Fanni Gergely: Exploring centrosome biology

Gergely investigates the roles of centrosomes in mitosis and beyond.

PHOTO COURTESY OF FANNI GERGELY

Fanni Gergely

Encouraged by her parents to study abroad, Fanni Gergely left Budapest, Hungary, for Peterhouse College at the University of Cambridge, UK, with the intention to study theoretical physics. To her surprise, she developed an interest for experimental sciences during an internship with Simon Maddrell, which was further confirmed by a short stay in Daniel St. Johnston's group studying *Drosophila* oogenesis. Fanni joined Jordan Raff's lab at the Wellcome/CRC (now Gurdon) Institute, to pursue her PhD. Her project focused on cloning and characterizing the mammalian homologues to D-TACC, then–newly identified microtubule-binding proteins that play a role in mitosis.

After being awarded a Junior Research Fellowship by Gonville and Caius College and a Dorothy Hodgkin Fellowship by the Royal Society, she joined Colin Taylor's group in the Department of Pharmacology, University of Cambridge, to learn about membrane biology and signaling in her postdoctoral studies. However, she returned to mitosis when she found a role for the microtubule polymerase ch-Tog in maintaining spindle bipolarity. Through her postdoc, Fanni moved her attention to the interplay between mitosis and genome stability, and, in particular, concentrated on how centrosomes define spindle poles. In 2005, she was awarded a Royal Society University Research Fellowship to work on centrosomes at the University of Cambridge. She became a tenure-track group leader at the Cancer Research UK Cambridge Institute (CRUK CI) in 2006 and received tenure in 2012. We contacted her to learn more about her exciting research and career.

> "A complex picture [of centrosomes] is emerging, with tissue-specific and ubiquitous phenotypes, so we are in this for the long haul."

Tell us more about your transition from membrane biology to mitosis.

In Colin Taylor's group, my aim was to decipher how inositol trisphosphate receptors are retained at the endoplasmic reticulum and use this information to target them to the plasma membrane for electrophysiology assays. Instead, we discovered that these calcium channels were retained at the endoplasmic reticulum via their transmembrane domains, which meant that mutating their targeting sequences would have rendered them inactive. This was disappointing, but the results coincided with the emergence of siRNA technology, and I was itching to try it out on the TACC genes. Now back as a postdoc in Jordan's lab, I had discovered that TACC3 and its binding partner ch-Tog/XMAP215, a highly conserved microtubule polymerase, are required for chromosome alignment in mitosis. I found a role for ch-Tog in maintaining spindle bipolarity—cells depleted of ch-Tog exhibited striking multipolar spindles in the presence of normal centrosome numbers. This study marked my return to the mitosis field and got me interested in the link between mitosis and genome stability, and, in particular, how centrosomes define spindle poles—questions my group is still investigating.

What interested you about centrosome biology?

Centrosomes are clearly important for mitotic spindle function, but their roles are not restricted to mitosis. The core structure of centrosomes, the centriole, is essential for growing the primary cilia, a sensory and signaling organelle present in many cell types. Moreover, through their ability to organize microtubules, centrosomes contribute to cell polarity and migration and fulfill specialized functions such as those at the immunological synapse during cytotoxic T cell killing (1). There could be further cell type–specific functions still waiting to be discovered.

My group has addressed centrosome biology on different levels ranging from the roles of individual components to the function of the organelle as an entity (2). We have recently described how a conserved centrosomal protein, in a complex with the microtubule motor, helps to link centrosomes with spindle poles. Remarkably, cells with supernumerary centrosomes seem to have hijacked the same complex to promote the clustering of centrosomes into pseudo-bipolar spindles, a survival tactic (3). By disrupting essential centrosomal proteins in vitro, we discovered important roles for the centrosome in the regulation of spindle assembly and genome stability (4).

What are you currently working on, and what is up next for you?

Toward the end of my PhD studies, I stained cancer tissues with antibodies against centrosomal and mitotic spindle proteins and was struck by how abnormal these structures were. From the work of many groups, including mine, we learned that mutations in several centrosomal genes cause growth defects such as abnormally small brain and dwarfism. I still find this dichotomy of growth-promoting and growth-suppressing abilities of centrosomes compelling.

In order to address the physiological significance of centrosomes, we recently turned to mouse models. A complex picture

Downloaded from http://rupress.org/jcb/article-pdf/215/3/294/1603606/jcb_2153pi.pdf by guest on 08 February 2026

Text and Interview by Melina Casadio
mcasadio@rockefeller.edu

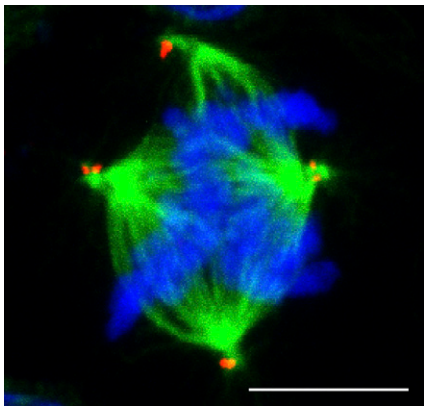

IMAGE COURTESY OF PAVITHRA L. CHAVALI

Deleting CEP215 compromises the connection between centrosomes and spindle poles and impairs centrosome clustering in cells with excess centrosomes. Microtubules are in green, and centrioles in red. Scale bar, 5 µm.

is emerging, with tissue-specific and ubiquitous phenotypes, so we are in this for the long haul. Being based in a Cancer Research UK Institute facilitates collaborations with clinicians, creating the opportunity to study centrosome biology in primary tumor samples. We hope to bring our knowledge from basic cell biology and mouse models to understand the origin of centrosome abnormalities in cancers and find out whether they can be exploited for treatment.

What kind of approach do you bring to your work?

At heart I am a geneticist and a cell biologist, but in the lab we use every approach we think is necessary. Proteomics has become increasingly important over the years, and more recently we started using next generation sequencing. Our research has also benefited greatly from an expanding list of collaborators that includes structural biologists, chemists, clinical geneticists, and oncologists.

What did you learn during your PhD and postdoc that helped prepare you for being a group leader? What were you unprepared for?

In today's world, when mobility is regarded as an essential part of the scientific journey, I often get asked (and I sometimes wonder) how I ended up staying in Cambridge for such a long time and without intending to do so. I liked the place—I greatly appreciated the lack of hierarchy, the intellectual freedom, the density of smart people, and the generosity of the society. However, my main reason for staying was the personal funding (and its no-strings-attached nature) I received continually between 2000 and 2013. The Junior Research Fellowship by Gonville and Caius College and the Royal Society's two fellowship schemes—the Dorothy Hodgkin Fellowship and the University Research Fellowship—were instrumental to my development as an independent scientist.

I enjoyed my PhD and postdoc, mostly because I was given freedom over my projects. As a result, I try not to be overly prescriptive and let people find aspects of their projects they enjoy, so that they can develop these further. I was lucky enough to have worked with gifted and dedicated people. However, nobody prepares you for the challenges that are external to the lab. Individuals can experience real traumas in their personal lives whilst in the lab; as their mentor, you need to find the right balance of empathy and distance to allow the work to continue. This may be the hardest aspect of managing people.

> "Having a long-term plan is useful, but... sometimes it is more helpful ...to think of your future in small, digestible chunks."

What is the best advice you have been given?

As somebody who is prone to procrastination, I was told to follow the elephant rule (how do you eat an elephant? One bite at a time.) I break big tasks into little ones and just focus on the first minor task. Another equally great piece of advice is to take risks; I am grateful to Bruce Ponder for encouraging me to turn down an offer in exchange for a possible position in a then virtual institute.

What are your hobbies?

I was about to say that independent films, because I ran a film club for 18 years, but since the birth of my daughter two years ago, I have hardly watched a movie, unless on an airplane, let alone organized a club. I hope to resume this hobby at some point in the future. On the plus side, there will be loads of "new" films waiting. I also like literature and classical music.

What do you think you would be if you were not a scientist?

I am fascinated by archeology, especially ancient civilizations. I also enjoy architecture and design, but whether I would be any good at either, I don't know.

What has been your biggest accomplishment outside of the lab?

This is a hard one. Possibly keeping my daughter alive and contented for two years! And participating in my family's life (at least in spirit) over the past 20 years while working in the UK.

Any tips for a successful research career?

Everyone tells you that you must have a 5- or even a 10-year plan. Having a long-term plan is useful, but I find that sometimes it is more helpful and less stressful to think of your future in small, digestible chunks (similarly to the elephant rule). Not worrying about a 10-year plan also makes it easier to take some risk. Finally, you need a support network; in my case the generosity of my parents, my grandmother, and siblings has been essential for me to get this far. And without my extremely supportive partner, I would probably never make it to work.

1. Zyss, D., et al. 2011. *J. Cell Biol.* 195:781–797.
2. Sir, J.H., et al. 2011. *Nat. Genet.* 43:1147–1153.
3. Chavali, P.L., et al. 2016. *Nat. Commun.* 7:11005.
4. Sir, J.H., et al. 2013. *J. Cell Biol.* 203:747–756.

PHOTO COURTESY OF KJ PATEL

Gergely next to an ancient Greek theatre on a foggy day in Palazzolo Acreide, Sicily.

Downloaded from http://rupress.org/jcb/article-pdf/215/3/294/1603606/jcb_2153pi.pdf by guest on 08 February 2026