



RESEARCH CONFERENCES

ESF-EMBO Symposium

Cell Polarity and Membrane Traffic

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava) • Spain
23 -28 May 2009

Chair: **Anne Spang**, Biozentrum University of Basel, CH
Co-Chair: **Ian G. Macara**, University of Virginia, US

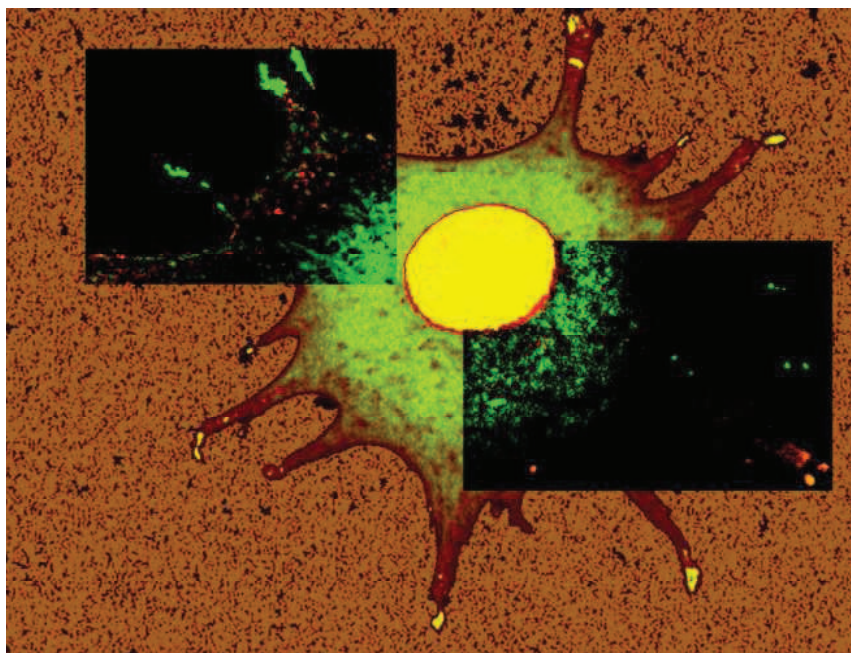
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Highlights & Scientific Report



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Conference Highlights

Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)

About 150 scientists from Europe, the US and Japan gathered at the Costa Brava to bring together the historically separated fields of polarity and intracellular transport. Cell polarity establishment and maintenance was in the past mostly studied in the context of development, while intracellular transport was associated mainly with biochemistry. With the introduction of new, fast and high resolution imaging techniques, transport and polarity related processes could be imaged in real time. Using these imaging techniques researchers from both fields came to the realization that no polarity is established without membrane traffic and that a number of molecules transported in the secretory and endocytic pathways play an essential role to generate polarity. This is most obvious at the plasma membrane, where polarity signaling pathways must be initiated and tightly controlled. One prominent way to control the signaling is by limiting the number of receptors at the plasma membrane, which is achieved by coupled endo- and exocytosis. The roles of the exocyst, a complex, which promotes fusion of transport containers at the plasma membrane, and of the Rab GTPases, Rab5 and Rab11, one essential for endocytosis and the other for recycling material to the plasma membrane were widely discussed. Endocytosis as well as membrane and protein delivery to the plasma membrane depends on the cytoskeleton. Misregulation of the cytoskeleton or interfering with the function of molecular motors has hence a tremendous effect on the maintenance of polarity. Loss of polarity in an epithelium can lead to tumor formation. The identification of members of the endocytic machinery as tumor suppressors underscores the importance membrane transport in tumorigenesis.

Not only proteins are asymmetrically distributed, a large number of mRNAs are not just stochastically localized in cell, but rather transported to specific sites. These mRNAs may encode transcriptional repressors in dividing cells to give one daughter cell a different cell fate over the other daughter cell. In other instances e.g. in the *Drosophila* egg chamber, mRNA is transported from nurse cells into the oocyte and anchored at specific locales. Similarly to proteins, mRNA may have address labels (in most instances more complicated ones) that allow the correct targeting and the timely expression of the protein encoded by the mRNA.

Moreover, novel imaging methods such as STED and light sheet based microscopy were discussed. With the increasing repertoire of imaging techniques, higher resolution and faster image collection is possible on one hand, but also less invasive and destructive methods become available, both of which will allow to produce high quality dataset and advance our understanding of membrane transport in polarity establishment.

Finally, a large variety of model systems were used in the studies presented at the conference. The beauty is that despite all of this diversity, the basic principles seem to be conserved as the same players popped up in different systems.



I hereby authorize ESF – and the conference partners to use the information contained in the above section on 'Conference Highlights' in their communication on the scheme.

Scientific Report

Executive Summary

(2 pages max)

The goal of the ESF/EMBO Conference on Cell Polarity and Membrane Traffic aimed to bring together people from different fields and to initiate discussions and collaborations. This goal was met beyond our expectations! The meeting was very vibrant and intense discussion took place after each oral presentation. Also the discussions at the posters went on way beyond the official poster session time. Given the number of outstanding posters, the poster prize committee had a hard time to select the winners. The organizers wish to thank again the committee for their efforts! Three poster prizes were awarded worth 1x 250€ and 2x 100 € complemented by annual subscriptions to Nature Cell Biology, EMBO reports and Trends in Cell Biology. For the scientific report please go to the section below. In addition to the 27 invited presentation, 10 posters were selected for oral presentation. Thus offering the young researchers a very good opportunity to talk about their research in front of the plenum.

About 180 researchers applied to the Conference. At the end about 150 scientists participated in the ESF/EMBO Conference on Cell Polarity and Membrane Traffic. Thanks to the support from ESF, EMBO, EMBO-YIP, Roche, Biochemical J., Zeiss, Microsynth, AHF and the Catalunya Region, about 36% of the conference budget was spent to pay the registration/travel for young researchers. In total 36 allowances were allocated. Moreover, we could offer an open bar every night after the sessions, which fostered the interactions between the conference participants. The venue was much appreciated by the attendees. The location at the sea is spectacular, and we had fantastic weather. The helpful staff even installed a TV cable in the conference room so that the participants could follow the Football European Champions League final. Both transits to and from the venue were well organized and went very smoothly.

The organization on-site as well as the before the meeting went very smoothly and was very efficient thanks to the great efforts by Jean Kelly, our conference officer. It has been a delight to interact with her.

Over all, we think that we had an excellent meeting which greatly stimulated discussions and research effort in the future.

Scientific Content of the Conference

(1 page min.)

- Summary of the conference sessions focusing on the scientific highlights
- Assessment of the results and their potential impact on future research or applications

The conference was like a firework. The stage was set by our keynote speaker Yuh Nung Jan, a Howard Hughes Investigator from the University of California, San Francisco. Dr. Jan is one of the world's most eminent developmental biologists, who has made many important contributions to our understanding of neuronal development. He effortlessly covered the topics from the secretory pathway to the regulation of dendritic scaling in *Drosophila* through miRNA.

The first day was mostly devoted to membrane traffic. Kai Simons surprised the audience by the amount of different lipid species present in the cell, and by the accuracy these different species can be measured and assigned various organelles and transport containers. Catherine Rabouille presented a novel unconventional secretion pathway in which the mRNAs of the core constituents of the pathway are localized to a specific site and then translated to assist the secretion of integrins. The complexity of RNA localization was reviewed in an interesting talk by Anne Ephrussi. A re-occurring theme was the role of the exocyst and the small GTPase Rab11 on the secretion side and components of the endocytic route in polarity maintenance and cell integrity. The exocyst

is a complex at the plasma membrane, which is essential for vesicle function at the plasma membrane and hence also essential for secretion. Keith Mostov provided interesting insights into the links between cell polarity proteins and the vesicle traffic machinery. Philippe Chavrier reported that cell invasion is triggered by the secretion of metalloprotease MT1, which degrades the extracellular matrix. David Bilder reported that mutations in a component of the ESCRT complex, which sorts proteins into the degradation pathway or Rab5 and other early endocytosis factors cause neoplasia, most likely through upregulation of Crumbs, which is an apical domain determinant. Jordi Casanova and Yohanns Bellaiche discussed the role of another small GTPase of the Rab family, Rab11 and the exocyst in tracheal lumen formation and E-cadherin localization in epithelial cells, respectively. Whereas Pilar Perez and Patrick Brennwald explored the relationship between exocyst components and Cdc42 and Rho3, two GTPases required for polarity establishment and maintenance in different systems.

We also took into account one of the reviewer's suggestion, to include a session on new imaging methods and computational biology. This was an interesting and very much appreciated session with talks on light-sheet microscopy and on super-resolution STED microscopy by Ernst Stelzer and the Hell lab, respectively, and mathematical modeling of gradient formation and membrane traffic covered by Hans Meinhardt and Matthias Weiss. The theme of this more 'technical' session was continued with a more 'applied' talk by Gaudenz Danuser on speckle microscopy and the coupling of actin dynamics to endocytosis.

The conference highlighted many links between vesicle transport and cell polarity, in multiple types of organism. Much of the machinery for vesicle transport and polarity is conserved among these different organisms, which gave coherence to the sessions and enabled participants to benefit from advances made using these various model systems. There was a broad recognition that both the vesicle traffic and cell polarity fields would benefit from collaborations and interactions. The power of using quantitative imaging and mathematical modeling was also highlighted, and will likely impact many future research projects.

We chose to report here just some of the highlights not to loose momentum. We would like to point out that the talks chosen from the abstracts were of extremely high quality and reported cutting edge research.

Forward Look

(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe*
- *Identification of emerging topics*

The meeting was extremely productive in terms of the very high quality of the oral and poster presentations and the excellent spirit of discussions, data and idea exchange. We expect that new collaborations have been launched at the conference between people from different fields. Despite the realization that polarity and intracellular transport are intimately intertwined, we still have a very long way to go. We have just begun to scrape at the surface. The emerging concept of the interplay between intracellular transport and polarity/cell asymmetry needs to be further explored and better understood. Much is still to be learnt about the regulation of the signaling at the plasma membrane. We expect great developments in the near future and this is why we would

like to have another meeting in 3 years.

In the future the merging field will probably move towards organ development. Already a few presentations explored the connection between membrane transport and polarity in terms of tube formation. This event is key in the development of branched organs like the vasculature, lung, kidney and mammary gland. During the meeting models for trachea (the *Drosophila* equivalent of a lung) and mammary gland development were presented. We expect to see more models and a wider exploration of the existing models in the near future. For a long time, not too much attention was paid to the 3D structure of cells. People were/are using tissue culture cells, preferentially those, which are flat in culture to facilitate imaging, reducing the complexity to a 2D problem. However cells in an organism do not live in isolation, they have neighbors with which they interact and communicate, and as in an epithelium form a tight boundary, one site exposed to a lumen (e.g. in the gut or the lung or the vasculature) and the other side of the boundary in close contact with basement membrane. The maintenance of this boundary is extremely important. Loss of the boundary, which is a consequence of loss of polarity, causes the loss of e.g. the blood-brain barrier, which would have a deadly effect. We expect in the future a better understanding of the maintenance of polarity and epithelial connectivity.

We also foresee a stronger connection with stem cell field. The understanding we gain from generating asymmetry in *Drosophila* oocytes and *C.elegans* one-cell embryos or even in yeast *S. cerevisiae* will turn out to uncover mechanisms by which also determinants are asymmetrically segregated during stem cell division, whereby one cell is a copy of the mother cell, while the second daughter cell will go on to a different cell fate and differentiate.

▪ Is there a need for a foresight-type initiative?

The time might not be quite right for a foresight-type initiative, since the fields are just getting to know each other.

Atmosphere and Infrastructure

▪ *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

The participants thought that the meeting was very important and successful. Many participants mentioned that it was the most useful and exciting conference they have attended. There was an anonymous vote to hold another meeting on the same topics in 3 years; the chairs have been selected. The participants were very happy with the location and the accommodations. If possible people would like to go back to the same place.