Cell News

Newsletter of the German Society for Cell Biology

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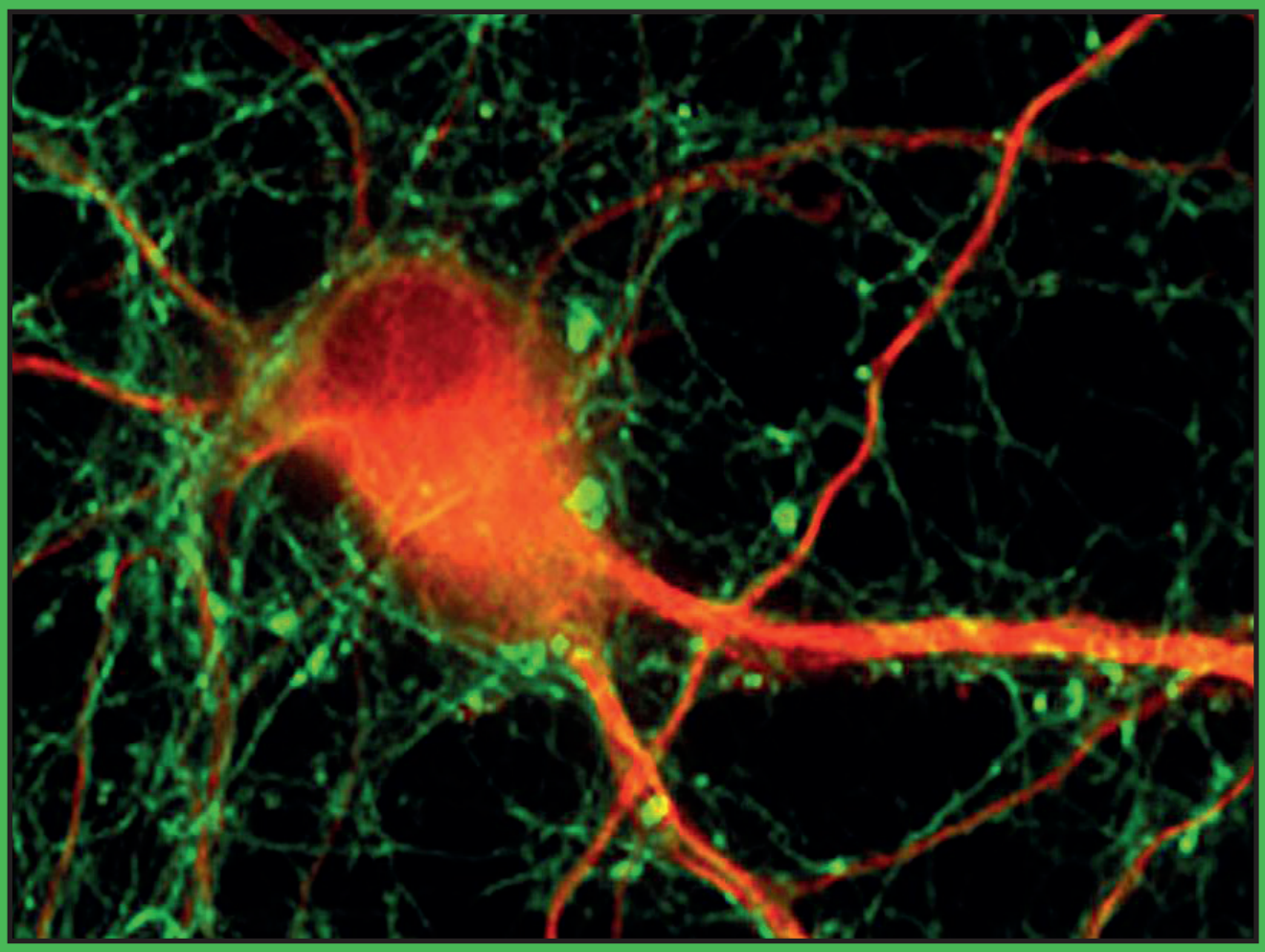

- International Meeting Regensburg
- Special Interest Meeting Potsdam
- International Meeting Potsdam
- Annual International Dictyostelium Conference Potsdam

DGZ

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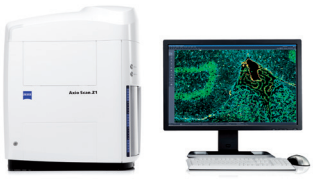

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Cover image: The image shows a primary rat hippocampal neuron, 21 days in vitro. The cell has been fixed and stained with antibodies against Tau (green color) and MAP2 (red color). In physiological conditions Tau is an axonal protein and is only present in the axons. MAP2 is a dendritic protein and is only present in the cell body and the dendrites. In pathological conditions such as Alzheimer Disease, Tau becomes mis-localized (missorting of Tau) and appears in the cell body and the dendrites. Hans Zempel.

PREFACE

Dear colleagues,

this is my first preface as the president of the DGZ. On behalf of all members of the executive committee, I would like to thank you for your votes in the elections for the new executive committee and advisory board. We really feel honored and we would like to thank you for your confidence. The election of Prof. Carien Niessen (vice president), Oliver Gruss (CEO), Klemens Rottner (Vice CEO) and myself (president) was approved at our last member meeting held during the International DGZ Meeting 2014 in Regensburg.

New bylaws

On the member meeting, we also have ratified new bylaws. These new bylaws were necessary to allow for the the legal possibility to perform our next elections through an online system. We prefer such an online ballot, not only for reasons of convenience and costs but also likely allows us to mobilize a higher number of voters. In the course of this bylaws modification we have also updated a few other aspects. You can read about all changes in the minutes of the member meeting, which are published together with the new bylaws in this issue of Cell News. For legal reasons the bylaws have to be published in German, I apologize to those of our readers who do not understand German.

Next International Meeting in Cologne

We are happy to announce that **the next International Meeting of the DGZ will be held from March 24–27, 2015, in Cologne**. I am very grateful to Carien Niessen that she has agreed to organize the meeting together with her colleagues (Angelika Noegel, Thorsten Hoppe, Sara Wickström, and Sandra Iden) at the university campus. On a program workshop, we have recently defined a cocktail of interesting topics for an exciting meeting. You will find a little preview at the bottom of this page. The German Society of Cell Biology is aware of gender issues and promotion of young scientists. Thus, we are proud to announce a roughly equal balance of male and female chairpersons in our Symposia, Plenary Lectures and dedicated Young Scientist Sessions (see below).

Future meetings

With regard to meetings in the near future, I would also like to invite you to register for our special interest meetings this summer. Registration for "Life at the Edge - The Nuclear Envelope In Nucleoplasmic Transport, Genome Organization And Cell Cycle Regulation" is still open until June 2nd (www.nuclearenvelope2014.com), and until July 7th you can also register for the "Annual International Dictyostelium Conference" (www.dicty2014.de), which is held under the auspices of the DGZ this year. Both meetings will take place at the Seminaris Hotel in Potsdam at the Lake Templin.

Promotion of young scientists

As you can read in the minutes of the member meeting, we have consolidated our finances in 2013 and are eager to increase our assets again in 2014. As soon as we feel able to do so, we will again organize a Young Scientist Meeting, since promotion of young researchers should in my opinion be one of the major objectives of our society. Following this objective, we have decided to include Young Scientist Sessions in our International Meeting in Cologne 2015. These sessions will be held as satellite meetings in the morning of March 24th. So if you are a young postdoc willing to organize a symposium on an interesting topic in cell biology, don't hesitate to contact the DGZ office for further details. We are able to organize rooms, sponsor registration fees for your speakers and to give some additional, financial support.
I would also like to encourage young scientists to submit an article on their scientific work for publication in Cell News. You'll find the instructions for authors at http://zellbiologie.de/cellnews/for-authors . You can take the articles of our price winners in the current issue as examples.

Finally, for those of you who have not yet come across my research, please have a look inside this issue of CellNews. There you can find a review on my favorite scientific topic. Even if you are not a young scientist anymore, please feel invited to use CellNews as platform to introduce yourself or your research group the Cell Biology community in Germany and even beyond. You'll find a broad audience and keep your copyrights. CellNews is YOUR journal and the DGZ is YOUR society. We as the executive committee appreciate any kind of input and contributions.

Yours,
Ralph Gräf (president)

International DGZ meeting

March 24 – 27 2015 in Cologne.

Topics will include among others:

1. cell biology of aging
2. cell polarity
3. neurobiology
4. mitochondria
5. new actin functions
6. signal transduction and trafficking
8. Immunity

DGZ Member Meeting – Minutes

March 18 – 21, 2014, Regensburg, Germany

DGZ Member Meeting
19.3.2014 in Regensburg
Time: 1 pm - 2 pm
Attendees: 30 Members

TOP1: Confirmation of the minutes of the DGZ Member Meeting 2013.
The CEO, Prof. Oliver Gruss, asked the present members if there were any concerns about or comments on the minutes of the last members' meeting in Heidelberg in 2013. No issues were raised and the minutes therefore accepted.

TOP2: The president's annual report
The president, Prof. Eugen Kerkhoff, thanked the organizers of last year's International Meeting in Heidelberg for their excellent organization and the outstanding programme. The DGZ has appreciated to carry out this meeting as a joint meeting with the Society for Developmental Biology (GfE). Unfortunately, the current executive board of the GfE is not in support of performing their biennial meeting again as a joint meeting with our International Meeting in 2015. The city and venue of our International Meeting in 2015 is still a matter of discussion, since attempts to organize it in München or Düsseldorf have failed.

The president reported about the novel developments of our journal Cell News. Cell News is now an online journal with a convenient and professionally designed homepage. Due to the short time since its launch as an online journal there is currently no statistics on the traffic on the journal website. The DGZ is in negotiations with Dr. Dagmar Gebauer from the European Journal of Cell Biology (Elsevier) for a closer collaboration for publishing our review articles as full publications in EJCB and to make EJCB the publishing organ of the DGZ. Cell News should be continued for publication of short articles, news from our society and our field of work.

TOP3: Financial report
The CEO, Prof. Oliver Gruss (OG), presented the financial report for 2013. Moreover, he informed the members that, in 2013, the society has gained 49 new members and lost 76 members. Currently the society has 1111 members.
After a drop in our assets in 2012 due to unexpected expenses from our meetings, we have consolidated our finances in 2013. There were no unusual financial bookings in 2013. Our assets by December 31, 2014, amounted to 40,280.09 €. Taken into account that the salary for our secretary Mrs. Sabine Reichel-Klingmann was billed for 1.5 years by the DKFZ, this is almost exactly the same amount as by the end of 2012. OG explained that Mrs. Sabine Reichel-Klingmann now holds a permanent contract with the DKFZ. Although her salary will still be afforded by the DGZ in the future, she legally is a tenured employee of DKFZ. The executive board is eager to increase our assets again in 2014 in order to have more flexibility in its work.

TOP4: Auditors' report
On behalf of the two auditors (Prof. Dabauvalle and Prof. Mannherz) Prof. Mannherz reported that records were checked and found correct.

TOP5: Approval of the executive board
Prof. Mannherz applied to discharge the executive board. His petition was accepted with the following result: yes (26), abstention (4; executive board), no (0)

TOP6: DGZ elections 2014
Vorstand:
Ralph Gräf, Präsident: yes (151), no (1), abstention (10)
Carien Niessen, Vizepräsidentin: yes (137), no (3), abstention (20)
Oliver Gruss, Geschäftsführer: yes (150), no (0), abstention (10)
Klemens Rottner, Sekretär (in future: Vizegeschäftsführer) yes (147), no (2), abstention (11)

Ralph Gräf, Carien Niessen, Oliver Gruss and Klemens Rottner accepted their election as president, vice president, chief executive officer and secretary, respectively.

Ergänzungswahl zum Beirat:
Thomas Dresselhaus: yes (131), no (2), abstention (25)
Volker Gerke: yes (146), no (2), abstention (12)
Doris Wedlich: yes (139), no (7), abstention (13)

The elected members of the Advisory Board, Prof. Doris Wedlich, Prof. Volker Gerke and Prof. Thomas Dresselhaus were present and also accepted their election.

Wahl der Kassenprüfer:
Marie-Christine Dabauvalle: yes (146), no (2), abstention (12)
Hans-Georg Mannherz: yes (145), no (1), abstention (11)

Ergänzungswahl zur Preisjury:
Zoya Ignatova: yes (132), no (3), abstention (20)
Frank Schnorrer: yes (135), no (2), abstention (20)
Walter Witke: yes (140), no (1), abstention (15)

TOP7: Changes in the DGZ bylaws
The DGZ bylaws needed to be updated. The new president, Prof. Ralph Gräf, went through the bylaws point by point and mentioned any desired change. (1) New members will be notified on their membership by a letter from the DGZ office. (2) Honorary members of the DGZ should be appointed by the executive board instead of being elected. (3) Cancelation of the membership should be notified to the DGZ office instead of the secretary (vice CEO, see below). (4) Members will be informed about the upcoming members' meeting and its minutes through publication in the DGZ journal (Cell News). (5) To avoid confusion of the German term "Sekretär" for the executive board member with our secretary in the DGZ office, the former secretary within the executive board should now be called vice chief executive officer (vice CEO), in German "Vizegeschäftsführer". (6) Elections should also be possible through an anonymized online election procedure instead of the current postal voting procedure. (7) The allowed number of members in the advisory board will be changed to "8 – 12" instead of 12.

All abovementioned changes were accepted with the following result: yes (28), abstention (2), no (0).

TOP8: Other
none

New bylaws

(beschlossen auf der Mitgliederversammlung am 19. März 2014 in Regensburg)

For legal reasons bylaws have to be published in German.

§ 1 Name und Sitz des Vereins, Eintragung ins Vereinsregister

Der Name des Vereins lautet: "Deutsche Gesellschaft für Zellbiologie"
(englische Bezeichnung: German Society for Cell Biology)
Der Sitz des Vereins ist Heidelberg. Der Verein ist ins Vereinsregister unter der Nr. 888 beim Registergericht des Amtsgerichts Mannheim eingetragen.

§ 2 Zweck der Gesellschaft

(1) Die Deutsche Gesellschaft für Zellbiologie verfolgt ausschließlich und unmittelbar gemeinnützige Zwecke im Sinne des Abschnitts "Steuerbegünstigte Zwecke" der Abgabenordnung.
(2) Ihr Zweck ist die Förderung der Wissenschaft.
(3) Dieser Satzungszweck wird verwirklicht insbesondere durch die Vertretung der Interessen der Zellbiologie als selbständiger, multidisziplinärer und fachintegrierender Wissenschaft innerhalb und außerhalb der Bundesrepublik Deutschland. Die Gesellschaft soll Informationen ausländischer und internationaler Zellbiologievereinigungen über Aktivitäten auf dem Gebiet der Zellbiologie und verwandter Wissenschaften (Tagungen, Methodenkurse, Kooperationsprojekte, Stipendien, Wissenschaftleraustausch etc.) an ihre Mitglieder vermitteln und umgekehrt entsprechende Informationen aus dem deutschen Bereich an die betreffenden ausländischen oder internationalen Institutionen weiterleiten. Sie soll ferner in begrenztem Maß zur Finanzierung bestimmter wissenschaftlicher Aktivitäten im In- und Ausland beitragen und als zentrale Informationsstelle über Angebot und Nachfrage von Arbeitsstellen und Stipendien für Zellbiologen dienen. Die Gesellschaft soll Arbeitstagungen und Kongresse durchführen und Vorschläge zur Verbesserung des Standes der deutschen Zellbiologie auf bestimmten Arbeitsgebieten entwickeln.

§ 3

(1) Die Gesellschaft ist selbstlos tätig; sie verfolgt nicht in erster Linie eigenwirtschaftliche Zwecke.
(2) Mittel der Gesellschaft dürfen nur für die satzungsmäßigen Zwecke verwendet werden.
(3) Es darf keine Person durch Ausgaben, die dem Zweck der Gesellschaft fremd sind, oder durch unverhältnismäßig hohe Vergütungen begünstigt werden.
(4) Bei Auflösung der Gesellschaft oder bei Wegfall ihres bisherigen Zweckes fällt das Vermögen des Vereins an die Deutsche Forschungsgemeinschaft, die es unmittelbar und ausschließlich für gemeinnützige Zwecke zu verwenden hat.

§ 4 Mitgliedschaft

Die Gesellschaft besteht aus aktiven und aus Ehrenmitgliedern, außerdem kann es fördernde Mitglieder geben. Aktives Mitglied kann auf schriftliches Gesuch hin jeder auf einem zellbiologischen Gebiet arbeitende Wissenschaftler werden. Die Mitgliedschaft wird gültig mit der schriftlichen Bestätigung seitens der Geschäftsführung, in jedem Fall aber erst nach Zahlung des Beitrages für das laufende Jahr. Ehrenmitglieder werden vom Vorstand ernannt und sollten hervorragende Zellbiologen mit einer als gesichert angesehenen wissenschaftlichen Leistung sein. Sie sind von der Beitragszahlung befreit. Ihre Zahl wird auf 20 beschränkt.
Mitgliedschaft und Ehrenmitgliedschaft ist nicht auf Bürger der Bundesrepublik Deutschland beschränkt.
Die Mitgliedschaft erlischt durch Austritt oder Tod. Der Austritt aus der Gesellschaft kann jeweils zum Ende des Kalenderjahres nach schriftlicher Mitteilung an das Sekretariat der Gesellschaft erfolgen.
Mitglieder, welche während zwei aufeinander folgender Jahre ihren Beitrag nicht gezahlt haben, können nach fruchtloser, erneuter Mahnung mit zweiwöchiger Fristsetzung und Hinweis auf die Ausschließungsmöglichkeit durch den Vorstand vom Verein ausgeschlossen werden.

§ 5 Die Organe der Gesellschaft
Organe der Gesellschaft sind:

(1) Die Mitgliederversammlung
Die Mitgliederversammlung soll in der Regel einmal jährlich - nach Möglichkeit im Frühjahr - mindestens aber alle zwei Jahre stattfinden. Einladungen dazu mit der Tagesordnung sollen spätestens vier Wochen vor dem Termin allen Mitgliedern und Ehrenmitgliedern von der Geschäftsführung durch Veröffentlichung in der Mitgliederzeitschrift bekannt gegeben werden. Die Mitgliederversammlung behandelt insbesondere folgende Tagungsordnungspunkte:

1. Bestätigung des Protokolls der letzten Sitzung
2. Jahresbericht des Präsidenten mit anschließender Diskussion
3. Geschäfts- und Kassenbericht des Geschäftsführers und seines Vizegeschäftsführers
(Bericht über das abgelaufene Kalenderjahr)
4. Bericht der beiden Rechnungsprüfer
5. Entlastung des Vorstandes
6. Genehmigung des Budgets und Festsetzung des jährlichen Mitgliederbeitrages
7. Bekanntgabe des Wahlergebnisses und Amtseinführung des neuen Vorstandes und des Beirats
8. Kommissionsberichte
9. Wahl von besonderen Kommissionen
10. Weitere Tagesordnungspunkte

Anregungen zur Gestaltung der Tagesordnung sind an die Geschäftsführung zu richten. Anträge von Mitgliedern auf Aufnahme von weiteren Tagesordnungspunkten sind jedoch nur zu berücksichtigen, wenn sie von mindestens fünf Mitgliedern schriftlich fünf Wochen vor der Versammlung bei der Geschäftsführung eingegangen sind. Die Versammlungen werden vom Präsidenten und bei dessen Verhinderung von den weiteren Vorstandsmitgliedern in der Reihenfolge ihrer Funktionsbenennung gem. Abschnitt II berufen und geleitet. Die Protokolle sind vom Versammlungsleiter und dem Vizegeschäftsführer des Vereins zu unterschreiben. Bei Verhinderung des Vizegeschäftsführers hat der Versammlungsleiter eine andere Person zur Protokollführung und zur Unterschrift unter das Protokoll zu bestimmen. Das Protokoll der Mitgliederversammlung soll von der Geschäftsführung allen Mitgliedern durch Veröffentlichung in der Mitgliederzeitschrift bekannt gegeben werden.

(2) Der Vorstand
Der Vorstand des Vereins im Sinne des § 26 besteht aus
1. Dem Präsidenten
2. Dem Vizepräsidenten
3. Dem Geschäftsführer
4. Dem Vizegeschäftsführer. Dieser ist auch Stellvertreter des Geschäftsführers.

Die Vorstandsmitglieder werden aus dem Kreis der aktiven Mitglieder durch geheime Wahl gewählt. Dies kann entweder über Briefwahl oder über ein anonymisiertes Verfahren per online-Abstimmung über eine gesicherte Internetverbindung erfolgen. Das Ergebnis der Wahl wird durch einen Wahlausschuss festgestellt, der vom Vorstand bestimmt wird und dem zwei Vorstandsmitglieder angehören. Über das Wahlergebnis ist ein Protokoll anzufertigen und von diesen zwei Vorstandsmitgliedern zu unterschreiben. Das Ergebnis der Wahl wird auf der Mitgliederversammlung bekannt gegeben. Erreicht ein Kandidat im 1. Wahlgang die absolute Mehrheit, so ist er gewählt. Im 2. Wahlgang stehen diejenigen Personen zur Wahl, die im 1. Wahlgang die höchste und zweithöchste Stimmenzahl erreicht haben.
Der Präsident führt und repräsentiert die Gesellschaft, der Vizepräsident steht ihm zur Seite und vertritt ihn gegebenenfalls. Der Geschäftsführer leitet die Geschäfte der Gesellschaft, ihm zur Seite steht der Vizegeschäftsführer. Zur Vertretung des Vereins sind der Präsident und der Vizepräsident allein berechtigt. Von den übrigen Vorstandsmitgliedern sind jeweils zwei gemeinschaftlich zur Vertretung des Vereins berechtigt.
Die Amtsperiode eines Vorstands beginnt nach der Annahme der Wahl und Amtseinführung auf der Mitgliederversammlung. Sie endigt, vorbehaltlich der Amtsniederlegung, mit wirksamer Berufung des Amtsnachfolgers. Neue Vorstandswahlen sollen alle zwei Jahre stattfinden.
Bei vorzeitigem Ausscheiden eines Vorstandsmitglieds sind die übrigen Vorstandsmitglieder berechtigt, von sich aus Amtsnachfolger zu wählen oder einzelne Vorstandsmitglieder mit zwei Ämtern zu betrauen.
Der gesamte Vorstand oder ein einzelnes Vorstandsmitglied kann auf Antrag von mindestens zehn Mitgliedern der Mitgliederversammlung mit mehr als der Hälfte der abgegebenen Stimmen abgewählt werden. Die Abberufung erfordert eine unmittelbar anschließende Neuwahl.

(3) Der Beirat
Der Beirat berät den Vorstand in allen Planungen und Zielsetzungen die über die Amtsperiode des Vorstandes hinausgehen. Der Beirat besteht aus drei verdienten Mitgliedern der Gesellschaft, die von den aktiven Mitgliedern alle zwei Jahre gewählt werden. Die Amtsperiode dieser Mitglieder beträgt 2 Jahre. Der Wahlmodus für diese Beiratsmitglieder ist der gleiche wie für die Wahl des Vorstandes. Außer diesen gewählten Mitgliedern gehören dem Beirat an: (1) der Präsident der letzten Tagung (jeweils bis zur nächsten Tagung, d.h. ein Jahr) und (2) der jeweils aus seinem Amt ausgeschiedene Präsident (für 2 Jahre). Zusätzlich werden vom jeweiligen Vorstand weitere Beiratsmitglieder für eine Amtsperiode von 2 Jahren benannt, um auf eine Gesamtzahl von 8 bis 12 Beiratsmitgliedern zu kommen. Eine Wiederwahl bzw. eine Wiederbenennung ist möglich. Die Amtsperiode der Beiratsmitglieder beginnt nach Annahme der Wahl und Amtseinführung auf der Mitgliederversammlung bzw. nach der Benennung.

(4) Rechnungsprüfer
Die Mitgliederversammlung wählt für zwei Jahre zwei Rechnungsprüfer. Diesen sowie dem Präsidenten und Vizepräsidenten muss der jährliche Kassenbericht bis zum 1. Februar des darauf folgenden Jahres vom Geschäftsführer und seinem Vizegeschäftsführer vorgelegt werden. Die Rechnungsprüfer sind unbegrenzt wieder wählbar.

(5) Kommissionen und Delegationen
Die Gesellschaft kann durch die Hauptversammlung oder durch den Vorstand zur Lösung bestimmter Aufgaben Kommissionen einsetzen und Delegationen zur Vertretung auf wissenschaftlichen oder gesellschaftlichen Veranstaltungen entsenden. Die Mitglieder der Kommission werden auf eine bestimmte Zeit, maximal aber zwei Jahre, auf Vorschlag mit der einfachen Mehrheit der Mitgliederversammlung gewählt. Die Kommissionen und Delegationen organisieren ihre Arbeit kollegial nach eigenem Ermessen.

(6) Außerordentliche Versammlung der Gesellschaft
Auf schriftliches Verlangen von mindestens einem Drittel der Mitglieder der Gesellschaft ist der Vorstand verpflichtet, unter Angabe der Tagesordnung eine außerordentliche Mitgliederversammlung einzuberufen. Eine solche kann nötigenfalls auch durch die Mehrheit des Vorstandes beschlossen werden.

§ 6 Satzungsänderungen
Änderungen der Satzung können nur in der Mitgliederversammlung mit Zweidrittelmehrheit der anwesenden Mitglieder erfolgen, entsprechende Anträge sind - wie oben für Tagesordnungspunkte angegeben - frühzeitig einzureichen und werden der Einladung zur Mitgliederversammlung beigefügt. Bei der Bekanntgabe der Tagesordnung und Einladung der Mitglieder zur Versammlung genügt die Erwähnung des Tagesordnungspunktes "Satzungsänderung", ohne dass die zu beschließende Änderung im Einzelnen angegeben werden muss.

§ 7 Bestimmungen für die Auflösung der Gesellschaft
Die Auflösung der Gesellschaft kann als Tagesordnungspunkt Nummer 1 von mindestens 30 Mitgliedern oder der Mehrheit des Vorstandes beantragt werden. Wenn sich mehr als zwei Drittel der bei der Hauptversammlung abgegebenen Stimmen für eine Auflösung der Gesellschaft aussprechen, ist der Vorstand gehalten, binnen 14 Tagen alle registrierten Mitglieder innerhalb vier Wochen zu einer schriftlichen Entscheidung über die Auflösung der Gesellschaft aufzurufen. Sprechen sich mehr als zwei Drittel der schriftlich abgegebenen Mitgliedstimmen für die Auflösung des Vereins aus, so ist diese binnen 14 Tagen vom Vorstand festzustellen und dem Vereinsregister anzumelden. Die Zweckbestimmung des Vermögens regelt § 3 (4).

Nikon Young Scientist Award 2014

Hans Zempel

Background

In Alzheimer Disease (AD), the connection of the two major pathological hallmarks, deposition of the extracellular Amyloid-beta (Aβ) in the form of plaques, and aggregation of the intracellular protein Tau, is not well understood. Genetic evidence from AD and Down Syndrome (Trisomy 21), and models thereof, has suggested that aberrant production of Aβ is upstream of Tau aggregation, but also points to Tau as a critical effector in the pathological process (Bloom, 2014; Ittner and Gotz, 2010; Morris et al., 2011). Yet, the cascade of events leading from increased levels of Aβ to Tau-dependent toxicity remains a matter of debate, hindering rational developments of therapies for AD and related dementias.

Results

To elucidate the pathological cascade leading to neurodegeneration in AD, we established a system to model the effects of Aβ on Tau. In mature rodent primary neurons, Tau is present in several isoforms, is sorted into the axonal compartment and excluded from the somatodendritic compartment, similar to the adult human brain. To trigger AD-like pathological changes of Tau, we exposed primary neurons to a pre-aggregation form of Aβ (oligomeric Aβ), which is thought to be the toxic trigger in AD (Haass and Selkoe, 2007; Karran et al., 2011). We investigated changes of Tau and related cellular pathologies using biochemical methods, fluorescence microscopy including live cell imaging, and electron microscopy.

After exposure to oligomeric Aβ, Tau becomes mislocalized (missorted) into the somatodendritic compartment. This missorting of Tau correlates with a loss of synapses specifically in dendrites containing missorted Tau. This loss of synapses could link the mislocalization of Tau to the cognitive decline observed in AD patients. One of the key features discovered here is that in neurons showing missorted dendritic Tau, there is a dramatic loss of microtubules (Zempel and Mandelkow, 2012). As tracks of intracellular traffic, microtubules are of great importance, particularly for neurons whose extended processes require a highly efficient transport system based on microtubule-dependent motor proteins. Treatment of neurons with Aβ oligomers leads

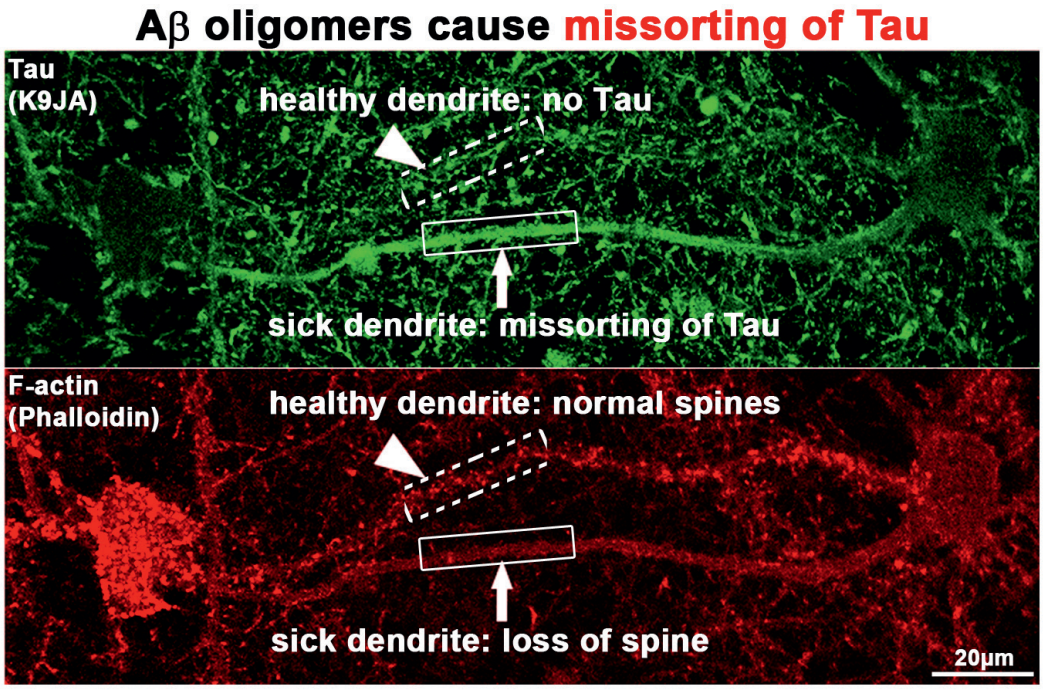

Figure 1. Aβ oligomers induce missorting of Tau into dendrites. Missorting of Tau correlates with loss of spines. Example of two nearby dendrites after treatment with Aβ oligomers of primary hippocampal neurons aged for 23 days *in vitro*. Tau is stained with a total Tau antibody (K9JA, green color). Spines are dendritic protrusions that contain high amounts of filamentous actin (f-actin; stained with phalloidin, red color) and are indicative of healthy synapses. The lower dendrite shows the presence of missorted Tau and loss of spines (box with solid outline, arrows), while the upper dendrite (dotted box, arrowheads) is free of Tau and contains numerous spines. Adapted from (Zempel et al., 2010).

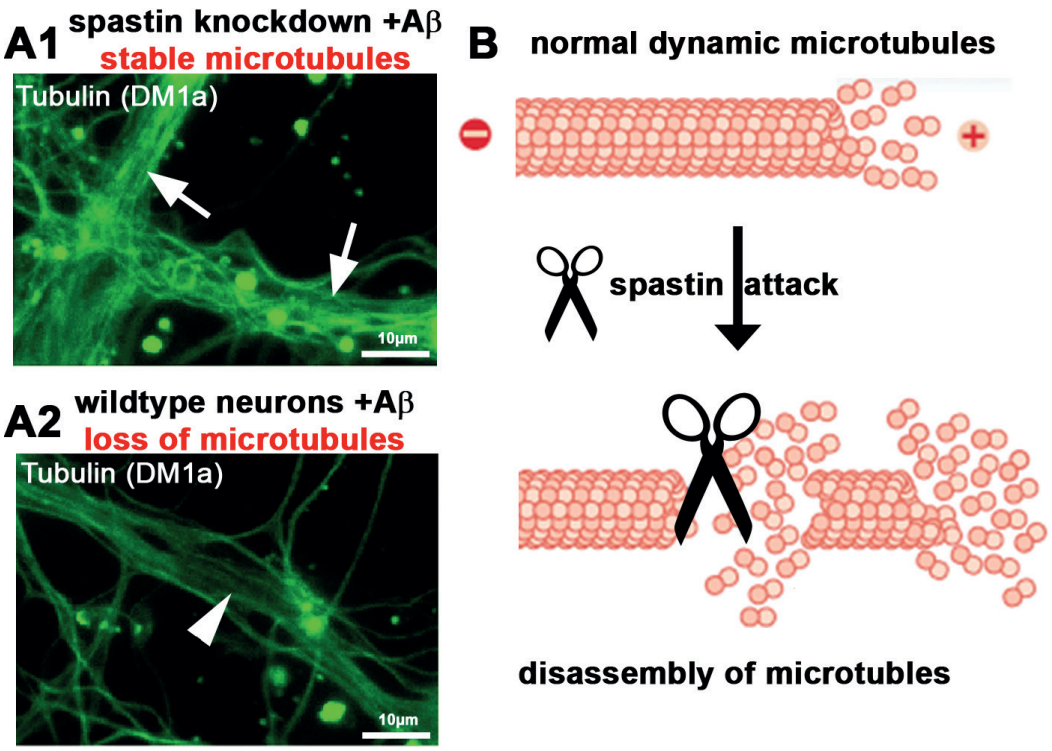

Figure 2. Spastin executes microtubule loss after invasion of dendrites by Tau and TTLL6.
Spastin was silenced using shRNA with a vector coexpressing RFP (5d) in primary hippocampal neurons aged 16 days in vitro, cells were then treated with 1µM Aβ for 3h. A: Silencing of spastin results in stable microtubules after Aβ treatment. Cells expressing shRNA (arrows, A1), show no microtubule reduction. Neighbouring untransfected cells with normal spastin levels show loss of microtubules in dendrites after Aβ exposure (A2, arrowheads).
B: Schematics of spastin mediated microtubule disassembly in dendrites in presence of missorted Tau.
Modified from (Jean and Baas, 2013; Zempel et al., 2013).

to missorting of Tau into dendrites, with subsequent decay of microtubules. Consequently, mitochondria, vesicles, and other cargo suffer from traffic jams in these dendrites. Neurofilaments that are usually transported along microtubules from the soma into the axon, become also mislocalized to the somatodendritic compartment, which indicates impaired transport. Remarkably, this loss of microtubules and synapses, aberrant mitochondria and neurofilament distribution depends on Tau, as in neurons derived from Tau knockout mice (TauKO) these pathological changes do not occur (Zempel et al., 2013).

In search for the causes of microtubule breakdown in dendrites, we found that the decay of microtubules is executed by spastin, a microtubule severing enzyme. Spastin in turn is recruited by polyglutamylation of microtubules, conferred by the enzyme TTLL6 (Tubulin-Tyrosin-Ligase-Like-6), a microtubule modifying ligase (Lacroix et al., 2010). TTLL6 catalyzes the addition of polyGlu residues within the C-terminal tail of α-tubulin, which in turn leads to the recruitment of the microtubule severing protein spastin and subsequent destruction of microtubules. TTLL6 is mislocalized from the soma into dendrites by a Tau dependent mechanism, involving an interaction of TTLL6 with Tau's N-terminal half (Zempel et al., 2013).

Tau is a microtubule associated protein (MAP) capable of binding to and stabilizing microtubules. Proper axonal sorting of Tau depends on intact Tau-microtubule interactions (Kanai and Hirokawa, 1995). In the pathological condition of Tau missorting, however, Tau is phosphorylated at a number of sites, including the KXGS-motifs in the repeat domain of Tau (Thies and Mandelkow, 2007; Zempel et al., 2010). These sites regulate the binding of Tau to microtubules and are targets of the Microtubule-Affinity-Regulating Kinase (MARK), which in mature neurons is most active in growth cones and the somatodendritic compartent, but not in axons (Timm et al., 2011). When phosphorylated at the KXGS-motifs, Tau cannot bind and stabilize microtubules, and can become missorted (Li et al., 2011). Phosphorylation of Tau at the KXGS-motifs is essential for the loss of microtubules, the loss of synapses mediated by Tau missorting, the translocalization of Tau into spines, and destruction of spines and synapses (another pathological hallmark of AD). Contrary to earlier views, the majority of missorted Tau in the soma and the dendrites does not originate by retrograde flow from the axon, but from newly synthesized protein that is not properly routed into the axon anymore (Zempel et al., 2013).

Significance and Implications for Therapeutic Approaches

A key result is the identification of a novel reaction cascade implicated in the missorting of the Tau protein in neurons affected by AD. The results reveal a multi-step pathway leading from the exposure of neurons to Aβ oligomers towards Tau-dependent synaptic deficits. We identified new contributors and functions in the pathological cascade of AD, centered around missorting of Tau into the somatodendritic compartment. This includes the decay of dendritic microtubules mediated by TTLL6 and spastin, leading to Tau-dependent loss of spines in a phosphorylation dependent manner. It provides an explanation for the well-

known reduction of microtubules in AD and might contribute to neurodegeneration in other Tau-dependent pathological states. The mechanistic description could lead to the development of new therapeutic strategies. For example, we showed that downregulation of spastin prevents loss of microtubules and missorting of Tau, two key events in Alzheimer pathology.

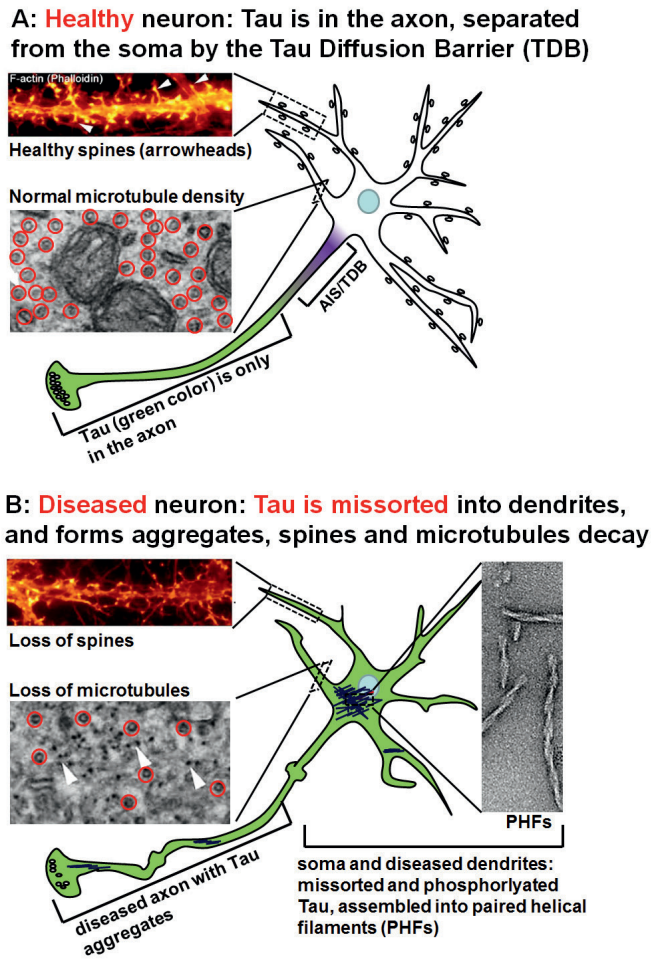

Figure 3. In Alzheimer Disease, Tau is missorted into the soma and the dendrites, causing loss of spines and microtubules.
A: In mature healthy neurons, the Tau diffusion barrier (TDB, depicted in magenta) within the axon initial segment (AIS) is established, Tau (green) is sorted into the axon. Dendrites display dense spines (upper panel, spine staining with phalloidin) and dense microtubules (lower panel: highlighted by red circles in cross sectioned dendrite imaged by electron microscopy (TEM)).
B: In diseased or stressed neurons (e.g. exposed to elevated Aβ as shown here, Tau mutations or traumatic injury), Tau (green) is missorted into the soma and the dendrites, axons become distorted and develop varicosities. Dendrites retract, lose their spines (upper panel), and microtubule density (lower panel, red circles) is reduced. Dendrites are invaded by neurofilaments (NF, indicated by white arrowheads). Missorted Tau in diseased neurons assembles into paired helical filaments (PHFs, panel to the right: TEM of aggregated recombinant human Tau).
Images are modified from (Mandelkow and Mandelkow, 2012; Zempel et al., 2013; Zempel et al., 2010).

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Hans Zempel studied Biochemistry at the Berlin Free University and obtained his MSc in the group of Ulrich Pison at the Charité, Berlin. He then moved to Japan to study the clinical part of medical school in Tokyo Medical and Dental University. For his PhD he then joined the laboratory of Eva-Maria and Eckhard Mandelkow at the Max-Planck-Unit for Structural Molecular Biology at DESY, Hamburg, and later at the German Center for Neurodegenerative Disease at CAESAR, Bonn, where he worked on the analysis of cell models of Alzheimer Disease and Frontotemporal Dementia.

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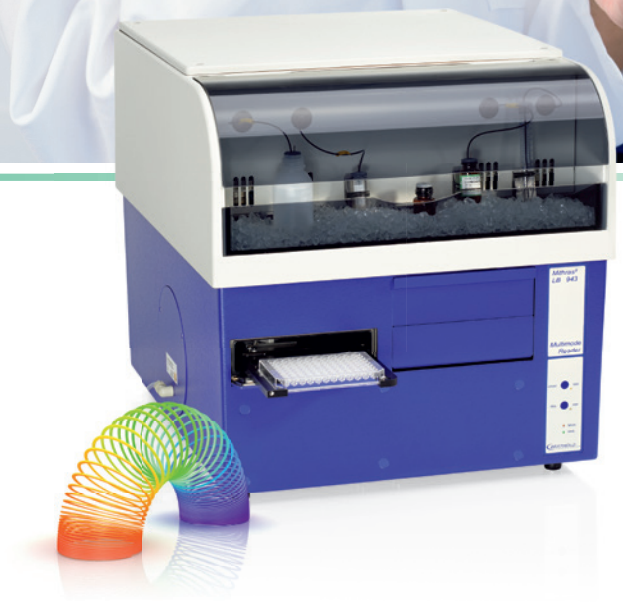

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Werner Risau Prize 2014
Coupling of angiogenesis and osteogenesis by a specific vessel subtype in bone

Anjali P. Kusumbe

In the mammalian skeletal system, growth of the vascular network is regulated by signals provided by chondrocytes and other bone cells, among which the vascular endothelial growth factor (VEGF) is studied best1. Conversely, blood vessels are thought to influence the osteogenic generation of new bone2. In addition to historic studies highlighting the close proximity of vascular and osteoblastic cells, potential roles of angiogenic blood vessel growth in fracture healing have been proposed3. It also has been suggested that alterations in the skeletal microvasculature might be linked to compromised hematopoiesis and osteogenesis in human subjects with primary osteoporosis or at old age4,5. However, direct evidence for such disease-causing or age-related alterations is lacking and our understanding of the normal organisation, functional specialization and precise function of the skeletal vasculature is incomplete. The precise overall organization of the skeletal vasculature has remained poorly understood because of technical difficulties associated with the processing of bone combined with the loss of crucial 3D information in thin tissue sections. Revised immunohistochemistry protocols have now allowed us to image the bone vasculature at high resolution.

In addition to revised immunofluorescence protocols, we visualised bone vessels with a combination of EC specific, tamoxifen-inducible Cdh5(PAC)-CreERT2 and Rosa26-mT/mG Cre reporter transgenic mice6,7. Imaging of the bone microvasculature with both approaches uncovered structurally distinct capillary subsets. Endothelial tubes in the metaphysis resembled straight columns that were interconnected by distal vessel loops or arches. In contrast, diaphyseal capillaries displayed the highly branched pattern characteristic for the sinusoidal vasculature of bone marrow (Fig. 1a, b). At the interface between metaphysis and diaphysis, the two vessel types were connected confirming that they were part of one continuous vascular bed (Fig. 1b).

The different vessel types were distinguishable by immunostaining with specific cell surface markers. Columnar tubes and arches in the metaphysis and endosteal endothelial cells (ECs) were strongly positive for CD31/PECAM1 and Endomucin (Emcn), while sinusoidal vessels in the diaphysis displayed only weak CD31 staining and slightly lower Emcn expression (Fig. 1c). A distinct CD31hi/Emcnhi endothelial subset could be also identified and separated from CD31lo/Emcnlo cells in single cell suspensions of long bones(Fig. 1d). Quantitative analysis by flow

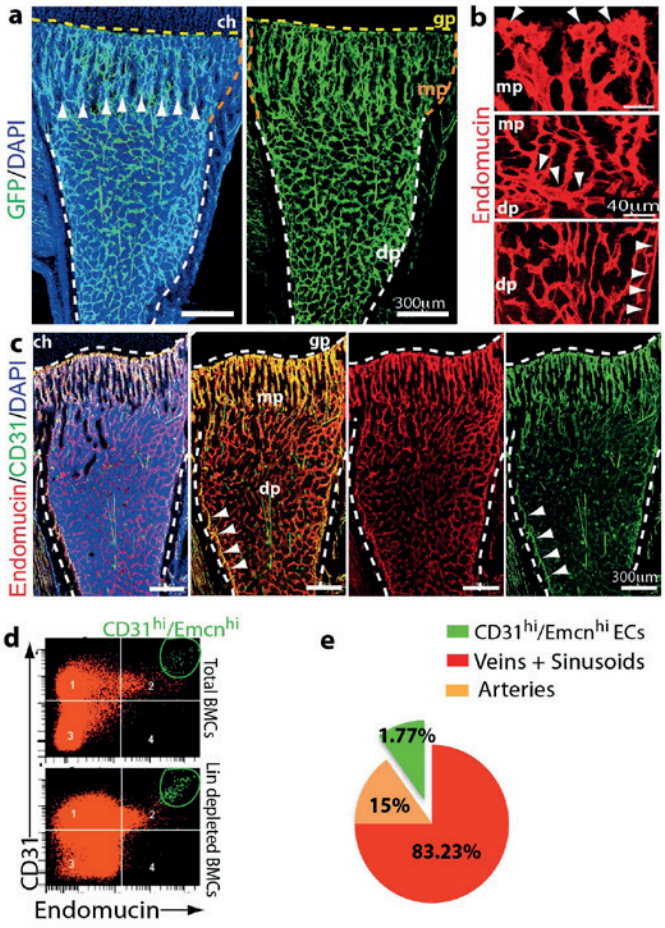

Figure 1. Identification of a distinct vessel subtype in murine bone. a, Representative tile scan confocal images of the GFP+ (green) endothelium in 4 week-old Cdh5(PAC)-CreERT2 x Rosa26-mT/mG double transgenic tibia. Nuclei, DAPI (blue). Yellow dotted line marks growth plate (gp). Note distinct organisation of microvessels in metaphysis (mp) and diaphysis (dp) as well as their connections (arrowheads). b, Maximum intensity projections of Endomucin+ (red) column vessels in metaphysis (mp, arrowheads mark distal protrusions) and highly branched sinusoids in diaphysis (dp). Central panel shows interconnections (arrowheads) between both vessel subtypes. c, Confocal tile scan of 4 week-old tibia images showing distinct patterns of CD31+ (green) and Endomucin+ (red) ECs. Nuclei, DAPI (blue). Strong CD31 and Endomucin signals mark capillaries in metaphysis (mp) and endosteum (arrwoheads). d, Representative flow cytometry dot plots showing the distinct CD31hi Endomucinhi EC subset in lineage (lin) depleted bone marrow cells. e, Pie chart showing the relative abundance of EC subtypes in 4 week-old long bone. CD31hi/Emcnhi cells represent 1.77±0.01% (mean ± s.d.m of 7 mice) of total ECs.

cytometry showed that CD31hi/Emcnhi cells represented only a small fraction of total ECs (Fig. 1e). The observations above established the existence of spatial and phenotypic heterogeneity in the bone endothelium. On the basis of these findings, we propose the following terminology for bone microvessels: type H for the small CD31hi/Emcnhi subset and type L for the CD31lo/Emcnlo sinusoidal vessels.

Immunostaining showed that Osterix+ osteoprogenitors, which will give rise to osteoblasts and osteocytes8, were selectively positioned around type H but not type L endothelium (Fig. 2a). Despite the low frequency (~1.77%) of type H endothelial cells (ECs) in the bone endothelial cell fraction and ~0.015% in total bone marrow (Fig. 1e), the majority of Runx2+ (82.63±1.8%), collagen 1α+ (74±3.3%) and Osterix+ cells (70±1.9%) were located directly adjacent to CD31hi/Emcnhi vessels (Fig. 2b,c).

To understand this distribution pattern of osteoblastic cells, the expression of mRNAs for secreted growth factors with known roles in osteoprogenitor survival and proliferation was analysed in freshly purified ECs from long bone. Pdgfa, Pdgfb, Tgf1, Tgf3, and Fgf1 transcripts were significantly higher expressed in type H relative to type L ECs (Fig. 2c). Accordingly, the two bone capillary EC subsets have specific expression profiles suggesting specialized functional properties.

It has been previously reported that osteoblast numbers declines during aging9. Our analysis of bone endothelium during ageing illustrated pronounced reduction of type H vessels, which were much more abundant in juvenile (4 week-old) mice compared to (11 week-old) adults, and were nearly absent in aged (70 week-old) animals (Fig. 2d). EC proliferation was high within the type H subpopulation in juvenile mice and declined rapidly in adulthood (Data not shown). In contrast, the rate of type L EC proliferation did not differ significantly between juvenile and older animals (Data not shown).

HIF-1α controls physiological and pathological neo-angiogenesis2. To investigate HIF-1α function in the postnatal bone endothelium, inducible EC-specific loss-of-function mice (Hif1aiΔEC) were generated by combining loxP-flanked Hif1a alleles (Hif1alox/lox)10 and Cdh5(PAC)-CreERT2 transgenics. Following tamoxifen administration from postnatal day (P) 10 to P14, analysis of Hif1aiΔEC mutants at P20 revealed striking vascular defects. Type H endothelium was strongly reduced in metaphysis and endosteum (Fig. 3a), the number of diaphyseal type L vessels and ECs was comparable to control littermates.

The von Hippel-Lindau (VHL) E3 ubiquitin protein ligase controls the stability and thereby biological activity of HIF-1α and other substrates11. Inducible, EC-specific targeting of the murine Vhl gene with the same strategy as described above for Hif1a led to pronounced expansion of type H endothelium and metaphyseal vessel columns and the surrounding osteoprogenitors (Fig. 3c,d). Osteoprogenitors were significantly reduced in Hif1aiΔEC samples (Fig. 3a,b).

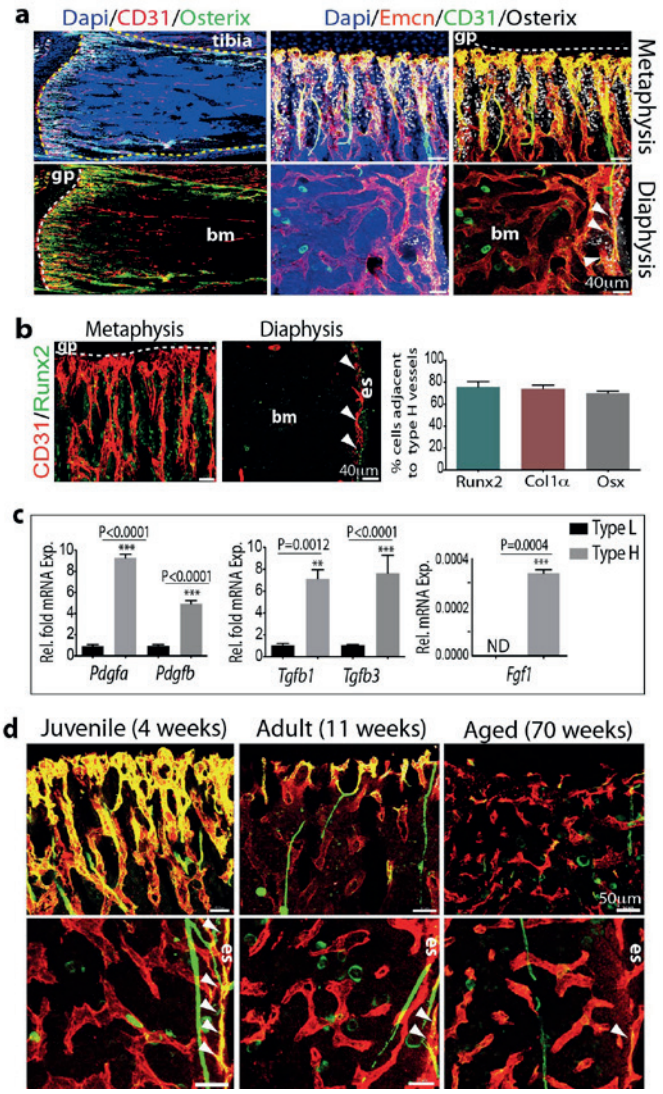

Figure 2. Association of osteoprogenitor cells with type H ECs and decline of type H ECs in aged bones.
a. Confocal images of 4 week-old tibia with the indicated immunostainings. Nuclei, DAPI (blue). Growth plate (gp) and bone marrow cavity (bm) are marked. Osterix+ are found in proximity to CD31hi/Emcnhi (type H) ECs in metaphysis and endosteum (arrowheads). b, Representative confocal images (left panel) of immunostained 4 week-old tibia showing association of Runx2+ osteoprogenitors (green) with CD31+ (red) vessels in metaphysis and endosteum (es). Minimum exposure was used to capture CD31 fluorescence to project only cells with high CD31 intensity. Quantitative analysis (right panel) of proximity (≤20μm) of Runx2+, Collagen1α+ (Col1α) and Osterix+ (Osx) to nearest type H vessel. Mean±s.e.m, n=5. c, qPCR analysis of growth factor expression (normalised to Actb) by CD31hi/Emcnhi ECs relative to CD31lo/Emcnlo ECs sorted from murine tibia. Data represent mean±s.e.m (n=4-6). P values, two-tailed unpaired t-test. d, Representative confocal images of CD31 (green) and Endomucin (red) immunostained tibia sections at 4, 11 and 70 weeks. Note age-dependent decline of CD31hi/Endomucinhi ECs in metaphysis (upper panel) and in endosteal (es, arrowheads) region in diaphysis (lower panel) of bone.

Prolyl-4-hydroxylases (PHDs) modify HIF-1α and thereby mark the protein for degradation under normoxic conditions. Accordingly, PHD inhibitors, such as deferoxamine mesylate (DFM), enhance HIF-1α stability and activity12. Next, we tested whether DFM promotes CD31hi/Emcnhi ECs, neo-angiogenesis and osteogenesis in aged animals. While long bones of aged, 64 to 70 week-old mice treated with vehicle control contained very few CD31hi/Emcnhi vessels, DFM administration led to substantial expansion of type H endothelium (Fig. 3e) and emergence of vessel-associated Osterix+ cells (Fig. 3f). Furthermore, μ-CT examination showed that 6 weeks of DFM treatment led to significantly increased bone mass (Fig. 3g,h). While the activity of DFM is not restricted to ECs and is likely to affect multiple cell populations, the findings above argue for crucial roles of endothelial HIF in controlling bone angiogenesis, type H vessel abundance, endothelial growth factor expression, and osteogenesis.

Above finding that capillaries in the skeletal system of mice can be subdivided into type H and type L endothelium on the basis of morphological, molecular and functional criteria should be hugely beneficial for future studies in basic and medical research. CD31hi/Emcnhi capillaries at the distal end of the arterial network in bone might represent the central building block of a metabolically specialised tissue environment with privileged access to oxygen and nutrients, which is likely to influence the growth potential and metabolism of other cell types. This is not only relevant for osteoblastic cells but potentially also for hematopoietic stem and progenitor cells, which preferentially home to the metaphysis after transplantation13.

We also propose that type H ECs mediate local growth of the vasculature and provide niche signals for perivascular osteoprogenitors. Type H vessel formation and the expression of potential angiocrine factors for osteoblastic cells are enhanced by HIF and by Notch signalling14. Thus, the abundance of CD31hi/Emcnhi ECs may be useful as diagnostic readout for the growth status of the bone vasculature and its pro-osteogenic capacity. Our results also indicate that specific molecular pathways can be used to boost type H vessel formation and osteogenesis. This might be of great importance for conditions involving compromised fracture healing or loss of bone mass. Ageing and post-menopausal estrogen deficiency are major risk factors for osteoporosis, and estrogen can promote angiogenesis15. Accordingly, decline of type H vessels and the concomitant reduction of osteoprogenitor cells could potentially offer a compelling explanation for the loss of bone mass during ageing and might enable therapeutic

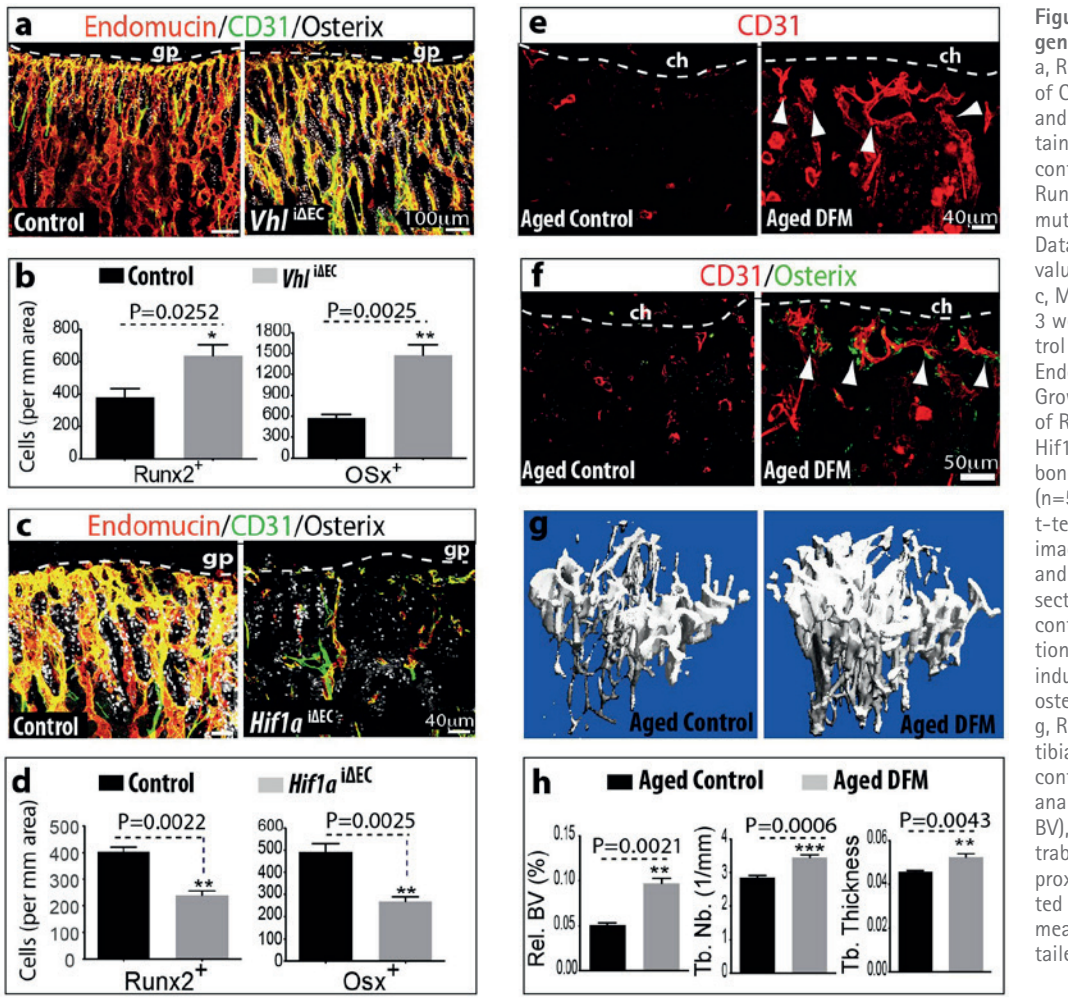

Figure 3. Type H ECs couple angiogenesis and osteogenesis.
a, Representative confocal images of CD31 (green), Endomucin (red) and Osterix (white) immunostained, 3 week-old VhliΔEC and control tibiae. b, Quantitation of Runx2+ and Osterix+ in VhliΔEC mutants and littermate controls. Data represent mean±s.e.m (n=5). P values, two-tailed unpaired t-test. c, Maximum intensity projections of 3 week-old Hif1aiΔEC and control tibia stained for CD31 (green), Endomucin (red) and Osterix (white). Growth plate, gp. d, Quantitation of Runx2+ and Osterix+ cells in Hif1aiΔEC mutant and control long bone. Data represent mean±s.e.m (n=5). P values, two-tailed unpaired t-test. e, f, Representative confocal images of CD31 (red, f) or CD31 and Osterix (green, g) stained tibia sections from aged DFM-treated and control mice. Low intensity projection shows only CD31hi cells. DFM induces CD31hi vessels and Osterix+ osteoprogenitors. Chondrocytes, ch. g, Representative μ-CT images of tibias from aged DFM-treated and control mice. h, Quantitative μ-CT analysis of relative bone volume (Rel. BV), trabecular number (Tb. Nb), and trabecular thickness (Tb. Thickness) in proximal tibia from aged DFM-treated and control mice. Data represent mean±s.e.m (n=5). P values, two-tailed unpaired t-test.

improvement of osteogenesis in elderly people.

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Coevolution of centrosomes and nuclear lamina

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In most eukaryotes microtubule organization is tightly associated with the nuclear envelope (NE). The nuclear envelope consists of an outer and inner membrane. The outer nuclear membrane (ONM) is directly connected both to the endoplasmic reticulum and, at the nuclear pore complexes (NPCs), to the inner nuclear membrane (INM). The perinuclear space separates the INM and ONM and is directly linked to the lumen of the ER. In metazoans, the INM is associated with the nuclear lamina mainly consisting of specialized intermediate filaments (IF) called lamins (Herrmann et al., 2007). The lamin-based nuclear lamina is indirectly connected with all cytoplasmic cytoskeletal elements through so-called LINC (linker of nucleoskeleton and cytoskeleton) complexes (Crisp et al., 2006). These complexes consist of a SUN-protein in the INM and a KASH-domain protein in the ONM, while the respective KASH and SUN domain interact within the perinuclear space. On the cytoplasmic side, individual KASH domain proteins interact directly or indirectly with actin filaments, IFs or the centrosome and, thus, with microtubules. At the nuclear face, Sun proteins bind to lamins and NPCs (Starr and Fridolfsson, 2010). In addition, lamins associate with chromatin and are involved in formation of lamina-associated heterochromatin domains. Thus, they also regulate gene expression and differentiation (Van Bortle and Corces, 2013). Due to the many binding activities of lamins, especially to cytoskeletal elements, the nucleus serves also as an abutment against mechanical forces for the whole cell (Dahl et al., 2004). While centrosomal structures are found in most eukaryotes except higher plants, until recently little was known about the molecular basis of the nuclear lamina in organisms other than metazoans. Meanwhile comparative cell biology and database analyses of centrosomal structures and the nuclear lamina have provided novel insights into early events in eukaryotic evolution (Fig. 1).

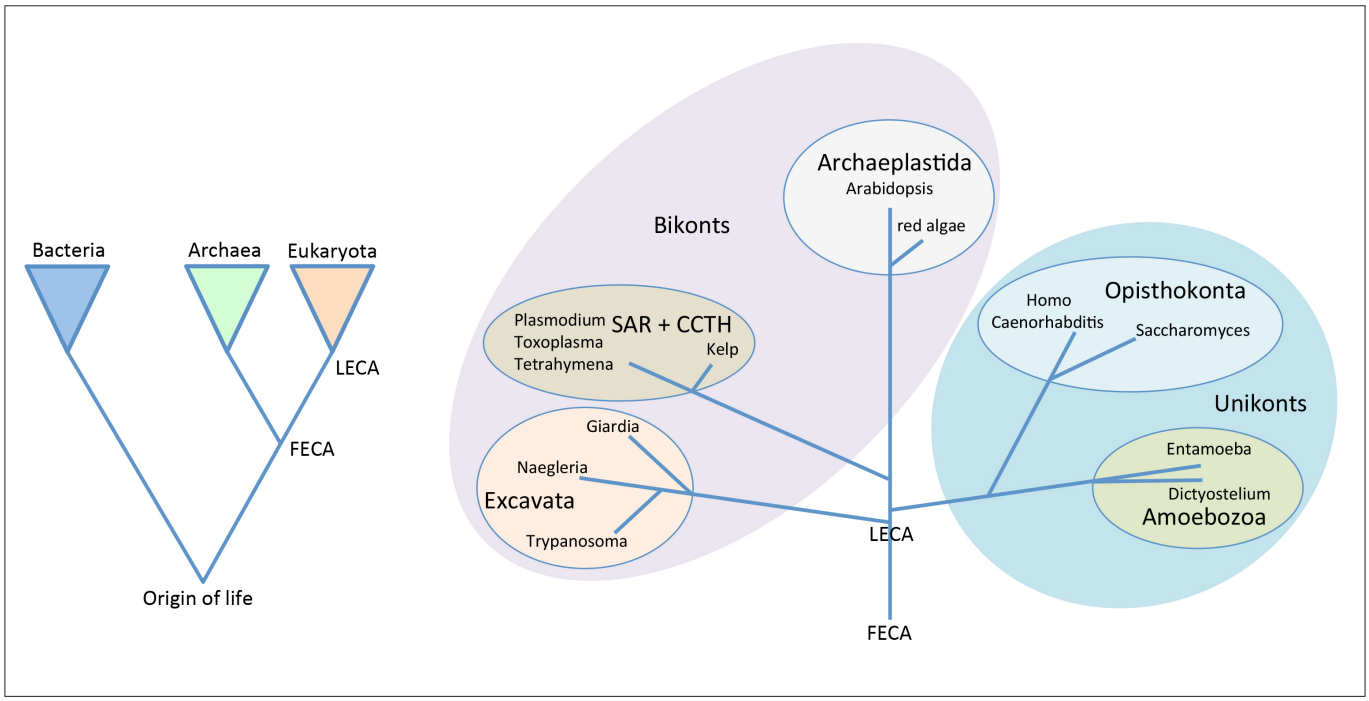

Figure 1.
Tree of life and phylogenetic tree of eukaryotes. (A) Three-domain-tree of life based on rRNA sequences (Pace, 2006). (B) Current view of eukaryotic evolution (Adl et al., 2012). FECA/LECA = first/last eukaryotic common ancestor; SAR-CCTH = Stramenophile, Alveolata, Rhizaria + Cryptophyta, Centrohelida, Telonemia, Haptophyta. Original figure corrected by the author (06/11/2014)

Centrosomes in different eukaryotes

Centrosomes are tiny non-membranous organelles harboring many different functions, most of which are somehow related to microtubule organization. They generally consist of a central, highly organized structure embedded in a matrix serving as a scaffold for microtubule nucleation complexes. If present, centrosomes serve as the main microtubule-organizing centers (MTOCs) and thus they are essential for the whole cell architecture in all organisms using the microtubule system to position their organelles to the right place. Since the major function of microtubule nucleation and organization is shared by all organisms containing an MTOC as a clearly discernable single organelle, I use the term "centrosome" for all these kinds of organelles whether they contain centrioles or not.

Mononucleated cells generally contain only one centrosome. It duplicates once in each cell cycle and contributes to organization of the mitotic spindle, whereby each of the duplicated centrosomes organizes microtubules at the two spindle poles. Centrosomes or at least their precursors have been invented very early in eukaryotic evolution since they are present in all eukaryotes except higher plants (see Fig. 1 for a current model of the eukaryotic tree of life). Eukaryotic evolution has engendered different types of centrosomes. The most common type is found among the opistokonts in animals, but also in unicellular bikonts and lower plants. It is characterized by centrioles consisting of a nine-fold symmetrical, cylindrical arrangement of short microtubules and associated proteins (Fig. 2A). In G1 the centrosome contains two centrioles and after duplication in S-phase, each centriole (now called mother centriole) has born one premature daughter centriole in a perpendicular orientation at its side. Thus, the centrioles are the duplicating unit of the centrosome. They are embedded in a so-called pericentriolar matrix (PCM) mainly consisting of scaffolding proteins that bind microtubule nucleation complexes and regulators of microtubule dynamics. The presence of centrioles is inevitably coupled to the existence of cilia or flagellae. This is because the mother centriole also serves as the basal body of the primary cilium, which has signaling and sensory functions (Kim and Dynlacht, 2013). Besides these non-motile primary cilia there are also cells using single or several cilia for cell locomotion or transport of fluids. Cells containing more than one cilium have means to amplify centriole number independently of canonical, cell cycle-synchronized centriole duplication.

Opposed to centriolar centrosomes are acentriolar centrosomes, sometimes also called nucleus associated bodies (NABs) or spindle pole bodies (SPBs) found among the unikonts in fungi and amoebozoans. These often possess layered core structures instead of centrioles and are best characterized in yeasts and Dictyostelium amoebae (Fig. 2B). In budding yeast the SPB mainly consists of a stack of three plaques and is permanently inserted into the nuclear envelope. It organizes a very simple intra-nuclear and extra-nuclear microtubule cytoskeleton, which is mainly required for nuclear positioning and chromosome segregation during mitosis. In the amoebozoan Dictyostelium, the centrosome (NAB) also contains a three-layered core structure, which in addition is surrounded by a corona reminiscent of a PCM (Fig. 2B). Although being attached to the nuclear envelope this centrosome is entirely located in the cytosol during interphase by contrast to the budding yeast SPB. The Dictyostelium centrosome enters the nuclear envelope only upon centrosome duplication during mitosis, in a manner reminiscent of the situation in fission yeast (Ding et al., 1997; Ueda et al., 1999). It organizes a radial microtubule cytoskeleton very similar to that of animal cells. However, due to their amoeboid locomotion and the absence of ciliated gametes these cells need no centrioles. Since their centrosomes seem to fulfill all known functions of centrosomes except cilia formation, this organism offers the possibility to use comparative biology to identify the proteins essential for all those centrosomal func-tions unrelated to cilia formation.

If different centrosome types of animals, yeasts and amoebozoa are compared, a surprisingly short list of general centrosomal components emerges. It includes the proteins of the γ-tubulin small complex (γ-TuSC; γ-tubulin, gamma-tubulin complex-associated proteins GCP2, GCP3) required for microtubule nucleation, EB1, TACC and XMAP215 for microtubule dynamics and stabilization, centrin, Cep192/SPD2, and centrosomin (Cnn) as scaffolding proteins, kinases from the polo, aurora, NIMA and Cdk family regulating duplication and spindle organization, and the dynein motor protein (Still et al., 2004; Carvalho-Santos et al., 2010; Carvalho-Santos et al., 2011) suggesting that these proteins comprise the most ancient centrosomal protein inventory. I have added Cnn, which was originally identified in Drosophila (Megraw et al., 1999; Lucas and Raff, 2007) to the list, since recent experimental and database analyses in Dictyostelium suggest that this protein is not only conserved in humans (CDK5Rap2; (Fong et al., 2008)) and fission yeast (mto1; (Samejima et al., 2005)) but also in Dictyostelium, where two putative orthologues, CP148 (Kuhnert et al., 2012) and DDB_G0282851 (http://dictybase.org), have been identified.

One of the intriguing questions is which of the extant centrosome structures represents the most ancient type. For many decades the amoeboid cell state was regarded as being ancestral and thus the acentriolar MTOCs in fungi and amoebozoans were thought to represent a primitive centrosome type. Meanwhile, comparative biology has taught us that most likely LECA (last eukaryotic common ancestor) already possessed one or two centrioles associated with a cilium, since centrioles are found in all major eukaryotic subgroups (Cavalier-Smith, 2010; Hodges et al., 2010) (Fig. 1). Thus, the absence of centrioles in higher plants, fungi and most amoebozoans is considered a result of secondary loss due to abandonment of locomotion by ciliary or flagellar beating in these organisms. In this light, the most initial purpose of centrosomes was to initiate formation of a cilium, whereby the centriole served as a basal body for nucleation and tethering of ciliar microtubules and determined the nine-fold symmetry of microtubule arrangements within the cilium. Indeed, ciliates for example employ centrioles only

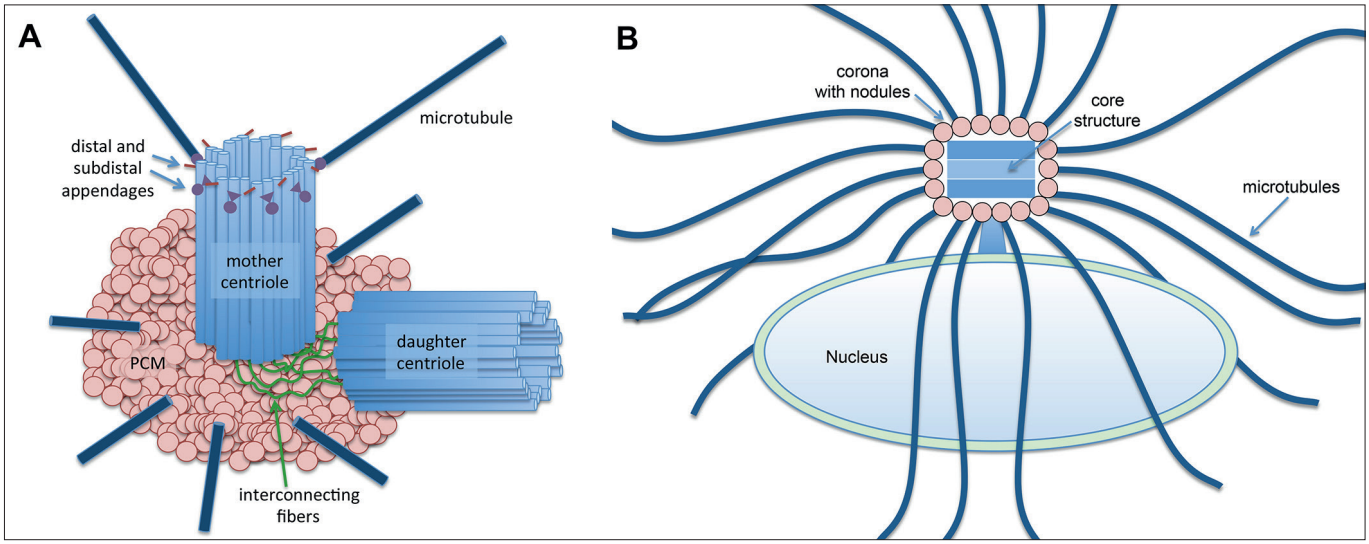

Figure 2.
Different centrosome types of animals and Dictyostelium. (A) Centriole-containing animal centrosome. (B) Acentriolar Dictyostelium centrosome. See text for further descriptions.

in their function as basal bodies for cilia formation, while their mitotic spindle poles are devoid of centrioles (Pearson and Winey, 2009). Thus, it is possible that centrioles were initially only passive passengers of spindle poles, whereby their association with the spindle ensured their equal distribution into the two daughter cells (Friedländer and Wahrman, 1970; Pickett-Heaps, 1971; Debec et al., 2010). This view is supported by the fact that centrioles are dispensable for mitotic spindle formation as it has been shown e.g. by laser ablation experiments vertebrate cells (Khodjakov et al., 2000; Khodjakov and Rieder, 2001) or RNAi-based depletion of the essential centriole component DSas-4 in Drosophila (Basto et al., 2006). However, in these experiments it became clear that centrioles are required for the formation of astral microtubules and cilia.

Cavalier-Smith proposed that the precursor of centrosomes in the prekaryote was a membrane and chromatin-associated microtubule nucleation center with a dual centromere/centrosome function (Cavalier-Smith, 2010). It has duplicated during eukaryotic evolution, with a centrosome staying attached to the plasma membrane associated with ciliary microtubules and microtubules building the pellicula and a microtubule nucleation center attached to endomembranes, which later built up the nuclear envelope. This may originally have led to an intranuclear microtubule nucleation center whose function was organization of the intranuclear spindle and an extranuclear centrosome stabilizing the cell surface through organization and attachment of pellicular microtubules and a motile cilium/flagellum, respectively. This split of labor of an intranuclear microtubule nucleation center and an extranuclear centrosome is realized for example in discicristata such as Euglena and trypanosomes (Ratcliffe, 1927). In this light the tight association of a nucleus-associated centrosome with clustered centromeres during the entire cell cycle as in fission yeast or the amoebozoan Dictyostelium would be a primitive attribute. Cavalier-Smith (Cavalier-Smith, 2010) also suggested that centrin played a key role in the assembly of the primitive microtubule nucleation complex at centromeres. Centrins belong to the calmodulin family of calcium-binding proteins and are ancient eukaryotic signature proteins (Hartman and Fedorov, 2002). Their function can generally be described as connectors between microtubular structures and membrane-bound structures. Thus, they are constituents of calcium-sensitive fibers connecting basal bodies to membranes and they play a role in centrosome duplication as for example in budding yeast, where Cdc31p (the yeast centrin) is a major constituent of the half bridge, which serves as the assembly platform for the nascent new SPB upon SPB duplication. There are several centrin isoforms (four in human cells) that in most species can be grouped into two subfamilies, one comprising human centrin-2-like proteins and one comprising yeast Cdc31p/centrin-3-like proteins. These subfamilies obviously arose very early in eukaryotic evolution since their members are present in both unikonts and bikonts (Bornens and Azimzadeh, 2007). Thus, loss of one subfamily is likely to be a secondary effect. Cavalier-Smith suggested that loss of centrin paralogues in yeasts occurred upon loss of centrioles/basal bodies with the attached rootlets and pellicle structures except one paralogue associated with the nuclear centrosome, where it is required for centrosome attachment to the nucleus and centrosome duplication (Cavalier-Smith, 2010). Yet, one cannot generalize a role of the centrin-3 like isoforms for centrosome duplication and nuclear functions, since e.g. in flies and nematodes centrin-3 is missing and centrin-2 is required for this job (Bornens and Azimzadeh, 2007). Furthermore, it is centrin-2 which serves a function in nucleotide excision repair after DNA damage as part of the xeroderma pigmentosum group C complex (XPC complex) within the nucleus (Araki et al., 2001; Dantas et al., 2012). The two existing centrin paralogues

(CenA and CenB) of the amoebozoan Dictyostelium cannot be assigned to either of the two subfamilies. However, both are predominantly associated with the nucleus, with CenA (originally called DdCrp) being concentrated at centromeres and to a lesser extent at the centrosome, and CenB inside the nucleus (Daunderer et al., 2001; Mana-Capelli et al., 2009). While the exact function of CenA is unknown, CenB is important for nuclear architecture and centrosome attachment to the nucleus. The latter function is also found in budding yeast, where Cdc31p together with its binding partner Sfi1p forms the half bridge, which tethers the nascent SPB to the nuclear envelope (Li et al., 2006).

Centrosomal LINCs to the nuclear lamina

The nuclear envelope is underlaid by a morphologically distinct lamina first described in an amoeba (Pappas, 1956). Yet, until recently, the nuclear lamina was characterized on a molecular level only in metazoans. Here its major components are type V intermediate filaments called lamins. They have a size of 60-80 kDa and consist of an approx. 370 aa coiled coil domain preceded by a short head domain and followed by a tail domain. The head domain possesses a CDK1 phosphorylation site at its end, and the tail domain includes a basic nuclear localization sequence, an Ig-fold domain and a CaaX-box at its end. The latter is the target for C-terminal prenylation, which is required for proper assembly of a lamin filament network at the NE. Recent studies have characterized nuclear lamina proteins in Trypanosoma (discicristates), higher plants and Dictyostelium (DuBois et al., 2012; Krüger et al., 2012; Ciska et al., 2013). While NMCP (nuclear matrix constituent proteins) of higher plants and NUP-1 in trypanosoma are clearly functionally analog to lamins, they do not appear to be evolutionary related to lamins or to each other. Although they are also long coiled coil proteins they show no sequence similarity to lamins. In contrast the NE81 protein found in four amoebozan species so far (Dictyostelium discoideum, D. falciparum, D. purpureum, Polysphondylium pallidum) is not only functionally analog to lamins, it also shows clear sequence similarity to lamins, similar regulation and post translational processing and should thus be considered a bona fide lamin (Batsios et al., 2012; Krüger et al., 2012). This pushed the evolutionary origin of lamins from their first appearance in metazoans back to the origin of unikonts or even earlier (Devos et al., 2014). It is rather likely that LECA possessed a nuclear lamina, however, it is unclear whether it was composed of NUP-1-like, NMCP-like or lamin-like proteins. LECA could have had a complex lamina composed of all three types of proteins and all except one protein family could have been lost during evolution in different eukaryotic groups. Alternatively, plants and discicristata may have replaced a lamin-based lamina by NUP-1 or NMCPs, respectively.

By contrast to the composition of the lamina itself, nuclear attachment of the centrosome to the lamina is an ancient feature, since it is found in almost all vegetative eukaryotic cells possessing a clearly discernible centrosomal organelle. This is in line with the hypothesis stated above that the precursor of the centrosome has split into a plasma membrane associated unit required for membrane architecture and locomotion and a nuclear unit involved in mitotic spindle organization (Cavalier-Smith, 2010). The idea that the latter had a dual centromere/centrosome function is supported by the fact that both structures are still very closely associated with each other during the entire cell cycle, as for example in fission yeast or Dictyostelium where centromeres are clustered close to the inner nuclear membrane and permanently associated with the SPB/centrosome at the cytoplasmic face of the nucleus (Kaller et al., 2006; King et al., 2008; Schulz et al., 2009). In Dictyostelium this linkage involves a conserved set of proteins that is now known for its role in centrosome attachment to the nucleus in all major eukaryotic groups. It includes Sun-family proteins, dynein and nuclear lamina proteins (Schulz et al., 2009). Sun proteins are widespread in all major eukaryotic groups. In most organisms they are concentrated at the inner nuclear membrane and interact with proteins of the KASH-family in the outer nuclear membrane forming a so-called LINC complex (Stewart-Hutchinson et al., 2008; Starr and Fridolfsson, 2010; Rothballer and Kutay, 2013). Different KASH proteins manage direct or indirect connection to all three cytoskeletal filament systems (microtubules, actin filaments, intermediate filaments). With regard to the centrosome they interact with dynein, which in turn helps to keep the centrosome close to the nucleus through its microtubule-binding and microtubule minus end-directed motor activity. Sun proteins are also linked to the nuclear lamina and this linkage is of crucial importance for proper centrosome/nucleus attachment (Schneider et al., 2011).

The linkage of Sun-proteins with nuclear lamina proteins has so far been proven in metazoans (Haque et al., 2006) and plants (Graumann, 2014) and, thus, it is very likely that this holds true for amoebozoans as well. Consistent with that the Dictyostelium lamin NE81 is also required for centrosome/nucleus attachment and interference with NE81 function caused phenotypes similar to Sun1 disruptions in this organism (Xiong et al., 2008; Schulz et al., 2009; Krüger et al., 2012). This suggests that lamins were ancestrally involved in centrosome attachment to the nucleus and have coevolved with Sun-proteins. In this light the absence of Sun-proteins in discicristata were in agreement with the substitution of lamins by NUP-1. Yet, coevolution is not strictly necessary, since plants have Sun-proteins but NMCPs instead of lamins. A requirement of KASH-domain proteins for centrosome/nucleus attachment is also not universal, since bona fide KASH domain proteins appear to be absent in Dictyostelidae. Yet, this condition may be caused by secondary loss, since the classical SUN/KASH-based LINC complexes are found in almost all branches of the tree of life except some amoebozoans and discicristates (Field et al., 2012). Especially the ubiquitous presence of Sun-proteins and their conserved capacity to bind directly to chromatin tempted Cavalier-Smith to propose that this binding activity was the key step in the original attachment of proto-ER membranes to heterochromatin during the formation of the nucleus in the first eukaryotic common ancestor (FECA) (Cavalier-Smith, 2010).

As the nuclear envelope is connected to all cytoskeletal filament systems, which in are turn linked to the plasma membrane, Cavalier-Smith has suggested that "lamins and the intermediate filament protein family as a whole have evolved in the ancestral animal (sponge) to increase the mechanical strength of the giant oocyte nucleus when the ancestor of animals evolved oogamy" and that "the mechanical robustness of the lamina may have made it essential for it to be reversibly disassembled at mitosis" (Cavalier-Smith, 2010). Thus he proposed that open mitosis has coevolved with the lamina in the ancestral animal. However, we now know that lamins (NE81) are already present in Dictyostelidae, i.e. amoebozoans. Since, Dictyostelium has a more closed type of mitosis, comparable to fungi such as Aspergillus (De Souza and Osmani, 2007), which clearly possess no lamins, these two issues are not likely to be interlinked. Dictyostelium most likely has solved the problem to soften the nuclear envelope in order to allow karyokinesis by disassembly of NE81 networks while disassembled NE81 still stays associated with the nuclear envelope through its prenyl anchor (Krüger et al., 2012).

Outlook

Further clarification of the evolution of the nuclear envelope and centrosomes will arise from further analyses of nuclear envelope proteins interacting with the nuclear lamina in various organisms and functional characterization of further centrosomal proteins in organisms with acentriolar centrosomes. Of special interest in this respect is the acellular slime mold Physarum polycephalum. It exists in different life forms, including an amoeboid form with centriole-containing centrosomes and an open mitosis and syncycial plasmodia with acentriolar MTOCs and a closed mitosis (Tanaka, 1973; Wright et al., 1988; Solnica Krezel et al., 1991). Theoretically this allows comparative cell biology within one organism especially if the ongoing, difficult Physarum genome project will be finished (Glöckner et al., 2008).

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SPECIAL INTEREST MEETING

Seminaris SeeHotel Potsdam, Germany

June 10 – 13, 2014

MOLECULAR INSIGHT INTO MUSCLE FUNCTION AND PROTEIN AGGREGATE MYOPATHIES

ORGANIZERS

Dieter O. Fürst, University of Bonn | Harald Herrmann, DKFZ Heidelberg
Rolf Schröder, University Hospital Erlangen

SPEAKERS CONFIRMED

Ueli Aebi, Basel
Giselle Bonne, Paris
Thomas Braun, Bad Nauheim
Folma Buss, Cambridge
Yassemi Capetanaki, Athens
Gloria Conover, College Station
Kristina Djinovi-Carugo, Vienna
Elisabeth Ehler, London
Peter Gunning, Sydney
Rudolf A. Kley, Bochum
Leslie Leinwand , Boulder
Wolfgang Linke, Bochum
Dietmar Manstein, Hannover
Katrin Marcus, Bochum
Jennifer E. Morgan, London
Anders Oldfors, Gothenburg
Gabriella Piazzesi, Sesto Fiorentino
Roy Quinlan, Durham
Matthias Rief, München
Wolfgang Rottbauer, Ulm
Marco Sandri, Padova
Omar Skalli, Memphis
Theresia Stradal, Münster
Thomas Voit, Paris
Gerhard Wiche, Vienna

MEETING ORGANIZATION

Annika Bleckert, Legal Organizer (PCO) – MCI Deutschland GmbH
musclepam@mci-group.com

Abstract Submission Deadline: February 28, 2014
Registration Deadline: April 30, 2014
www.musclepam2014.de

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Molecular Insight into Muscle Function and Protein Aggregate Myopathies

10 – 13 July 2014, Potsdam

Organizers: Prof. Dr. Dieter O. Fürst, Institute for Cell Biology, University of Bonn
Prof. Dr. Harald Herrmann, Deutsches Krebsforschungszentrum Heidelberg
Prof. Dr. Rolf Schröder, University Hospital, Erlangen

Date: Start: 10.06.2014, 15:00 Uhr; End: 13.06.2014, 13:00 Uhr

Venue: Seminaris SeeHotel, Potsdam

Tuesday, June 10th, 2014

17:00 – 19:00 Opening Lectures

Keynote Lecture 1: Leslie Leinwand (Boulder, USA): Molecular basis of inherited cardiomyopathies
Keynote Lecture 2: Peter Gunning (Sydney, Australia): Diversity of the actin cytoskeleton and its implications for tropomyosin based muscle disease

20:00 *Dinner and get together*

Wednesday, June 11th, 2014

Session 1: Intermediate Filaments; Chair: Harald Herrmann (Heidelberg, Germany)

08:30 Gisèle Bonne (Paris, France): Lamin A/C myopathies: molecular insight from cell and animal models

09:00 Omar Skalli (Memphis, USA): The role of synemin in normal and diseased muscle

09:30 Yassemi Capetanaki (Athens, Greece): Desmin as a major player in Heart Failure

10:00 Rolf Schröder (Erlangen, Germany): The downstream pathology of point-mutated desmin: from aberrant localization and turnover of intermediate filaments over decreased biomechanical stability of muscle fibers to myopathy and cardiomyopathy

talks selected from the abstracts

10:30 Ralf Bauer (Heidelberg, Germany): AAV-mediated cardiac transfer of the desmin cDNA ameliorates progression of cardiomyopathy in desmin-deficient mice

10:45 Hendrik Milting (Bad Oeynhausen, Germany): No evidence for lysosomal degradation of mutant desmin causing severe cardiomyopathies and cytosolic protein aggregates

10:30 Coffee and Discussion

Session 2: IF-Associated Proteins; Chair: Gisèle Bonne (Paris, France)

11:30 Gerhard Wiche (Vienna, Austria): Plectinopathies: from cell and animals models to potential treatments

12:00 Gloria Conover (Galveston, USA): Nebulin – getting it clear with desmin

talks selected from Abstracts

12:30 Petra Zugschwerdt (Heidelberg, Germany): How are intermediate filaments integrated into cellular structures by synemin and nestin?

12:45 Robert Stehle (Cologne, Germany): Biomechanical characterization of plectindeficient skinned fibres and myofibrils from mouse psoas muscle

13:00 Lunch Break

14:00–15:30 Poster Session I with Coffee and Discussion

Session 3: Protein quality control; Chair: Rolf Schröder (Erlangen, Germany)

15:30 Roy Quinlan (Durham, UK): The functional role of alphaB-crystallin for muscle maintenance

16:00 Wolfgang Rottbauer (Ulm, Germany): VCP & VCP binding partners: lessons from functional genomics in zebrafish

16:30 Marco Sandri (Padova, Italy): Regulation of the autophagic system in striated muscle wasting

17:00 Jörg Höhfeld (Bonn, Germany): BAG3-mediated mechanotransduction is essential for muscle maintenance

17:30 Norbert Frey (Kiel, Germany): Novel pathways in protein degradation

18:00 Christoph Clemen (Cologne, Germany): VCP – PSMF1 interaction: a switching system to regulate 26S proteasome activity

18:30 Dinner

20:00 After-Dinner-Talk; Ueli Aebi (Basel, Switzerland): Actin: from Structural Plasticity to Functional Diversity

Thursday, June 12th, 2014

Session 4: Motor proteins; Chair: Gabriele Pfitzer (Cologne, Germany)

08:30	Jennifer Morgan (London, UK): Mouse muscle stem cells: Different satellite cells?
09:00	Folma Buss (Cambridge, UK): The role of myosins in autophagy
09:30	Theresia Stradal (Braunschweig, Germany): Molecular regulation of actin-based cellular protrusions
10:00	Dietmar Manstein (Hannover, Germany): From molecular structure to the pathophysiology of motor protein-linked diseases
10:30	Gabriella Piazzesi (Florence, Italy): In situ studies of muscle myosin II mechanics and structural dynamics
11:00	**Coffee and Discussion**

Session 5: Titin; Chair: Kristina Djinovič-Carugo (Vienna, Austria)

11:30	Wolfgang Linke (Bochum, Germany): Titin and its role in cell signalling
12:00	Anders Oldfors (Gothenburg, Sweden): Clinic, genetic and pathiophysiological aspects of HMERF
12:30	Michael Gotthardt (Berlin, Germany): Following titin along the myofibril – a visual and omics approach to sarcomere biology
13:00	**Lunch Break**

14:00 – 15:30 Poster Session II with Coffee and Discussion

Session 6: Filamin C; Chair: Dieter Fürst (Bonn, Germany)

15:30	Rudolf Kley (Bochum, Germany): Proteomic profiles in myofibrillar myopathies talks selected from Abstracts
16:00	Yvonne Leber (Bonn, Germany): Filamin C is a highly dynamic protein involved in fast repair of myofibrillar microdamage
16:15	Sibylle Molt (Bonn, Germany): Aciculin interacts with filamin C and Xin and is essential for myofibril assembly, remodeling and maintenance
16:30	Frédéric Chevessier-Tünnesen (Erlangen, Germany) W2710X filamin C knock-in mice: a physiological model for filamin C-related myofibrillar myopathies
16:45	Andreas Unger (Bochum, Germany): Intracellular translocation of chaperones/cochaperones in human skeletal muscle myopathies: an immunoelectron microscopical study
17:00	**Coffee and Discussion**

17:30 – 18:30 Highlights from the Posters; Chair: Harald Herrmann (Heidelberg, Germany)

17:30	Stamatis Papathanasiou (Athens, Greece): Epithelial Cytoskeleton in Cardiac Muscle: A Novel Compensatory Mechanism
17:45	Oliver Friedrich (Erlangen-Nürnberg, Germany): 'The bad Architect' – The structural basis of progressive weakness revealed by multiphoton microscopy in degenerative myopathies associated with cellular remodeling or protein aggregates.
18.00	Sri Krishna Raja Kiran Kalepu (Ulm, Germany): Adult Human Skeletal Muscle WNTSignalling Pathway and its Associated Molecules in Ageing and Disease.
18:15	Euripides De Almeida Ribeiro (Vienna, Austria): Structural basis of human Z-disk – actinin regulation by PIP2.

18:30 – 19:30 Matthias Rief (Munich, Germany): Mechanics of single molecules

20:00 *Social event (Wine tasting)*

Friday, June 13th, 2014

08:30 – 09:30 Plenary talk; Thomas Braun (Bad Nauheim, Germany): Regenerative capacity of striated muscle tissue

Session 7: Advanced Experimental Approaches; Chair: Jennifer Morgan (London, UK)

09:30	Elisabeth Ehler (London, UK): A central role of the intercalated disc for cardiomyocyte growth
10:00	Katrin Marcus (Bochum, Germany): Quantitative methods in proteomics
10:00	**Coffee and Discussion**
11:00	Bettina Warscheid (Freiburg, Germany): Dissecting Signaling Processes In and Out of the Z-Disc by Functional Proteomics
11:30	Kristina Djinovič-Carugo (Vienna, Austria): Lessons from integrative structural biology

12:00 – 13:00: Plenary talks; Conrad Weihl (St. Louis, USA): Function and dysfunction of autophagy in protein aggregate myopathies

Departure

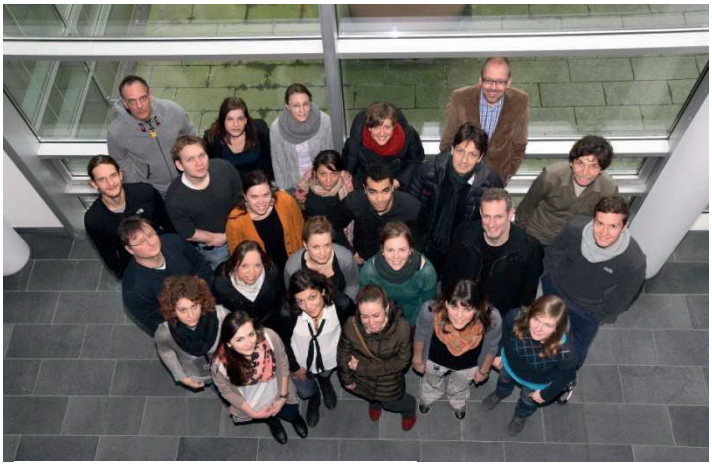
Research Training Group 1459

The interdisciplinary Research Training Group (GRK) 1459 “Sorting and Interactions between Proteins of Subcellular Compartments” was founded in 2008 and consists of scientists from the University Medical Center Hamburg-Eppendorf, the Institute of Biochemistry at the University Kiel, and the Bernhard-Nocht-Institute for Tropical Medicine in Hamburg. Eleven PhD students and five MD students are funded by the Deutsche Forschungsgemeinschaft (DFG). The general topic of the Research Training Group is sorting and transport of selected proteins within the Golgi apparatus and endosomal compartments. Missorted proteins may lead to loss of function in their target organelles, which may affect the wellbeing of the cell and the organism as a whole. By focussing on selected model proteins, basic mechanisms of the biogenesis of intracellular compartments as well as the balance of membrane transport between organelles and the interplay between cytosolic and membrane proteins will be investigated. The majority of projects address sorting and transport processes under pathological conditions in cells derived from patients or mouse models of human diseases or cells infected by bacteria or in parasite cells.

The PhD and MD students go through a three year curriculum of academic as well as non-academic courses in molecular and cellular biology, biochemistry, infectiology, microbiology, and molecular biomedicine. The Research Training Group offers a continuous educational program including monthly seminars with leading international guest scientist (among others J. Rothman, S. Schmid, J. Nunnari, J. Bonifacino, K. Simons, A. Helenius, T. Rapoport, R. Jahn, G. Warren, D. Owen, and S. Pfeffer), lectures on “Molecular Cell Biology of Subcellular Compartments”, project-specific practical courses, annual retreat with external reviewers, a three month scientific cooperative stay abroad and the organization of an international symposium every two years.

This year the PhD students are preparing the 3rd International Symposium on “Protein Trafficking in Health and Disease” (www.trafficking-symposium2014.de). The meeting will take place from **September 10th to 12th 2014** in Hamburg, Germany.

The graduates of the GRK 1459 invite PhD students and young postdocs from all over Europe to come to Hamburg, meet leading scientists in the field of protein trafficking, establish contacts and present and discuss their own projects.



GRK Members, February 2014

Life at the Edge:
The Nuclear Envelope in Nucleocytoplasmic Transport, Genome Organization and Cell Cycle Regulation

International Meeting of the German Society for Cell Biology (DGZ)

Potsdam, July 23-26, 2014
Seminaris Seehotel Potsdam

ORGANIZERS

Birthe Fahrenkrog
Université Libre de Bruxelles

Ralph Kehlenbach
Universität Göttingen

CONFIRMED SPEAKERS

Wolfram Antonin, Tübingen
Peter Askjaer, Sevilla
Martin Beck, Heidelberg
Günter Blobel, New York
Yuh Min Chook, Dallas
Valérie Doye, Paris
Roland Foisner, Wien
Susan Gasser, Basel
Pierre-Emmanuel Gleizes, Toulouse
Dirk Görlich, Göttingen
Ed Hurt, Heidelberg
Naoko Imamoto, Saitama
Ulrich Kubitscheck, Bonn
Ulrike Kutay, Zürich
Mike Rout, New York
Thomas Schwartz, Boston
Irina Solovei, München
Bas van Steensel, Amsterdam
Susan Wente, Nashville

additional speakers will be selected from the abstracts

REGISTRATION
deadline 2 June 2014
ABSTRACT submission
deadline 2 May 2014

www.zellbiologie.de

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photography by Ralph Gräf, Potsdam

Life at the Edge: The Nuclear Envelope in Nucleo-cytoplasmic Transport, Genome Organization and Cell Cycle Regulation

23 – 26 July, 2014, Potsdam

Molecular exchange between the nucleus and the cytoplasm is mediated by nuclear pore complexes (NPCs), which are embedded in the nuclear envelope (NE). Proteins of the NPCs and the NE play important roles in genome organization and cell cycle regulation, underlining their importance for cellular and organismal health. We are only beginning to understand the complexity in the interplay between the NE, the genome and the cell cycle. The meeting will start with a keynote EMBO lecture given by Günter Blobel. The following sessions will focus on the structural analysis of NE proteins, NE-genome interactions, NE assembly and disassembly, aspects of nucleocytoplasmic transport and the link between NE proteins and cell cycle regulation. A poster session as well as several short talks selected from the abstracts will provide ample opportunities for in-depth discussions.

Dicty 2014

Annual International Dictyostelium Conference

August 3rd - August 7th

Potsdam, Germany

Further information and registration at www.dicty2014.de

Organizers: Ralph Gräf, Carsten Beta, Sascha Thewes

DGZ

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FUTURE MEETINGS

Annual international Dictyostelium conference – Dicty 2014

from August 3rd – 7th, 2014, Potsdam,

Dictyostelium is a well known model organism, which was the basis for numerous pioneering papers in cell biology. The Dictyostelium conference is the annual highlight for Dictyostelium researchers from all over the world. Its tradition reaches back to 1969 where the first meeting was held in La Jolla (USA). Since 1981 it is an annual meeting, each year organized by different researchers from USA, Japan, Australia and Europe in their individual home countries. This year the meeting is organized by Ralph Gräf, Carsten Beta (both University of Potsdam) and Sascha Thewes (Freie Universität Berlin) and it will be held under the auspices of the DGZ. These meetings traditionally have no invited speakers, but their inspiring, collaborative and interdisciplinary atmosphere always attracts also the frontmost researchers of the field to present their newest, often unpublished data. Just register to the meeting, if you are interested in the fields of chemotaxis, development, cytoskeleton, membrane trafficking, gene regulation, pathogen interactions, disease models and evolution. The price is all-inclusive and you'll also enjoy the beautiful vicinity of the Lake Templin and Potsdam with its UNESCO world heritage. More information and registration at www.dicty2014.de

ASCB-IFCB Joint meeting in Philadelphia

USA – December 6–10, 2014

Dear Society Member,

Our meeting this year will be held jointly with the American Society of Cell Biology, from December 6-10, in Philadelphia, Pennsylvania, USA. As the premier meeting for biomedical research worldwide, ASCB/offers a great opportunity for you to learn about the latest research in your field and network with leaders and peers in cell biology, biophysics, stem cells, and genomics, to name a few. This meeting is a wonderful chance for you to present your science and to meet in person many of the prominent names you know from the literature. It will also be a great occasion to promote cell biology as a world science.

To encourage you to present your science in Philadelphia, the ASCB is offering 50% off ASCB membership to IFCB members. This qualifies you for the ASCB-member rates for registration and abstract submission. ASCB also is offering special travel awards to attendees from developing nations. Every constituent society in the IFCB has been invited to host an open information session in Philadelphia where members can highlight training, visiting fellowship, and funding opportunities in their home country.

As one attendee at the 2013 ASCB Annual Meeting noted, "The meeting is a perfect combination of high-profile talks, networking opportunities, professional development, teaching resources, and FUN!" We hope you will be able to join us in Philadelphia. To learn more about the 2014 ASCB/IFCB Meeting and obtain a discount code to attend, please go to http://www.ascb.org/2014meeting/ifcb.

A reminder: if you need a visa for the U.S., you should register for the 2014 ASCB/IFCB by August 5 in order to receive a formal letter of invitation so you can schedule your visa interview in a timely manner.

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