations have been suggested as causes or risk factors for Parkinson's disease, the low penetrance of some mutations and the low disease concordance in relatives suggests that there must be interactions between multiple factors. We suggest that multiple hits' that combine toxic stress, for example, from dopamine oxidn. or mitochondrial dysfunction, with an inhibition of a neuroprotective response, such as loss of function of parkin or stress-induced autophagic degrdn., underlie

selective neuronal death. We discuss the properties of substantia nigra dopamine neurons that might make them particular targets of such multiple hits.

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  Abstract: Neuromelanin (NM) isolated from the substantia nigra of the human brain is found to contain a series of dolichoic acids (dol-CA) containing 14-20 isoprene units. This is the first observation of dol-CA in a natural system. Using internally spiked nor-dolichol and nor-dolichoic acid standards, the concentrations of dolichol (dol) and dol-CA present in NM were determined. Remarkably, dol was only four times as abundant as dol-CA in NM. The distribution of dol-CA chains lengths in NM also differed from that of dol, suggesting that the enzyme(s) responsible for the conversion of dol to dol-CA prefer a dolichol substrate containing 19 isoprene units.

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  Abstract: Agents suppressing microglial activation are attracting attention as candidate drugs for neuroprotection in Parkinson s disease (PD): While different mechanisms including environmental toxins and genetic factors initiate neuronal damage in the substantia nigra and striatum in PD, there is unequivocal evidence that activation of neuroinflammatory cells aggravates this neurodegenerative process. It was shown that following an acute exposure to the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and other toxins the degenerative process continues for years in absence of the toxin. Reactive microglia has been observed in the substantia nigra of patients with PD, indicating that this inflammatory process might aggravate neurodegeneration. By releasing various kinds of noxious factors such as cytokines or proinflammatory molecules microglia may damage CNS cells. The stimuli triggering microgliosis in Parkinsonian syndromes are unknown so far: However, analysis of neuronal loss in PD patients shows that it is not uniform but that neurons containing neuromelanin (NM) are predominantly involved. We hypothesized that extraneuronal melanin might trigger microgliosis, microglial chemotaxis and microglial activation in PD with subsequent release of neurotoxic mediators. The addition of human NM to microglial cell cultures induced positive chemotactic effects, activated the pro-inflammatory transcription factor nuclear factor kappa B (NF-kappaB) via phosphorylation and degradation of the inhibitor protein kappaB (IkappaB), and led to an upregulation of TNF-alpha, IL-6 and NO. These findings demonstrate a crucial role of NM in the pathogenesis of Parkinson s disease by augmentation of microglial activation, leading to a vicious cycle of neuronal death, exposure of additional neuromelanin and chronification of inflammation. Antiinflammatory drugs may be one of the new approaches in the treatment of PD.

6. Genetics, molecular and developmental biology

(Dr. F. Beermann)

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  Endothelin 3 Induces Skin Pigmentation in a Keratin-Driven Inducible Mouse Model. J Invest Dermatol, 2007.
  Abstract: Endothelin 3 (Edn3) encodes a ligand important to developing neural crest cells and is allelic to the spontaneous mouse mutation occurring at the lethal spotting (ls) locus. Edn3(ls/ls) mutants exhibit a spotted phenotype due to reduced numbers of neural crest-derived melanocyte precursors in the skin. In this study, we show that when Edn3 is driven by the keratin 5 promoter and thereby placed proximal to melanocyte lineage cells, adult mice manifest pigmented skin harboring dermal melanocytes. Using a tetracycline inducible system, we show that the postnatal expression of Edn3 is required to maintain these dermal melanocytes, and that early expression of the Edn3 transgene is important to the onset of the hyperpigmentation phenotype. Crosses into Edn3(ls/ls) mutants demonstrate that the Edn3 transgene expression does not fully compensate for the endogenous expression pattern. Crosses into tyrosine kinase receptor Kit(Wv) mutants indicate that Edn3 can partially compensate for Kit's role in early development. Crosses into A(y) mutant mice considerably darkened their yellow coat color suggesting a previously unreported role for endothelin signaling in pigment switching. These results demonstrate that exogenous Edn3 affects both precursors and differentiated melanocytes, leading to a phenotype with characteristics similar to the human skin condition dermal melanocytosis.

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7. Tyrosinase, TRPs, other enzymes

(Pr. J.C. Garcia-Borron)

8. Melanosomes

(Prof. J. Borovansky)

Melanosome trafficking, movement and distribution have received much attention recently: Two reviews deal with the function of myosins (*Coudrier, Eichler et al*), two papers postulate the role of Rab27A-Myrip-myosin VIIa complex in the melanosome motility in the RPE (*Klomp et al, Lopes et al*). A new method suitable for the in vivo melanosome tracking has been reported (*Toprak et al*).
The demonstration of aberrant melanosomes in metastatic myxoid melanoma cells (*Inoue et al*) and in conjuctival melanoma (*Kabasawa et al*) cannot any more be considered a surprising finding – the list of tumours with the incidence of aberrant melanosomes has already become too long. Changes of normal melanosome ultrastructure were described in epidermal melanocytes in slaty mice (*Hirobe&Abe*) and the rescue of melanosome maturation by the excess of tyrosine was observed in cultured recessive yellow melanocytes (*Hirobe et al*). Melanosomes in the extracutaneous melanocytes of amphibian testes were characterized by Zieri et al. The occurence of giant melanosomes in the choroid melanocytes was induced by bevacizumab injections (*Peters et al*).

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Requirement of dynactin p150(Glued) subunit for the functional integrity of the keratinocyte microparasol. J Invest Dermatol 127(7): 1736-1743, 2007.

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Myosin in melanocytes: to move or not to move? Pigment Cell Res 20(3): 153-160, 2007.
Comments: The role of myosins and different molecular mechanisms by which they contribute to the distribution, the movement and the biogenesis of melanosomes in epidermal melanocytes and RPE cells has been reviewed.

- Eichler TW, Kögel T, Bukoreshtliev NV, Gerdes HH.
The role of myosin Va in secretory granule trafficking and exocytosis. Biochemical Society Transactions 34(5): 671-674, 2006.
Comments: Concise and nicely illustrated review. Melanosomes are mentioned mainly in the paragraph devoted to myosin Va-related diseases.

- Hirobe T, Abe H.
Changes of melanosome morphology associated with the differentiation of epidermal melanocytes in slaty mice. Anat Rec (Hoboken) 290(7): 795-800, 2007.
Comments: Differences in the morphology and in the maturation of melanosomes in cultured epidermal melanocytes between those derived from wild type and slaty mutant were studied by means of electron microscopy. In wild type ((DCT+) almost all melanosome were elliptical stage IV organelles. In slaty melanocytes stage III melanosomes were mainly present in 3 different forms: spherical melanosomes with granular deposition of melanin, elliptical fibrillar melanosomes and mixed types. With the advancing age of the mouse cell donor spherical and mixed type melanosomes were gradually decreasing in slaty melanocytes -*see also Hirobe, Wakamatsu, Ito / Zool Sci- below. As for the mixed melanosome see Sato et al / Cell Structure Function 10: 421-425, 1985*.

- Hirobe T, Abe H, Wakamatsu K, Ito S, Kawa Y, Soma Y, Mizoguchi M.
Excess tyrosine rescues the reduced activity of proliferation and differentiation of cultured recessive yellow melanocytes derived from neonatal mouse epidermis. Eur J Cell Biol 86(6): 315-330, 2007.
Comments: The murine recessive yellow (MC1r(e)) is a loss-of-function mutant in melanocortin receptor 1 for α-MSH. The results obtained suggest that the MC1r(e) mutation affects the proliferation and differentiation of melanocytes; L-tyr was shown to rescue the reduced proliferative and differentiative activities by stimulating tyrosinase activity, TRP1 and TRP2 expressions as well as melanosome maturation.

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Excess tyrosine stimulates eumelanin and pheomelanin synthesis in cultured slaty melanocytes from neonatal mouse epidermis. Zoological Sci 24: 209-217, 2007.
Comments: The content of melanin was measured in the cultured epidermal melanocytes and in their supernatants in serum-free primary cultures derived from wild type and slaty mouse melanocytes. The addition of L-tyrosine increased the content of phaeo- and eumelanin in cultured slaty melanocytes and even stronger in culture supernatants. The eu- and phaeomelanin contents in culture supernatants from 7.5-day-old slaty melanocytes supplemented with L-tyrosine were even higher than those from wild-type melanocytes. *See also Hirobe et al / Eur J Cell Biol 85(6): 537-549, 2006*.

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  Metastatic myxoid melanoma with partial regression of the primary lesion. J Cuth Pathol 34(6): 508-512, 2007.
  Comments: Aberrant stage 3 melanosomes with various sized vesicles within the unit membrane were intermingled with normally looking melanosomes in the lymph node metastatic cells. The regressing primary site was not examined ultrastructurally.

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  Case of corneally displaced malignant conjunctival melanoma. */In Japanese/* Nippon Ganka Gakki Zasshi 111(2): 102-106, 2007.
  Comments: Ultrastructural study of the pigmented tumour cells in the cornea revealed the presence of aberrant granular melanosomes.

- Klomp AE, Teofilo K, Legacki E, Williams DS.
  Analysis of the linkage of MYRIP and MYO7A to melanosomes by RAB27A in retinal pigment epithelial cells. Cell Motil Cytoskeleton 64(6): 474-487, 2007.
  Comments: The relationship among Myrip(= myosin 7A interacting protein), Rab27a and myosin7A was examined with studies of mouse RPE in primary culture (including live-cell imaging), analyses of mutant retinas and RPE cell fractionation experiments. In RPE cells Rab27A, Myrip and myosin7A were all associated with melanosomes. Analyses of mutant mouse provided genetic evidence that Myrip is linked to melanosomes via Rab27A but showed that recruitment of Myrip to apical RPE is independent of melanosomes and Rab27A. It has been concluded that the Rab27A-Myrip-myosin7A complex functions in melanosome motility in the RPE.

- Lopes VS, Ramalho JS, Owen DM, Karl MO, Strauss O, Futter CE, Seabra MC.
  The ternary Rab27a-Myrip-Myosin VIIa complex regulates melanosome motility in the retinal pigment epithelium. Traffic 7(8): 486-499, 2007.
  Comments: Rab27a- Myrip - myosin VIIa complex was demonstrated to play a functional role in melanosome motlity in retinal pigment epithelium. Significant and similar alterations were observed when any one of these three components of the complex was missing as studied in ashen- (Rab27a defective), shaker1 (myosin VIIa mutant) and in the cells with knockdowned Myrip expression. I expect that this modern, first class paper will become a fundamental „compulsory“ reading on the melanosome motility in the RPE.

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  Ultrastructural findings in the primate eye after intravitreal injection of bevacizumab. Am J Ophthalmol 143(6): 995-1002, 2007.
  Comments: Bevacizumab, protein inhibitor of vascular endothelial growth factor, has been repeatedly tested for the treatment of various malignancies and ocular pathological situations */see e.g. Gerber HP&Ferrara N /Cancer Res 65(3): 671-680, 2005/*. This time intravitreal application of bevacizumab was reported to induce various ultrastructural changes in the choriocapillaries of Cynomolgus monkeys´eyes: choroidal melanocytes contained giant melanosomes on days 1 to 7 after the injection of bevacizumab.

- Toprak E, Balci H, Blehm BH, Selvin PR.
  Three-dimensional particle tracking via biphocal imaging. Nano Letters 7(7): 2043-2045, 2007.
  Comments: Biphocal imaging method (using a single CCD camera) enabling three-dimensional tracking of both fluorescent and non-fluorescent particles has been introduced and applied to several systems including in vivo melanosome tracking. Two to five nm accuracy with 2-50ms time resolution was achieved.

- Zieri L, Taboga SR, De Oliveira C.
  Melanocytes in the testes of Eupemphix natterei (Anura, Leiuperidae): Histological, Stereological and Ultrastructural aspects. Anat Rec 290: 795-800, 2007.
  Comments: Description of extracutaneous pigmentary system in the testis of the anuran amphibian Eupemphix natterei. Melanocytes occupied 0.71±0.33 mm3, were found to be in contact with neighbour melanocytes, myoid cells, Leidig cells and fibroblasts, and contained a large amount of melanosomes. Transmission EM revealed round and ovoid melanosomes of variable size and with indistinct margins. The authors have concluded that the described pigment cell type is not a component of the melanomacrophage system.

9. Melanoma experimental, cell culture

(Dr. R. Morandini)

Microencapsulation of recombinant cells is a recent approach to gene therapy which does not depend on genetic modification of the patient's own cells. Recombinant cell lines secreting a desired therapeutic gene product can be implanted into different patients, requiring the same product replacement or a therapeutic protein delivery. Graft rejection is avoided by enclosing these cells in immuno-isolation devices whose permeability excludes the host's immune mediators but permits the transit of nutrients and recombinant gene products. The capsules, or bioreactors, permit the release of recombinant proteins that may assert their effects in the tumor microenvironment. Such system has been used by Zhang et al. (2007); they describe a method to systemically inhibit tumor growth by in vivo culture of anti-angiogenic endostatin-secreting Chinese hamster ovary cells (CHO) in microcapsules as small as 200 µm in diameter. Peritoneal administrations of these microcapsules inhibit the growth of melanoma cells more than 65 % and enhance the survival of treated mice by 27 days post-treatment.
Hu (2007) has developed an original technique for the isolation, purification and cultivation of human conjunctival melanocytes. The author compares 2 methods: (1) various enzyme digestion methods or (2) enzyme-microdissection method (with dispase). The best results are obtained by the use of the second. This method provides a valuable source of large numbers of human conjunctival melanocytes.

A. Signal transduction and cell culture

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- Elco CP, Sen GC. **Stat1 required for interferon-inducible but not constitutive responsiveness to extracellular dsRNA**. J Interferon Cytokine Res. 27(5):411-24, 2007.

- Lee SO, Chun JY, Nadiminty N, Lou W, Gao AC. **Interleukin-6 undergoes transition from growth inhibitor associated with neuroendocrine differentiation to stimulator accompanied by androgen receptor activation during LNCaP prostate cancer cell progression**. Prostate. 67(7):764-73, 2007.

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B. Melanin and cell culture

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C. 3D cell culture and/or skin reconstitution

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D. Other tools and cell culture

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Claudin-1 overexpression in melanoma is regulated by PKC and contributes to melanoma cell motility. Oncogene. 26(26):3846-56, 2007. Epub 2006 Dec 11.

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E. Melanoma Experimental

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ANNOUNCEMENTS & RELATED ACTIVITIES

Calendar of events

2007 16th Annual Growth Factor and Signal Transduction Symposium. Senescence, Aging and Cancer

July 26–29, Ames, Iowa, USA

Contact: Symposium Office,
3208 Molecular Biology Building,
Iowa State University, Ames, IA 50011-3260, USA
Phone: +1 515 294 7978
Fax: +1 515 294 2244
E-mail: gfst@iastate.edu
Web site: http://www.bb.iastate.edu/~gfst/homepg.html

2007 First World Meeting of Interdisciplinary Melanoma Centers

September 5–8, Barcelona, Spain

Contact: Apartado Correos 14.040
08080 Barcelona, Spain
Tel. +34 690 846097
Fax +34 932 057230
Email: sbc@sbc-congresos.com
Web site: www.melanomacentersmeeting.com

2007 7th Congress of BADV

September 6-8, Riga, Latvia

Contact: Professor Andris Rubins
Tel: +371 2948 1725
Fax: +371 736 1615
E-mail: info@badv.lv
Web site: www.badv.lv

2007 37th Annual ESDR Meeting

September 5–8, Zürich, Switzerland

Contact: ESDR Office
7 Rue Cingria, CH - 1205 Geneva, Switzerland
Tel: +41 22 321 48 90
Fax: +41 22 321 48 92
E-mail: office@esdr.org
Web site : www.esdr.org

2007 14th Annual meeting of the PanAmerican Society for Pigment Cell Research

September 13-16, Chicago, IL, USA

Contact: Caroline LePoole
E-mail: ilepool@lumc.edu
Web site: paspcr.med.umn.edu/ ; www.paspcr2007.org

2007 21st World Congress of Dermatology

October 1-5, Buenos Aires, Argentina

Contact: E-mail: info@dermato2007.org
Web site: www.dermato2007.org

2007 Perspectives in MELANOMA XI

October 3-4, Huntington Beach, California, USA

Contact: IMEDEX
4325 Alexander Drive
Alpharetta, Georgia
30022-3740 USA
Tel: +1 (770) 751 7332
Fax : +1 (770) 751 7334
E-mail: meetings@imedex.com
Web site: www.imedex.com

2007 The 23rd IUSTI-Europe Conference on Sexually Transmitted Infections and HIV/AIDS

October 11-14, Cavtat/Dubrovnik, Croatia

Contact: Spektar Putovanja
Tkalciceva 15
HR-10000 Zagreb
Croatia
Tel: 385 1 4862 600, 4862 607
Fax: 385 1 4862 622
Email: kongres-derma@mef.hr
Web site: www.iustieurope2007.org

2007 XIVth Meeting of the European Society for Pigment Cell Research

October 14-17, Bari, Italy "Pigment Cells and their environment"

Contact: Prof Rosa Cicero
E-mail : r.cicero@biolgene.uniba.it
E-mail : espcr@gruppotriumph.it
Web site: www.espcr.org

2007 The IV International Melanoma Congress

November 1-4, NY City, USA

Contact:
E-mail: MBerwick@salud.unm.edu
Web site: www.melanomacongress07.net

2007 XXVII Symposium of the ISDP

November 9-11, Malaga, Spain

Contact: E-mail: intsocdermpath@aol.com
Web site: www.intsocdermpath.org

2007 26th PAD & 5th SARAD Conference of Dermatology

November 15-18, Lahore, Pakistan

Contact: Professor Atif Kazmi
Department of Dermatology, King Edward Medical University
Mayo Hospital, Lahore, Palistan
Tel: +92 42 735 4094
Fax + 92 42 735 3043
E-mail: atifkazmi80@yahoo.com
Web site: www.padsarad2007.com

2007 20th Annual Meeting of the Japanese Society for Pigment Cell Research (JSPCR)

November 25-26, Matsumoto City, Japan

Contact: Prof. Toshiaki Saita, Shinsyu University
Web site: wwwsoc.nii.ac.jp/jspcr/

2007 21th Annual Meeting of the Japanese Society for Pigment Cell Research (JSPCR)

December 8-9, Toyoake City, Japan

Contact: Prof. Kazumasa Wakamatsu
E-mail: kwaka@fujita-hu.ac.jp
Web site: wwwsoc.nii.ac.jp/jspcr/

2008 66th Annual Meeting AAD

February 1-5, San Antonio (TX), USA

2008 Dermatologia Globale

April 23-26, Genoa, Italy

Contact: Dr Salvatore Noto
Via Luciano 15
20156 Milano
Tel.: +39 02 36 57 07 00
Fax: + 39 02 36 57 07 40
Email: info@allroundcongressi.it
Website: www.globaldermatology.info

2008 20th International Pigment Cell Conference (IPCC)

conjoined with

Vth International Melanoma Research Congress

May 7–12 Sapporo, Japan

Contact: Secretariat Office
Toshiharu YAMASHITA (Sapporo Medical University, Japan)
Minami 1-jo, Nishi 16-chome Chuo-ku, Sapporo, Japan 060-8543
Phone: +81-11-611-2111
Fax: +81-11-613-3739
E-mail: ipcc-imrc2008@sapmed.ac.jp
Web site: www.e-convention.org/ipcc-imrc2008

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

May 14-17 , Kyoto, Japan

Contact: E-mail: office@esdr.org
Web site: www.esdr.ch

2008 9th Congress of the European Society for Pediatric Dermatology

May 15-17, Athens, Greece

Contact: Ms. Penelope Mitrogianni
Tel: +30 210 725 7693 Fax: +30 210 725 7532
e-mail: info@espd2008.com
Web site: www.espd2008.com

2008 5th EADV Spring Symposium

May 22-25, Istanbul, Turkey

Contact: Professor Mehmet Ali Gürer
Ayazmaderesi Cad. Karadut Sok. No:7
34394 Dikilitas - Istanbul, Turkey
Tel: +90 212 258 60 20 pbx Fax: +90 212 258 60 78
E-mail: info@eadvistanbul2008.com or president@eadvistanbul2008.com
Web site: www.eadv.org/istanbul2008

2008 17th Annual Congress of the European Academy of Dermatology Venereology

September 17-21, Paris, France

Contact: EADV PARIS 2008 CONGRESS OFFICE :
EADV 2008 MCI - 24, rue Chauchat
FR - 75009 Paris - France
Tel. : + 33 (0)1 53 85 82 70 Fax.: + 33 (0)1 53 85 82 83
E-mail: www.eadvparis2008.com

2009 6th EADV Spring Symposium

April 23 – 26, Bucharest, Romania

2009 Annual Meeting for the Society for Investigative Dermatology

May 6-9, Montreal, Quebec, Canada

Contact: Web site: www.sidnet.org

2009 39th Annual ESDR Meeting

September 9-12, Budapest, Hungary

2009 XVth Meeting of the ESPCR

September 20-23, Münster, Germany

Contact: Dr Markus Böhm
E-mail: bohmm@uni-muenster.de

2009 18th EADV Congress

October 7-11, Berlin, Germany

2010 40th Annual ESDR Meeting

September 8-11, Helsinski, Finland

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

BOYANO Maria Dolores
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Faculty of Medicine and Dentistry
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Communication from Blackwell

Announcement

Pigment Cell Research to become *Pigment Cell & Melanoma Research*

We are pleased to announce that *Pigment Cell Research*, the official journal of the International Federation of Pigment Cell Societies, has now also become the official journal of the Society for Melanoma Research (SMR).

To highlight the increased focus on melanoma research, the journal is changing its name from January 2008 to *Pigment Cell & Melanoma Research*.

Other journal developments to support the increased growth in melanoma research include:

- New Executive Editors: Ze'ev Ronai, Burnham Institute, La Jolla, USA and Shosuke Ito, Fujita Health University, Japan.
- Revised and expanded Editorial Board of melanoma research specialists.
- New 'News & Views' section to be launched.
- Revised Aims & Scope.

Revised Aims & Scope

Pigment Cell Research publishes manuscripts on all aspects of pigment cells including development, cell and molecular biology, genetics, diseases of pigment cells including melanoma. Papers that provide insights into the causes and progression of melanoma including the process of metastasis and invasion, proliferation, senescence, apoptosis or gene regulation are especially welcome, as are papers that use the melanocyte system to answer questions of general biological relevance. Papers that are purely descriptive or make only minor advances to our knowledge of pigment cells or melanoma in particular are not suitable for this journal.

Author Benefits

Publish your research papers in *Pigment Cell Research* and benefit from:

- Email manuscript submission.
- Rapid review process – average 21 days from submission to first decision.
- Low cost colour figures.
- Author services – track your paper online from acceptance to publication.
- Online early – article by article publishing leading to rapid publication times.
- Reach into more than 5,500 institutions worldwide with access to the journal.
- Online 'virtual' issues for melanoma, vitiligo and development.

Blackwell Publishing

Visit the website for further information on the journal and to read our special virtual issue on melanoma:

www.pigment.org