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ESF-EMBO Symposium

Cell Polarity and Membrane Traffic

Polonia Castle (Dom Polonii), Pultusk • Poland,
31 March - 5 April 2012

Chaired by: **Catherine Rabouille**, Hubrecht Institute for Developmental Biology and Stem Cell Research, NL
Co-Chaired by: **Keith Mostov**, University of California - San Francisco, US

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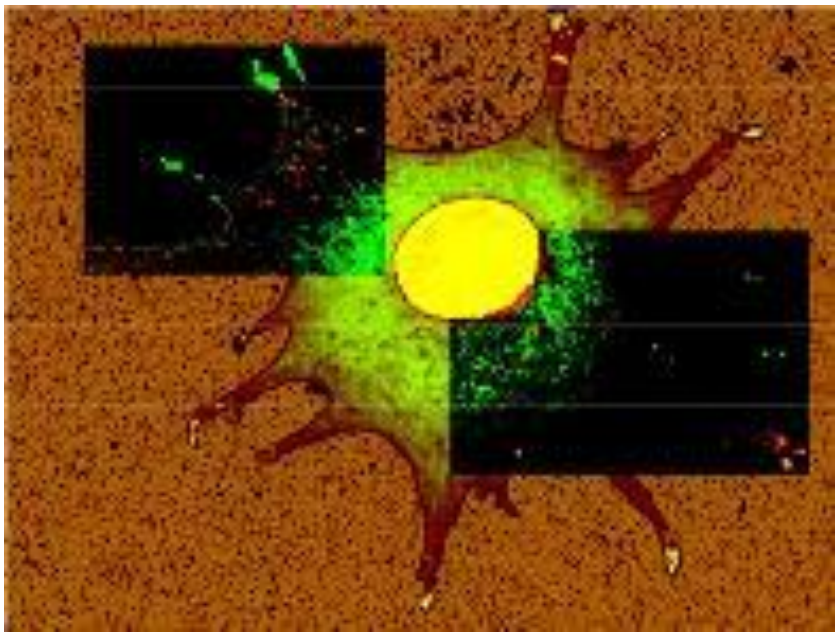

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Conference Highlights

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)

Cells are the basic building blocks of all life. All cells are spatially asymmetric or polarized. That is, although cells are sometimes depicted schematically in textbooks as simple spheres, they actually have highly complex and dynamic shapes to fulfill their diverse roles in organisms. For example, all interior and exterior surfaces of the body, such as the skin and the linings of the digestive, respiratory and urogenital systems, are lined by a layer of cells known generically as epithelial cells. In another example, cells frequently move, often as part of normal development, or to attack infectious microorganisms, or during the spread of cancers. Such moving cells are also polarized, with a front or leading edge, and a back or trailing tail. This asymmetry or polarity is defined by a set of defined components (Par complex) and structures (junctions).

All cells are surrounded by a membrane, a very thin layer composed of lipids and proteins, which is termed the plasma membrane. In higher or eukaryotic organisms, they also have internal membranes, which form internal structures also named organelles, such as the nucleus, Golgi apparatus, endosomes and lysosomes. Membranes are mostly made on a special organelle called the rough endoplasmic reticulum and are transported to the other organelles and the plasma membrane. Conversely, cells take up large molecules from the outside via small membrane carriers and send them to the cell interior in special organelles called endosomes and lysosomes. Collectively, membrane movement within the cell is called membrane traffic.

Cell polarity and membrane traffic are closely intertwined processes at several levels. A hallmark of cell polarity is that the plasma membrane is divided into several separate domains, each with a distinct composition of lipids and proteins and which serves distinct functions. For instance, polarized epithelial cells contain an apical surface, which faces the outside world, either the outside of the skin, or the lumen of organs such as the digestive or respiratory system, which is topologically equivalent to the outside world. These cells also contain a basolateral surface, which contacts adjacent cells and the interior of the organism. These two surfaces, apical and basolateral, contain completely different lipid and protein compositions, reflecting their specialized functions in exchange with the outside world, or interacting with other cells, respectively. The protein trafficking machinery must send newly made proteins and lipids to the correct apical or basolateral plasma membrane. Moreover, after these components reach the plasma membrane, they are generally internalized by a process termed endocytosis. There is a clear interplay between membrane traffic (exo and endocytosis) and the Par complex proteins, the junctional proteins and the definition of the basolateral/apical membrane.

This meeting focused on the latest advances in the intersection of the fields of cell polarity and membrane traffic, bringing together researchers in many fields of biological and biomedical science, to provide a unique forum to advance the subject.

☐ 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 overall combination of cell polarity and membrane traffic is nearly unique among conferences, the best precedent being the similar ESF/EMBO conference held three years ago in Spain (there organized by leader in the field, Anne Spang and Ian Macara). The combination produced many new and unexpected insights.

This ESF EMBO conference on Cell Polarity and Membrane Traffic was a great success, exceeding all of the expectations of the organizers and many of the participants. It brought together scientists from many diverse disciplines, including cell biology, biochemistry, medical science, metabolism, physiology, plant science (an often over-looked field), biophysics, computational/structural biology, imaging, materials science and related disciplines.

There was excellent gender balance (nearly 40% of attendees and 30% of the speakers were women) and geographic representation spanning the globe (23 nationalities over 17 countries) and all levels of scientific and economic development, both among speakers and participants. Quite a substantial amount of money was raised in sponsorship (from the Company of Biologists, the Wellcome Trust, the Foundation for Polish Science, Genentech, Abcam, Springer and Nature Reviews) and this allowed us to give a large number of travel and registration grants to many young people and people from overseas, people who would otherwise not have been able to come.

Several innovative features of the design of the conference greatly promoted interactions, especially between senior and more junior attendees, so that all participants in the conference were able to enhance their experience, benefits and networking. The conference covered an unusually wide mix of subjects, juxtaposing them in creative ways, such as sessions combining plant biology and immunology. We highlighted below only a few of numerous unexpected and exciting new scientific results that which were presented at this meeting.

1. Chairs of sessions were deliberately chosen from the ranks of graduate students, postdoctoral fellows, and young group leaders. This was to give these young people visibility and an early taste of leadership and involvement in the field. They took their duties very seriously in presenting the speakers and keeping with time.
2. The speakers (whether invited or selected) also kept their speaking time under control. For instance, out of the 40 minute slot, the invited speakers were instructed to use only 33, allowing ample question time and discussion before the next talk began. This worked well.
3. During the meals following each session, special tables were designated in the dining room for each speaker, where audience members could dine and converse in small groups with the speakers. This semi-formal setting was designed to help younger people feel comfortable to approach more established scientists and to overcome the all too common pattern in meetings where established scientists tend to sit and talk mainly with each other, while junior scientists have little personal contact with the senior people.
4. Half of the oral presentations were short talks, selected from submitted abstracts that complemented each session (that were organized by themes, see below). Indeed, several sessions were largely dominated by such talks. As is to be expected, several invited speakers cancelled at the very last minute, due to family medical emergencies, funerals, etc. We were able to select additional short talks from the submitted abstracts; such talks were particularly well received. This also gave exposure to many more delegates.
5. Almost all invited speakers were given the task to read at least 5 posters and interact with their presenters. They then reported on which they like the best. We were then able to award poster prizes, which were given to Aniko Keller-Pinter for her poster on Syndecan-4 (Nature Cell Biology subscription) and Alicja Drojdowska for her poster on Ctc1p (J. Cell Biology subscription).

Scientific Content of the Conference

(1 page min.)

▪ *Summary of the conference sessions focusing on the scientific highlights*

1. Nuclear migration. The keynote speaker Daniel St Johnston presented exciting data on nuclear migration in the Drosophila oocyte. Despite the early proposition that the nucleus was pulled by microtubules, it is now clear that the nucleus is pushed by small microtubules that are generated from the centrosome. Antoine Guichet presented a poster on the exact same subject reaching very similar conclusions. Sandrine Etienne-Manneville also broached on the same subject in human cells in culture,

2. Polarity in MDCK cells and cysts
Keith Mostov presented work from his lab on recovery from injury, using a novel system where epithelial cells grown as cysts in three-dimensional structures. In this system the dead cells are pushed out of the monolayer by actin-rich protrusions from neighboring cells and the surviving cells re-enter the cell cycle. Fernando Martin-Belmonte talked about how to members of the synaptotagmin-like protein family, Slp2 and Slp4 work in distinct steps in the process of forming lumens in epithelial cells . In a poster, Anne Muesch explicated how the polarity kinase Par1 determines whether cells form the conventional type of columnar organization, or with high Par1 activity, a hepatocyte-like polarity with the lumen encircling the cell

3. Junctions give direction to the Actin/myosin flow
Thomas Lecuit gave a beautiful talk on the visualization live of the myosin flow in polarized cells and showed that this flow is organized and constrained by junction, thus allowing polarized events to take place. Sandrine Etienne Manneville had similar data and show that this organization is necessary for migration of glioblastoma cells.

4. Endocytosis
Whereas Anne Spang presented her work on endosomal transport including new data on the role of Corvet and Hops, and Enrique Rodriguez Boulan spoke about the role of the adaptor protein AP-1 in the trafficking of plasma membrane proteins, Marta Miaczynska and Thomas Vaccari presented work integrating endosomal function and either signaling (TNF alpha) or development and polarity (Notch). Interestingly, Barry Thompson also proposed that polarity is maintained via the continuous recycling of Crumbs from the basolateral membrane to the apical one, where it is prevented from internalization by Cdc42.

5. Cadherin endocytosis.
Ian Macara presented work on mammalian Scribble, a gene well known in Drosophila as a polarity marker. He showed that mammalian Scribble has an unexpected role in controlling E-cadherin endocytosis and once endocytosed, prevents its interaction with the retromer in the endosomes, interaction that would send them back in the TGN. Interestingly, Helena Richardson also proposed alternative roles of Lgl and aPKC, two polarity factors.
Adam Grieve from Catherine Rabouille's lab presented data on the selective endocytosis of truncated E-cadherin. Last Sandrine Etienne-Manneville also showed that E-cadherin is constantly recycled from the lateral side to the leading edge of the migrating cells.

6. Asymetric cell division.
Marcos Gonzalez-Gaitan showed that the determining factor to make sara endosomes go to the anterior cells during the Drosophila SOP division is the higher concentration of microtubules in the posterior side of the mitotic spindle.
In the same session, Jurgen Knoblish shows that the stem cells in the Drosophila gut divide asymmetrically and that this asymmetry is defined by the same principles and polarity factors (Par and aPKC) as in the neuroblast.

7. Karin Reinish presented a complex but very clear talk on her work on deciphering the structure of small Rab activators. These activators falls into 4 categories, all rather different and her lab acquired X-ray structures of them.

This meeting was a resounding success, exceeding all of our expectations. There is a compelling need for an ongoing series of similar future meeting, due the unique way in which the conference brought together the fields of membrane traffic and cell polarity, along with many specific scientific disciplines, ranging from botany to biophysics, from medicine to computation.

8. Tools
Two very exciting tools were presented during the meeting. First, the Rab library for Drosophila allowing to localize and deplete Rab proteins that was built and presented in a short talk by Marko Brankatschk and used by Sebastian Dunst (Poster). The other is the RUSH system presented in a short talk by Frank Perez, allowing to follow secretion of any cargo using the secretory pathway after it is retained in the ER by binding to a streptavidin hook and released by addition of biotin.

9. Cilia
Ben Margolis presented very exciting data showing striking similarity between passage through the nuclear pore and the entering the cilia in their dependency for Ran GTP. This is a very original idea that he clearly illustrated. This session was completed by a talk from Wolfganf Kuehn on ciliopathy in kidney and an interesting link to TOR.

10. Marino Zerial finished the meeting by a beautiful lecture on a multi-disciplinary and quantitative approach to understanding endocytosis as well as a novel imaging technique to follow liver development and the role of the different cell types therein.

▪ *Assessment of the results and their potential impact on future research or applications*
This meeting was a resounding success, exceeding all of our expectations. There is a compelling need for an ongoing series of similar future meeting, due the unique way in which the conference brought together the fields of membrane traffic and cell polarity, along with many specific scientific disciplines, ranging from botany to biophysics, from medicine to computation.
The science presented was of amazing quality including the 20 short talks that complemented the session. Many exciting non-published data was presented and discussed in a friendly yet scholarly manner.

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*
One of the main new directions of the field over the next five to ten years will be an increasingly quantitative approach, increasing mathematical rigor, and increasing computer modeling. New methods, especially in imaging, permit ever more quantitative, large, multidimensional data sets to be obtained and data extracted by sophisticated computer methods. While mathematical modeling of polarity and morphogenesis dates back to the pioneering work of Turing in the 1950s and Meinhardt in the 1970s, new advances in computation are bringing us to a new, comprehensive approach where we can enumerate the entire universe of possible mathematical mechanisms that lead to polarization. This will soon revolutionize the field, and have manifold, unexpected impacts in all directions.

Another main direction will be the increasing emphasis on in vivo studies in vertebrate systems, especially zebrafish (only one short talk) and mouse (one invited talk).

A session on “Asymmetric localization of mRNAs” was missing from the programme. This was because the three speakers invited to cover this subject were unable to join us in Poland and decline the invitation (for different reasons). This should perhaps be remedied next time, although this particular subject is extremely well covered by an FASEB/EMBO meeting (the last one held in August 2011).

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

Yes, definitely as there are no other meetings on cell polarity, let alone cell polarity and membrane traffic. We believe that this is this unique combination that makes the meeting so rich and intense.
Two major leaders, one in the field of cell Polarity, Professor Daniel St Johnston, and the other in membrane traffic and polarity, Prof Enrique Rodrigez Boulan, clearly recognizes the need for such meeting and offered to organize the next one.

Business Meeting Outcomes

- *Election of the Organising Committee of the next conference*
- *Identified Topics*
- *Next Steps*

The meeting elected by popular acclaim for Prof Daniel St Johnston, Director of the Gurdon Institute in Cambridge, UK and Professor of Genetics at Cambridge University, to be the next chair of the meeting. Similarly, Prof. Enrique Rodriguez-Boulan of the Dyson Institute and Department of Cell and Developmental Biology at Weil Cornell Medical College in New York City, New York, USA, was elected co-chair. Both of these people are well-established leaders in the field, well respected and collegial, with excellent track-records in organizing scientific enterprises. Prof St. Johnston's background in Drosophila development complements Prof Rodriguez-Boulan's background in polarized membrane traffic in cultured mammalian cells.
The idea is to apply to the ESF for a meeting in the spring of 2014 as it is not clear what the ESF funding will be after this.
An alternative would be to make it an EMBO meeting but this will be discussed later if the ESF application does not go through,

Atmosphere and Infrastructure

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

It was the first time that an ESF/EMBO meeting was held in Pultusk (Poland), so it was a learning curve for both ESF and the hotel/infrastructure.
Some points were very positive, other negative, though the negative did not impinge too much on the moral and enjoyment of the delegates.

Positive

1. The atmosphere was particularly relaxed and good mannered, which contributed to many very extensive interactions, discussions and networking, especially between junior and senior scientists and between scientists from wealthy and less-developed countries. This was especially promoted by the innovative mechanisms described above. We are personally aware of new collaborations that resulted from this meeting and undoubtedly many more will result, which have yet not become known to us.

2. The ESF conference staff, Ms Caroline Nsenda and Ms Jean Kelly were excellent and very professional. The hotel provided very abundant and helpful staff (like a charming barman during the evening poster session) and during the conference itself (with the microphones and the computer/projectionist). We felt very welcome and well taken care of.

3. As for physical infrastructure, the Polonia Castle was very charming, providing historical rooms (conference hall, dining rooms and other public rooms for informal discussions) that were very attractive. The individual hotel bedrooms were spacious and well kept. The main hall for the conference room was comfortable, with good acoustics and conducive to discussions, both during the presentations and during the coffee breaks.

4.The food was good (although not outstanding, not as good or interesting as the food in the location of the previous ESF polarity meeting in St Feliu in Spain).

Negative:

1. The computer LCD projector was of low quality and overall inadequate in terms of resolution and brightness. As a result, some presentations were compromised as some images displaying color micrographs, that form the bulk of some talks, were not projected properly. This could easily be fixed with some investment in a better projector

2. The internet WiFi service in the hotel was uneven, some spots being very good (some rooms, public rooms in the hotel and conference room) and some very bad. At least for the invited speakers, this causes some problems as some of them are heads of institutes or department chairs and they need to have access to internet in their rooms. Since some areas are better than others, I would suggest to group the speakers around the spots of good reception.

In general, although the hotel had beautiful European charm, it was not completely up to date in terms of technology. This could be fixed with some investment, which would also benefit the hotel long term.

3. The hotel did not house all invited speakers in the main building of the castle and some (6) were located in the small building next door that was not as grand. The ESF representative managed to re-locate 4 of them to the castle, but this should imperatively be arranged much better next time. This together with the Wifi issue should be given particular attention.

4. Although the poster sessions were very well attended and led to numerous high quality discussions and interactions, the room itself was very poorly lit. Due to the poor lighting it was impossible to see many of the posters, especially the color micrographs, which were the heart of many of the posters. Several participants used lights from their mobile phone cameras to illuminate the posters, which although clever, indicated the severity of the problem. Again, this could easily be fixed, perhaps by bringing some supplemental lamps into the room.

5. A general concern was the lack of things to do in the small amount of free time allocated in the meeting.
-One issue was the weather at this time of year (31 March-4 April) which was cold, windy, rainy even sleety. This confined everyone almost entirely indoors, giving little opportunity to explore the local environs of Pultusk.
-The other issue is that Pultusk is a rather small and boring town where there is nothing to do. One hour is enough to explore whatever charms it has.
It is also too far from Warsaw to go and visit the city (even though we could have tried to squeeze this during the free afternoon with packed lunch). This was a pity, since most of the participants had never been to Poland and would have enjoyed a bit of sightseeing, which could have been combined with informal scientific discussions. This would have also given a chance to contribute to the local economy.
This was in striking contrast to the prior setting in Spain, where meals and coffee breaks were almost all taken outdoors, and where participants could explore the local environs during the small amount of free time.

6.The bus service between the airport and the hotel was poor, and was 45 to 60 minutes late in leaving in both directions. Passengers were forced to stand outside in the cold wind, which was very unpleasant, especially for those who come from warmer climates. For the return to the airport this forced many participants to pay for expensive taxi fair. It was a blemish on an otherwise excellent meeting. This could be fixed by improving the performance of the bus company or by choosing a different bus company.

Of course, all these points should be fixed but it needs to be stressed that despite all this, the meeting was a big success, which should be reflected in the questionnaire.

In conclusion, we understand and approve the push from EMBO and ESF to organize meetings in East Europe as a way to promote scientific research and help interactions with national initiatives. In this regard, the financial contribution of the Foundation for Polish Science toward the registration fees of 4 young Polish researchers (plus one invited speaker) has to be noted as a very positive sign.

However, the question is whether it would be possible to have these meetings closer to a main city, whether in Poland or in other East-European countries to overcome some of the points raised above especially point 5.

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Date & Author: 16 April 2012

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