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.
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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).

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
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)
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
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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 2019

Federica Arbizzani, Sergio A Rincon, Anne Paoletti (2019 Jun 21)
Increasing ergosterol levels delays formin-dependent assembly of F-actin cables and disrupts division plane positioning.
Journal of cell science : DOI : jcs.227447

Isabelle Loiodice, Marcel E Janson, Penny Tavormina, Sebastien Schaub, Divya Bhatt, Ryan Cochran, Julie Czupryna, Chuanhai Fu, Phong T Tran (2019 Mar 7)
Quantifying Tubulin Concentration and Microtubule Number Throughout the Fission Yeast Cell Cycle.
Biomolecules : DOI : E86

Lara Katharina Krüger, Jérémie-Luc Sanchez, Anne Paoletti, Phong Thanh Tran (2019 Feb 27)
Kinesin-6 regulates cell-size-dependent spindle elongation velocity to keep mitosis duration constant in fission yeast.
eLife : DOI : 10.7554/eLife.42182

Year of publication 2017

Kinesin-5-independent mitotic spindle assembly requires the antiparallel microtubule crosslinker Ase1 in fission yeast.
Nature communications : 15286 : DOI : 10.1038/ncomms15286

Sergio A Rincon, Miguel Estravis, Florent Dingli, Damarys Loew, Phong T Tran, Anne Paoletti (2017 Feb 7)
SIN-Dependent Dissociation of the SAD Kinase Cdr2 from the Cell Cortex Resets the Division Plane.
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]