© 2017. Published by The Company of Biologists Ltd | Journal of Cell Science (2017) 130, 2775-2779 doi:10.1242/jcs.208660

MEETING REPORT

Meeting report – Cellular dynamics: membrane–cytoskeleton interface

Joshua N. Bembenek[1,*], Xenia Meshik[2] and Vasilios Tsarouhas[3]

ABSTRACT

The first ever 'Cellular Dynamics' meeting on the membrane–cytoskeleton interface took place in Southbridge, MA on May 21-24, 2017 and was co-organized by Michael Way, Elizabeth Chen, Margaret Gardel and Jennifer Lippincott-Schwarz. Investigators from around the world studying a broad range of related topics shared their insights into the function and regulation of the cytoskeleton and membrane compartments. This provided great opportunities to learn about key questions in various cellular processes, from the basic organization and operation of the cell to higher-order interactions in adhesion, migration, metastasis, division and immune cell interactions in different model organisms. This unique and diverse mix of research interests created a stimulating and educational meeting that will hopefully continue to be a successful meeting for years to come.

Imaging and computational analysis of cellular dynamics

This meeting aimed to bring together many different biologists looking at different aspects of membrane and cytoskeletal biology, and how these systems function in concert to achieve the diverse functions of a cell. These lofty goals were well encapsulated by new research utilizing light-sheet microscopy to obtain unprecedented views into cellular behavior. In recent years, novel interactions between organelles have been discovered, such as that between the ER and mitochondria during mitochondrial fission or transfer of lipids between various organelles. A major limitation in our understanding of organelle interactions is our ability to be able to observe only one or two organelles at a time. To overcome this and to begin to obtain a comprehensive view of organelle dynamics, Jennifer Lippincott-Schwartz (HHMI Janelia Research Campus, Ashburn, USA) utilized lattice light-sheet microscopy (LLSM) developed in Eric Betzig's lab combined with multispectral unmixing to simultaneously image six different fluorophores to label compartments in 3D (Valm et al., 2017). With these new tools, interactions between numerous organelles could be observed over time and quantified in control and perturbed cells, providing new insight into the dynamic organization of the cell and how it is regulated.

Tomas Kirchhausen (Harvard Medical School, Boston, USA) shared insight into membrane trafficking dynamics during cell division in single cells in culture, as well as in zebrafish eye and ear tissues (Aguet et al., 2016). Owing to new developments by his collaborator Eric Betzig, adaptive optics combined with LLSM imaging now allow improved clarity of deep-tissue imaging and made it possible to quantify the dynamics of individual clathrin vesicles. These initial talks provided a glimpse into what the future of cellular imaging might hold, but also clearly indicated a significant need for data management and analysis. Toward this end, Erik Welf from Gaudenz Danuser's lab (University of Texas Southwestern, Dallas, USA) presented his analysis of cellular migration using microenvironmental selective plane illumination microscopy (meSPIM), which allows for isotropic resolution, combined with sophisticated image analysis tools that can segment surfaces of cells (Welf et al., 2016). This analysis is capable of defining different types of protrusions, thereby allowing precise quantification of cell dynamics and potentially providing insights into microdomains where signaling networks function to regulate changes in cell shape. While these spectacular examples show the promise of new and emerging imaging approaches for cell biology, the bulk of the talks demonstrated the progress that can be made – even with more traditional tools – as William Trimble (The Hospital for Sick Children, Toronto, Canada) humorously pointed out.

Ciliogenesis

Among the organelles that harbor fascinating interactions between the cytoskeleton and membrane is the cilium; it requires intricate modifications of the centriole and microtubule cytoskeleton, as well as directed membrane trafficking for its formation and maintenance, and, moreover, appears to be the location for newly discovered functions of known genes. One of the more surprising is the discovery that gated transport of the kinesin KIF17 into the ciliary compartment is regulated by nucleoporins, as initially described by Kristen Verhey (University of Michigan, Ann Arbor, USA). This research has now characterized the architecture of cilia-specific modules that establish the nucleoporins at the base of the cilia, including nephronophthisis (NPHP), Joubert (JBTS) and Meckel–Gruber (MKS) proteins (Takao et al., 2017). William Trimble presented his latest research on the function of septins, the so-called fourth cytoskeletal component (Fung et al., 2014). In particular, he questions the role of septins as diffusion barriers during yeast cell division and, instead, has identified other functions, including in regulating RhoA signaling. In this regard, septins localize along the length of the axoneme to regulate ciliary length via RhoA, and the loss of septins can be rescued by tethering a Rho-GEF protein to the centriole.

Finally, recent findings also reveal previously unappreciated connections between the Golgi and the cilium. For example, David Stephens (University of Bristol, Bristol, UK) showed that loss of giantin (GOLGB1), but not of other Golgi components, causes defects in cilia formation and a swelling at the tip of cilia due to disrupted retrograde transport. Giantin loss depletes dynein 2 and its regulators from the cilium (Bergen et al., 2017). Last but not least, David Glover (University of Cambridge, Cambridge, UK)

[1]Department of Biochemistry & Cellular and Molecular Biology, University of Tennessee, Knoxville, TN 37996, USA. [2]Department of Anesthesiology, Washington University in St. Louis School of Medicine, St. Louis, MO 63110, USA. [3]Department of Molecular Biosciences, Stockholm University, Stockholm, Sweden.

*Author for correspondence (bembenek@utk.edu)

Journal of Cell Science (2017) 130, 2775-2779 doi:10.1242/jcs.208660

presented another link between the Golgi and cilium as he described how the Golgi protein GORAB interacts with the core centriole protein SASS6 and affects the nine-fold symmetry of the centriole in cilia. Thus, the cilium continues to be a valuable system to explore the function of well known proteins and gain new insights into the interactions between the cytoskeleton and membrane-trafficking pathways.

Mechanisms of actin polymerization

Actin dynamics are instrumental in various cellular processes, from cytokinesis to transport and migration, and this meeting showcased fascinating new research into the mechanisms regulating actomyosin-driven cell contraction and protrusions. Michael Way (The Francis Crick Institute, London, UK) reported on the role of small GTPases RhoC and RhoD in cortical contraction. Following the observation that vaccinia virus-infected cells show increased blebbing and contraction, the Way lab showed that the vaccinia protein F11 is involved in the underlying pathway. RhoD at the plasma membrane acts through the kinase PAK6 to inhibit RhoC-mediated ROCK activation and the resulting cortical contraction. They now show that F11 antagonizes this process by binding to RhoD, thereby alleviating its inhibitory effect on RhoC (Durkin et al., 2017). These findings thus reveal a novel contractility mechanism that is independent of the more widely studied RhoA-mediated pathway. Another member of the Rho family of GTPases, CDC42, mediates actin nucleation through its interaction with Toca-1 (FNBP1L) and the N-WASP complex. Helen Fox (Gurdon Institute, Cambridge, UK) used frog egg extracts to identify two new binding partners of Toca-1, Ena and VASP. She explained how the cellular analysis of Toca-1 and its partners suggests a role for Toca-1 in filopodia formation. Chiara Zurzolo (Pasteur Institute, Paris, France) presented her latest insights into tunneling nanotubes (TNTs), actin-rich protrusions involved in cell-to-cell communication and transport. Using EM and tomography, her lab previously found that, despite being morphologically similar to filopodia, TNTs are in fact distinct structures formed through distinct mechanisms. For instance, in neuronal cells, inhibition of ARP2/3 or stimulation of the CDC42-IRSp53-VASP pathway promote TNT formation, whereas they inhibit filopodia formation (Delage et al., 2016). These insights are important for understanding TNT physiology and their possible role in neurodegenerative diseases, which, as Chiara proposed, could spread from cell to cell via TNTs (Abounit et al., 2016).

Actin cytoskeleton and mechanosensing

Interdisciplinary approaches for studying cellular dynamics have led to the physical and mathematical characterization of cytoskeletal properties. Margaret Gardel (University of Chicago, Chicago, USA) spoke about her efforts in characterizing stress fiber contraction by using a parameter termed 'stress relaxation time'. Using laser ablation and optogenetic control of RhoA, her group was able to identify the time scale for which stress fibers transition between solid-like and fluid-like behavior – in other words, the time it takes for stress fibers to recoil after removal of applied tension. She also identified zyxin as a mediator of stress fiber contraction and showed that LIM-domain proteins recruit zyxin to stress fibers (Oakes et al., 2017). Johanna Ivaska (University of Turku, Turku, Finland) shared interesting new data on interactions between mechanosensitive cells and the matrix in pluripotency and cancer. Her group found that the extracellular matrix (ECM) restricts cancer cells through the mechanosensitive downregulation of the histone demethylase JMJD1A (also known as KDM3A; Kaukonen et al., 2016). In a series of *in vitro* experiments using human induced pluripotency stem cells (iPSCs), Ivaska's group now show that contractions derived from an actin ring that encircles the edges of iPSC colonies are crucial for maintaining their pluripotency (Närvä et al., 2017).

Actin dynamics at the immune synapse

When T-cells interact with an antigen-presenting cell (APC), they establish a synapse that is triggered by intracellular signaling, adhesion interactions and dynamic actin-driven cortical rearrangements. John Hammer (National Heart, Lung, and Blood Institute, Bethesda, USA) reported his group's characterization of the actin dynamics that contribute to the formation of a mature immunological synapse. He showed that actin arcs migrate toward the center of branched actin at the edges of the synapse and are derived from formin-mediated foci at the plasma membrane. Remarkably, inhibition of ARP2/3 by CK666 removes all branched actin and causes the entire actin network to become arcs. The function of these arcs may be to focus clusters of receptors and adhesion molecules to the center of the synapse to promote robust T-cell– APC adhesion and T-cell receptor (TCR) signaling (Murugesan et al., 2016). Sudha Kumari from Darrell Irvine's lab (MIT, Cambridge, USA) investigated how the actin architecture controls the lifetime of the synapse after it has formed. Her work identified WASP-dependent actin tails accumulating around TCR clusters that promote adhesion points and enhance contractile stress, ultimately tuning mechanical forces at the synapse and T-cell effector function (Kumari et al., 2015). Arpita Upadhyaya (University of Maryland, College Park, USA) discussed their efforts in determining the mechanosensing properties of the immunological synapse. TCR signaling is sensitive to force, meaning that sustained signaling is more likely to occur on soft rather than stiff substrates. T-cell forces are dependent on myosin activity and microtubule dynamics that influence the Rho–Rock pathway (Hui and Upadhyaya, 2017). Therefore, the actin cytoskeleton spatially regulates the signaling pathways that govern the dynamic T-cell–APC interaction, which responds to forces and adhesion.

Mechanisms of cell polarity

Another theme of the meeting addressed recent insights into the mechanisms of epithelial cell polarity. Anthony Bretscher (Cornell University, Ithaca, USA) presented his group's latest findings for the role of ezrin in the apical domain of epithelial cells. They found that upon binding to phosphatidylinositol 4,5-bisphosphate (PIP2), ezrin undergoes a conformational change that allows the C-terminal domain of LOK (STK10) to wedge itself between the C-terminal domain and the FERM domain of ezrin, thus activating LOK kinase activity and mediating phosphorylation of the T567 residue of ezrin. As LOK is known to localize to apical membranes, this pathway ensures that dynamic ezrin phosphocycling occurs on the apical side of the cell, thereby maintaining cell polarity (Pelaseyed et al., 2017).

Adherens junctions (AJs) also have a role in determining apical–basal polarity. The protein Canoe (Cno) in *Drosophila* serves as a linker between AJs and the cytoskeleton, and is at the top of the hierarchy of proteins that position cell–cell AJs and so establish apical–basal polarity (Choi et al., 2013). Mark Peifer (University of North Carolina, Chapel Hill, USA) showed that Cno regulates AJs in a Rap1-dependent manner. His data suggest that there is an apical pool of active Rap1 that is important for recruiting Cno apically. Furthermore, he reported that this involves both the N-terminal Rap1-binding Ras association (RA) domains and an RA-independent effect of Rap1.

Journal of Cell Science (2017) 130, 2775-2779 doi:10.1242/jcs.208660

In addition to apical–basal polarity, planar cell polarity (PCP) is another important, but less widely studied, feature of tissues. David Sprinzak (Tel Aviv University, Tel Aviv, Israel) talked about a synthetic biology platform that his group has used to show that the protocadherins Fat4 and Dachsous1 (Ds1/DCHS1) form complexes at the cell boundary that exhibit localized feedbacks, whereby each complex promotes the formation of complexes with the same orientation (e.g. Fat4–Ds1), but inhibits those of opposite orientation (e.g. Ds1–Fat4). These complexes form clusters that are highly stable – thus driving these feedbacks.

Cell migration

Cell migration relies on both cytoskeletal and membrane dynamics and was therefore a widely discussed topic at the meeting. Deconstructing the mechanisms underlying cell migration can provide insights into normal cell function, as well as pathological processes such as cancer cell invasion.

Fascinating research has been conducted on the role of the nucleus in 3D migration. G. W. Gant Luxton (University of Minnesota, Minneapolis, USA) presented his lab's recent findings on the role of torsin-A (TOR1A) during rearward nuclear movement, which is instrumental in reorienting the centrosome towards the leading edge in migrating cells. He showed that torsin-A and its activator LAP1 were essential for the assembly of transmembrane actin-associated nuclear (TAN) lines, which couple the nucleus to perinuclear actin cables, as well as for the retrograde flow of these perinuclear actin cables. Their latest results suggest that rearward nuclear movement requires the homo-hexamerization of torsin-A, supporting the possibility that torsin-A functions as a molecular chaperone, like other AAA+ proteins (Saunders et al., 2017).

Keeping within this theme, David Graham (University of North Carolina, Chapel Hill, USA) reported on findings with enucleated fibroblasts that raised the possibility that, on 2D surfaces, the nucleus is not required for adhesion, polarization, or migration of fibroblasts. However, although cells lacking nuclei migrated well on 2D substrates with higher stiffness, which mimicked the stiffness of the fibroblasts' native environment, they showed inhibited migration in lower stiffness 2D substrates and in 3D collagen matrix. This inhibition is thought to be due to the role of the nucleus in cell contractility. Kenneth Yamada (NIH, Bethesda, USA) introduced the concept of the 'nuclear piston' that is employed during 3D movement. Unlike 2D migration, 3D or 'lobopodial' migration relies on intracellular pressure generated at the leading edge by the forward movement of the nucleus, creating rounded protrusions at the front instead of lamellipodia. Using techniques, such as particle image velocimetry (PIV) and vector mapping, his group investigated the modes of movement of different cells in 3D matrices. Their more recent work has focused on the role of BTBD7 in regulating adhesion and motility during morphogenesis in epithelial cells (Daley et al., 2017).

Free microtubule (MT) minus-ends are found in many differentiated cells and contribute to polarized motility. Anna Akhmanova (Utrecht University, Utrecht, The Netherlands) showed how mammalian CAMSAPs (calmodulin-regulated spectrin-associated proteins) stabilize MT minus-ends and highlighted their functions in polarized cell motility, thereby adding a piece to the puzzle of how MT minus-ends are formed and stabilized (Wu et al., 2016). Contrary to earlier reports, their work demonstrated that MT minus-ends do in fact undergo polymerization in cells and that this process is required for the deposition of CAMSAPs on the MTs. Anna further showed that Golgi-anchored MTs that are stabilized by CAMSAP2 are important for cell motility in a 3D matrix.

Cell migration that involves multiple cell types adds another level of complexity, as illustrated by Erik Sahai (The Francis Crick Institute, London, UK) who spoke about heterotypic junctions formed between cancer cells and cancer-associated fibroblasts (CAFs). These junctions comprise E-cadherin from the cancer cell and N-cadherin located on the CAF membranes, and their maturation requires actomyosin modulation. Importantly, through these junctions, CAFs exert mechanical forces on cancer cells, which allows invasion of cancer cells to occur (Labernadie et al., 2017).

Finally, the role of small GTPases in cell migration was also discussed. Giorgio Scita (FIRC Institute of Molecular Oncology, Milan, Italy) showed that RAB5A, a trafficking protein known to deliver vesicles to the leading edge in migrating cells, re-awakens the movement of kinetically-arrested epithelial monolayers during collective cell migration. Here, RAB5A acts concomitantly on cell–cell junctions to increase junctional line tension, promote cell polarization through the formation of directional lamellipodia and alter E-cadherin architecture to generate cell–cell adhesions (Malinverno et al., 2017). Sara Donnelly (Albert Einstein College of Medicine, New York, USA) then discussed the role of RAC3 in cancer cell invasion and ECM degradation by invadopodia. She showed that RAC3 is recruited to invadopodia by calcium integrin binding protein (CIB1), where it regulates the ARF-GAP GIT1, which is required for ECM degradation.

It was clear from these fascinating talks that migrating cells experience complex interactions with their surrounding environment, as well as with adjacent cells, and the findings presented in this session provided new insights into the mechanisms that regulate both individual and collective cell migration.

Endomembrane trafficking

WASH (Wiskott–Aldrich syndrome protein and SCAR homologue) is an evolutionarily conserved protein that is required for actin-dependent membrane scission and cargo trafficking in conjunction with the retromer complex. Daniel Billadeau (Mayo Clinic, Rochester, USA) spoke about the WASH-interacting proteins of the COMMD–CCDC22–CCDC93 (CCC) protein complex his group recently identified and how they regulate endosomal actin and cargo sorting. He showed that lack of CCC complex leads to a distortion of endosomal sorting and/or recycling of the low-density lipoprotein receptor (LDLR) (Bartuzi et al., 2016) and copper transporter ATP7A (Phillips-Krawczak et al., 2015), providing valuable insights into the mechanisms that regulate cholesterol and copper homeostasis, respectively. Gia Voeltz (University of Colorado, Bolder, USA) presented stunning live imaging illustrating dynamic contacts between ER tubules and endosomes at position of fission sites. Her observations propose that the ER exerts a non-traditional role to regulate the dynamics and biogenesis of cytoplasmic organelles, such as endosomes and mitochondria.

Eyal Schejter (Weizmann Institute of Science, Rehovot, Israel) highlighted previously unknown roles for the branched actin regulator ARP2/3 in exocytosis using a genetically tractable *in vivo* system to image the temporal and spatial dynamics of polarized large vesicle secretion. In particular, they found that, after the initiation of vesicle fusion to the apical membrane, the formin Diaphanous (Dia/DIAPH1) is recruited by Rho1 to generate the vesicle actin coat during secretion. Then, ARP2/3-mediated branched actin network in conjunction with myosin II forms a unique 'cage'-like structure around actin-coated vesicles, which is

Journal of Cell Science (2017) 130, 2775-2779 doi:10.1242/jcs.208660

crucial for efficient vesicle compression and content release (Rousso et al., 2016).

Erika Holzbaur (University of Pennsylvania, Philadelphia, USA) presented elegant live-imaging work showing that autophagosomes of primary neurons preferentially form at the axon tip and undergo retrograde transport back towards the cell body by a constitutive mechanism that is temporally and spatially regulated along the axon. Reduction in autophagy activity has been observed in a number of aging models, but the role of autophagy in aging and age-related diseases is still elusive. Their new and exciting findings from neurons of aged mice argue that autophagy-induced aging could be a contributing risk factor for neurodegenerative diseases.

The plant endomembrane pathway exhibits an increased complexity and specialization in the associated trafficking pathways, which may reflect their immovable lifestyle. Jenny Russinova (VIB, Ghent, Belgium) presented the current view of endomembrane trafficking of brassinosteroid insensitive 1 receptor (BRI1) and its ligand, BR hormone. Her group was able to visualize the endocytosis of BR–BRI1 complexes in living *Arabidopsis thaliana* cells (Luo and Russinova, 2017), which indicates that BR signaling is regulated by AP2 and ARF-GEF-dependent endocytosis. Notably, post-translational modifications of the BRI1 trafficking machinery are crucial for BR endocytosis, while trans-Golgi network/early endosome acidity is indispensable for functional secretion and recycling of BR signaling.

Cell division

Cell division is a highly dynamic process that involves the reconfiguration and coordinated action of every membrane and cytoskeletal system in the cell. Nasser Rusan (NIH, Bethesda, USA) spoke about his group's findings for septin-interacting protein 2 (SIP2) that binds to the centrosomal protein Asp at the midbody, and so shows a similar localisation to that of chromosomal passenger proteins. SIP2 depletion disrupts formation of the central spindle and causes cytokinesis failure. Interestingly, they showed that lack of SIP2 also leads to defects in neural development, suggesting that further investigation of this aspect might lead to a better understanding of how mutations of centrosomal proteins could give rise to brain defects such as microcephaly.

Andy Moore (University of Pennsylvania, Philadelphia, USA) addressed the dynamics of actin and mitochondria during cell division in tissue culture cells. He presented results from Erika Holzbaur's lab showing cycles of mitochondrial fission and motility that are driven by actin polymerisation, which they propose could represent a mechanism to properly partition mitochondrial components into daughter cells (Moore et al., 2016). Finally, Ronen Zaidel-Bar (Mechanobiology Institute, Singapore) highlighted the function of the F-actin crosslinker plastin (also known as fimbrin) during early *C. elegans* development. Although plastin colocalizes with all the F-actin at the cell cortex, it is particularly enriched in contractile structures. This suggests that plastin increases the connectivity within the cortex and facilitates long-range cortical rearrangements that are required during polarization and cytokinesis in a one-cell embryo (Ding et al., 2017).

Cell junction remodeling

Maintenance and remodeling of cells within tissues requires the regulation of junctions between cells and the extracellular matrix and with neighboring cells. Kathleen Green (Northwestern University, Chicago, USA) presented data showing that the desmosomal component desmoglein 1 (DSG1) is expressed in epidermal skin cells as they begin to stratify and is essential for differentiation and actin remodeling during epidermal morphogenesis. Her findings indicate that Dsg1 is recruited to the membrane by dynein and properly positioned by the dynein light chain Tctex-type1 to promote the delamination required for epithelial stratification. Cara Gottardi (Northwestern University, Chicago, USA) spoke about her group's recent efforts in uncovering the roles for α-catenin outside the adherens junction complex. She showed how α-catenin can be recruited to the plasma membrane independently of the cadherin–catenin complex and in a manner that depends on PI3K signaling and PIP3 binding. By using a forced-dimerization system, they were able to show that α-catenin 'homodimers' promoted filopodia and growth-cone-like protrusions through an unidentified mechanism, suggesting that extra-junctional α-catenin contributes to membrane events that are required to maintain cell–cell adhesion. In her presentation, Tsveta Malinova (Academic Medical Center, Amsterdam, The Netherlands) focused on the role of protein kinase C and casein kinase substrate in neurons protein 2 (PACSIN2) in endothelial junctions and showed that PACSIN2 is recruited to the VE-cadherin-based focal adherens junctions, where it inhibits internalization of the VE-cadherin complex (Dorland et al., 2016). Interestingly, PACSIN2 also promotes sprouting angiogenesis, suggesting it has important roles in endothelial junctions in response to angiogenic cues.

Lastly, Cheng-han Yu (The University of Hong Kong, Hong Kong) discussed the role of cytoskeletal proteins in podosomes. By using FRAP-based assays, his group found that myosin-Ie, and specifically its tail domain, TH12, are among the most stable components of the podosome core. Specifically, TH12 was found to bind to PIP3 and to impair F-actin polymerization, as well as to suppress matrix degradation and reduce migration speed. Together, these data point to the TH12 domain of myosin-Ie as a key regulatory component of the podosome.

Cell–cell fusion

Cell–cell fusion is a fundamental biological process required for conception, development and physiological maintenance of multicellular organisms, but the mechanistic links between fusogens and the actin cytoskeleton remain elusive. Guangshuo Ou (Tsinghua University, Beijing, China) showed that the bona fide cell–cell fusion protein epithelial fusion failure 1 (EFF1) and F-actin are enriched at the cortex of post-embryonic fusing cells. Results based on affinity purification and mass spectrometry analyses revealed that EFF-1 binds to the actin-binding protein spectraplakin (VAB-10A in *C. elegans*). Interestingly, EFF-1 does not bind to F-actin, but, instead, VAB-10A links EFF-1 to the actin cytoskeleton and so promotes cell-cell fusion. Based on this, he proposed that, VAB-10A induces a positive feedback between fusogens and the actin cytoskeleton to promote cell-cell fusion (Yang et al., 2017). Another outstanding question in cell-cell fusion is how cells decide to fuse. Sophie Martin (University of Lausanne, Lausanne, Switzerland) discussed the role of the formin protein, Fus1, which is induced upon pheromone signaling in the fission yeast *Schizosaccharomyces pombe*, in promoting the formation of an actin focus. More specifically, she showed that fusion is triggered by a local increase of MAPK at the fusion focus and driven by the positive feedback between formation of the actin focus and focalization of pheromone release (Dudin et al., 2016). But how is the decision to fuse precisely coordinated with cell growth? Martin presented evidence for a negative-feedback loop mechanism that prevents any premature fusion during early steps of mating

Journal of Cell Science

(Merlini et al., 2017 preprint). Cell–cell fusion was long thought to be a symmetrical process, to which the two cells contribute equally. However, Elizabeth Chen (UT Southwestern Medical Center, Dallas, USA) demonstrated in her talk that cell–cell fusion in *Drosophila* myoblasts is an asymmetric process in which, an 'attacking' cell injects invasive protrusions, mediated by F-actin, into the 'receiving' cell to promote cell fusion (Sens et al., 2010). Furthermore, she also presented more recent work illustrating that the cytoskeleton component spectrin dynamically accumulates at the fusogenic synapse within the 'receiving' cell in response to mechanical force. Here, the function of spectrin is to constrict the protrusions from the 'attacking' cell and to so ensure that proper cell–cell fusion occurs.

Concluding remarks

This meeting brought together the latest research from some of the top scientists in the field to create a more complete picture of dynamic cell behavior. While the diverse topics stretched attendees outside their normal comfort zones, the meeting created wide opportunities for learning and thinking outside the box. With these fascinating talks, this inaugural meeting was a clear success and set a high precedent for any future 'Cellular Dynamics' meetings.

References

Abounit, S., Bousset, L., Loria, F., Zhu, S., de Chaumont, F., Pieri, L., Olivo-Marin, J. C., Melki, R. and Zurzolo, C. (2016). Tunneling nanotubes spread fibrillar alpha-synuclein by intercellular trafficking of lysosomes. *EMBO J.* **35**, 2120-2138.

Aguet, F., Upadhyayula, S., Gaudin, R., Chou, Y.-Y., Cocucci, E., He, K., Chen, B.-C., Mosaliganti, K., Pasham, M., Skillern, W. et al. (2016). Membrane dynamics of dividing cells imaged by lattice light-sheet microscopy. *Mol. Biol. Cell* **27**, 3418-3435.

Bartuzi, P., Billadeau, D. D., Favier, R., Rong, S., Dekker, D., Fedoseienko, A., Fieten, H., Wijers, M., Levels, J. H., Huijkman, N. et al. (2016). CCC- and WASH-mediated endosomal sorting of LDLR is required for normal clearance of circulating LDL. *Nat. Commun.* **7**, 10961.

Bergen, D. J. M., Stevenson, N. L., Skinner, R. E. H., Stephens, D. J. and Hammond, C. L. (2017). The Golgi matrix protein giantin is required for normal cilia function in zebrafish. *Biol Open*.

Choi, W., Harris, N. J., Sumigray, K. D. and Peifer, M. (2013). Rap1 and Canoe/afadin are essential for establishment of apical-basal polarity in the Drosophila embryo. *Mol. Biol. Cell* **24**, 945-963.

Daley, W. P., Matsumoto, K., Doyle, A. D., Wang, S., DuChez, B. J., Holmbeck, K. and Yamada, K. M. (2017). Btbd7 is essential for region-specific epithelial cell dynamics and branching morphogenesis in vivo. *Development* **144**, 2200-2211.

Delage, E., Cervantes, D. C., Pénard, E., Schmitt, C., Syan, S., Disanza, A., Scita, G. and Zurzolo, C. (2016). Differential identity of filopodia and tunneling nanotubes revealed by the opposite functions of actin regulatory complexes. *Sci. Rep.* **6**, 39632.

Ding, W. Y., Ong, H. T., Hara, Y., Wongsantichon, J., Toyama, Y., Robinson, R. C., Nédélec, F. and Zaidel-Bar, R. (2017). Plastin increases cortical connectivity to facilitate robust polarization and timely cytokinesis. *J. Cell Biol.* **216**, 1371-1386.

Dorland, Y. L., Malinova, T. S., van Stalborch, A.-M. D., Grieve, A. G., van Geemen, D., Jansen, N. S., de Kreuk, B. J., Nawaz, K., Kole, J., Geerts, D. et al. (2016). The F-BAR protein pacsin2 inhibits asymmetric VE-cadherin internalization from tensile adherens junctions. *Nat. Commun.* **7**, 12210.

Dudin, O., Merlini, L. and Martin, S. G. (2016). Spatial focalization of pheromone/MAPK signaling triggers commitment to cell-cell fusion. *Genes Dev.* **30**, 2226-2239.

Durkin, C. H., Leite, F., Cordeiro, J. V., Handa, Y., Arakawa, Y., Valderrama, F., and Way, M., . (2017). RhoD inhibits RhoC-ROCK-dependent cell contraction via PAK6. *Dev. Cell* **41**, 315-329.e7.

Fung, K. Y. Y., Dai, L. and Trimble, W. S. (2014). Cell and molecular biology of septins. *Int. Rev. Cell Mol. Biol.* **310**, 289-339.

Hui, K. L. and Upadhyaya, A. (2017). Dynamic microtubules regulate cellular contractility during T-cell activation. *Proc. Natl. Acac. Sci. USA* **114**, E4175-E4183.

Kaukonen, R., Mai, A., Georgiadou, M., Saari, M., De Franceschi, N., Betz, T., Sihto, H., Ventelä, S., Elo, L., Jokitalo, E. et al. (2016). Normal stroma suppresses cancer cell proliferation via mechanosensitive regulation of JMJD1a-mediated transcription. *Nat. Commun.* **7**:12237.

Kumari, S., Depoil, D., Martinelli, R., Judokusumo, E., Carmona, G., Gertler, F. B., Kam, L. C., Carman, C. V., Burkhardt, J. K., Irvine, D. J., (2015). Actin foci facilitate activation of the phospholipase C-γ in primary T lymphocytes via the WASP pathway. *Elife* **4**.

Labernadie, A., Kato, . T., Brugués, . A., Serra-Picamal, X., Derzsi, S., Arwert, E., Weston, A., González-Tarragó, V., Elosegui-Artola, A., Albertazzi, L. et al. (2017). A mechanically active heterotypic E-cadherin/N-cadherin adhesion enables fibroblasts to drive cancer cell invasion. *Nat. Cell. Biol.* **19**:224-237.

Luo, Y. and Russinova, E. (2017). Quantitative microscopic analysis of plasma membrane receptor dynamics in living plant cells. *Methods Mol. Biol.* **1564**, 121-132.

Malinverno, C., Corallino, S., Giavazzi, F., Bergert, M., Li, Q., Leoni, M., Disanza, A., Frittoli, E., Oldani, A., Martini, E. et al. (2017). Endocytic reawakening of motility in jammed epithelia. *Nat. Mater.* **16**, 587-596.

Merlini, L., Khalili, B., Dudin, O., Michon, L., Vincenzetti, V. and Martin, S. G. (2017). Feedback inhibition of Ras activity coordinates cell fusion with cell-cell contact. *BioRxiv*.

Moore, A. S., Wong, Y. C., Simpson, C. L. and Holzbaur, E. L. (2016). Dynamic actin cycling through mitochondrial subpopulations locally regulates the fission-fusion balance within mitochondrial networks. *Nat. Comms.* **7**, 12886.

Murugesan, S., Hong, J., Yi, J., Li, D., Beach, J. R., Shao, L., Meinhardt, J., Madison, G., Wu, X., Betzig, E. et al. (2016). Formin-generated actomyosin arcs propel T cell receptor microcluster movement at the immune synapse. *J. Cell Biol.* **215**, 383-399.

Närvä, E., Stubb, A., Guzman, C., Blomqvist, M., Balboa, D., Lerche, M., Saari, M., Otonkoski, T. and Ivaska, J. (2017). A strong contractile actin fence and large adhesions direct human pluripotent colony morphology and adhesion. *Stem Cell Rep.* **9**, 67-76.

Oakes, P. W., Wagner, E., Brand, C. A., Probst, D., Linke, M., Schwarz, U. S., Glotzer, M. and Gardel, M. L. (2017). Optogenetic control of RhoA reveals zyxin-mediated elasticity of stress fibres. *Nat. Commun.* **8**, 15817.

Pelaseyed, T., Viswanatha, R., Sauvanet, C., Filter, J. J., Goldberg, M. L., and Bretscher, A., . (2017). Ezrin activation by LOK phosphorylation involves a PIP2-dependent wedge mechanism. *Elife* **6**.

Phillips-Krawczak, C. A., Singla, A., Starokadomskyy, P., Deng, Z., Osborne, D. G., Li, H., Dick, C. J., Gomez, T. S., Koenecke, M., Zhang, J.-S. et al. (2015). COMMD1 is linked to the WASH complex and regulates endosomal trafficking of the copper transporter ATP7A. *Mol. Biol. Cell* **26**, 91-103.

Rousso, T., Schejter, E. D. and Shilo, B.-Z. (2016). Orchestrated content release from Drosophila glue-protein vesicles by a contractile actomyosin network. *Nat. Cell Biol.* **18**, 181-190.

Saunders, C. A., Harris, N. J., Willey, P. T., Woolums, B. M., Wang, Y., McQuown, A. J., Schoenhofen, A., Worman, H. J., Dauer, W. T., Gundersen, G. G. et al. (2017). TorsinA controls TAN line assembly and the retrograde flow of dorsal perinuclear actin cables during rearward nuclear movement. *J. Cell Biol.* **216**, 657-674.

Sens, K. L., Zhang, S., Jin, P., Duan, R., Zhang, G., Luo, F., Parachini, L. and Chen, E. H. (2010). An invasive podosome-like structure promotes fusion pore formation during myoblast fusion. *J. Cell Biol.* **191**, 1013-1027.

Takao, D., Wang, L., Boss, A. and Verhey, K. J. (2017). Protein interaction analysis provides a map of the spatial and temporal organization of the ciliary gating zone. *Curr. Biol.* (in Press).

Valm, A. M., Cohen, S., Legant, W. R., Melunis, J., Hershberg, U., Wait, E., Cohen, A. R., Davidson, M. W., Betzig, E. and Lippincott-Schwartz, J. (2017). Applying systems-level spectral imaging and analysis to reveal the organelle interactome. *Nature* **546**, 162-167.

Welf, E. S., Driscoll, M. K., Dean, K. M., Schäfer, C., Chu, J., Davidson, M. W., Lin, M. Z., Danuser, G. and Fiolka, R. (2016). Quantitative multiscale cell imaging in controlled 3D microenvironments. *Dev. Cell* **36**, 462-475.

Wu, J., de Heus, C., Liu, Q., Bouchet, B. P., Noordstra, I., Jiang, K., Hua, S., Martin, M., Yang, C., Grigoriev, I. et al. (2016). Molecular pathway of microtubule organization at the Golgi apparatus. *Dev. Cell* **39**, 44-60.

Yang, Y., Zhang, Y., Li, W.-J., Jiang, Y., Zhu, Z., Hu, H., Li, W., Wu, J.-W., Wang, Z.-X., Dong, M.-Q. et al. (2017). Spectraplakin induces positive feedback between fusogens and the actin cytoskeleton to promote cell-cell fusion. *Dev. Cell* **41**, 107-120.