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**Our team explores how the cytoskeleton is organized, how it controls the establishment of functional membrane domains devoted to polarized cell growth or cell division, and how it is remodeled at mitotic entry for the assembly of the mitotic spindle and contractile ring, two complex molecular machines promoting chromosome segregation and cytokinesis. Most our studies are performed in the fission yeast where cell organization is stereotyped and the cytoskeleton relatively simple.**

We combine classical molecular genetics with state-of-the-art live cell microscopy approaches in combination with micro-fabricated devices to control cellular environment. More recently, we have started exploring evolutionary conserved pathways in mammalian cells.

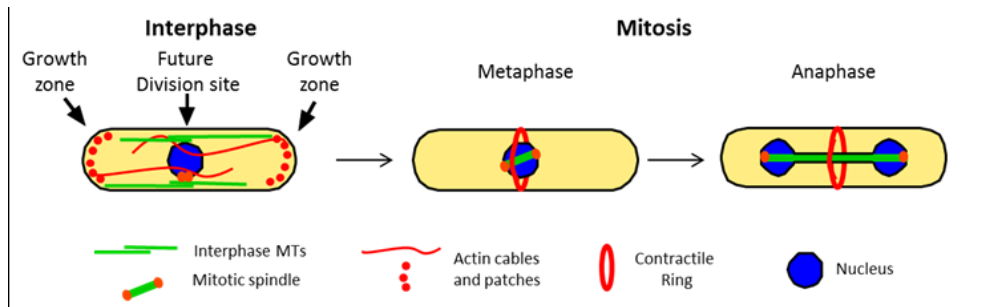


Figure 1: Organization of functional spatial domains by microtubules (MTs) and actin. MTs - assembled in symmetrical antiparallel bundles - position the nucleus in the middle where cell division will take place; MTs also dictate actin-dependent sites of polarized cell growth.

## Microtubule-based functions (Phong Tran).

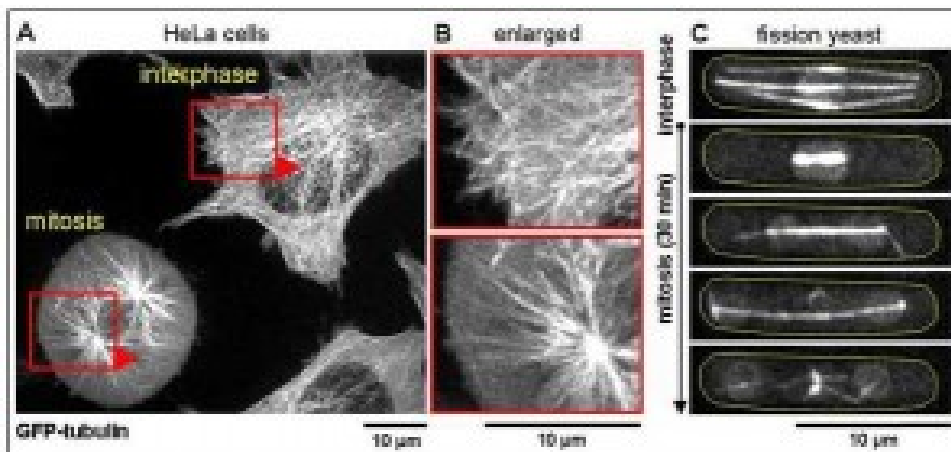


Figure 2 : Fission yeast is a good model to study the MT cyto-skeleton. (A) HeLa cells expressing GFP-tubulin. Shown are interphase and mitotic cells. (B) Enlarged images. (C) Interphase fission yeast has only 3-5 MT bundles. Mitotic fission yeast has a relatively simple spindle that resembles an elongating bar.

We are interested in understanding how cell polarity and cell division are orchestrated by the cytoskeleton. Our previous studies in fission yeast have shown that bundles of microtubules can direct new sites of actin-dependent polarized cell growth; and microtubules organize the mitotic spindle for chromosome segregation. Cytoskeletal architecture and dynamics are influenced by associated proteins such as motors and bundlers, and

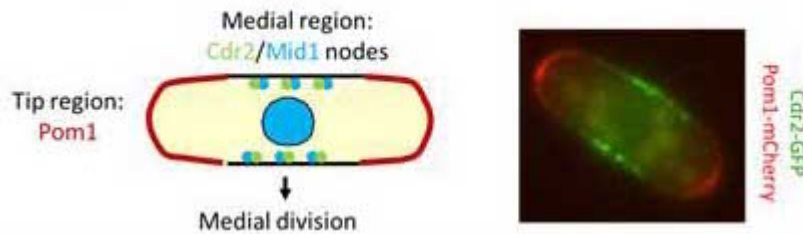


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regulatory proteins such as kinases and phosphatases. A long-term goal is to understand the molecular mechanisms by which these proteins function, and establish potential evolutionary conservation between yeast and man. Our plan is to (1) identify the molecular components of the cell shape and cell division pathway, (2) define the interactions of known (and newly discovered) cytoskeletal proteins and their roles in cell polarity and cell division, and (3) develop and apply advanced optical imaging analysis, and nanotechnology methods to the yeast and mammalian cell systems (Fig. 2).

### **Spatio-temporal regulation of cell division (Anne Paoletti)**

### Pom1-dependent control of Cdr2/Mid1 medial nodes assembly



*Figure 3: Spatio-temporal regulation of cell division in fission yeast. Contractile ring Node precursors are composed of the two major components Cdr2 and Mid1. Their assembly is restricted to the middle by Pom1 kinase which forms a gradient emanating from the cell tips. Pom1 lowers Cdr2 affinity for membrane lipids and also inhibits Cdr2 clustering dependent on Mid1/Cdr2 interaction.*

Our aim is to determine how cell division is controlled in time and space to guarantee a correct segregation of chromosomes and an equal partitioning of the cytoplasm between sister cells. Our past work showed that in fission yeast, it involves medial cortical nodes organized by the SAD kinase Cdr2 and the anillin-like protein Mid1 that define the position of the division plane in interphase and trigger medial assembly of the contractile ring during mitosis. Cdr2 nodes are restricted to the medial cortex by the DYRK kinase Pom1 which forms gradients emanating from the cell tips (Figure 3). Our most recent work shows that Pom1 prevents Cdr2 node assembly at cell tips by reducing Cdr2 affinity for membrane lipids and down-regulating Cdr2 clustering abilities depending on interactions with Mid1. Interestingly, Cdr2 also favors mitotic entry by inhibition of Wee1. This function is also inhibited by Pom1. However, Pom1 inhibition is relieved upon cell growth, allowing entry into mitosis and coupling mitosis entry to cell size. Our goal is now to characterize the function of additional components of medial cortical nodes that participate in division plane positioning or mitotic promoting functions. We also want to understand the signaling cascades and molecular mechanisms at play to remodel the nodes at mitotic entry when the

contractile ring starts assembling. We finally plan to address the evolutionary conservation of these pathways regulating cell division in higher Eukaryotes.

## Key publications

### Year of publication 2017

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Sergio A Rincon, Adam Lamson, Robert Blackwell, Viktoriya Syrovatkina, Vincent Fraisier, Anne Paoletti, Meredith D Betterton, Phong T Tran (2017 May 18)

**Kinesin-5-independent mitotic spindle assembly requires the antiparallel microtubule crosslinker Ase1 in fission yeast.**

*Nature communications* : 15286 : [DOI : 10.1038/ncomms15286](https://doi.org/10.1038/ncomms15286)

### Year of publication 2015

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Mercè Guzmán-Vendrell, Sergio A Rincon, Florent Dingli, Damarys Loew, Anne Paoletti (2015 Apr 17)

**Molecular control of the Wee1 regulatory pathway by the SAD kinase Cdr2.**

*Journal of cell science* : 2842-53 : [DOI : 10.1242/jcs.173146](https://doi.org/10.1242/jcs.173146)

Kathleen Scheffler, Refael Minnes, Vincent Fraisier, Anne Paoletti, Phong T Tran (2015 Apr 15)

**Microtubule minus end motors kinesin-14 and dynein drive nuclear congression in parallel pathways.**

*The Journal of cell biology* : 47-58 : [DOI : 10.1083/jcb.201409087](https://doi.org/10.1083/jcb.201409087)

Imène B Bouhrel, Midori Ohta, Adeline Mayeux, Nicole Bordes, Florent Dingli, Jérôme Boulanger, Guilhem Velve Casquillas, Damarys Loew, Phong T Tran, Masamitsu Sato, Anne Paoletti (2015 Mar 3)

**Cell cycle control of spindle pole body duplication and splitting by Sfi1 and Cdc31 in fission yeast.**

*Journal of cell science* : 1481-93 : [DOI : 10.1242/jcs.159657](https://doi.org/10.1242/jcs.159657)

### Year of publication 2014

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Kathleen Scheffler, Pierre Recouvreux, Anne Paoletti, Phong T Tran (2014 Nov 24)

**Oscillatory AAA+ ATPase Knk1 constitutes a novel morphogenetic pathway in**



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### **fission yeast.**

*Proceedings of the National Academy of Sciences of the United States of America* : 17899-904 :

[DOI : 10.1073/pnas.1407226111](https://doi.org/10.1073/pnas.1407226111)

Viktoriya Syrovatkina, Phong T Tran (2014 Sep 24)

### **Loss of kinesin-14 results in aneuploidy via kinesin-5-dependent microtubule protrusions leading to chromosome cut.**

*Nature communications* : 7322 : [DOI : 10.1038/ncomms8322](https://doi.org/10.1038/ncomms8322)