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MEETING REPORT

CYCLING TO DIVIDE: FROM SINGLE MOLECULES TO GLOBAL NETWORKS

CYCLER POUR SE DIVISER :

DE LA MOLECULE UNIQUE AUX RESEAUX GLOBAUX

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sbcf French Society for Cell Biology

JCB Journal of Cell Biology

EMBO

Institut JACQUES MONOD

eLife

Meeting Report
Cycling to Divide: From Single Molecules to Global Networks

General description

The 16th Jacques Monod conference in the series "Cell Cycle" took place May 13- 17, 2024, after a 5-year break due to the interruption of all Jacques Monod conferences during the pandemic for 2 years.

The generous support provided by **CNRS and Inserm** for the Jacques Monod conferences allows the organisation of this meeting at a registration fee that is affordable for most labs. The meeting was further supported by sponsors that the organisers were able to convince to additionally contribute. The organisers are very grateful to the **Sbcf, the French Society for Cell Biology** which is promoting cell biology research and enducation as well as outreach activities and which provided generous funding. The **Journal of Cell Biology** also provided significant financial help. The **Institut Jacques Monod** in Paris, and the journal **eLife** provided additional financial support. The EMBO YIP lecture of Andreas Bolland was supported by **EMBO. EMBO press** and **Communications Biology** provided a Flash talk prize and a Poster prize, respectively. Two independent committees were set up to select the best flash talk, and the best poster amongst junior participants (PhD students or postdocs).

The whole meeting would not have been possible without the organisational support by **Nathalie Babic of the CNRS**, who took care of all the logistics and financial aspects of the meeting. Her help was greatly appreciated, and she not only contributed significantly to the organisation of the meeting, but she was also present and of great help during the meeting.

The Jacques Monod conferences organized in Roscoff are well known in the field, because they are intimate enough that participants often know each other for discussions, yet large enough to get a general overview of the most recent developments in the field. We have tried to provide a gender- and age-balanced selection of speakers, taking into account the fact that a new generation of researchers contributing significantly to the field is emerging. Participants told us that they very much appreciated the friendly and constructive atmosphere of the meeting, even when controversial topics were discussed.

Roscoff is a beautiful setting to organize any meeting, and the walks from the lecture hall to the Gulfstream Hotel and back are relaxing breaks in the rather dense program. The excursion to the Ile-de-Batz was appreciated by the participants, also, because even though the weather forecast was not very positive, it did not rain and participants could walk around the island without getting wet. The food provided to participants at the Gulfstream Hotel was excellent, and as usual, the Dinner in the last evening was outstanding, with lots of seafood and animated discussion.

Summary of the lectures and discussions

The meeting started with a reception and dinner at the Gulfstream Hotel. After dinner, participants walked to the lecture hall to attend the welcome and keynote lecture of the meeting. As a keynote speaker we had invited Brenda Andrews, however, because of an accident just before the meeting she could not travel. Fortunately though, **Marie Hélène Verlhac** from the CIRB (College de France) in Paris, France, agreed to deliver a keynote lecture on a very short notice. She opened the meeting on Monday evening with a beautiful and interesting presentation on oocyte meiosis and how cortical contractions of the oocyte influence oocyte quality, and thus reproductive success. Her findings also apply to human oocytes, and are thus relevant for human reproductive health.

The next morning the meeting continued with a session entitled "A global view on cell cycle control", and a talk by **Silvia Santos**, from the Francis Crick institute in Lonodon, UK, who gave an exciting presentation on how the modulation of the cell cycle time is linked to differentiation of human embryonic stem cells. **Tony Ly** from the University of Dundee, UK talked about inhibitors of Cdk4 and Cdk6, which are used in cancer therapy, to better understand how they can induce cellular senescence and affect the immune phenotype. Next, **Allison Bardin** from the Curie Institute in Paris, France, talked about nucleotide sharing through gap junctions to encounter replication stress, in different drosophila tissues. **Theresa Zeisner** from the lab of Paul Nurse at the Francis Crick Institute then talked about the interplay of Cdk1 substrate phosphorylation and dephosphorylation during cell division in *S. pombe*.

The following session, entitled "Entry, cell size, and progression" started with a presentation by **Jan Skotheim** from Stanford University on Rb degradation and control of the G1/S transition, relevant also to understanding cell cycle control in cancer cells. **Silke Hauf** who works at Virginia Tech, USA, continued with a talk on how proper concentrations of Cyclin B may be achieved through translational regulation. **Alexis Barr** from the MRC in London, UK then continued with a presentation on Wee1, and how it synchronizes the G1/S transition by targetting Cdh1, an activator of the APC/C. **Ikui Amy** from the Brooklyn College in New York, USA then talked about an exciting model system she is using, namely the green algae, which undergo mutliple fission cycles. Her goal is to understand how replication is controlled during these very special cell divisions. Before lunch we had the first out of two Blitz poster sessions, where selected poster presenters were given the opportunity to present the main message of their poster in a 3 min oral presentation (the presenters were **Siyoung Choi, Catriona Conway, Erin Cutts, Luke Futcher, Monica Gobran, Malina Carmina Ilinca** and **Emilie Mathis**).

Lunch at the Gulf Stream Hotel was followed by the first poster session. Half of the posters (40 posters) were presented during the two hours of the session, whereby we asked half of those to be present in front of their poster during the first hour, and the other half during the second hour, so that poster presenters themselves had the chance to look at the other posters

during the same session. The poster session was very intense due to the high quality of the posters and the great interested they generated, leading to lively discussions.

After the poster session the meeting continued with the third session, entitled "Phosphatases". **Anna Castro** from the CRBM in Montpellier talked about FAM122A, a newly identified PP2A-B55 inhibitor, and its role for mitotic entry. **Lionel Pintard** from the Institut Jacques Monod in Paris, France, equally focused on PP2A-B55 inhibition. He is using *C. elegans* as a model system, with the aim of understanding how the PP2A-B55 inhibitor Ensa is regulated in the absence of a clear homolog of the Gwl kinase. **Zach Robert**, from the lab of Helfrid Hochegger in Brighton, UK, explained how a novel inhibitor of Gwl kinase was identified and how it can be used in different cell lines, thus demonstrating the relevance of targeting the Gwl and PP2A in cancer therapy. The last speaker of this session was **Monica Gotta**, from the University of Geneva in Switzerland, who talked about the kinase Plk1 and phosphatases in polarity establishment in C. elegans embryos.

The next session was entitled "Cyclins 1" and started with a presentation by **Andreas Boland** from the University of Geneva in Switzerland, who delivered an Embo Young Investigator talk on a binding pocket for Cyclin B1/Cdk1 which they have recently identified. He presented structural insights into the inhibition of Separase by Cyclin B1/Cdk1 and into the autocleavage activity of Separase. The next talk was given by **Iain Hagan** from the University of Manchester, UK, and President of the last Cell Cycle meeting in Roscoff, who talked about the spindle pole body in fission yeast, and how localized activity of mitotic kinases there feeds back to the cell cycle machinery. Then, **Julia Kamenz** from the University of Groningen in the Netherlands, presented the generation of a new single fluorophore biosensor to monitor Cdk1 activity in real time in Xenopus extracts.

After dinner at the Gulfstream Hotel, the evening continued with an evening session, that was entitled "How important is spatial control of mitotic kinases ?" **Toru Hirota**, from the Cancer Institute of the Japanese Foundation of Cancer Research in Tokyo, Japan, talked about the epigenetic environment at the centromere for Aurora B recruitment through H3K9 methylation which localizes HP1 and then Aurora B in a phosphoserine 10 dependent manner. He asked how ongoing transcription and HP1 recruitment are connected at the centromere. His talk was followed by a presentation by **Fanni Gergely** from the University of Oxford, UK who talked about Aurora A localization and association with binding partners such as CEP192 and TPX2 for localizaed activity. The last speaker of this session was **Kotak Sachin** from the Indian Institute of Science, in Bangalore, India. He focussed on the interplay of mitotic kinases and phosphatases as well as microtubule-depending mechanical forces for nuclear envelope disassembly in *C. elegans* embryos.

Wednesday morning started with a session entitled "Gametogenesis". The first talk was given by **Joao Matos** from the University of Vienna, Austria, whose lab studies how recombination

events are taking place in meiosis. He showed exciting data demonstrating the importance of Holliday junctions in the maintenance of the synaptonemal complex. **Katja Wassmann** from the Institut Jacques Monod in Paris and main organizer of the meeting provided insights into the control mechanisms impinging on Separase during the oocyte meiotic divisions, with a special focus on the transition from meiosis I into meiosis II. Her talk was followed by a presentation by **Andreas Heim,** from the lab of Thomas U. Mayer, at the University of Konstanz, Germany. He talked about the prolonged prophase I arrest that oocytes have to observe before resuming the first meiotic division. His work is focussed on tranlational repression mediated by 4E-T, which he found to be essential for downregulating protein synthesis and thus, maintaining prophase I arrest in frog as well as mouse oocytes.

After the coffee break, the next session, entitled "Cyclins II" started with a talk by **Julia Vorhauser** from the Insitute of Cancer Research in London, UK, working in the lab of Jörg Mansfeld. She presented data showing that p21 is a redox-regulated cell cyle inhibitor, and she proposes a model where the oxidation state of p21 regulates its interaction with Cdk4/6 versus Cdk2 to control its protein levels. Then, **Cirillo Luca**, from the Jonathan Pines lab also working at the Institute of Cancer Research in London, showed data on the spatial control of APC/C activity towards Cyclin B1. They found that APC/C as well as Cyclin B1 can interact with nucleosomes, and identified a nucleosome binding motif in Cyclin B1. **Pablo Lara-Gonzalez** from the University of California Irvine, USA, talked about an understudied Cyclin, namely Cyclin B3, and its role during early embryogenesis in *C. elegans,* where Cyclin B3 not only promotes the rapid divisions in embryos, but also seems to coordinate cell fate decisions by targeting two RNA binding proteins for degradation. This talk was followed by the second Blitz poster session, presented by **Caitlin Mellor, Marika Miot, Evanthia Pangou,Aanchal Udaynath Pareri, Lucas Takacs, Laura Tovini,** and **Noah Turner.** Finally, a short discussion on the new publishing model provided by eLife was moderated by two scientific editors of eLife present at the meeting, namely **Silke Hauf** and **Adele Marston**. The lively discussion allowed the audiance to better understand the submission process at eLife and seemed very helpful.

After lunch participants could enjoy some free time or participate at the excursion to the Ile de Batz. Eeverybody met again for the second poster session, which, as the first one, allowed for lots of discussions and interaction between the participants.

The session after the poster session was entitled "When things go wrong". It started with a talk by **Geert Kops**, from the Oncode Institute in Utrecht, in the Netherlands. Using expansion and super resolution microscopy he presented work showing that in contrary to the current belief, a single kinetocore is assembled of two functionally distinct units, each of which can form interactions with microtubule bundles, stabilized by condensin and cohesin complexes. Next followed a virtual talk by **Kruno Vukusic**, from tha lab of Iva Tolic at the Ruder Boskovic Institute in Zagreb, Croatia. His work is focussed on the connection between failures in chromosome congression and ehaustion of Cyclin A2 leading to chromosomal instability

across several cancer cell lines. This talk was followed by **Susanne Lens** from the Oncode Institute and Center of Molecular Medicine in Utrecht, Netherlands, who showed how aneuploidies may affect certain chromosomes preferentially in certain cancer types, such as colorectal cancers, due to the microenvironment that is specific to certain tumor types.

After this session the participants could enjoy a free evening in a restaurant of their choice in Roscoff. The next morning, talks started with a session entitled "Centrosomes and Centromeres". The session started with **Julien Dumont**, from the Institut Jacques Monod in Paris, who talked about different species of nematodes that are reproducing parthenogenetically, and the question of how they have adapted female meiosis to the fact that reproduction occurs without the presence of paternal genome, with a special focus on how proper centromsome number is achieved in the offspring. His talk was followed by a presentation given by **Karen Oegema** from the University of San Diego, USA. She talked about the mitotic stop-watch, which designs a mechanism that allows a cell to determine whether it has spent too much time in mitosis, resulting in apoptosis in the following cell cycle. She showed that cells are even able to detect accumulating delays during mutliple mitotic divisions to induce apoptosis. One selected speaker had cancelled her participation, however, **Arnault Echard** proposed to give a short talk at her place, which we gratefully accepted. He talked about cytokinesis abscission and the midbody remnant, which remains after abscission taking place at both sites of the midbody and is engulved by one of the daughter cells. The final talk of this session was given by **Warif El Yakoubi** from the lab of Takashi Akera at the NIH in the USA. He talked about differences in major satellite repeats at centromeres between distinct species of mice that function as reproductive barriers, because they lead to centromere stretching due to variations in condensin levels and thus, failures in chromosome segregation.

A photographer was present throughout the day, and during the coffee break participants were asked to go outside for a group picture before the next session, entitled "Chromosome structure". The following session started with a presentation by **Hironori Funabiki**, from the Rockefeller Institute in New York, USA. In his talk he proposed a novel model of how Aurora B kinase may phosphorylate certain substrates at kinetochores under conditions were there is less tension applied by the mitotic spindle and thus indicative of a merotelic attachment. He proposed that certain sites are masked when there is tension, and for this reason cannot be phsophorylated anymore. However, microtubule binding is required for a first phosphorylation, before masking occurs, indicating that there is a maturation process required for Aurora B to be prevented from phosphorylating substrates that are under tension. His talk was followed by a presentation given by **Frederic Beckouët**, from the Centre de Biologie Integrative, in Toulouse, France. He showed data on the structure of cohesin dependent loops, and their size and position is regulated. Then, **Adele Marston** from the University of Edinburgh and co-organizer of this meeting and main organizer of the next meeting presented her recent data showing that condesins bind interacting proteins through a SLiM (Short Linear Motif) which they identified in Sgo1. This interaction between condensin

and Sgo1 is necessary for biorientation of sister kinetochores and thus, correct chromsome segregation. Flora Paldi from the Giacomo Cavalli lab at the IGH in Montpellier, France, gave a presentation on epigenetic memory throughout cell division using mouse embryonic stem cells as well as mouse gastruloids. **Bethan Medina Pritchard** from the lab of Arockia Jeyaprakash presented results on CENP-A reloading after replication, when the amount per centromere is divided by half. The focus of the talk was on Mis18, required for CENP-A reloading through Plk1 self-primed phosphorylations, revealing a role for Plk1 in ensuring maintenance of centromere identity. The last session was entitled "SAC and cell cycle exit". **Elif Nur Firat Karalar** , EMBO Young Investigator at the Koc University in Istanbul, Turkey, gave a virtual presentation on the ciliopathy protein CCDC66. She showed that this protein regulates microtubule nucleation through both centrosomal and non-centrosomal pathways. CCDC66 can bundle microtubules in vitro, and her work shows that the roles of this protein are not limited to proper functioning of the cilia, but also mitotic progression and cytokinesis. **Simonetta Piatti**, from the CRBM in Montpellier, France, gave a presentation on Septins, which are required for cytokinesis. The have found that septins form a double ring at the bud neck in *S. cerevisiae*, which is essential for its function and that this depends on the mitotic exit network (MEN). Through phosphoproteome analysis they were able to identify the target of the MEN to reorganize Septins into a double ring. Izabela Sumara from the IGBMC in Illkirch, France, presented her work on the cytosolic assembly of nuclear pores during early interphase. The meeting ended with a final talk delivered by **Andrea Musacchio**, from the Max Planck Institute in Dortmund, Germany. He presented our current knowledge on the mitotic checkpoint complex, and how it assembles at the kinetochore, and focused on outstanding questions of how complex formation is modulated in response to microtubule interactions with the kinetochore.

Sessions:

Session I: A global view on cell cycle control
Session II: Entry, cell size and progression
Session III: Phosphatases
Session IV: Cyclins I
Session V: How important is spatial control of mitotic kinases ?
Session VI: Gametogenesis
Session VII: Cyclins II
Session VIII: When things go wrong
Session IX: Centrosomes and centromeres
Session X: Chromosome strucutre
Session XI: SAC and cell cycle exit

Conclusion and recommendations

Our conference, entitled "**Cycling to Divide: From Single Molecules to Global Networks**" was the first in the series since the pandemic, and eagerly awaited by the cell cycle community. As a consequence, the meeting was oversubscribed, and we (the organisers) had to select participants from the many excellent abstracts that have been submitted, attesting for the attractivity of the Jacques Monod conferences in the cell cycle field. In the selection, we aimed to propose an equilibrated program with participants chosen from different labs, so that there was at least one participant per lab that wanted to attend. Overall the meeting was a huge success. New technologies allow us to revisit major unresolved questions in this field from a new angle. A lasting impression from this meeting is the large number of impressive advances which stem from the integration of techniques supported by artifical intelligence. For example, Alphafold structural predictions became incredibly useful to develop working hypotheses that can be addressed by mutant approaches. Cell cycle questions can now be addressed in all their complexity in the context of the development of an organism, or during tumorigenesis. The field has moved forward with incredible speed since the last meeting took place, and it was a pleasure to see many new faces and junior researchers getting established with their own labs.
The only recommendation we may have for the next meeting would be the organization of a "beer poster session" in the evening, to have more time for discussion in front of the posters.

French summary

Notre conférence, intitulée « Cycler pour se diviser : de la molécule unique aux réseaux globaux » était la première de la série depuis la pandémie, et donc très attendue par la communauté du cycle cellulaire. En conséquence, la conférence a été sursouscrite et nous (les organisateurs) avons dû sélectionner les participants parmi les nombreux excellents résumés qui ont été soumis, attestant de l'attractivité des conférences Jacques Monod dans le domaine du cycle cellulaire. Lors de la sélection, nous avions pour objectif de proposer un programme équilibré avec des participants choisis venant des différents laboratoires, afin qu'il y ait au moins un participant par laboratoire souhaitant y assister. Dans l'ensemble, la réunion a été un énorme succès. Les nouvelles technologies nous permettent de revisiter des questions non résolues sous un nouvel angle. Ce qui a été le plus impressionnant, c’est probablement l’intégration de techniques appuyées par l’intelligence artificielle. Par exemple, les prédictions structurelles d’Alphafold sont devenues incroyablement utiles pour développer des hypothèses de travail pouvant être abordées dans les approches mutantes, grâce aux informations acquises avec ces prédictions structurelles. Les questions du cycle cellulaire peuvent désormais être abordées dans toute leur complexité dans le cadre du développement d'un organisme, ou lors de la tumorigenèse. Le domaine a progressé à une vitesse incroyable depuis la dernière conférence, et ce fut un plaisir de voir de nombreux nouveaux visages et jeunes chercheurs s'établir avec leurs propres laboratoires.