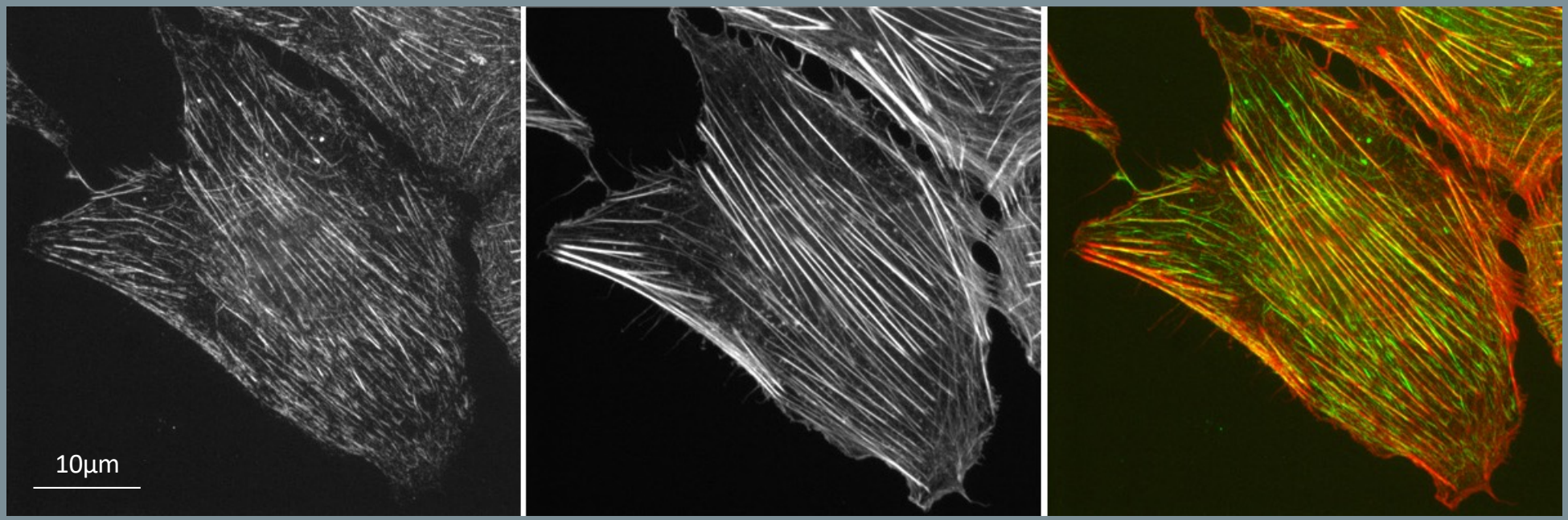
SEPTIN FILAMENTS

New cytoskeleton element

Septins Actin Septins Actin



STRUCTURE AND ASSEMBLY

of septin cytoskeleton

A family of 13 genes in humans

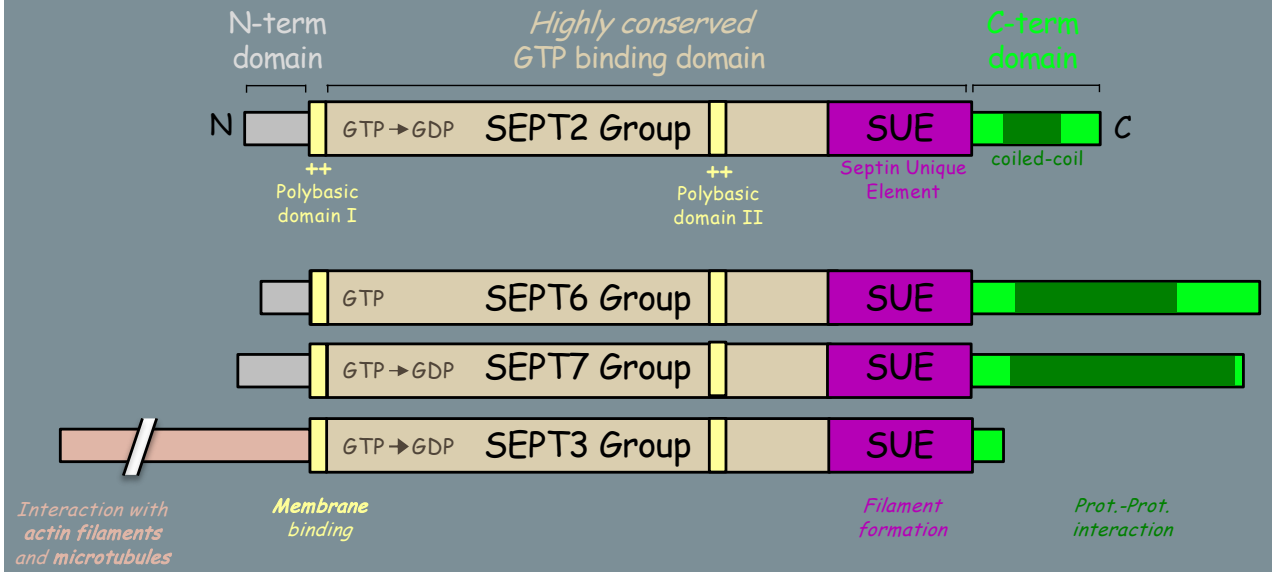
Coding for > 30 isoforms

SEPTINS were discovered in 1971 and named for their function in septation

Ubiquitous proteins, conserved from yeast to humans *(absent in plants)*

Primary structure

GTP-binding proteins, GTPase superfamily

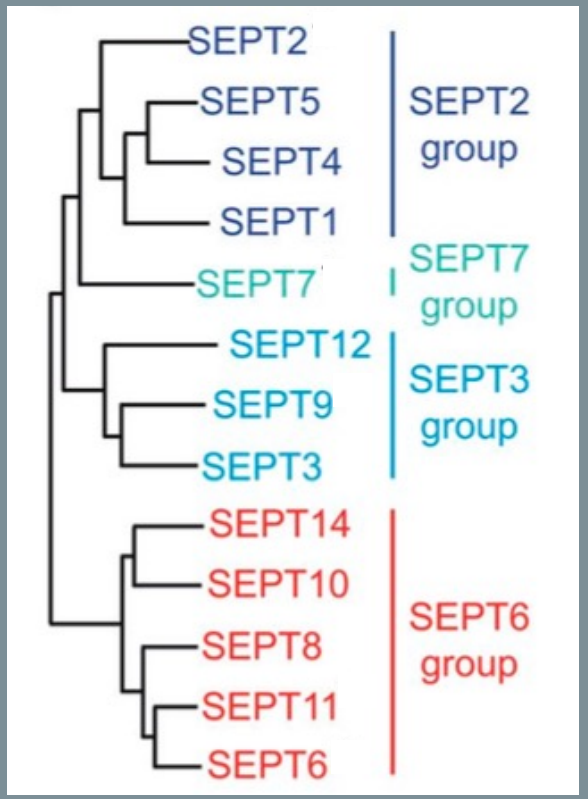


from Ribet et al., J. Cell Biol. (2017)

Omrane et al., iScience (2019)

Categorized into four groups

according to sequence homology



Kinoshita et al., J. Biochem. (2003)

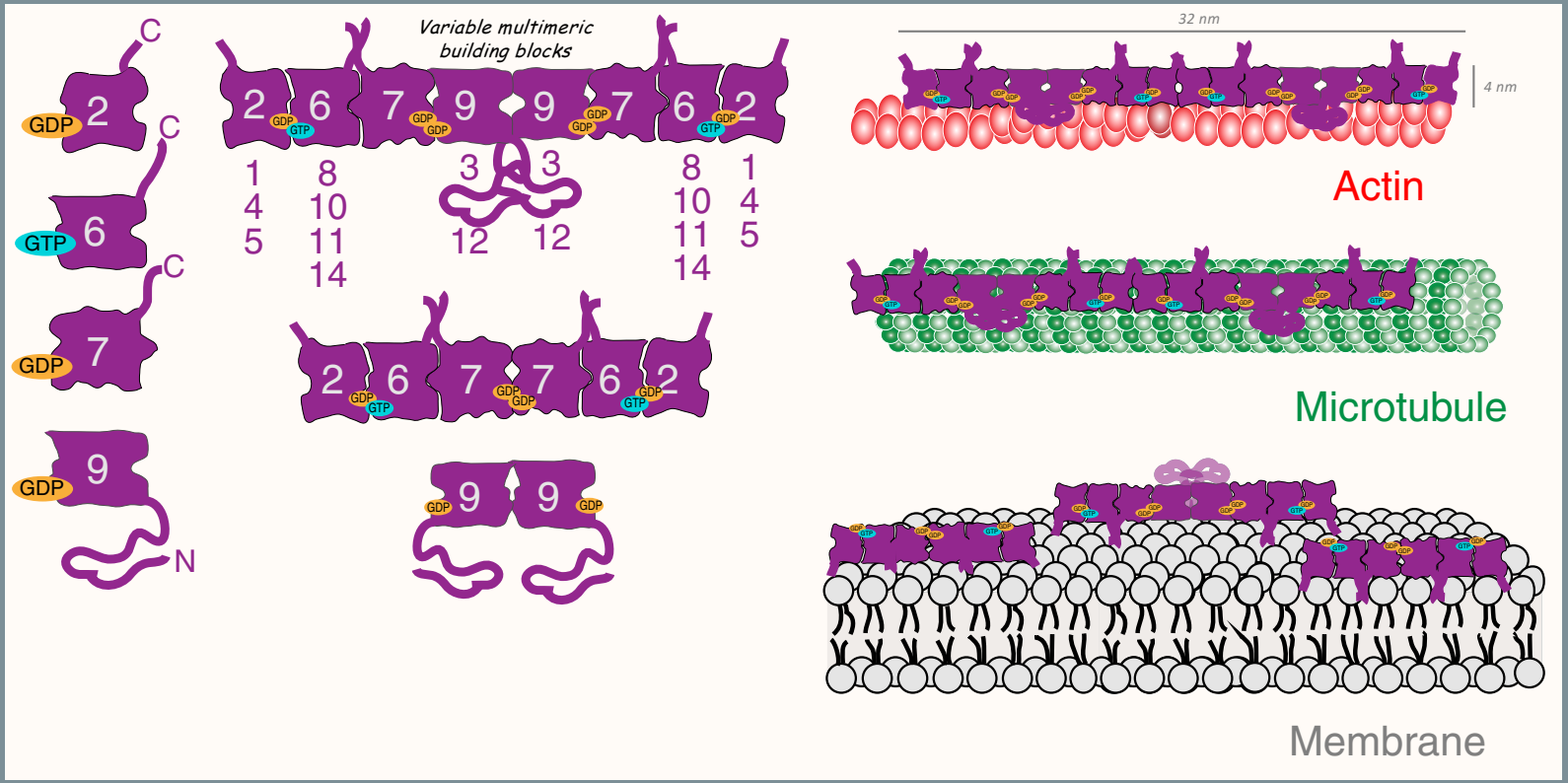
Oligomerization, filament formation and association with other cytoskeleton elements

4th cytoskeleton element

Mostowy et al., Nat. Rev. Mol. Cell Biol. (2012)

Non-polar filaments

Self-assembly into palindromic heteromers (*hexamers and octamers*)

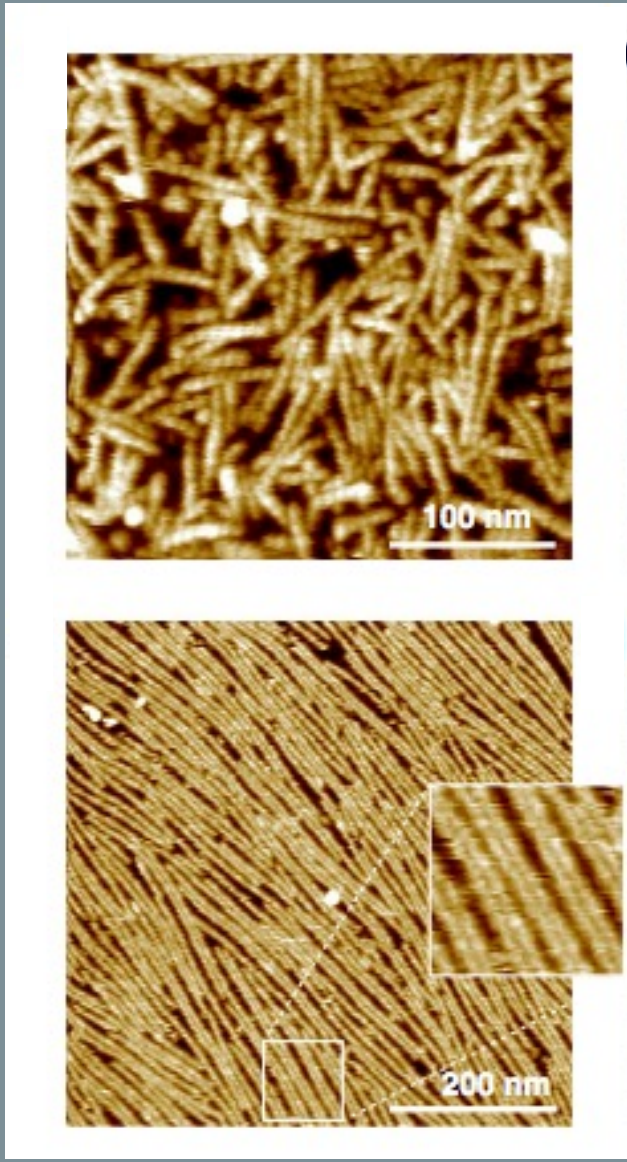


from Spiliotis and Nakos, Curr. Biol. (2021)

Mendonça et al., Cytoskeleton (2019) *Soroor et al., Mol. Biol. Cell (2021)*

End-to-end assembly of heteromers to form non-polar filaments

Hydrophobic epoxy surface



Disorganized filaments

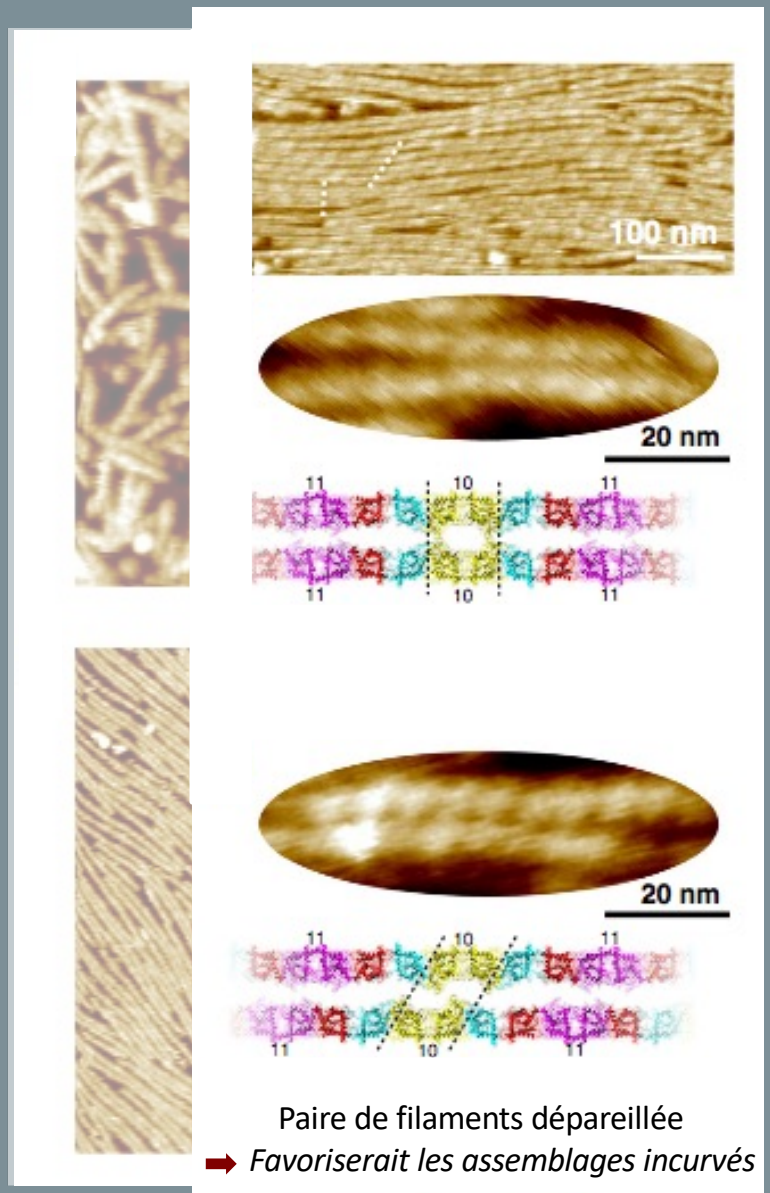
Paired filaments

Mica surface
negatively charged
like the plasma membrane

High-Speed Atomic Force Microscopy

Jiao et al., Nat. Com. (2020)

Variability of filament pairing



Matched filament pairs

Mismatched filament pairs

Paire de filaments dépareillée

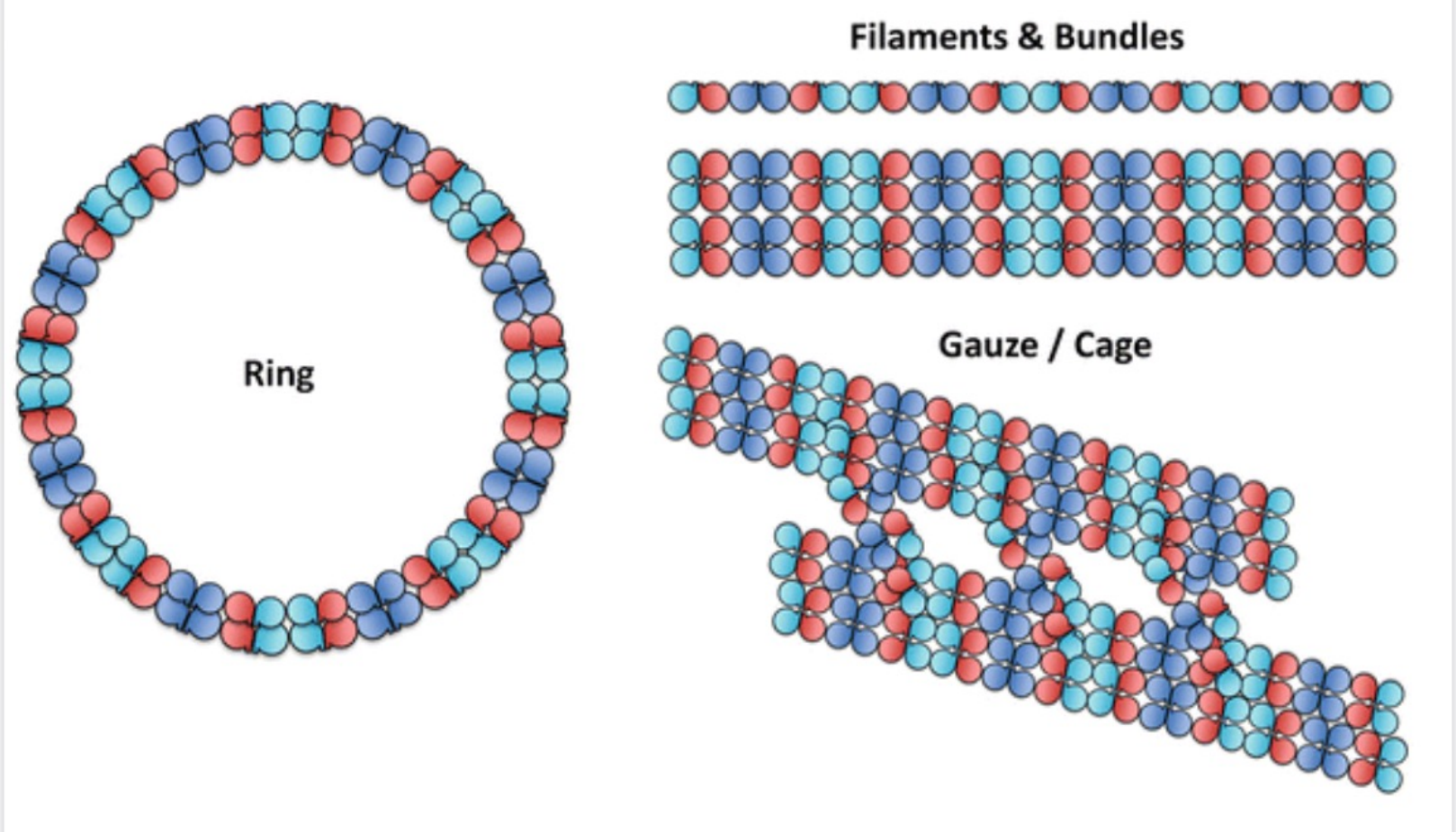
➡ *Favoriserait les assemblages incurvés*

High-speed Atomic Force Microscopy

Jiao et al., Nat. Com. (2020)

Self-assembly into higher-order structures

Single and paired filaments



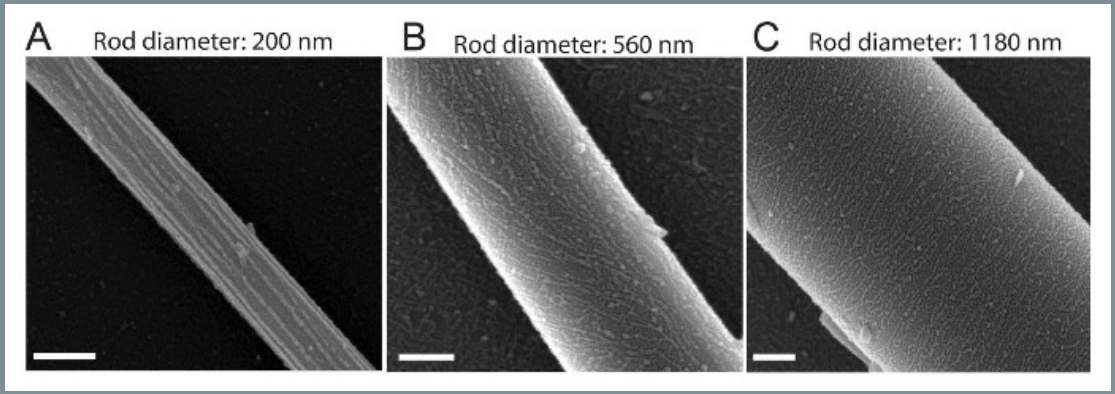
SUBCELLULAR LOCALIZATION

of septin cytoskeleton

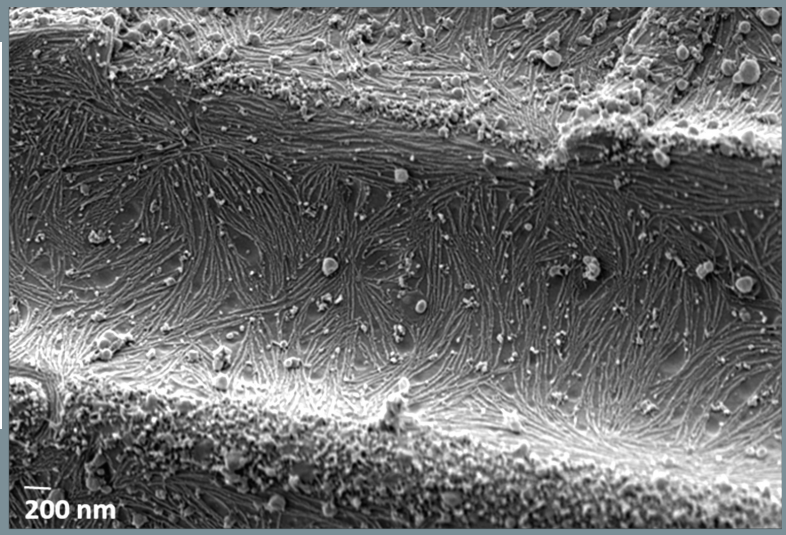
Binding of septins to the plasma membrane

Orientation of septin filaments according to membrane curvature

In vitro



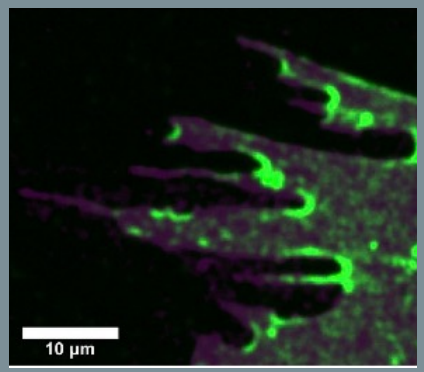
Cannon et al., J. Cell Biol. (2019)



Beber et al., Nat. Com. (2019)

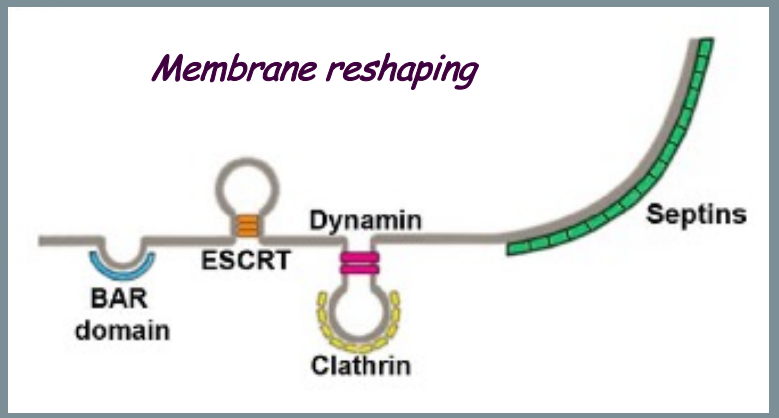
In vivo

Septins in a filamentous fungus



Septins in mammalian fibroblasts

Septins sense and bind to positive curvature



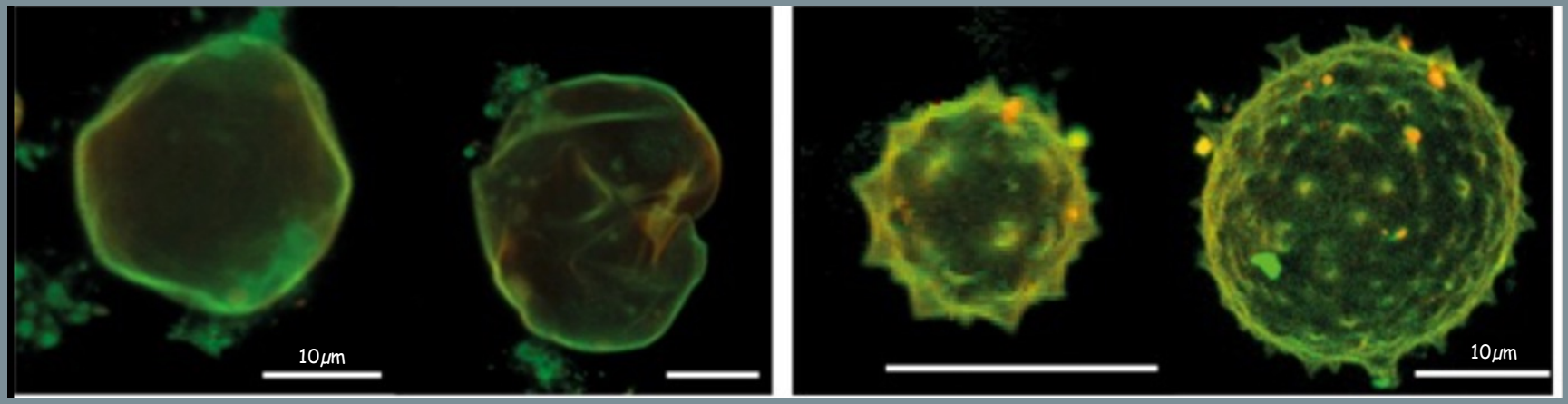
Bridges et al., J. Cell Biol. (2016)

Binding of septins to the plasma membrane

The binding of septin filaments reshapes the membrane of Giant Unilamellar Vesicles (GUV)

In vitro

3D reconstruction of confocal spinning disk images of GUVs in a solution of septins



200nM septins

600nM septins

Red = lipids
Green = septins

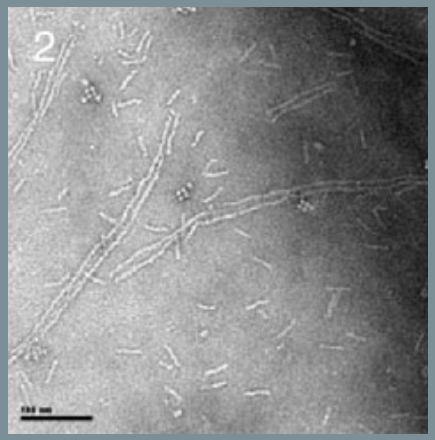
Formation of periodic spikes, while flattening smaller vesicles

Beber et al., Nat. Com. (2019)

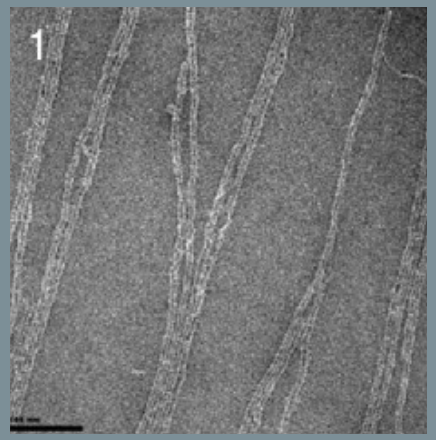
Binding of septins to phosphoinositide-rich membranes

In vitro

DOPC

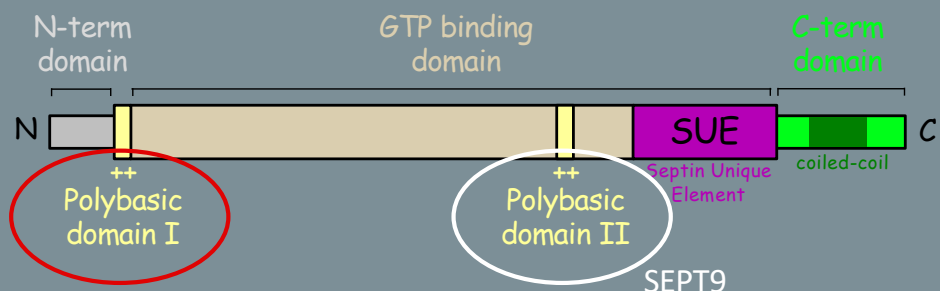


DOPC + PIP2



Bertin et al.,J. Mol. Biol. (2010)

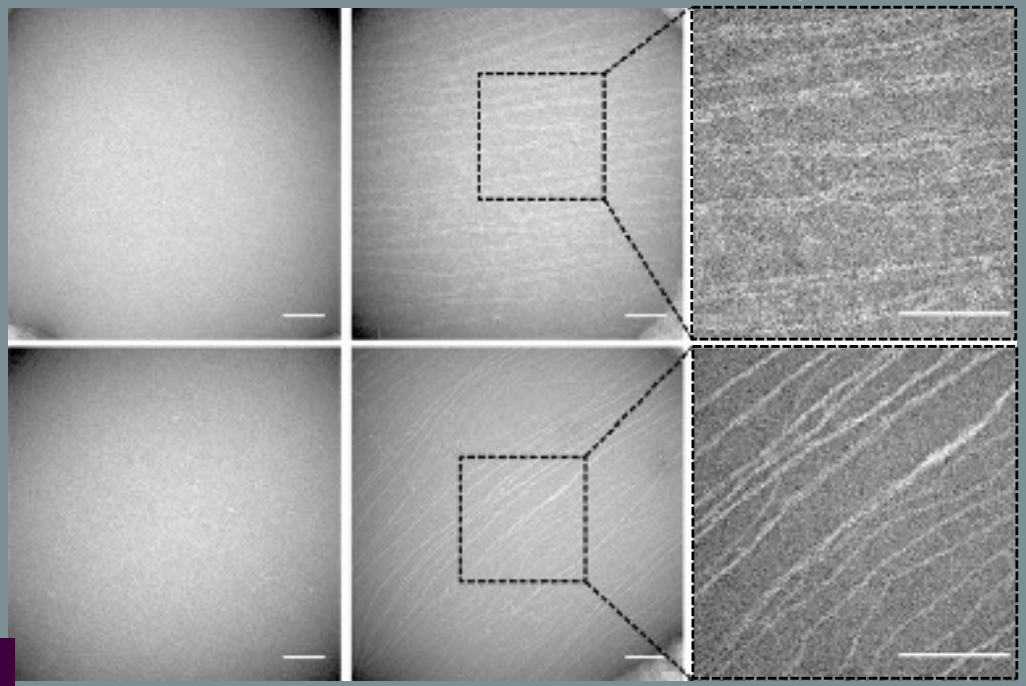
Primary structure



Omrane et al., iScience (2019)

DOPC

DOPC + PtdIns4,5P2



Specificity

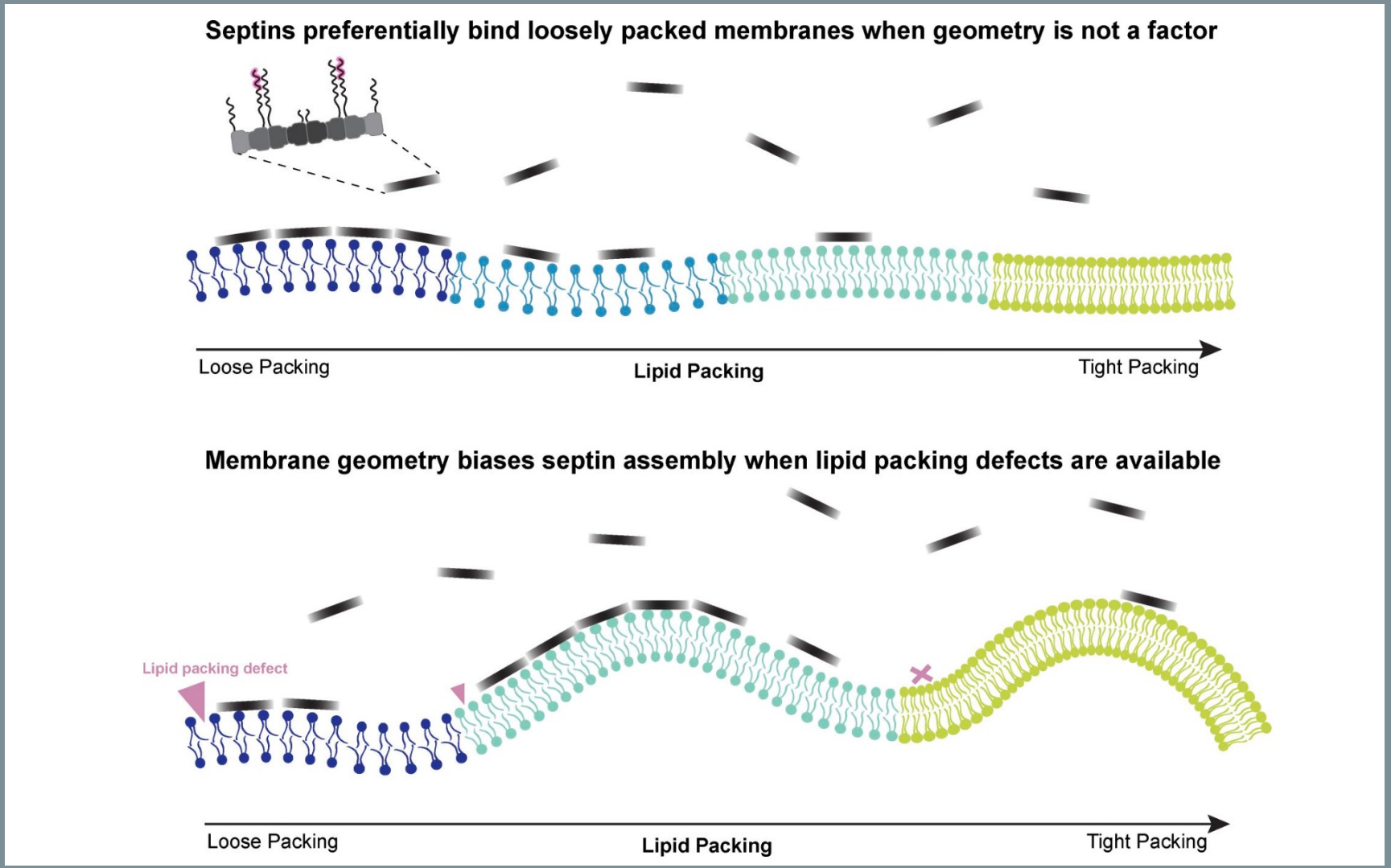
Plasma membrane
rich in PtdIns(4,5)P2

Golgi apparatus membrane
rich in PtdIns(4)P

Membrane of early endosomes
rich in PtdIns(3)P

DOPC = dioleoylphosphatidylcholine
Phosphoinositides = phosphorylated derivatives of phosphatidylinositol

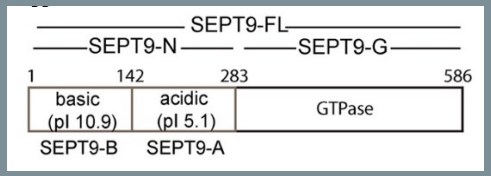
Lipid packing and local geometry influence septin curvature sensing



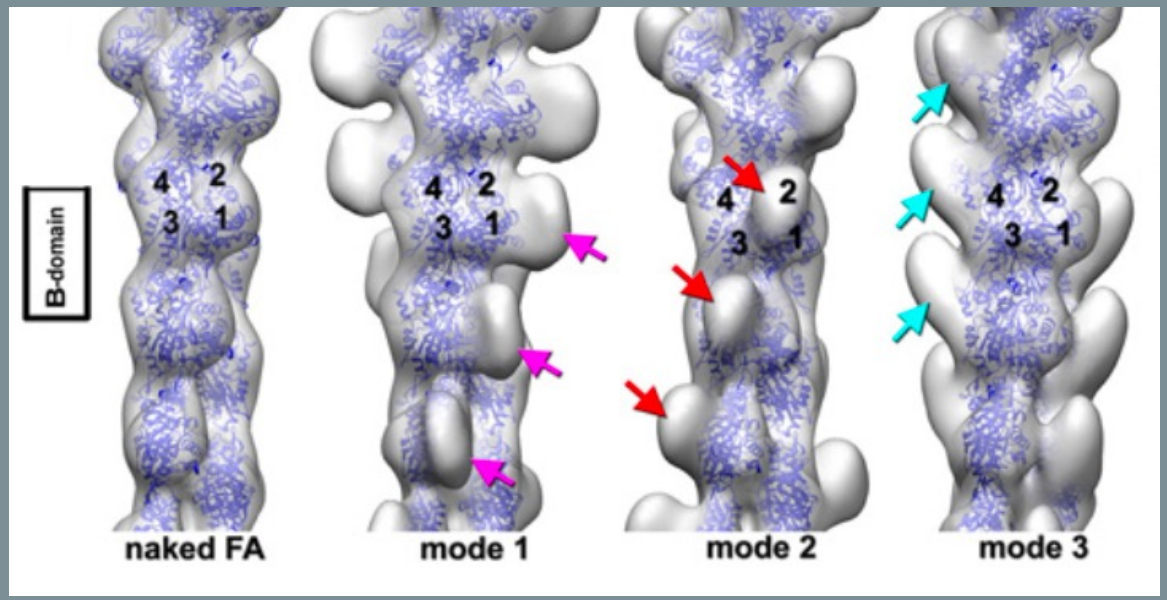
Curtis et al.,J. J. Cell Biol. (2026)

Association with other cytoskeletal elements

SEPT9 domains



SEPT9 interacts F-actin in a highly polymorphic fashion

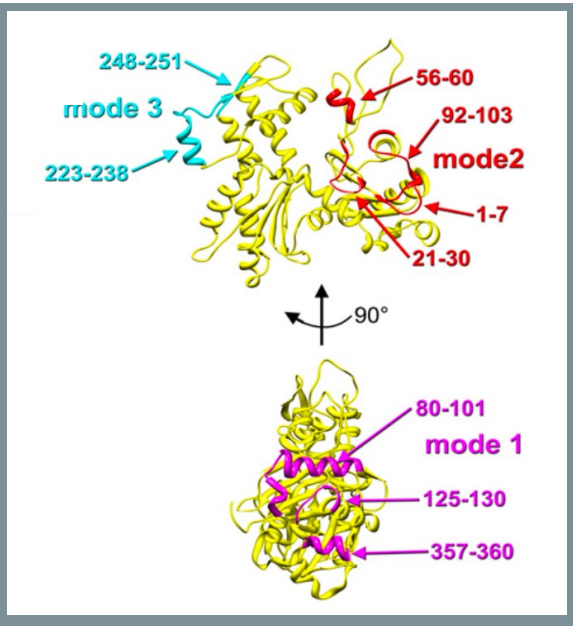


Smith et al.,J. Mol. Biol. (2015)

SEPT9 directly interacts with three sites on the surface of F-actin

Two of these sites overlap with the binding regions of myosin and cofilin

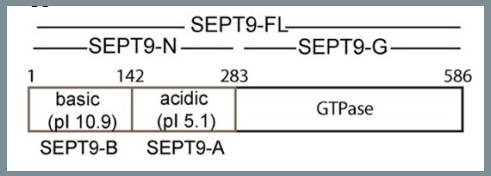
SEPT9 could maintain the integrity of growing and contracting actin filaments



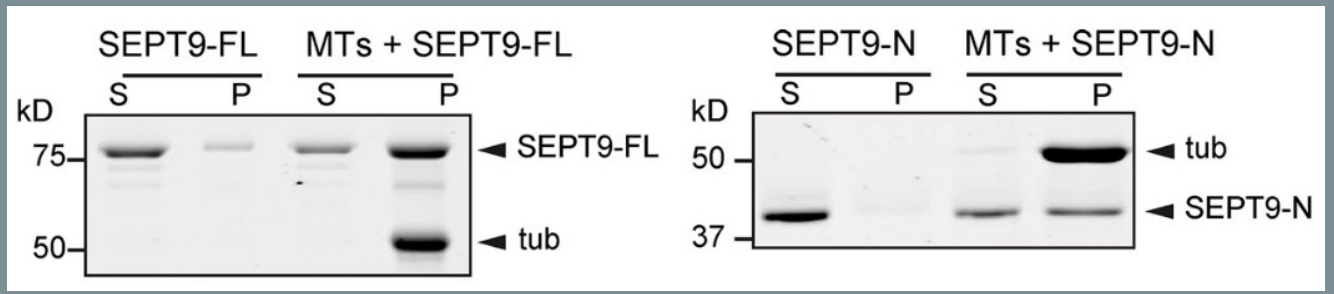
Actin monomer

Association with other cytoskeletal elements

SEPT9 domains

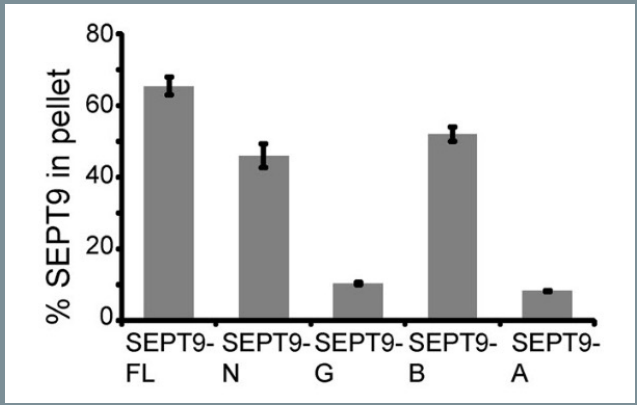


High speed sedimentation of pre-polymerized paclitaxel-stabilized microtubules with domains of SEPT9_i1



Coomassie stain gels

The basic domain (B-domain) of the N-terminal tail of SEPT9 is responsible for actin cross-linking

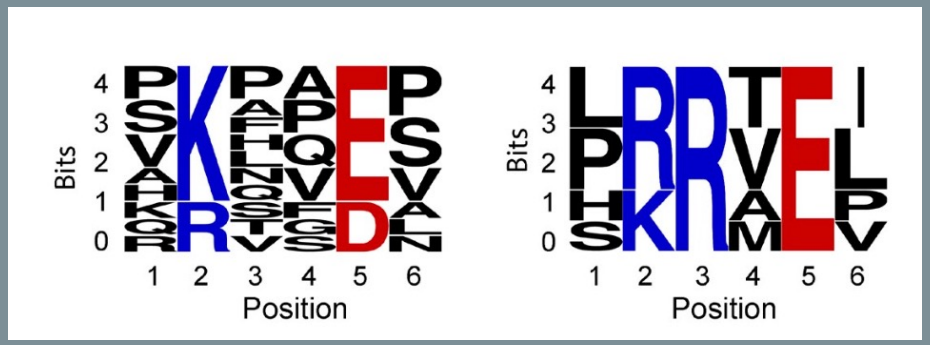


SEPT9 binds and bundles F-actin through its N-terminal basic domain

Bai et al.,J. Cell Biol. (2013)

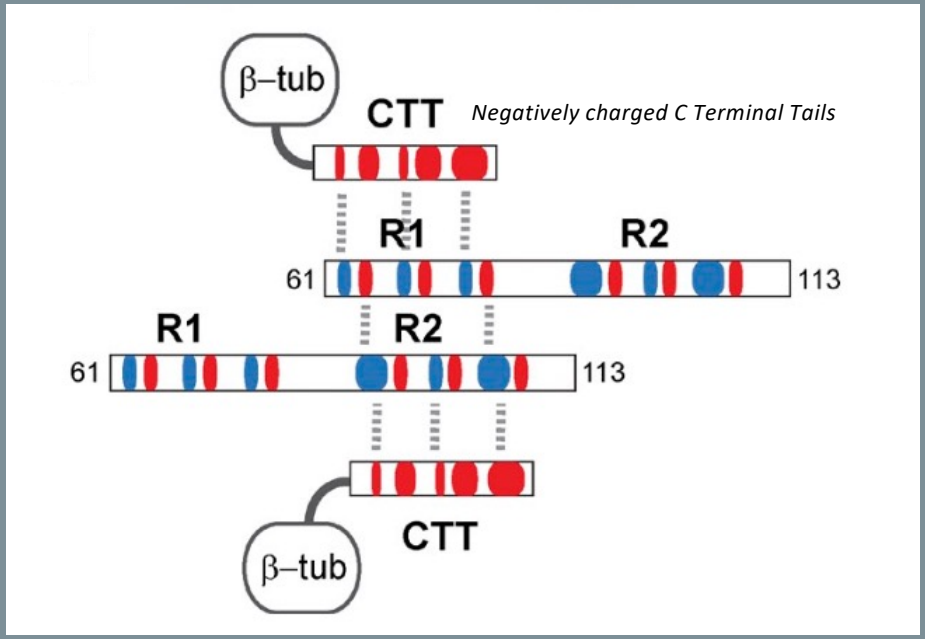
Association with other cytoskeletal elements

Alanine scanning mutagenesis



The K/R-x-x-E/D and R/K-R-x-E repeat motifs bind and bundle microtubules by interacting with the acidic C-terminal tails of β-tubulin.

Enabling septin–septin interactions that link microtubules together

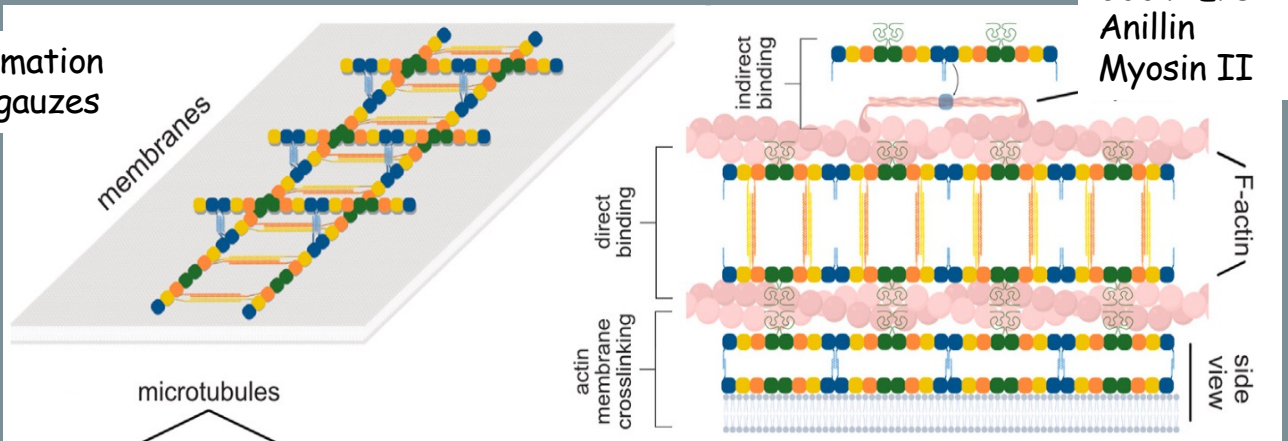


Affect intracellular microtubule bundling

Bai et al.,J. Cell Biol. (2013)

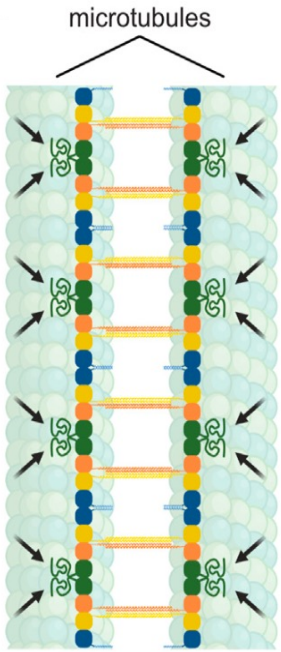
In summary

Formation of gauzes

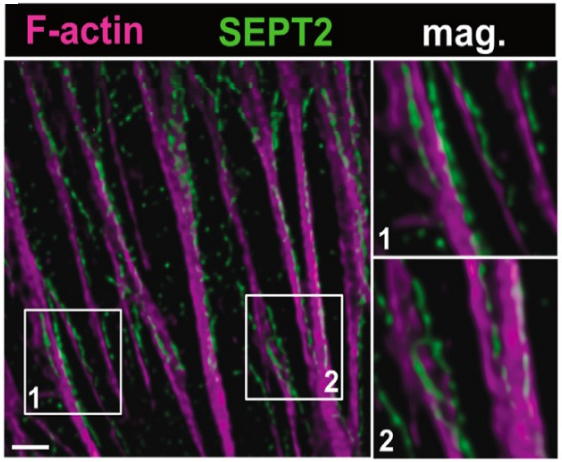


Cdc42EPs = Borg proteins
Anillin
Myosin II

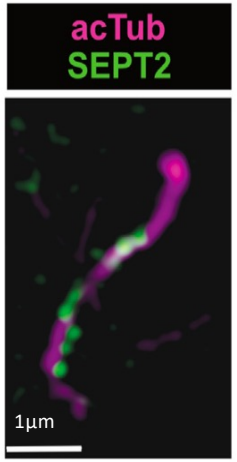
Direct interaction with microtubules



Ventral stress fibers



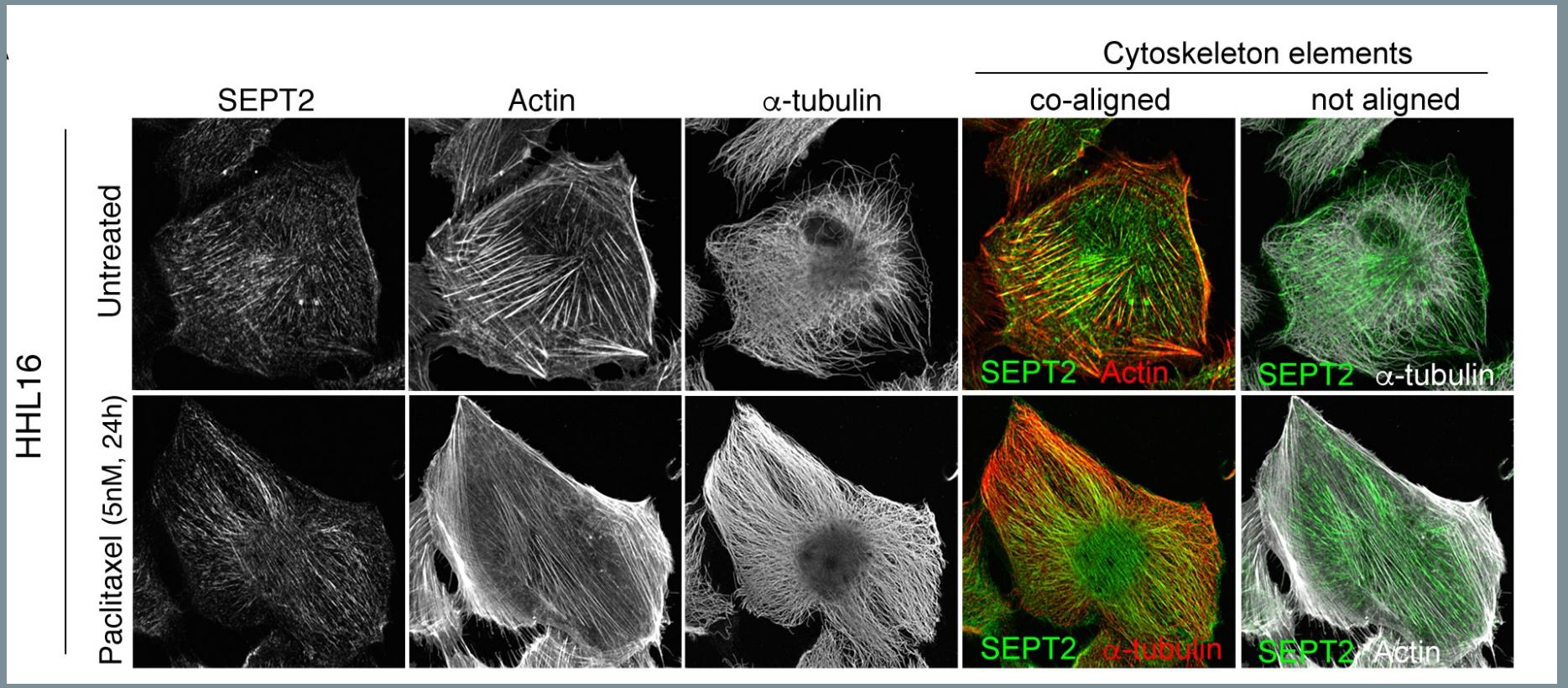
Primary cilium



Schampera and Schwan, Curr. Opin. Cell Biol. (2024)

Remodeling of the interplay between cytoskeletal elements
under pathological conditions

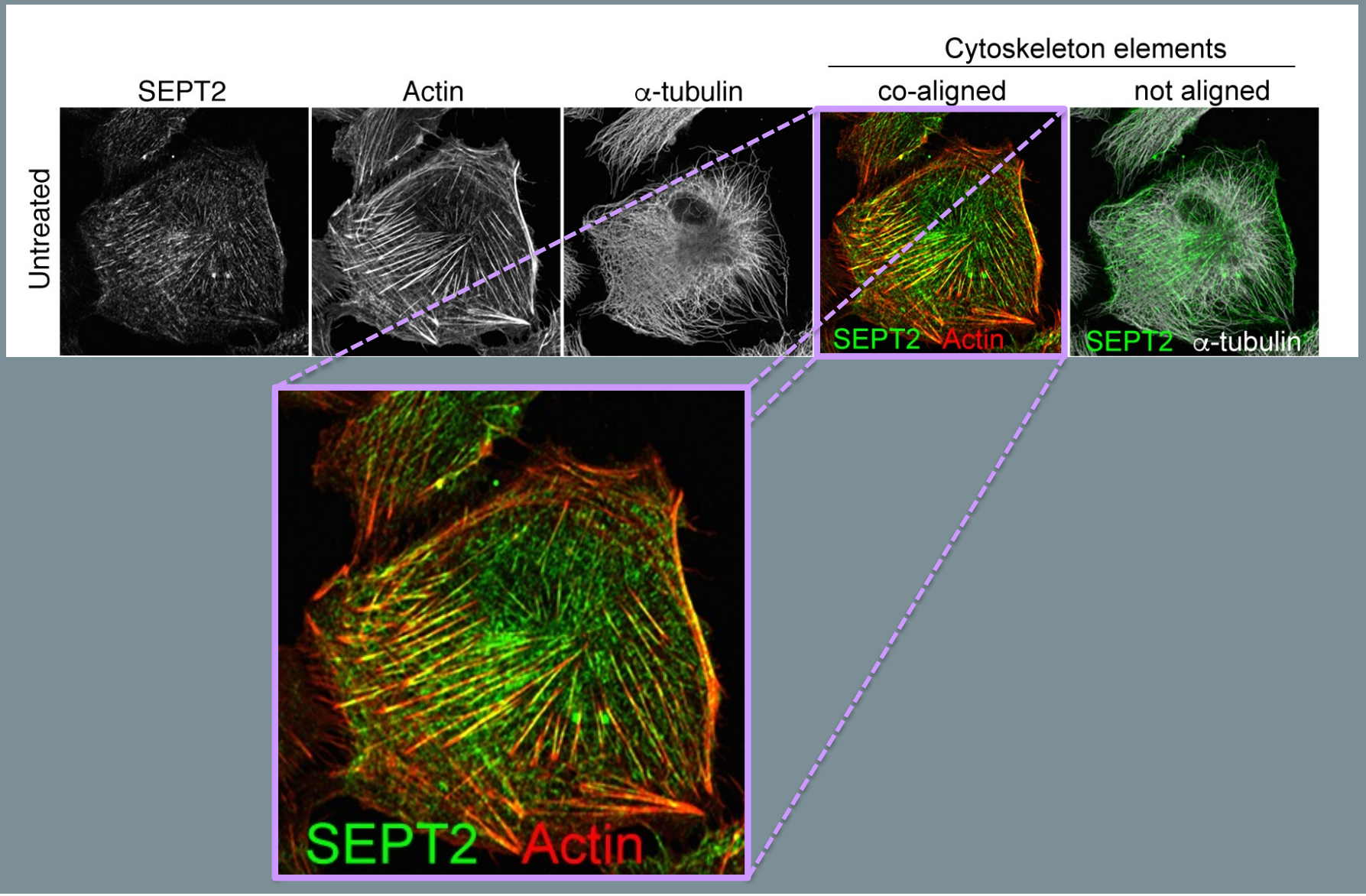
Co-alignment with sub-cortical actin and stress fibers



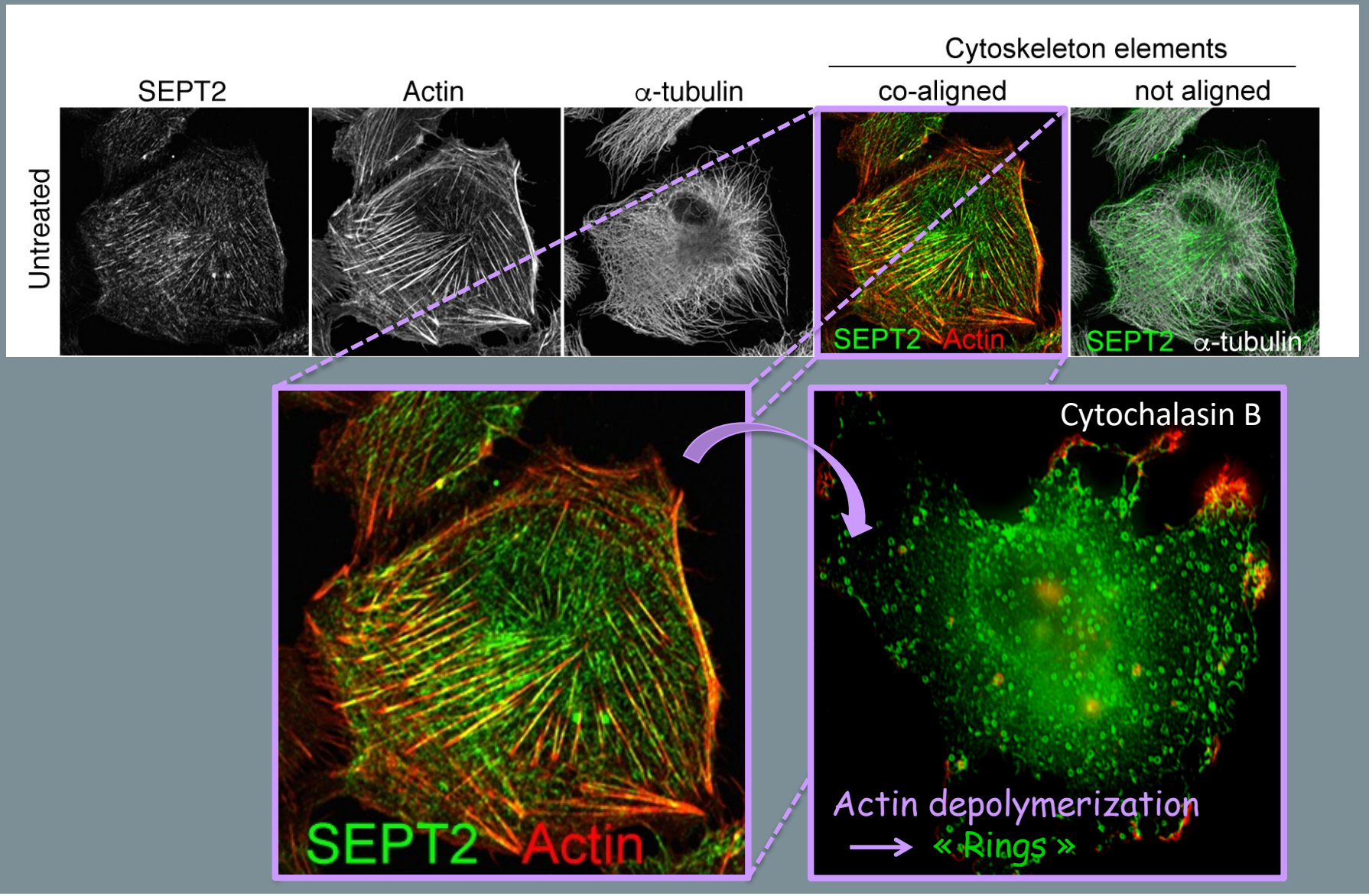
Targa et al., Cell Death Dis. (2019)

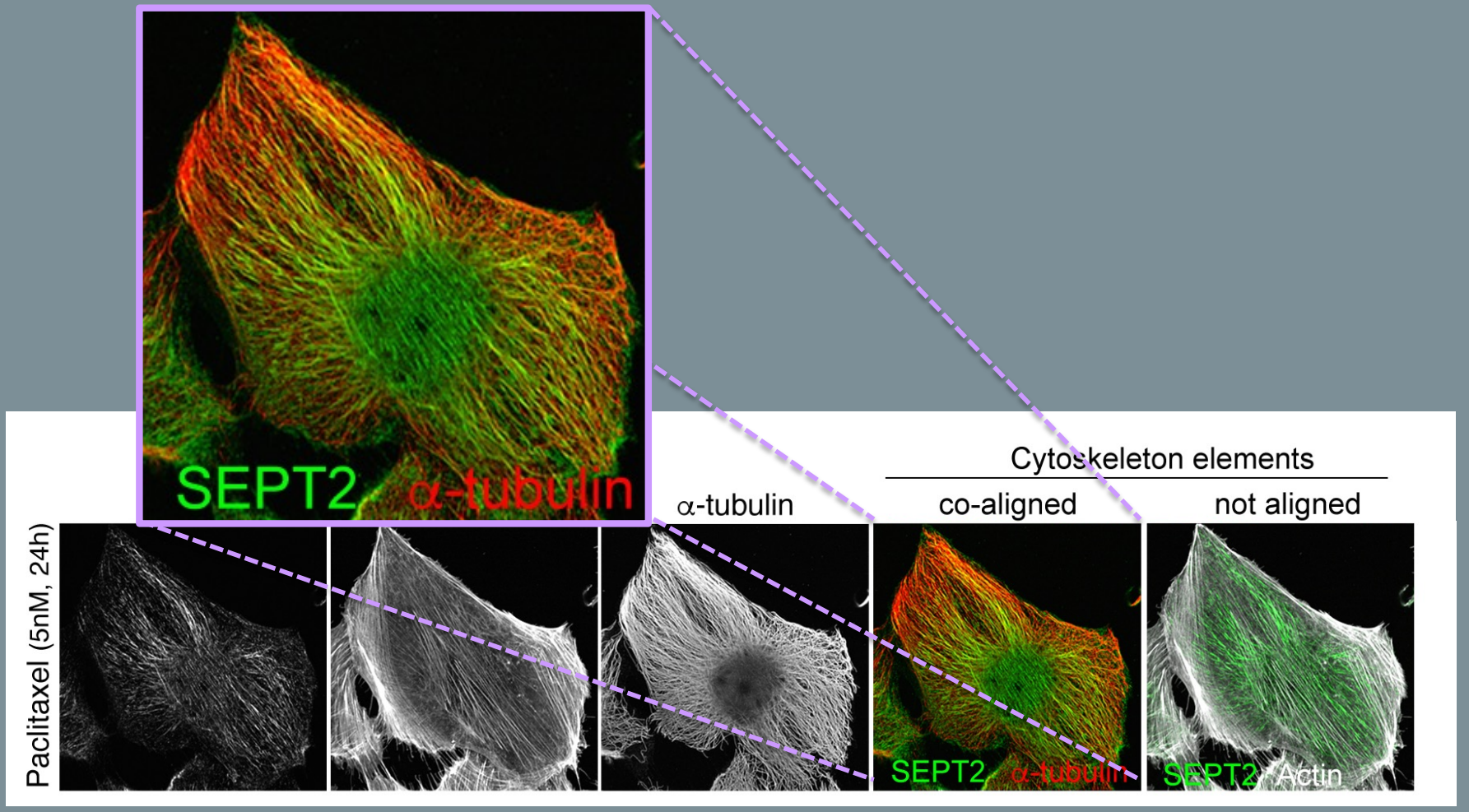
Co-alignment with microtubules
Upon Paclitaxel treatment

Co-alignment with sub-cortical actin and stress fibers



Co-alignment with sub-cortical actin and stress fibers





Co-alignment with microtubules

Upon Paclitaxel treatment

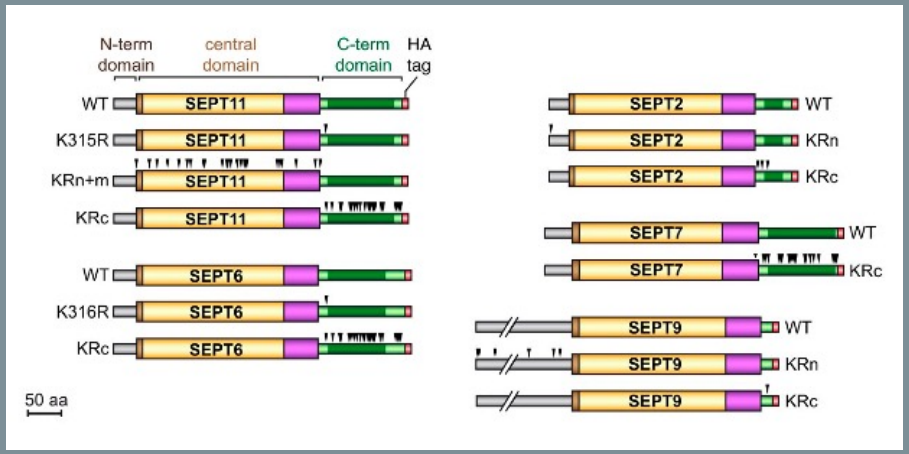
SEPTINS

Post-translational modifications

SUMOylation

Covalent binding of SUMO protéine(s) to one or more Lysines of the target proteins
→ thus regulating their biochemical properties

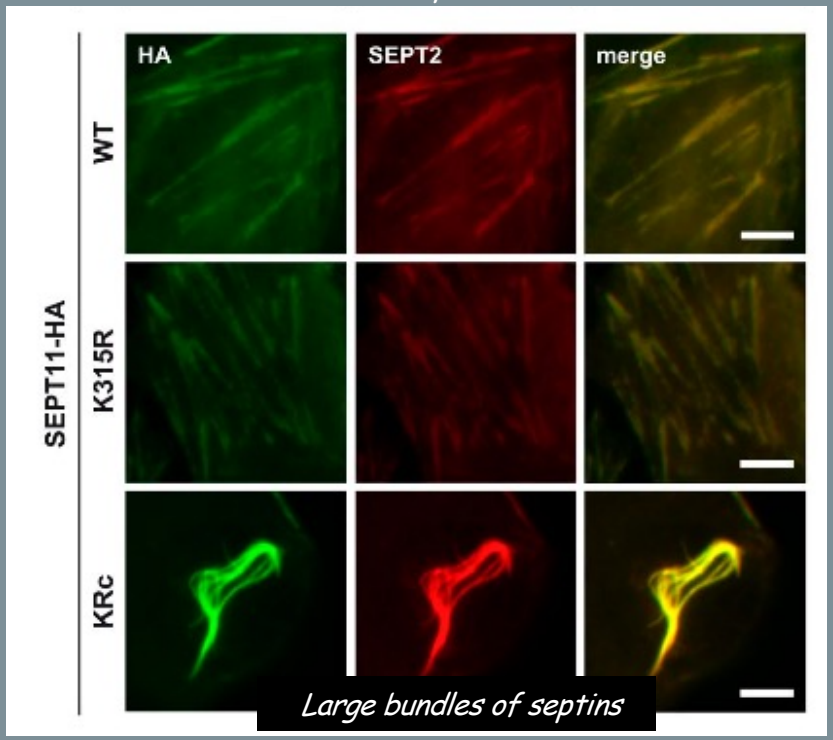
The septins of the 4 groups can be SUMOylated



SUMOylation impacts septin filamentation and localization

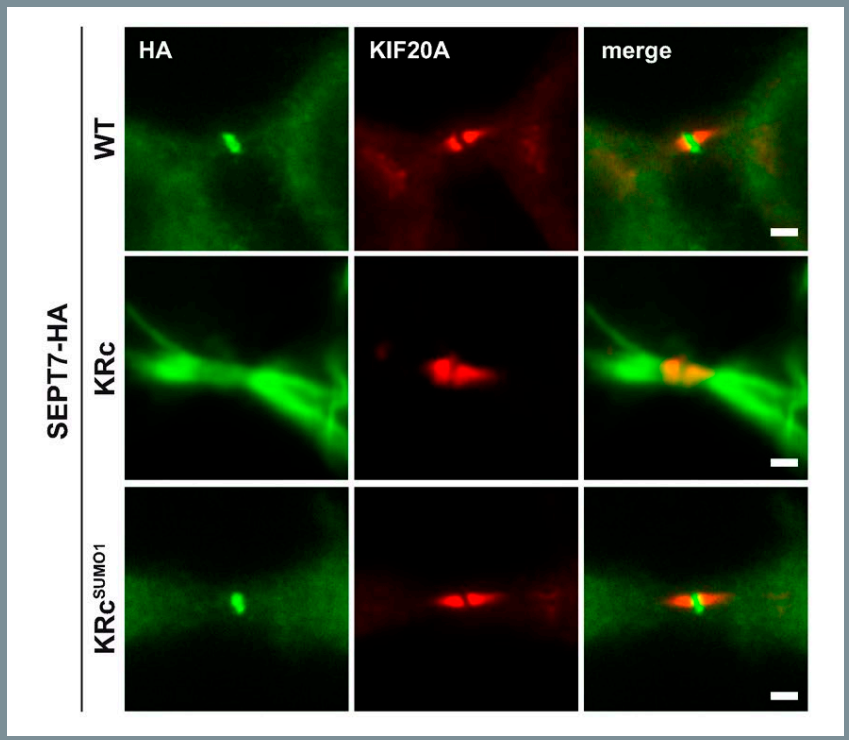
Impact on cytokinesis

Interphase cells



Large bundles of septins

Mitotic cells



KRc: all lysines replaced by arginines

KIF20A: midbody marker

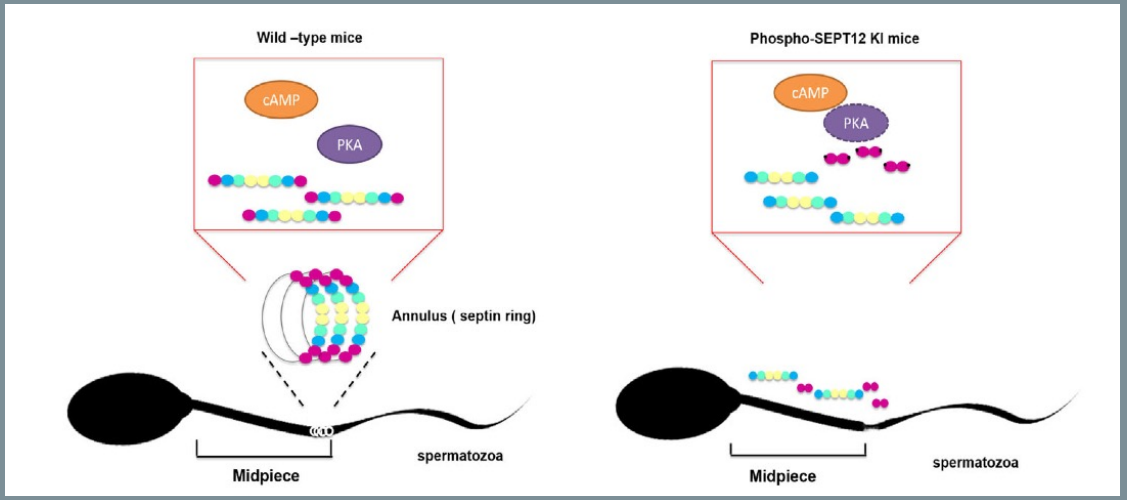
Ribet et al., J. Cell Biol. (2017)

Phosphorylation

Phosphorylation dissociate septine complexes, leading to the loss of the annular space

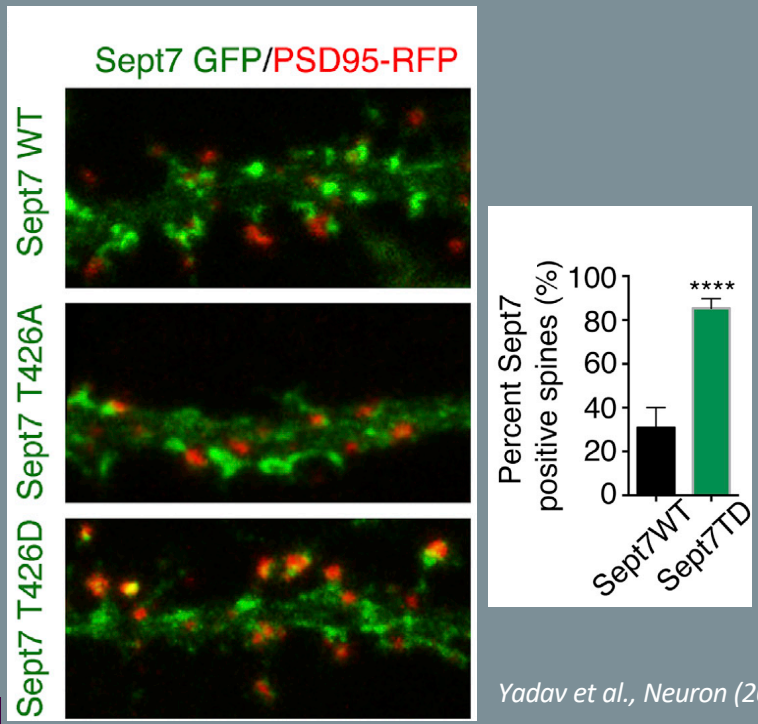
Impact on sperm motility

Lin et al., Cytoskeleton (2019)

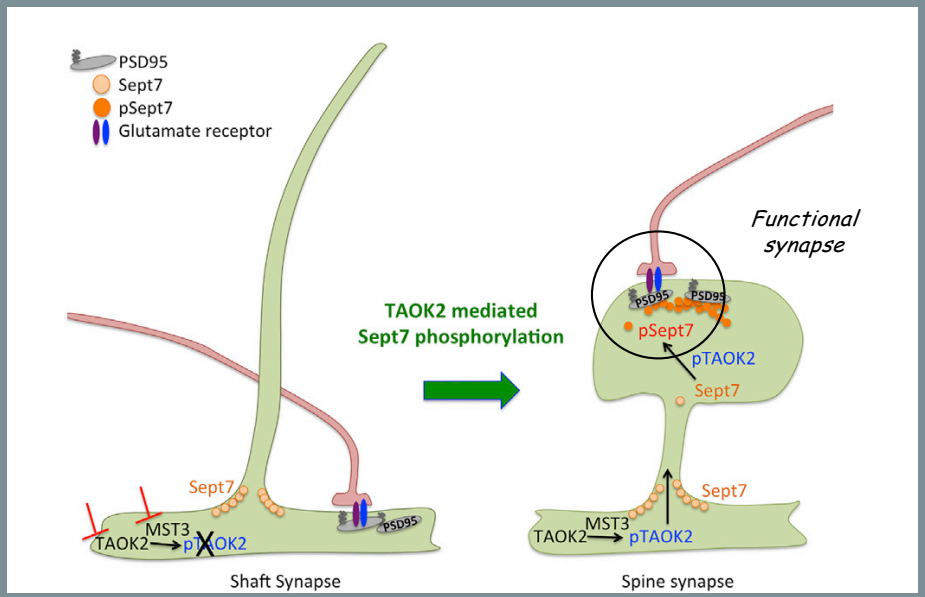


Phosphorylation can result in a change of septin localization

Impact on dendritic spine maturation



Yadav et al., Neuron (2017)



ROLES OF SEPTINS

at the molecular level

Scaffolds

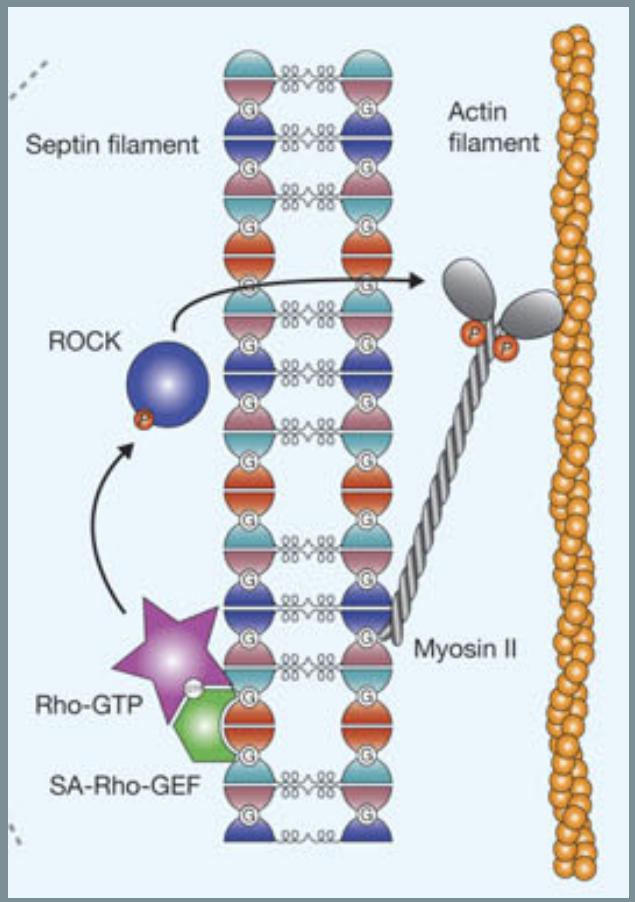
Diffusion barriers

Examples as scaffolding proteins

Phosphorylation of Myosin II by ROCK kinase

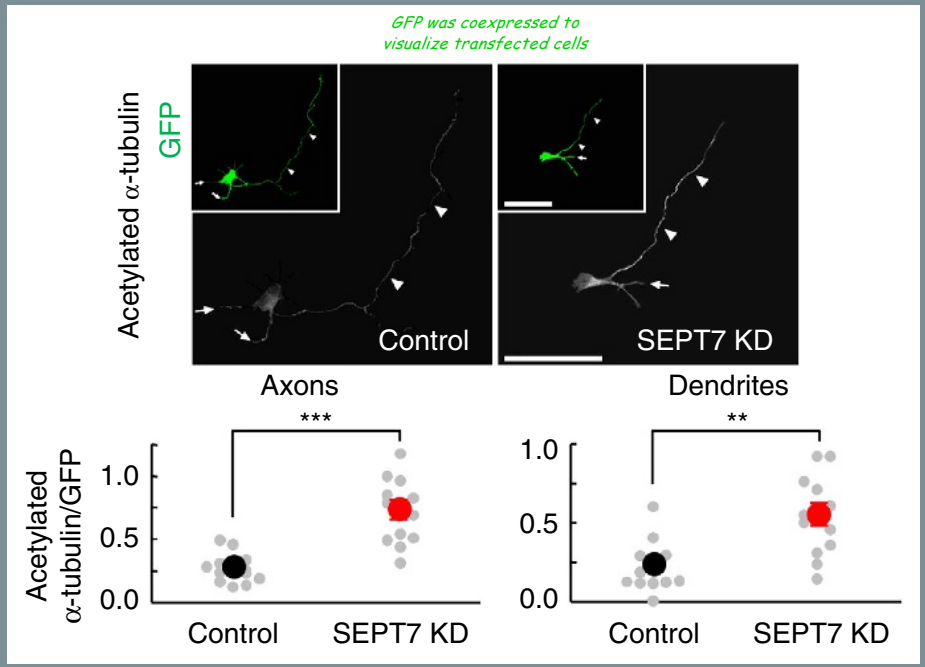
Septin filaments along stress fibers scaffold proteins for myosin activation

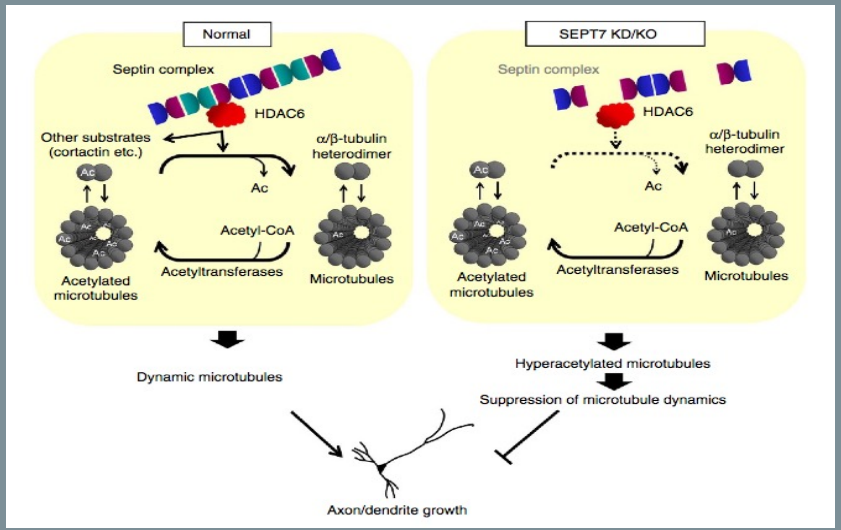
➡ *Muscle contraction / Division & Cell migration*



Joo et al., Dev. Cell (2007)
Beise and Trimble, J. Cell Sci. (2011)

Regulation of microtubule acetylation level

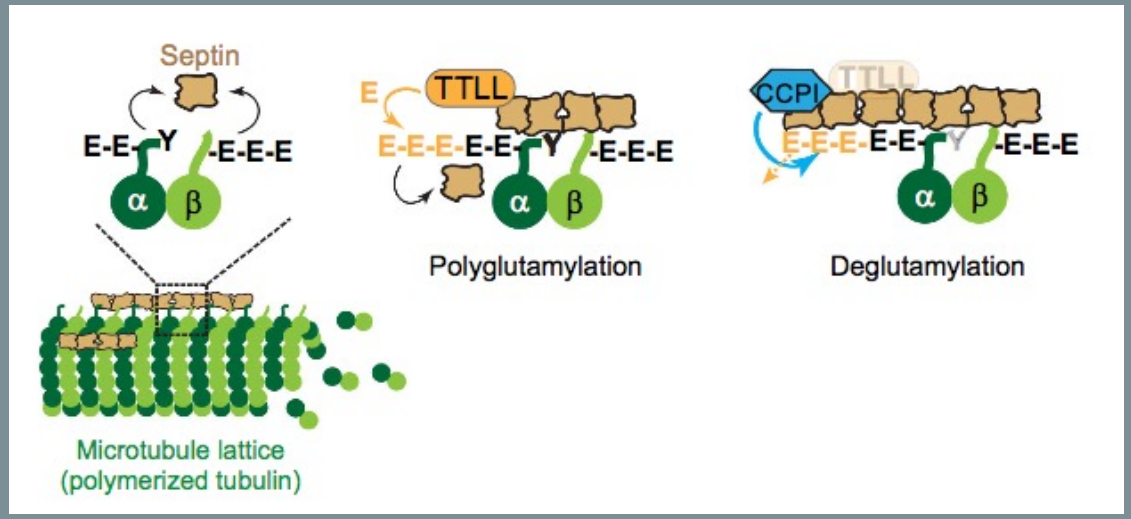




Ageta-Ishihara et al., Nat. Commun. (2013)

Examples as scaffolding proteins

Regulation of microtubule polyglutamylation level



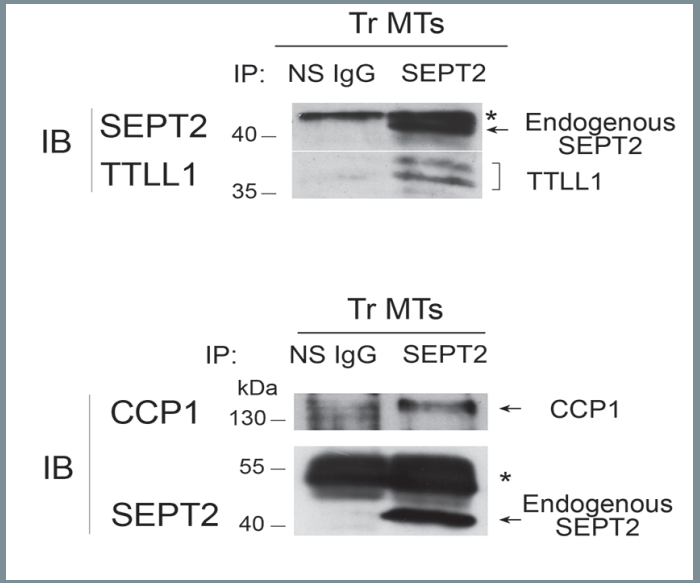
Spiliotis, J. Cell Sci. (2018) d'après Froidevaux-Klipfel et al., Oncotarget (2015)

Facilitates the recruitment of CLIP170 and MCAK
Recovery of microtubule dynamic instability

➡ *Reduced efficacy of chemotherapy*

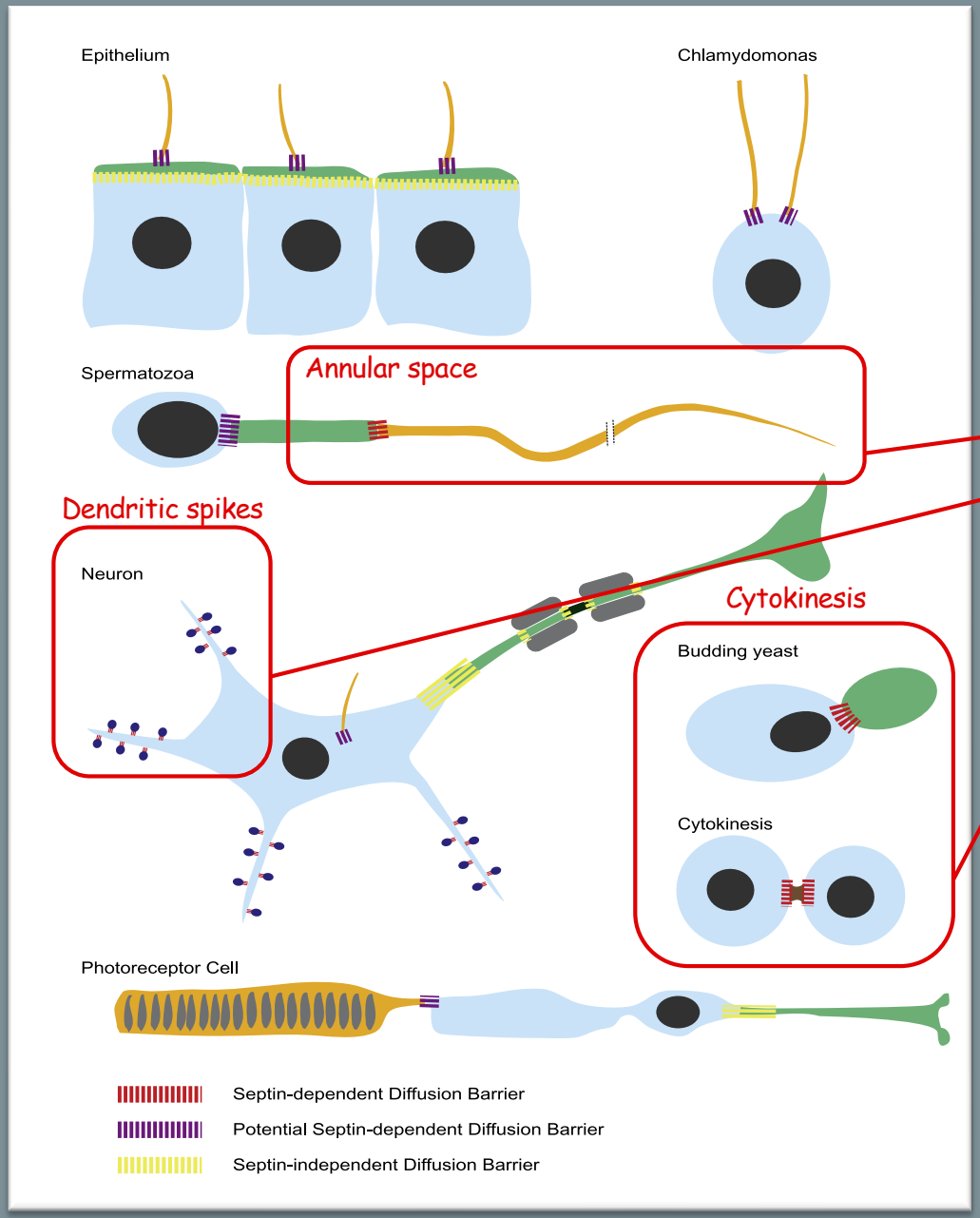
➡ *Taxane resistance*

Co-immunoprecipitation experiments



Froidevaux-Klipfel et al., Oncotarget (2015)

Examples as diffusion barriers



Examples where the role of septins has been clearly demonstrated

Caudron and Barral, Dev. Cell (2009)

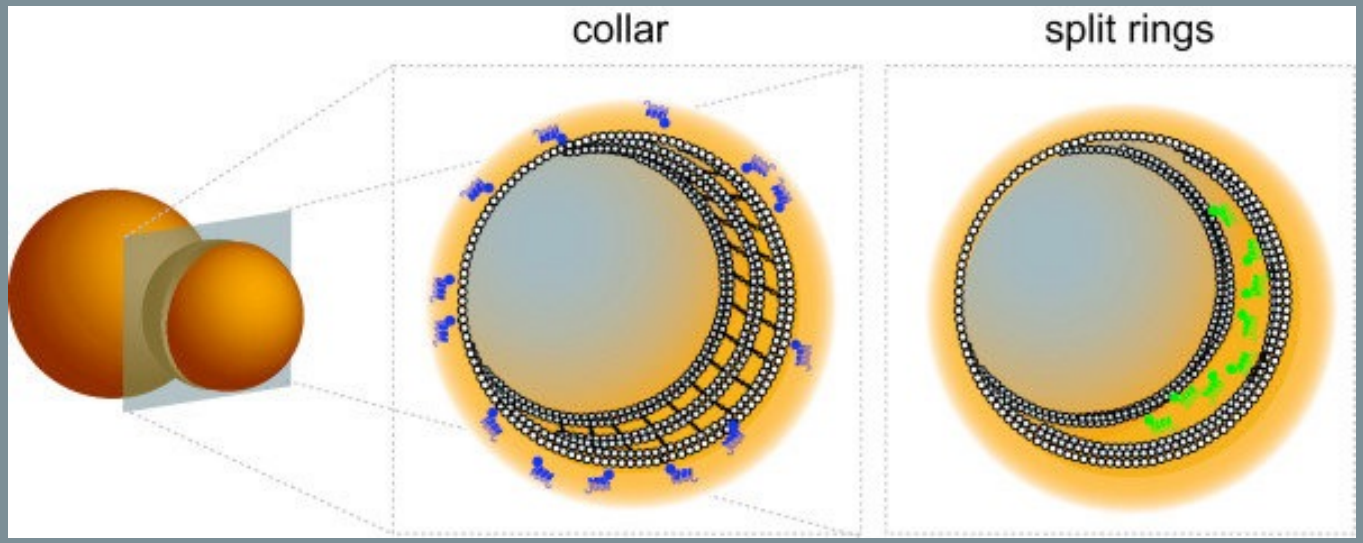
Examples as diffusion barriers

During cell division

By establishing a diffusion barrier during bud growth,
septins play a role in cell polarity

Before cytokinesis, proteins (in blue) are Retained in the bud

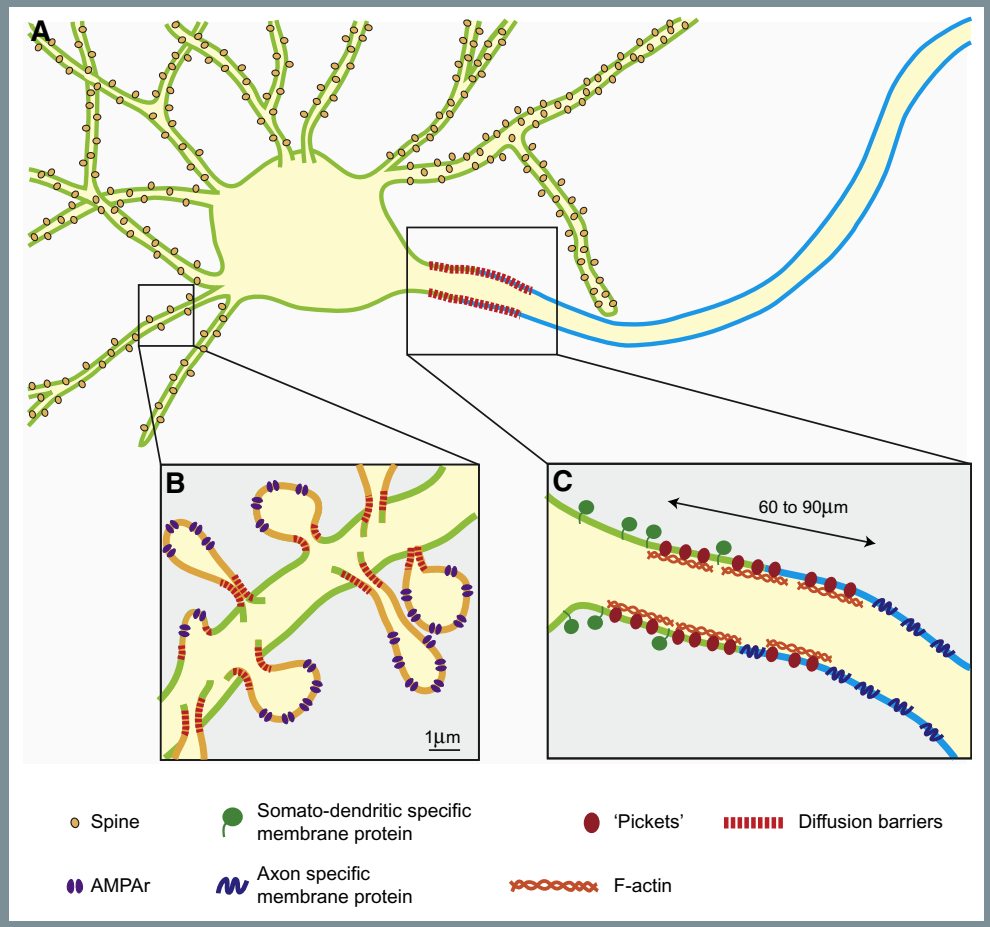
At the onset of cytokinesis, This same proteins (in green) are then accumulated in the neck



McMurray and Thorner, Cell Div. (2009)

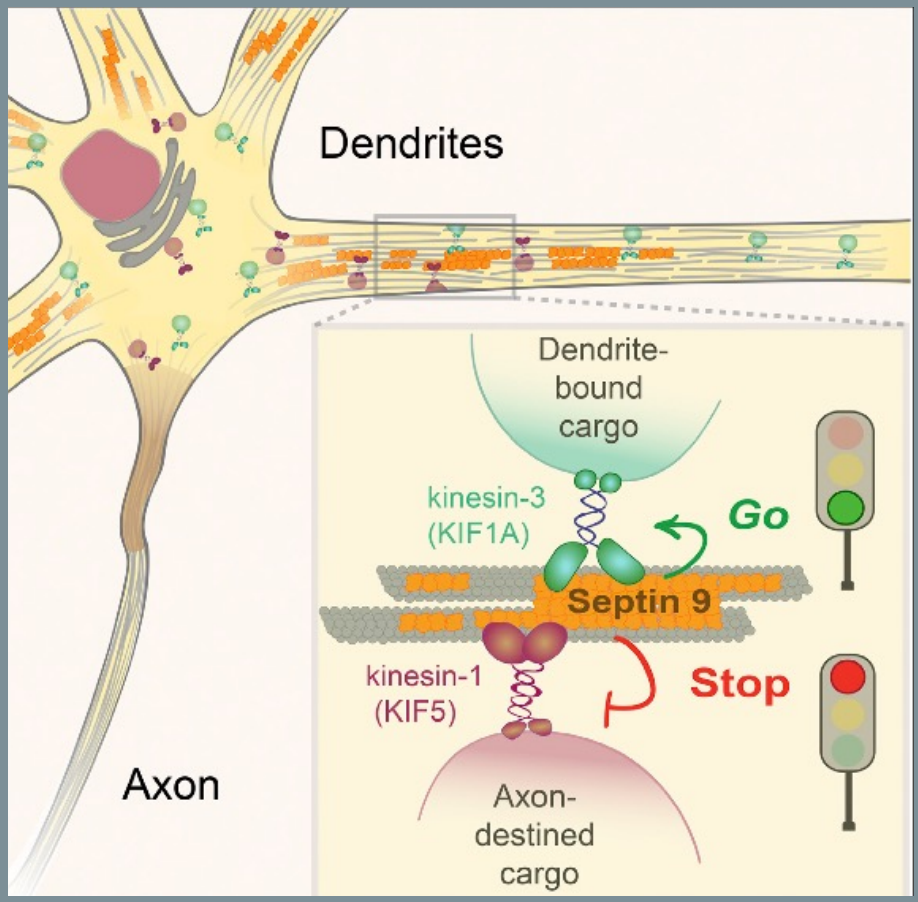
Examples as diffusion barriers

In neurons



Caudron and Barral, Dev. Cell (2009)

Directional sorting ensured by SEPT9 at the dendrite entrance



Karasmanis et al.,Dev. Cell (2018)

INVOLVEMENT OF SEPTINS

in a wide range of cell functions

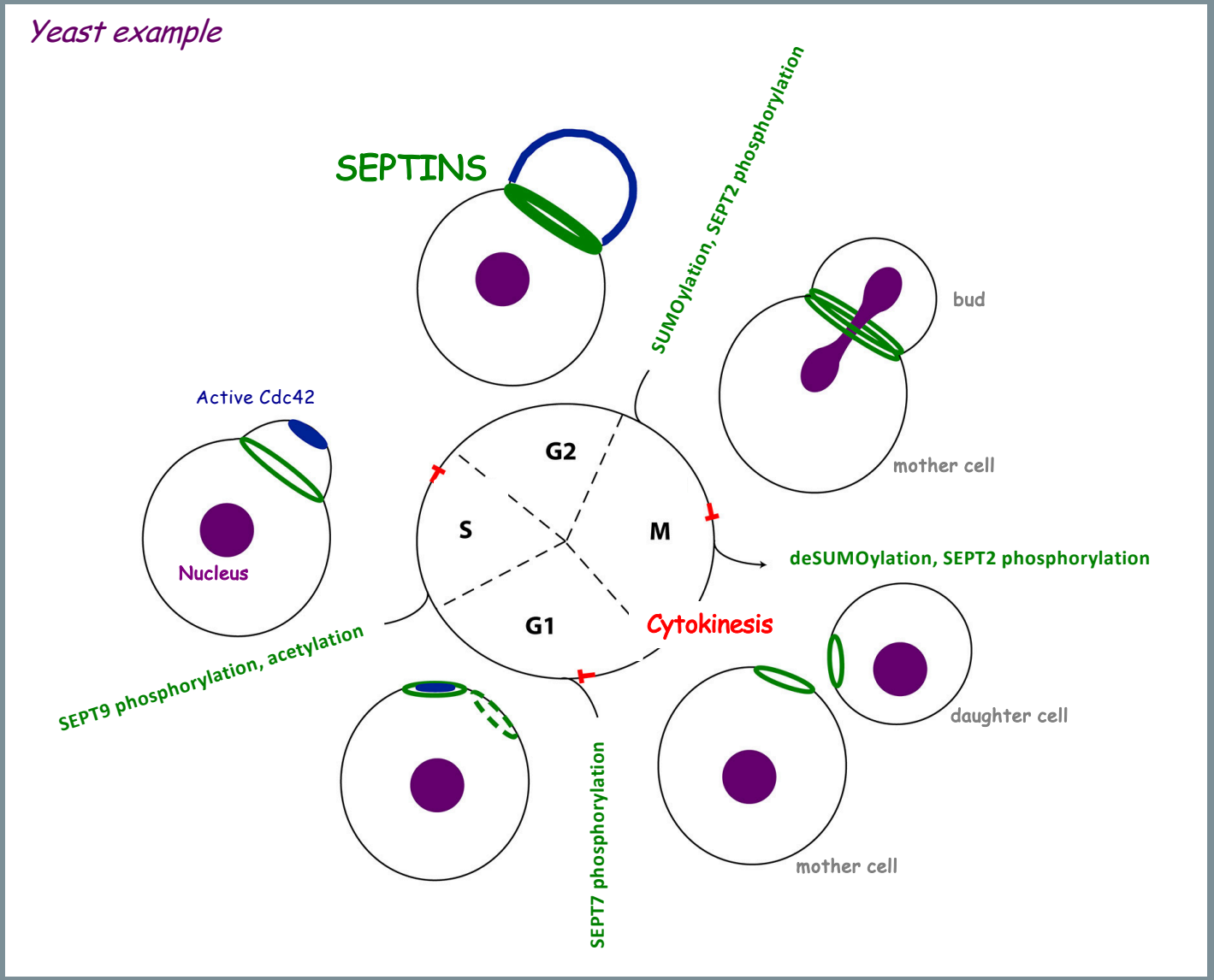
- ✓ Cytokinesis
- ✓ Vesicular traffic
- ✓ Cell polarity
- ✓ Cell migration
- ✓ Cytoskeleton dynamicity
- ✓ Pathogen internalization
- ✓ Apoptosis

- ✓ Oncogenesis
- ✓ Neurodegeneration
- ✓ ….

see Peterson and Petty, Clin. Genet. (2010)

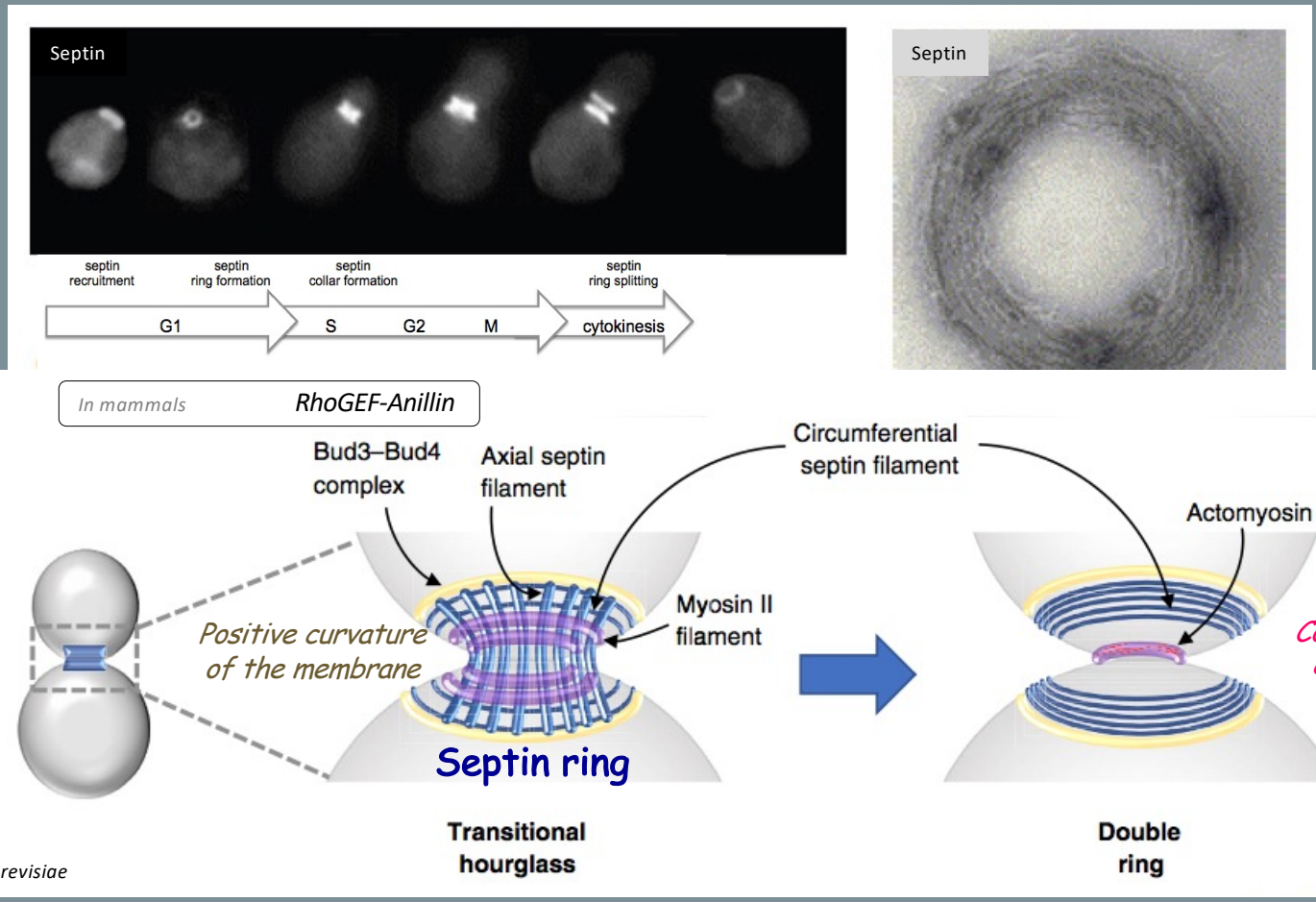
Cell cycle

Yeast example



Glomb and Gronemeyer, Front. Cell Dev. Biol. (2016)

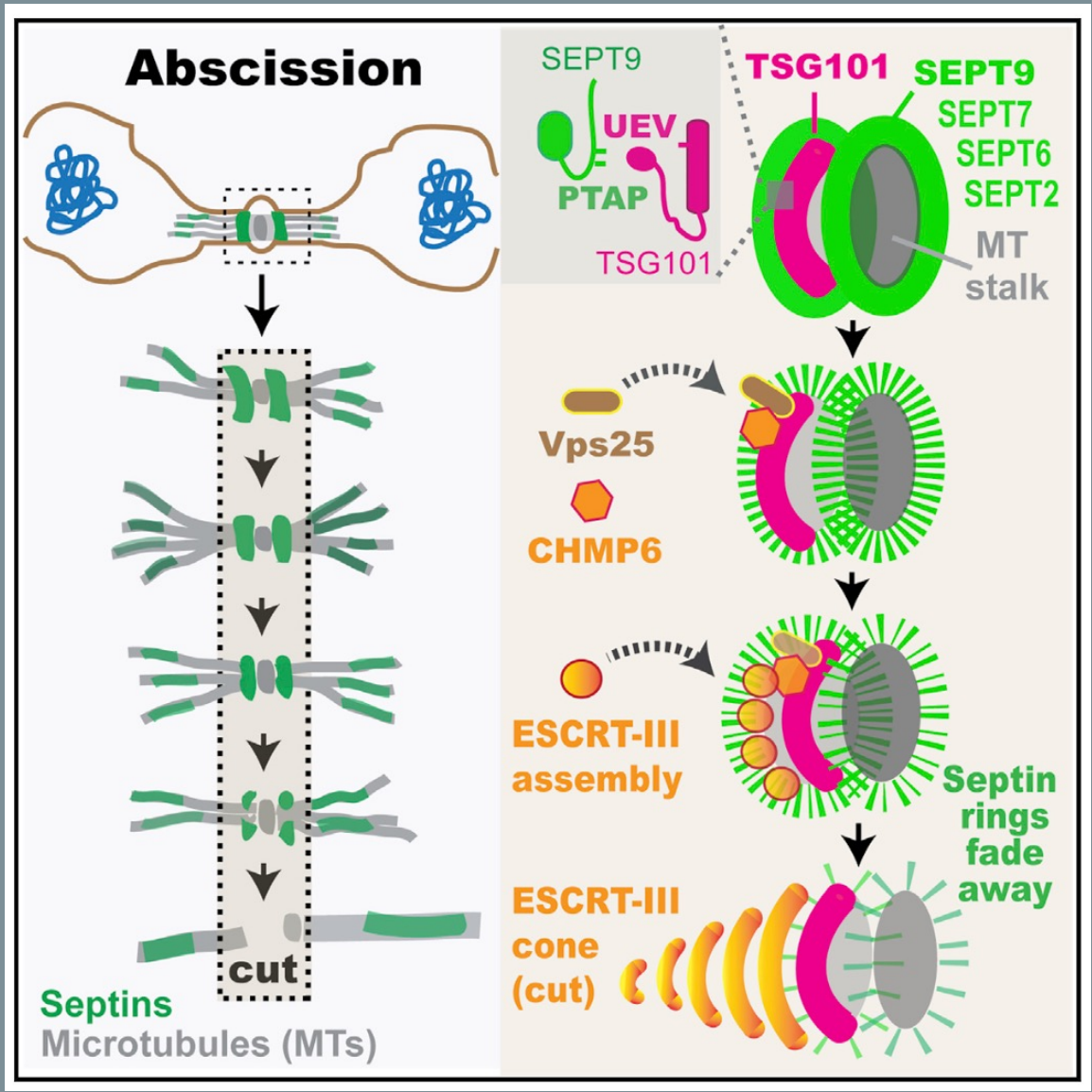
Crucial role of septins during cytokinesis



The dynamic organization of septin filaments allows for final constriction

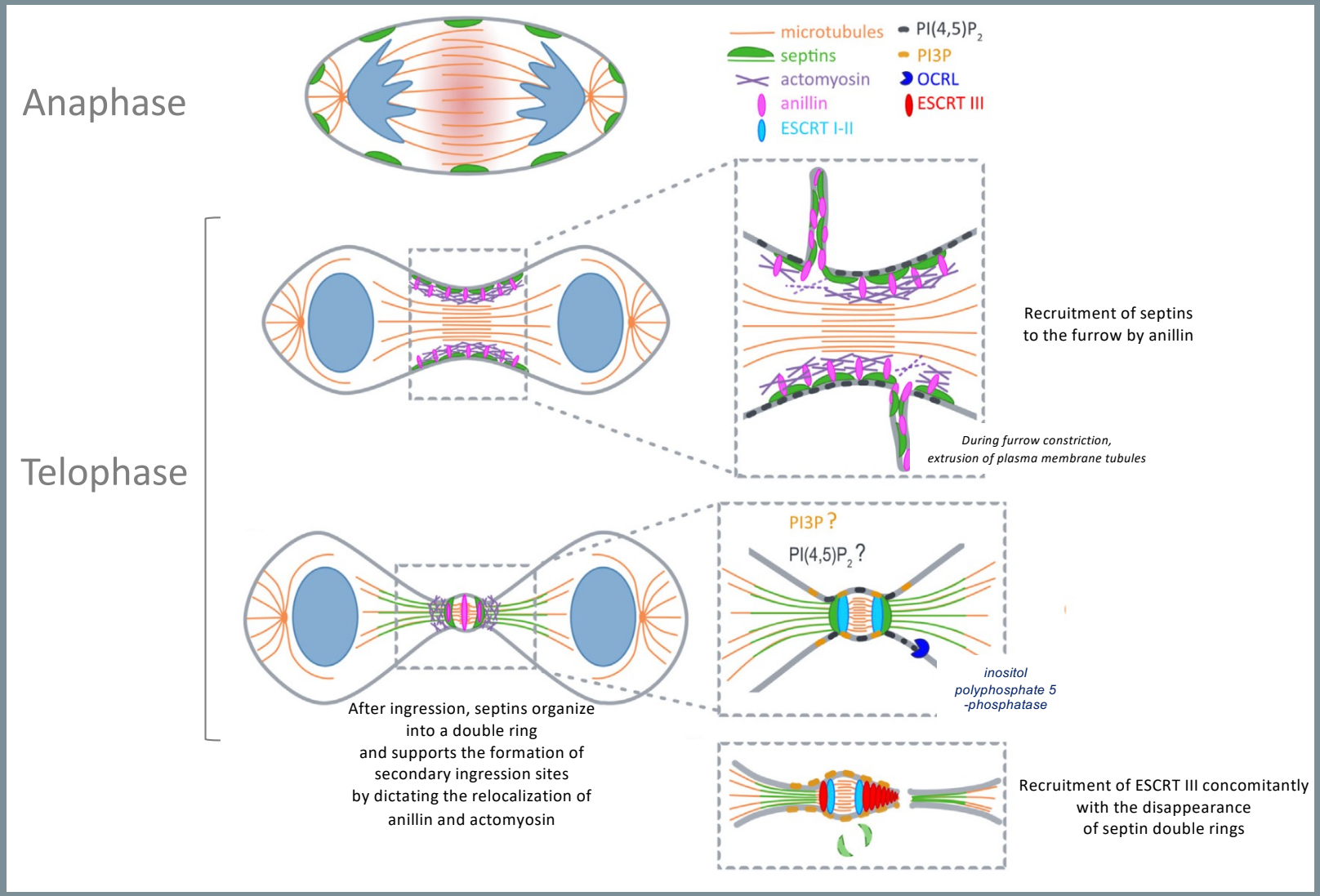
Piatti, Curr. Biol. (2020)
Chen et al., Curr. Biol. (2020)

Similar mechanism during ammalian cytokinesis



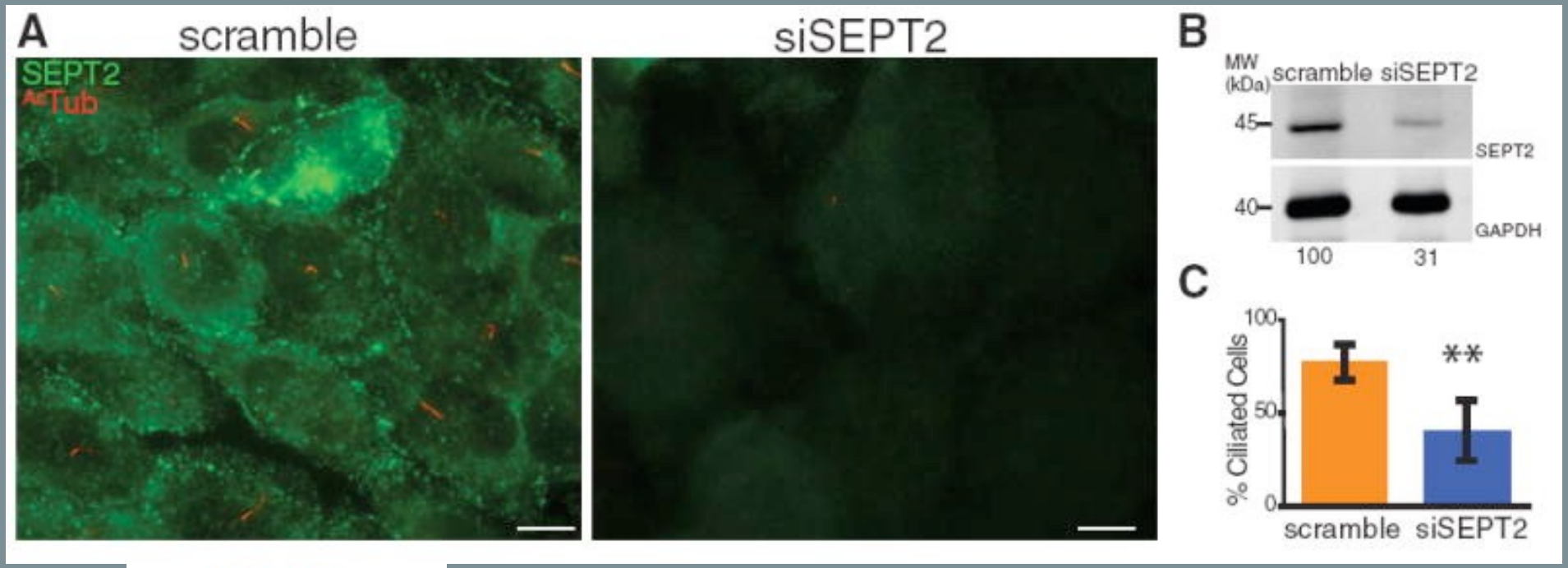
Karasmanis et al., Curr. Biol. (2019)

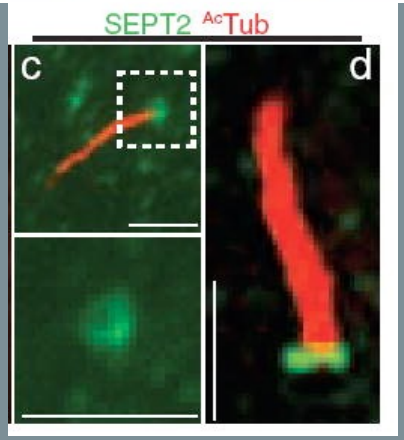
Similar mechanism during ammalian cytokinesis



Russo and Krauss, Front. Cell Dev. Biol. (2021)

Primary cilium integrity





Hu et al., Science (2010)

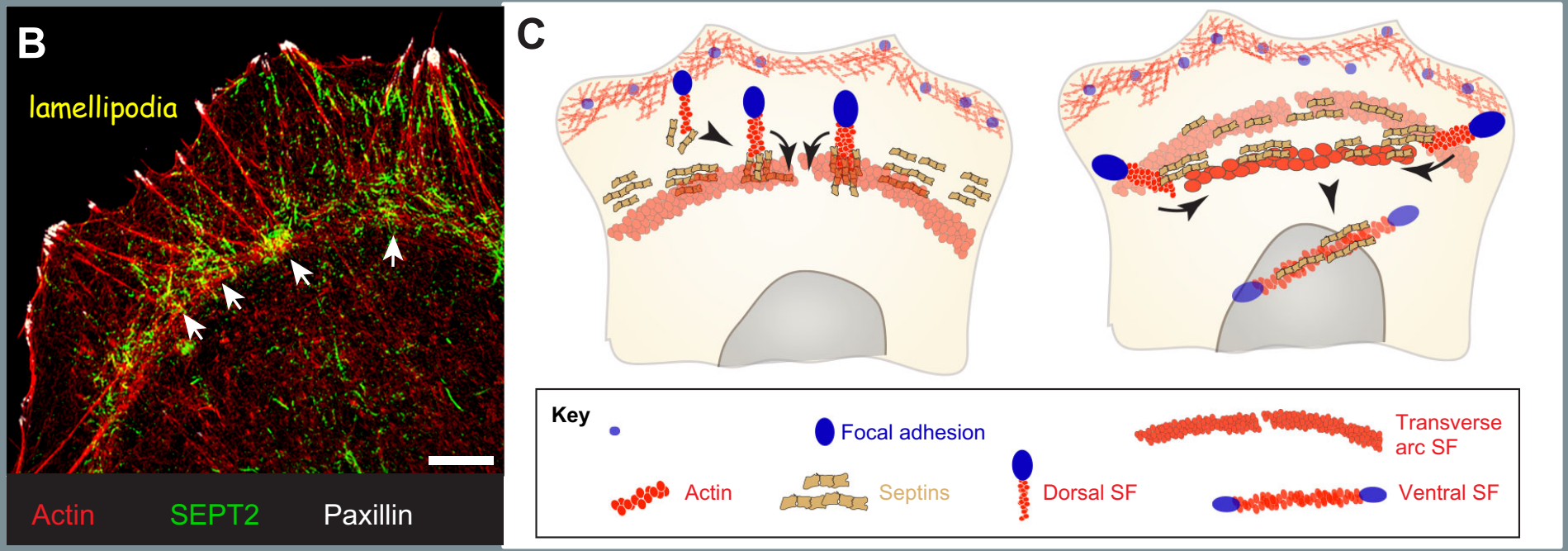
Disrupting this diffusion barrier at the base of the cilium results in:

- *The loss of localization of membrane proteins within the cilium*
- *The inhibition of the Sonic Hedgehog signaling pathway*
- *The inhibition of ciliogenesis*

Migration

Septins are essential for the migration of various cell types,
including epithelial cells, fibroblasts, lymphocytes and neurons

Septins coordinate the organization and contractility of actomyosin in the lamellipodia

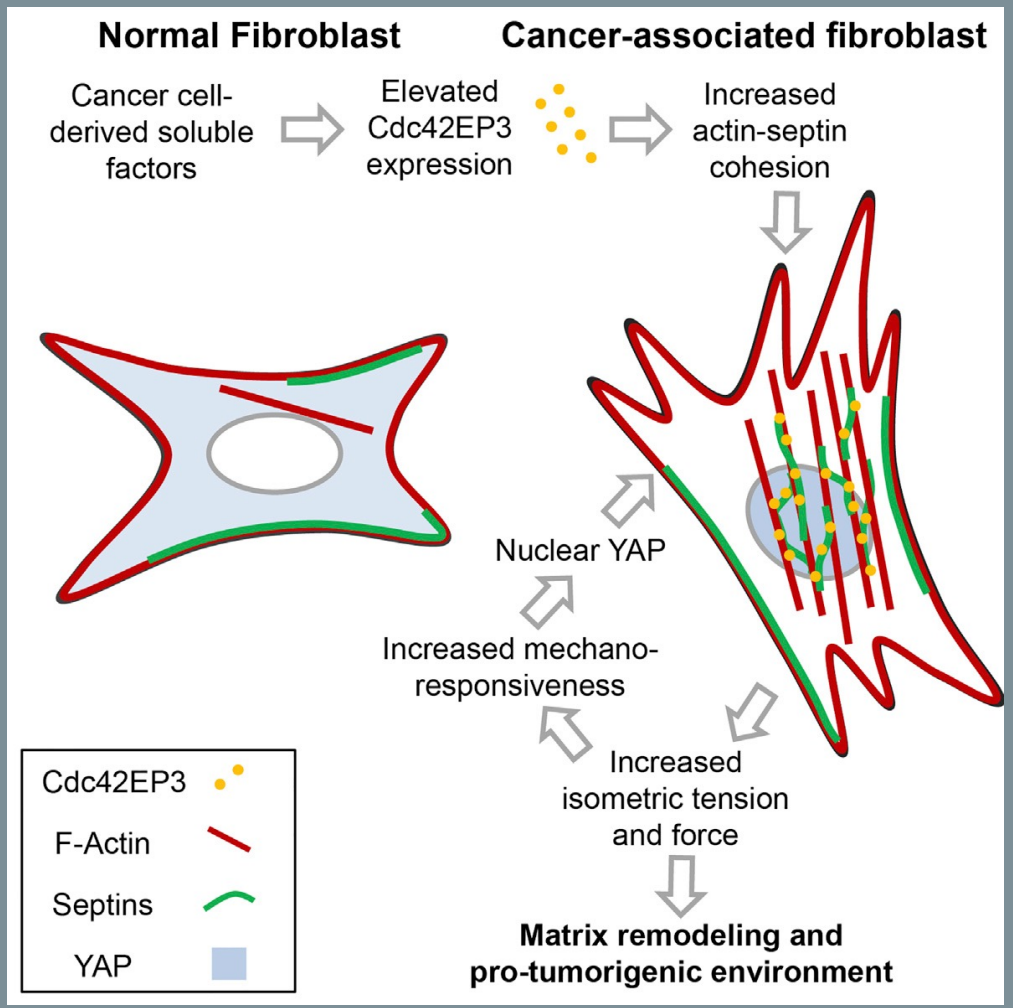


Spiliotis, J. Cell Sci. (2018)

SEPT9 interacts directly with actin filaments and functions as an actin stress fiber cross-linking protein that promotes the maturation of nascent focal adhesions and cell migration

Mechanotransduction

Role of septins in the response to changes in the cell environment and the nuclear translocation of the regulator of gene expression YAP



Activated fibroblasts → CAFs

Protumorigenic role

Calvo et al., Cell Rep. (2015)

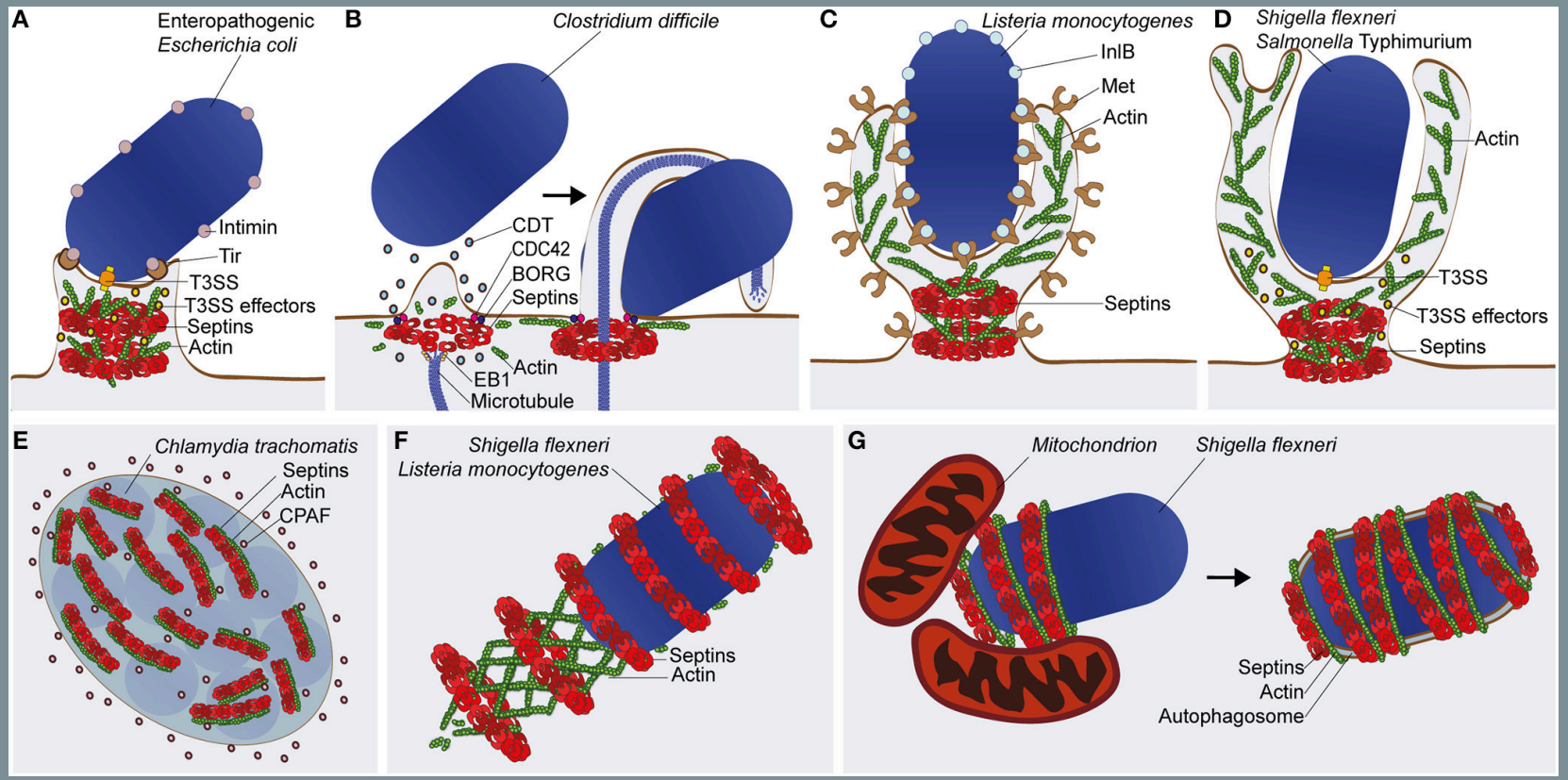
Pathogen internalization

Septins facilitate either internalization or degradation by autophagy

Rings remodel subcortical actin

Interaction with EB1 allows for the redirection of microtubule polymerization

Ring-shaped structures modify the membrane and facilitate bacterial entry



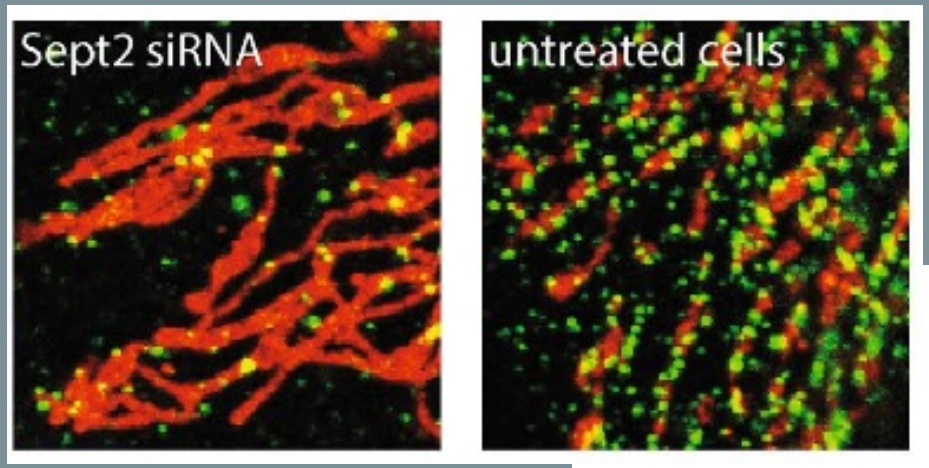
Septins coat the inclusion vacuole where bacteria survive and replicate

Unknown role of septin rings at the actin tail

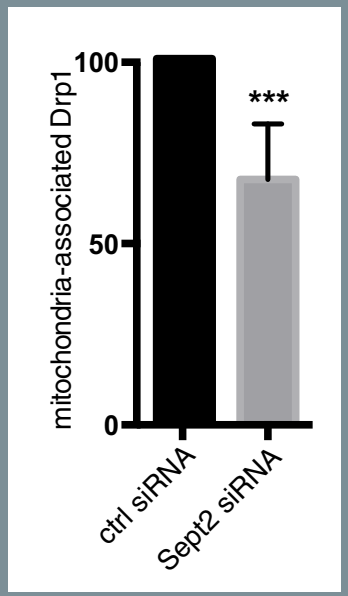
Cage-type structure assembly
Restriction of bacterial replication by autophagy

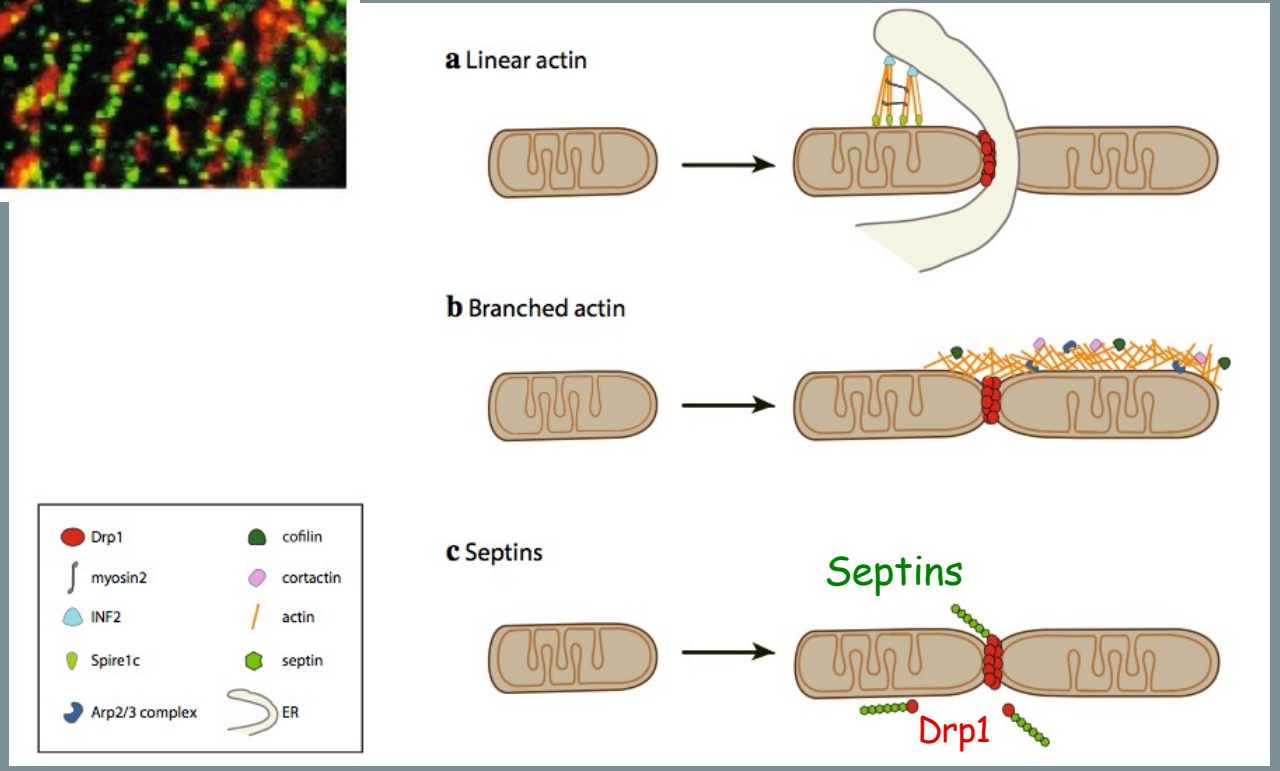
Torraca and Mostowy, Front. Cell Dev. Biol. (2016)

Mitochondrial fission



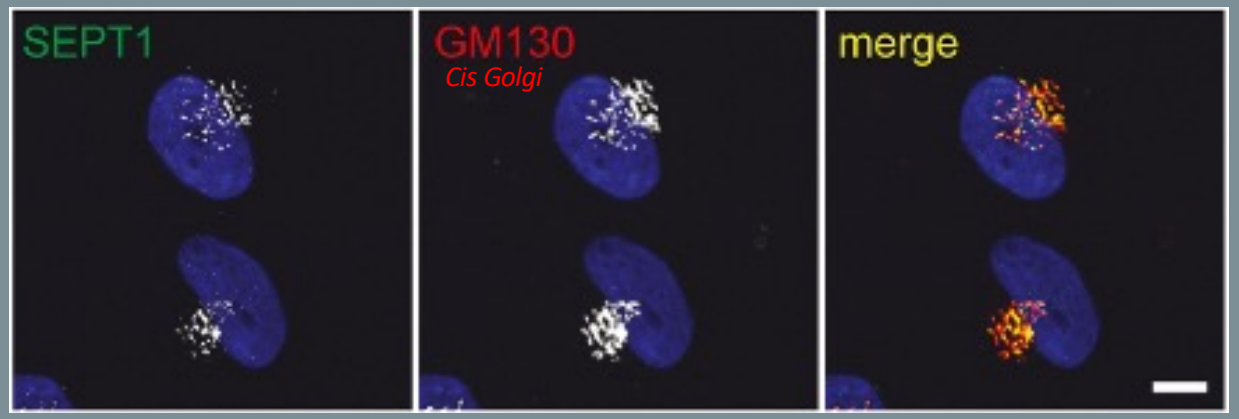
Pagliuso et al., EMBO Rep. (2017)



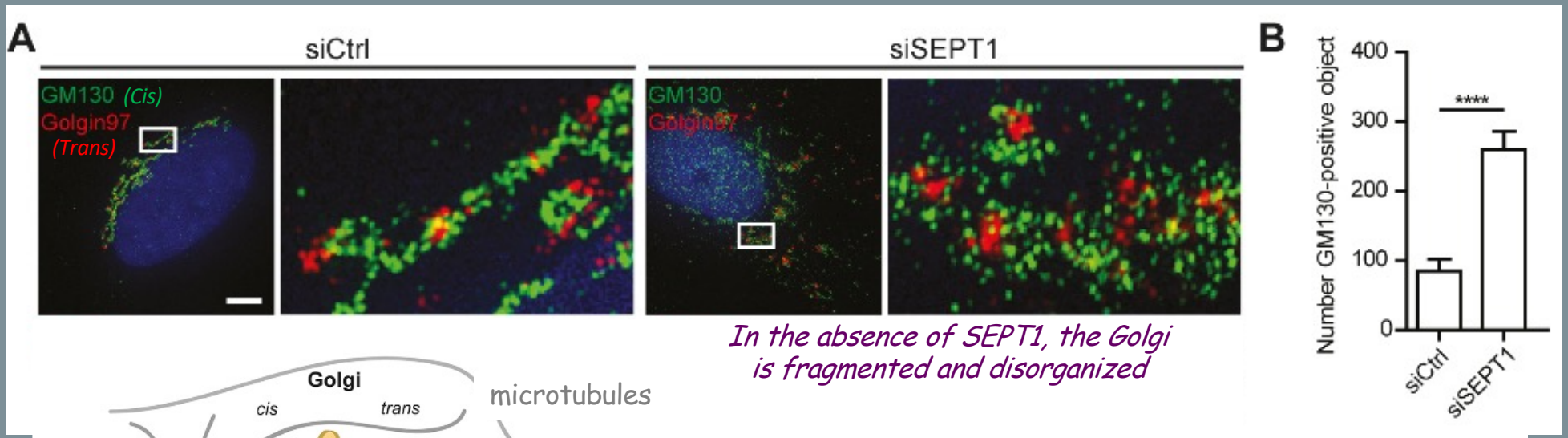


Mitochondrial localization of Drp1 relies on septins

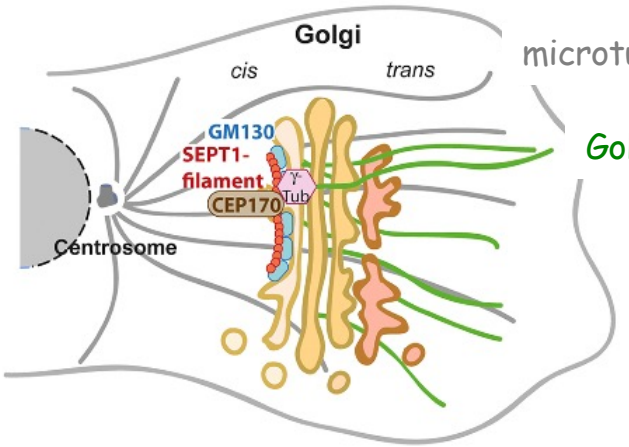
Maintaining the Golgi apparatus integrity



Song et al., J. Cell Sci. (2019)



In the absence of SEPT1, the Golgi is fragmented and disorganized



Golgi-derived microtubules

Nucleation of microtubules that originate at the Golgi

Regulation of protein stability

Septin- regulated protein	Septin(s) involved in regulation	Protein-septin interaction	Effect(s) of septins on protein stability	Molecular mechanism of septin-mediated effect	References
LCA	Septin 2 Septin 3 Septin 5 Septin 6 Septin 7 Septin 9 Septin 11	Dileucine motif (428L/429L) required for binding	Protect from ubiquitylation-dependent degradation	Unknown	Vagin et al., 2014
EGFR	Septin 9 Septin 2 Septin 7	Not demonstrated	Protects from ubiquitylation and degradation	Septin 9 competes with CBL for binding to CIN85	Diesenberg et al., 2015
ErbB2	Septin 2 Septin 9 Septin 7	Multiprotein complex with several septins	Protect from ubiquitylation and lysosomal degradation	Unknown	Marcus et al., 2016
HIF-1α	Septin 9	GTPase domain of septin 9 required for interaction	Protects from ubiquitylation and degradation	Septin 9 competes for RACK1 binding to HIF-1α	Amir et al., 2006, 2009; Golan and Mabjeesh, 2013; Vardi-Oknin et al., 2013
MET	Septin 2 Septin 11	Unknown	Differently modulate surface expression and association with the cytoskeleton	Unknown	Mostowy et al., 2011
JNK	Septin 9	GTPase domain of septin 9 required for interaction	Protects from degradation	Unknown	Gonzalez et al., 2009

Vagin and Beenhouwer, Front. Cell Dev. Biol. (2016)

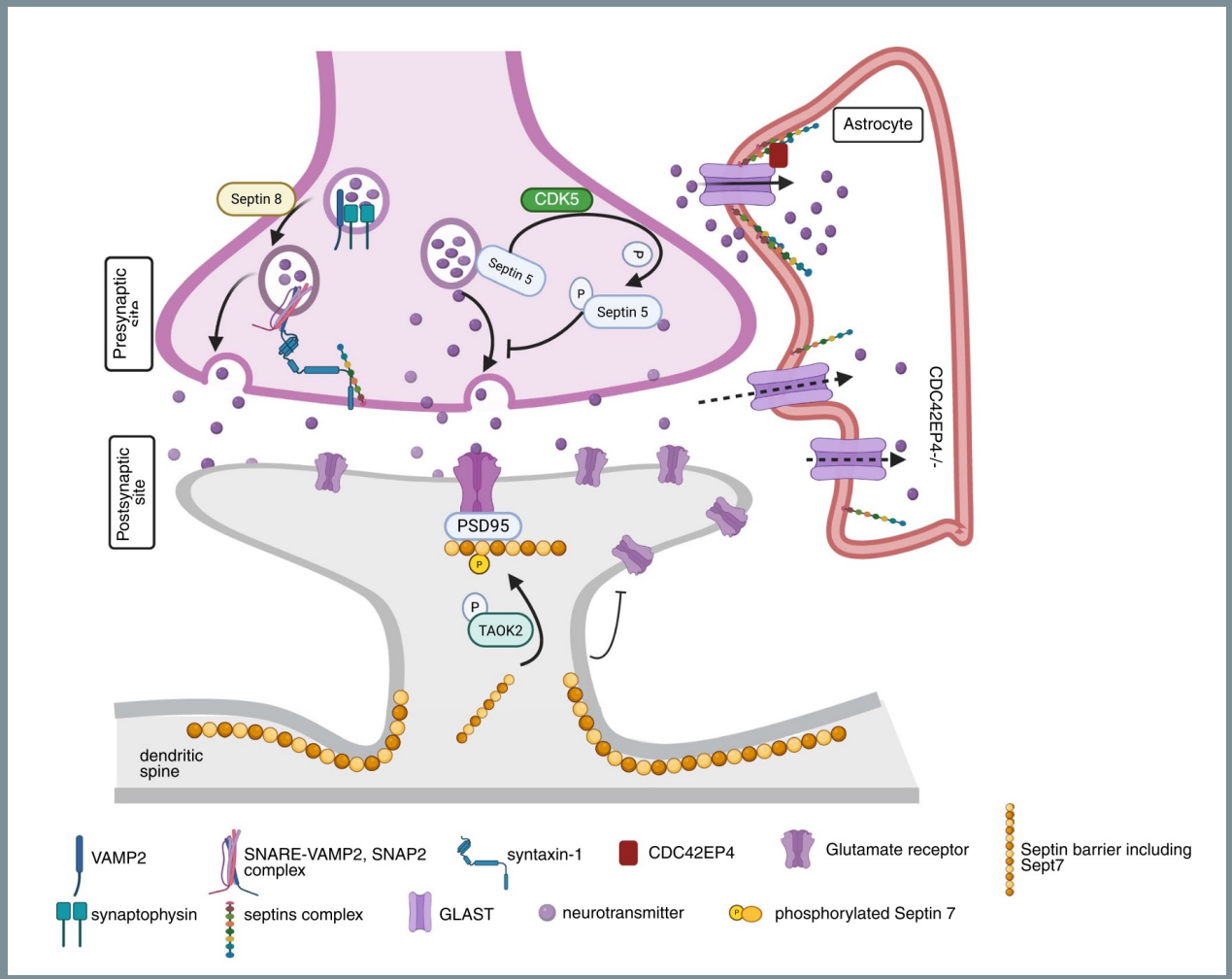
INVOLVEMENT OF SEPTINS

in human pathologies

Neurological disorders

Alterations in septin expression or assembly can disrupt synaptic architecture
Role in neuronal homeostasis

Septins regulate vesicular transport and neurotransmitter release at synapse



Alkhanjari et al., Cell Com. Signal. (2025)

Neurological disorders

Key regulators of neural development, including neurite outgrowth, spine morphology, and axon initial segment formation

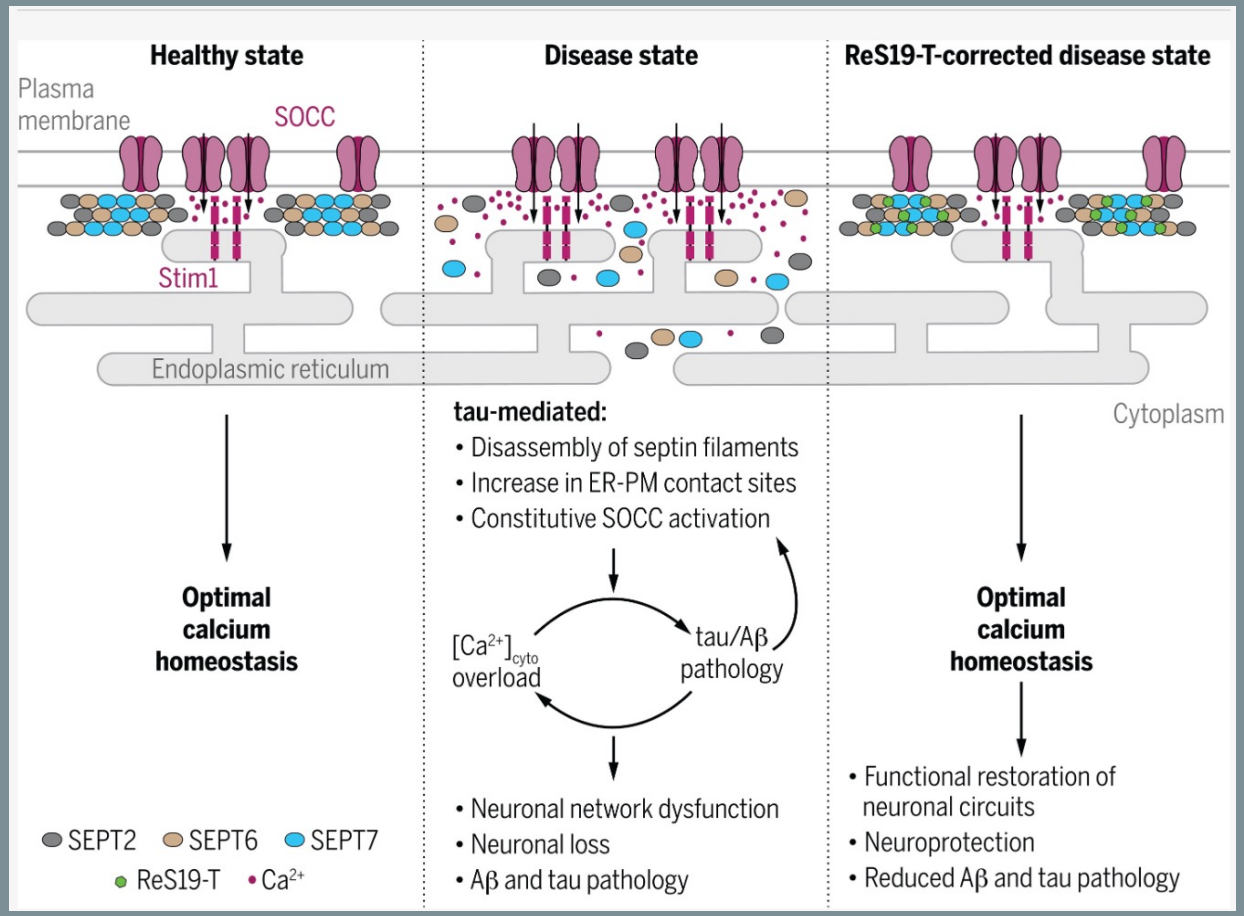
Implicated ina range of neurological disorders, including demyelinating diseases and Hereditary Neuralgic Amyotrophy

Abnormal septin aggregation in neurodegenerative diseases, such as Alzheimer's and Parkinson's disease

Neurological disorders

Abnormal Ca^{2+} signaling

Class of compounds able to restore Ca^{2+} homeostasis in tau pathology



SOCC = Ca^{2+} channel

Restrain Ca^{2+} entry

Restore septin filament assembly

Prevent neuronal loss

Septin cytoskeleton as a potential therapeutic target

Alkhanjari et al., Cell Com. Signal. (2025)

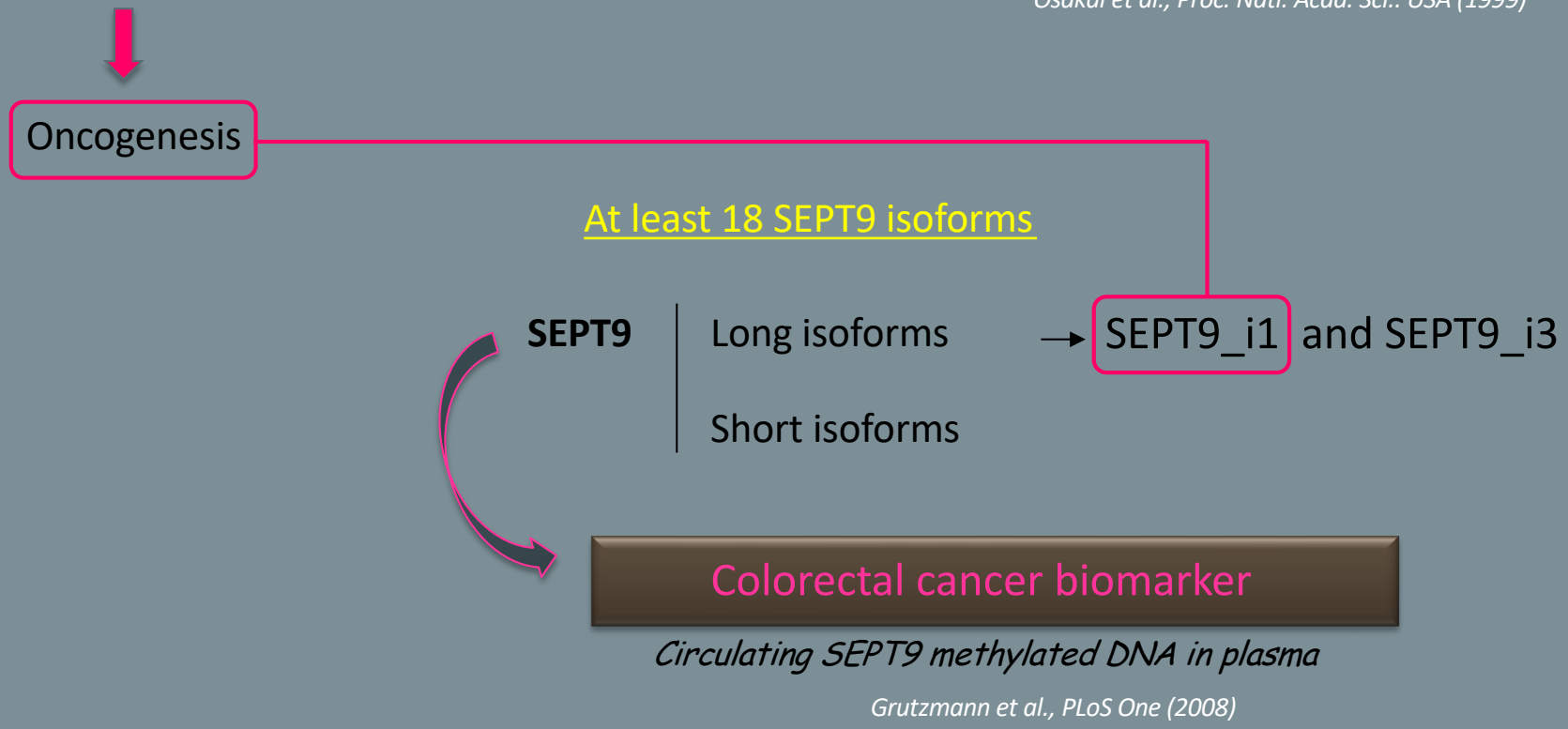
Cancerogenesis

- SEPT5, *MLL* gene translocation partner in acute myeloid leukemias

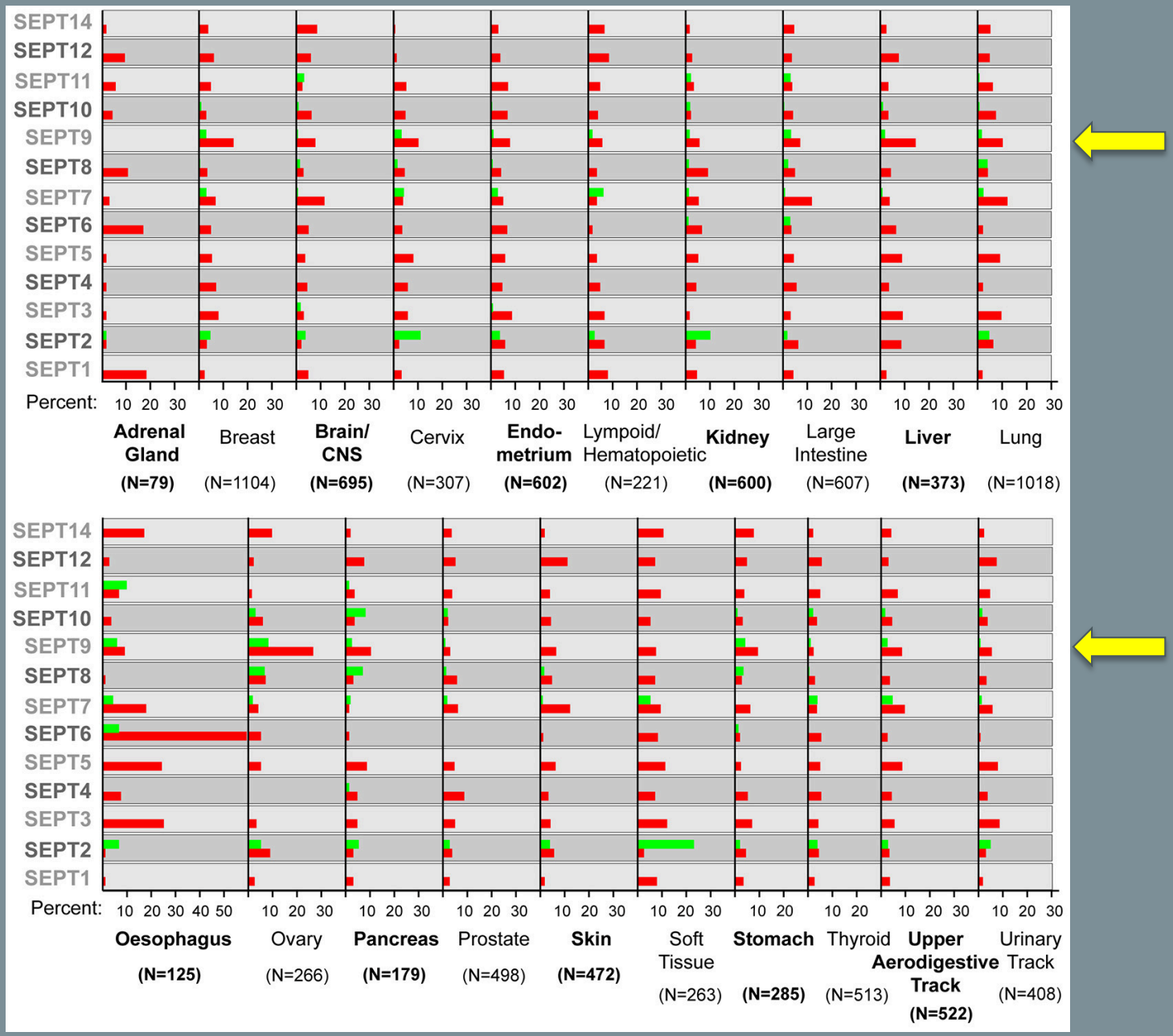
Megonigal et al., Proc. Natl. Acad. Sci.. USA (1998)

- Then SEPT9, SEPT6, SEPT2 and SEPT11 were also identified as fusion partners

Osakal et al., Proc. Natl. Acad. Sci.. USA (1999)

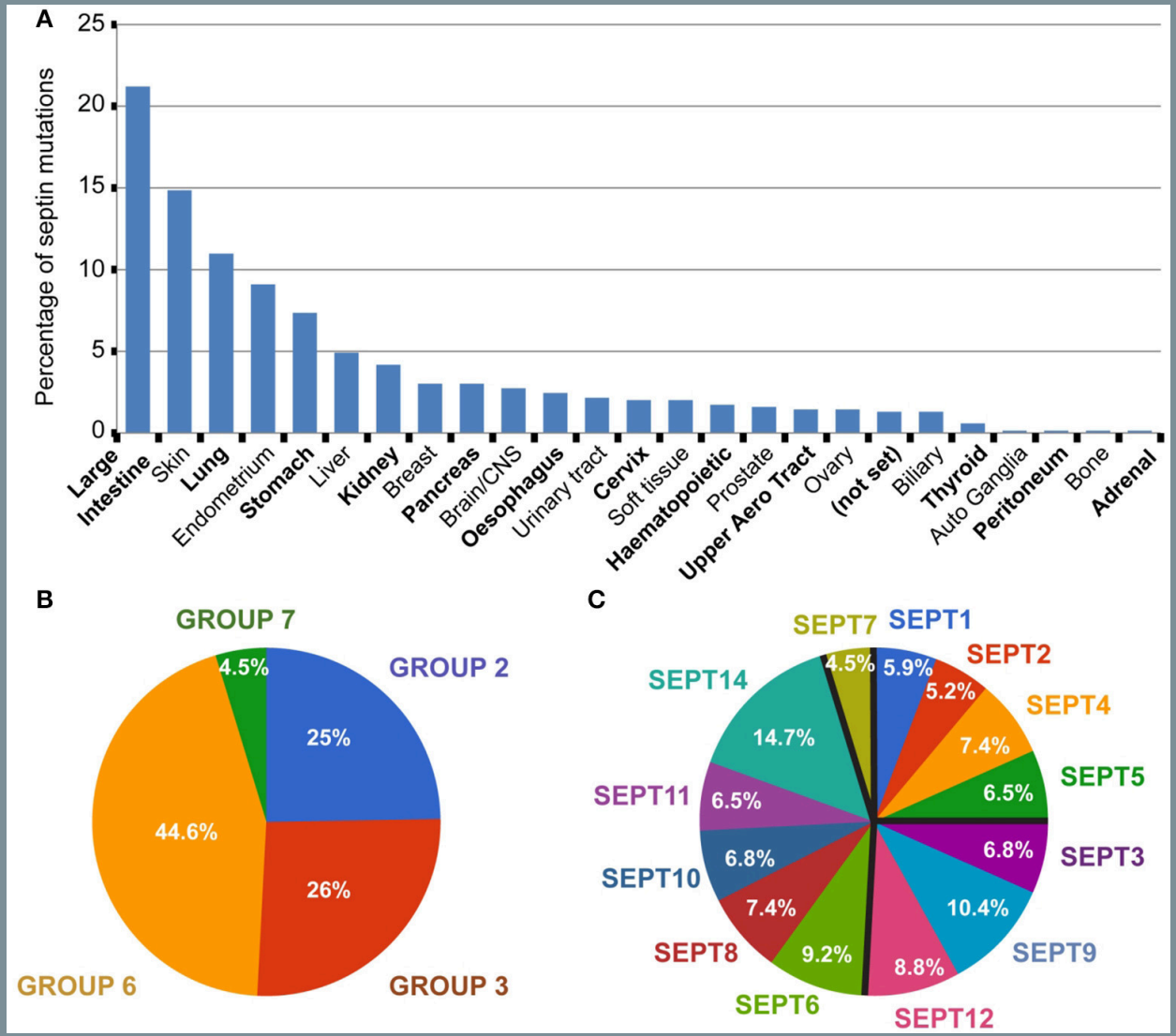


Percentage of tumor samples in which a septin is overexpressed (red) or underexpressed (green)



Angelis and Spiliotis, Front. Cell Dev. Biol. (2016)

Percentages of mutations found in septin genes in human cancers

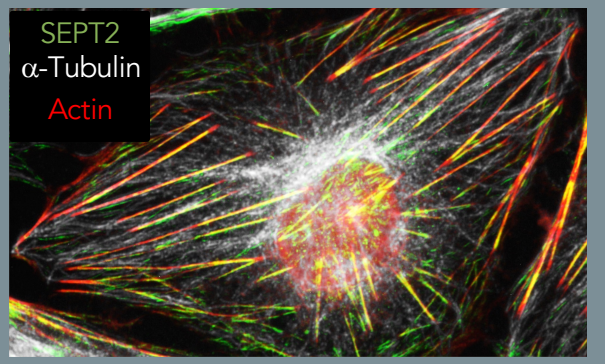


Angelis and Spiliotis, Front. Cell Dev. Biol. (2016)

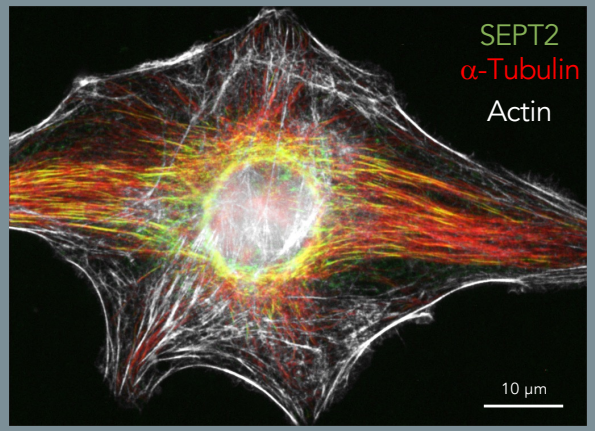
New mechanism of taxane resistance involving septins

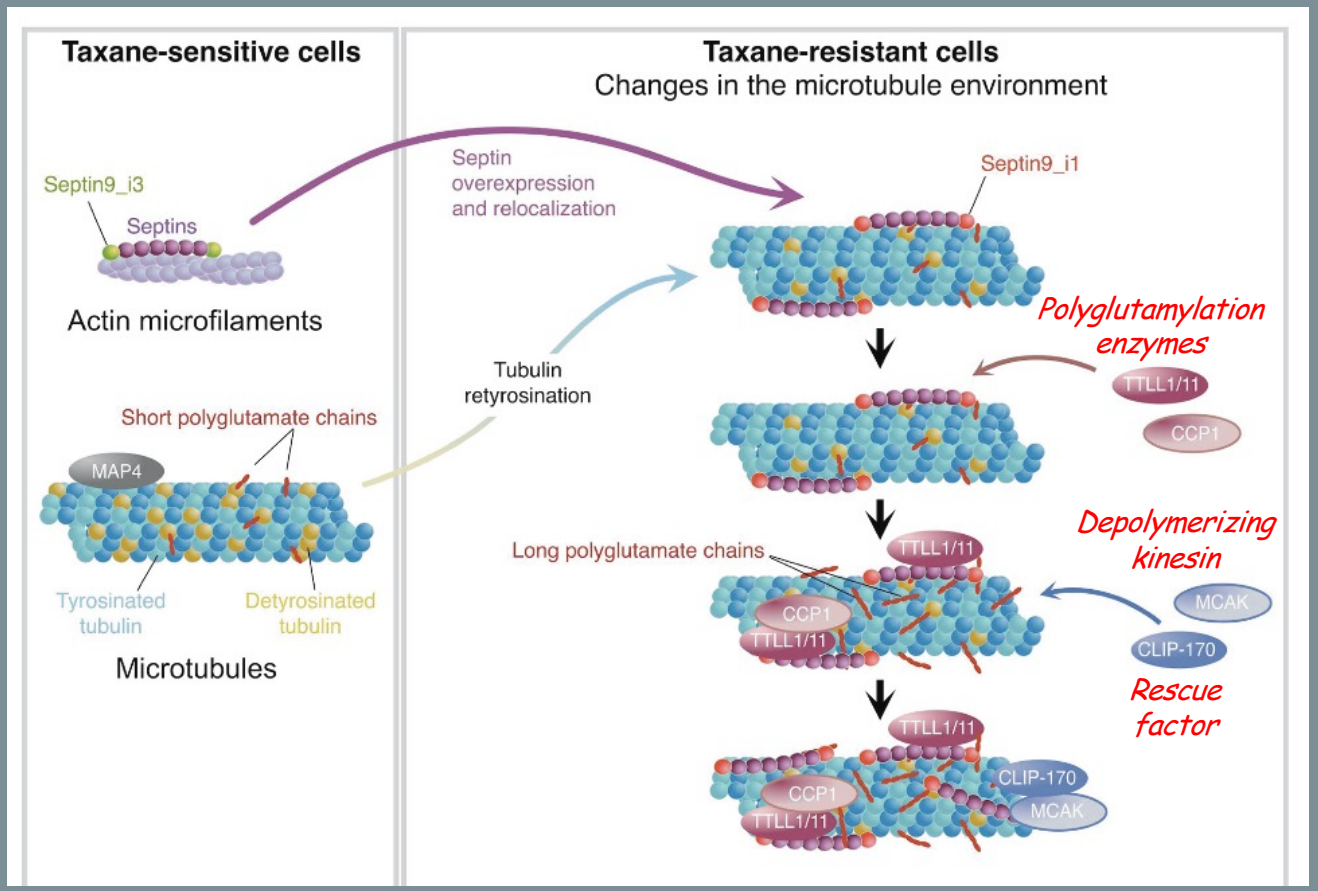
Subcellular relocalization of septin filaments

Sensitive cells



Resistant cells

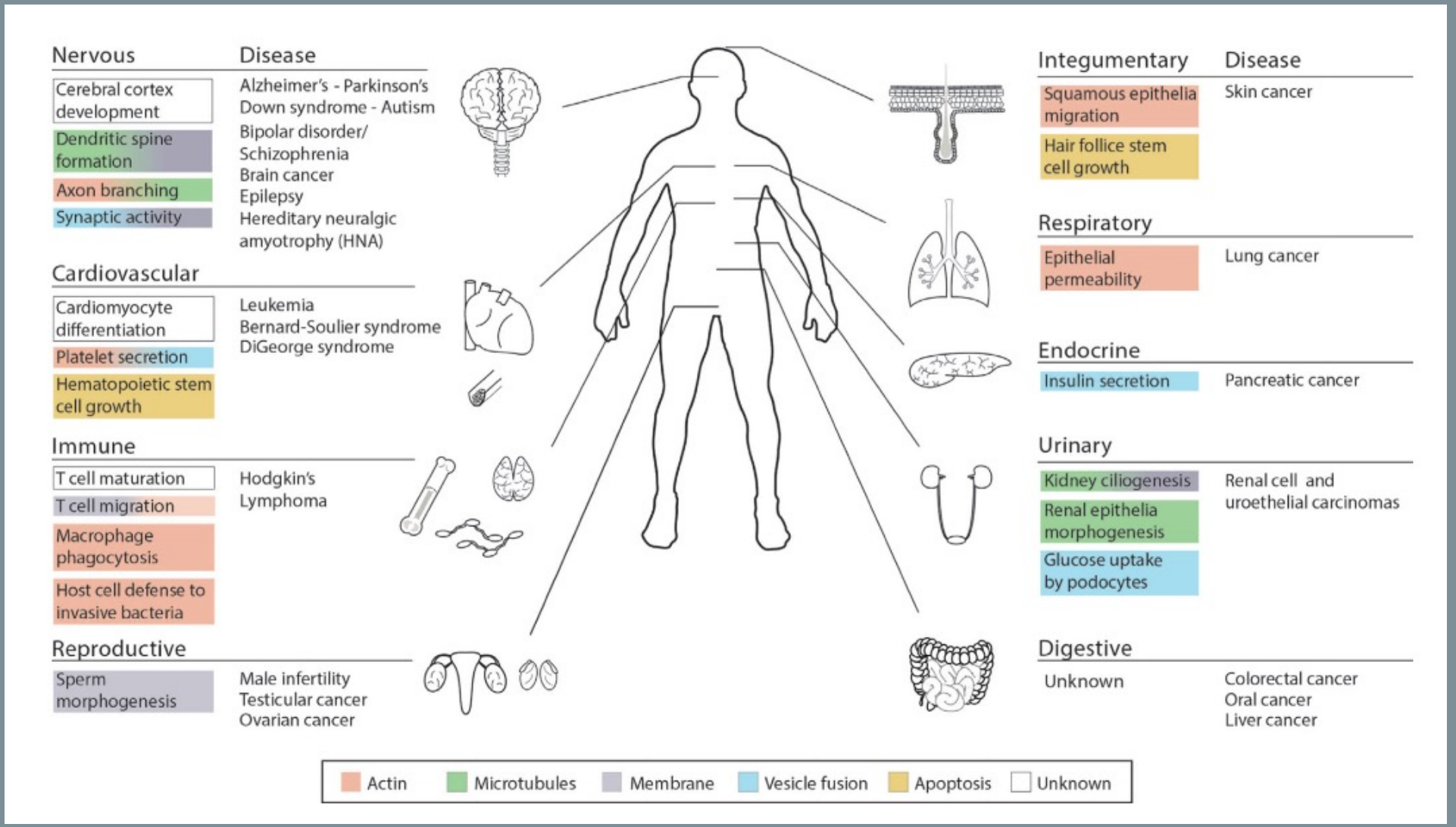




Restoration of microtubule dynamic instability

Froidevaux-Klipfel et al., Proteomics (2011) Froidevaux-Klipfel et al., Oncotarget (2015) Targa et al., Cell Death & Disease (2019) Salameh et al., Current Biology (2021)

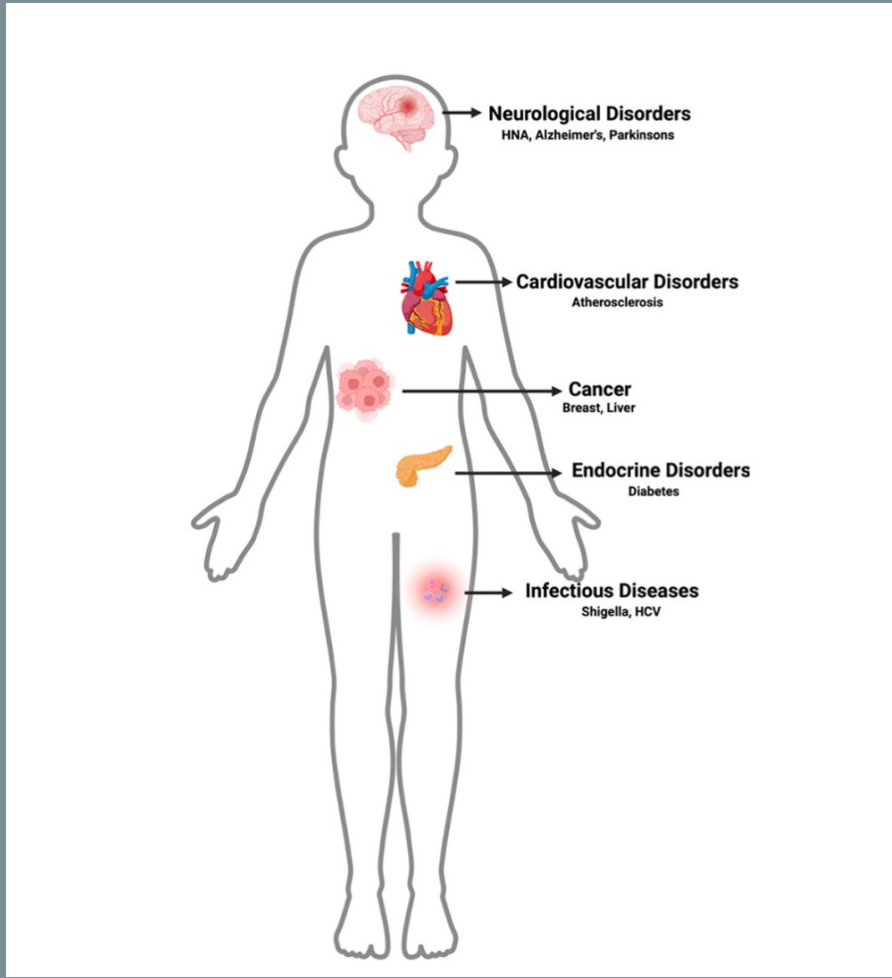
Septins and human pathologies



Dolat et al., Biol. Chem. (2014)

Septins and human pathologies

Pathological conditions associated with the unregulated expression of septins



Septins associated with the disease conditions

Septins	Disease-associated
SEPT1	Alzheimer's disease, cancer
SEPT2	Cancer, bacterial infections
SEPT3	Alzheimer's disease, cancer, Down's syndrome
SEPT4	Neurological disorders
SEPT5	Neurological disorders, cancer
SEPT6	Bipolar, cancer
SEPT7	Cancer, autophagy-related diseases, neurodegenerative disorders and metabolic conditions, mitochondrial disease, diabetes
SEPT8	Retinal degeneration
SEPT9	Neurological disorders, infections
SEPT10	—
SEPT11	ALS, viral infections, hormone-related diseases
SEPT12	bacterial infections, hormone-related
SEPT14	Neurological disorders, cancer

Das and Kunwar, J. Cell. Biochem. (2024)

OUR RESEARCH PROJECT

Septins and chemoresistance

Inserm UMR-S 1193

Team 5 « Cellular and molecular mechanisms of cell adaptation to stress and cancerogenesis »

Head: Pr Christian POÜS

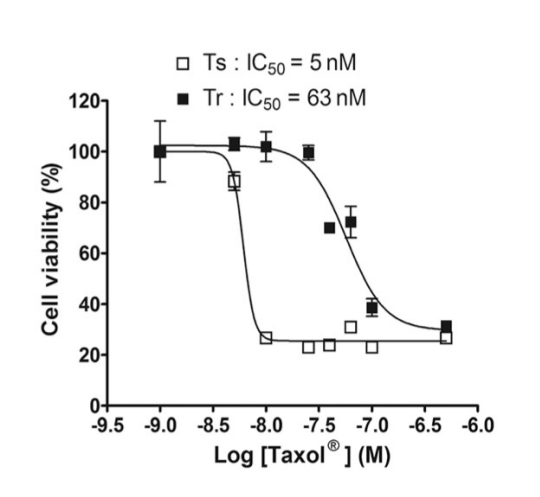
Proteomics 2011, *11*, 3877–3886 DOI 10.1002/pmic.201000789 3877

RESEARCH ARTICLE

Modulation of septin and molecular motor recruitment in the microtubule environment of the Taxol-resistant human breast cancer cell line MDA-MB-231

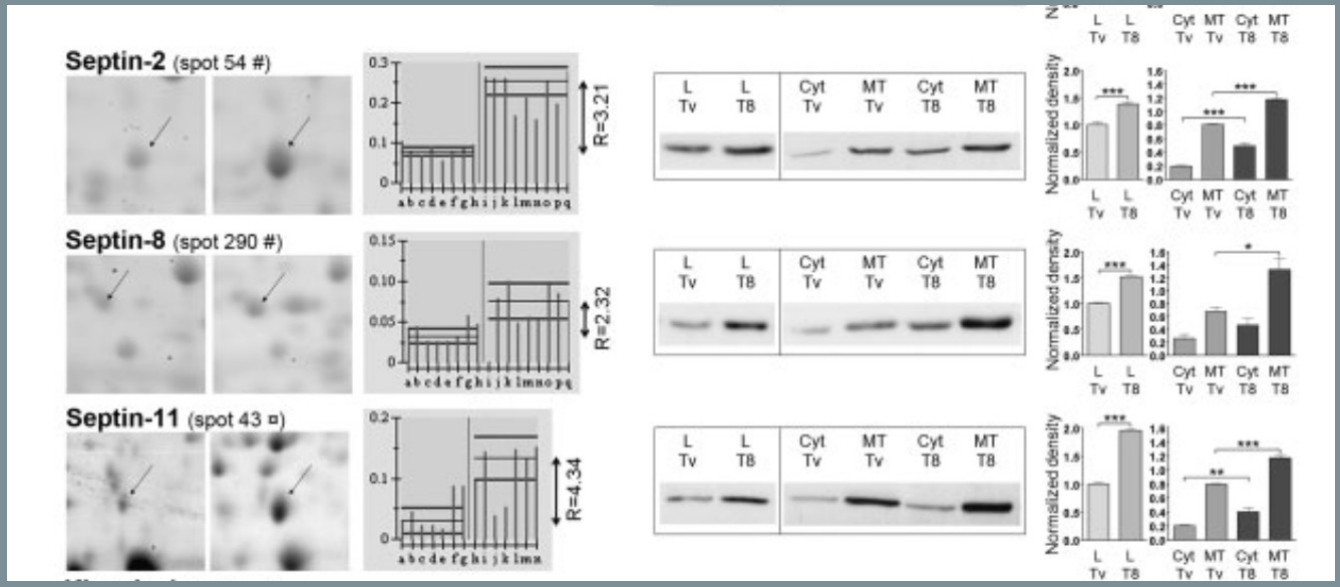
Laurence Froidevaux-Klipfel[1], Florence Poirier[2], Céline Boursier[2], Ronan Crépin[1], Christian Poüs[1,3], Bruno Baudin[1,4] and Anita Baillet[1]

Creation of a resistant cell line



Breast cancer cells MDA-MB 231

Proteomic analysis

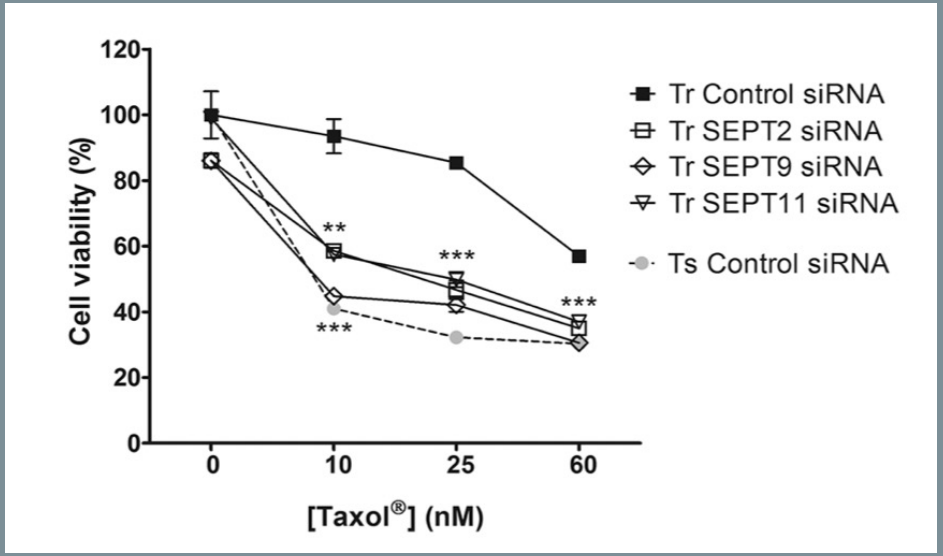


Overexpression and enhanced recruitment to microtubules of several septins

www.impactjournals.com/oncotarget/ Oncotarget, Vol. 6, No. 34

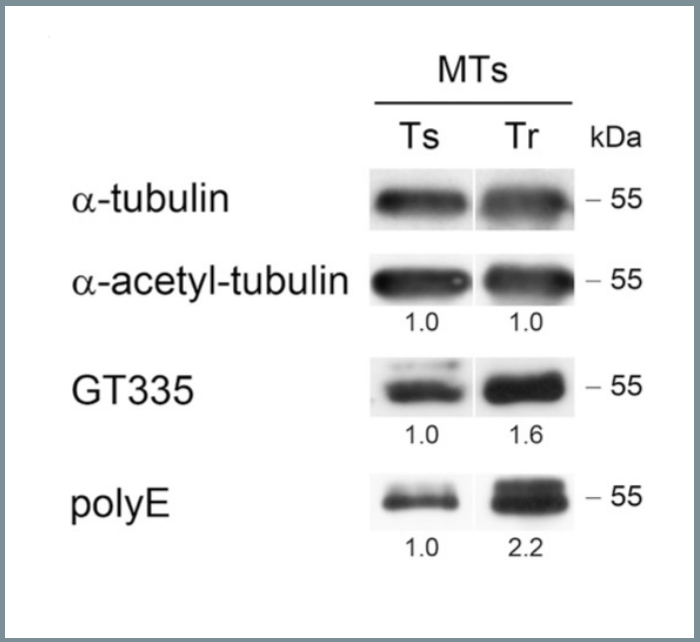
Septin cooperation with tubulin polyglutamylation contributes to cancer cell adaptation to taxanes

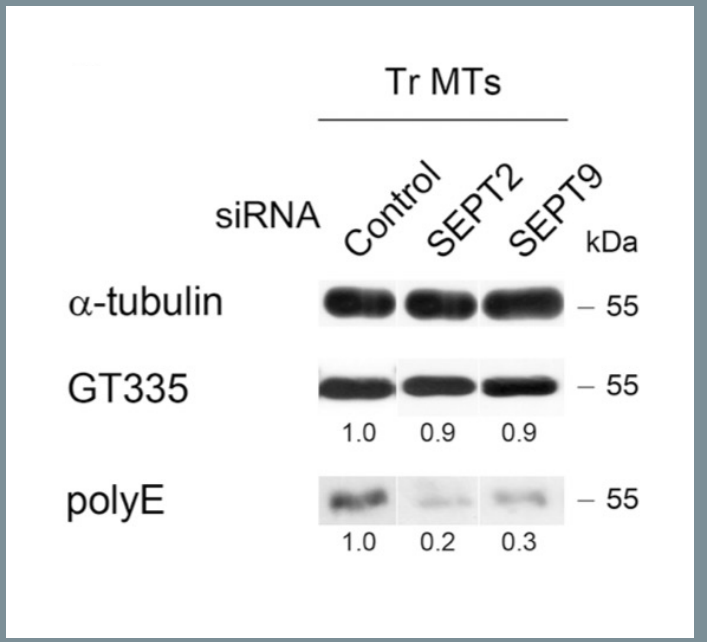
Laurence Froidevaux-Klipfel[1,*], Benjamin Targa[1], Isabelle Cantaloube[1], Hayat Ahmed-Zaïd[1], Christian Poüs[1,2], Anita Baillet[1]



Post-translational modifications of microtubules

Polyglutamylation





www.impactjournals.com/oncotarget/ Oncotarget, Vol. 6, No. 34

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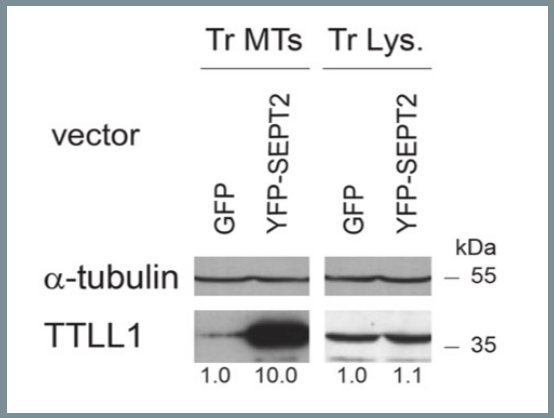
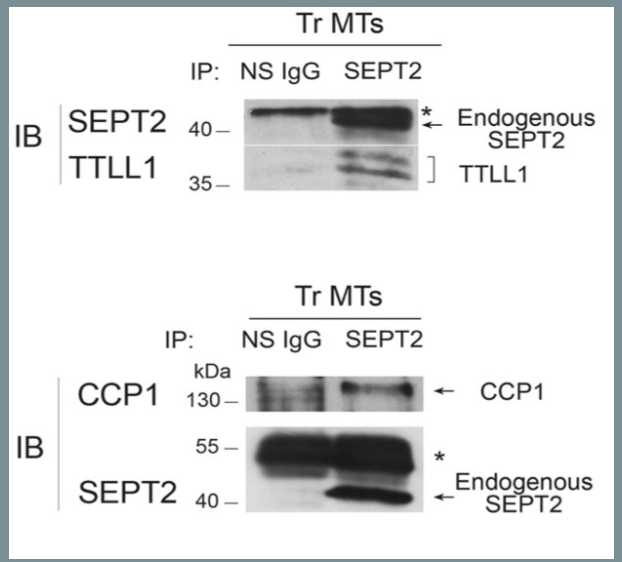
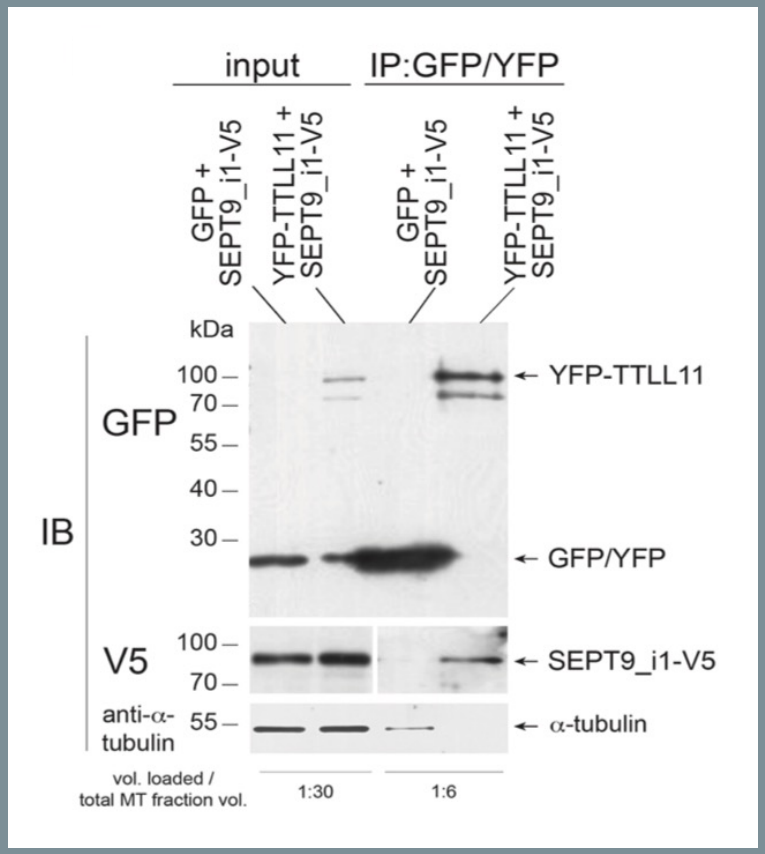
Septins recruit polyglutamylases and deglutamylases onto microtubules







Co-immunoprecipitation experiments

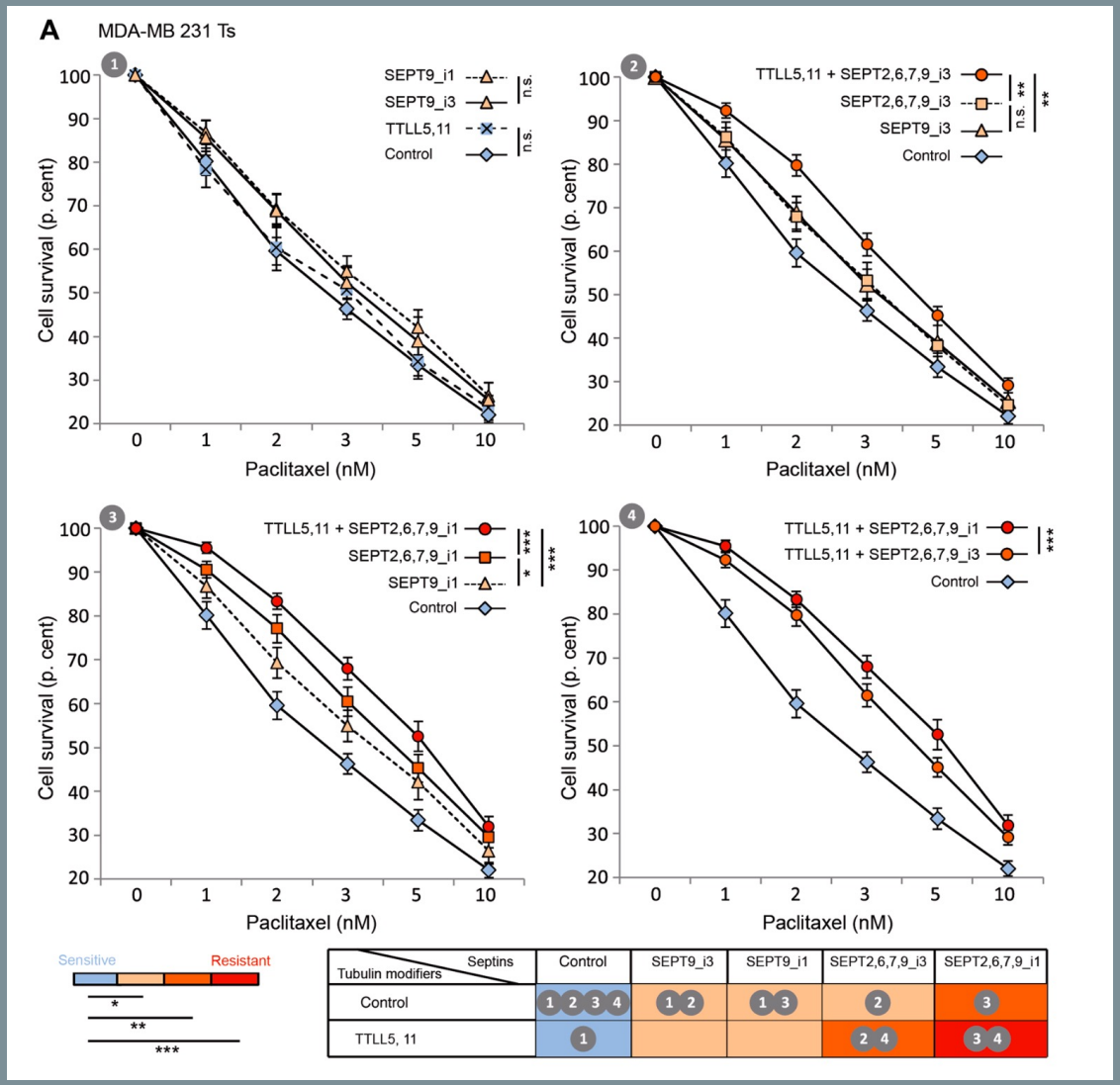
Targa et al. *Cell Death and Disease* (2019)10:54
https://doi.org/10.1038/s41419-019-1318-6

Cell Death & Disease

ARTICLE Open Access

Septin filament coalignment with microtubules depends on SEPT9_i1 and tubulin polyglutamylation, and is an early feature of acquired cell resistance to paclitaxel

Benjamin Targa[1], Laurence Klipfel[2], Isabelle Cantaloube[1], Joëlle Salameh[1], Béatrice Benoit[1], Christian Poüs[1,3] and Anita Baillet[1]



Overexpression of septins is sufficient to induce chemoresistance

Long-chain polyglutamylation of microtubles acts as an enhancer

Targa et al. *Cell Death and Disease* (2019)10:54
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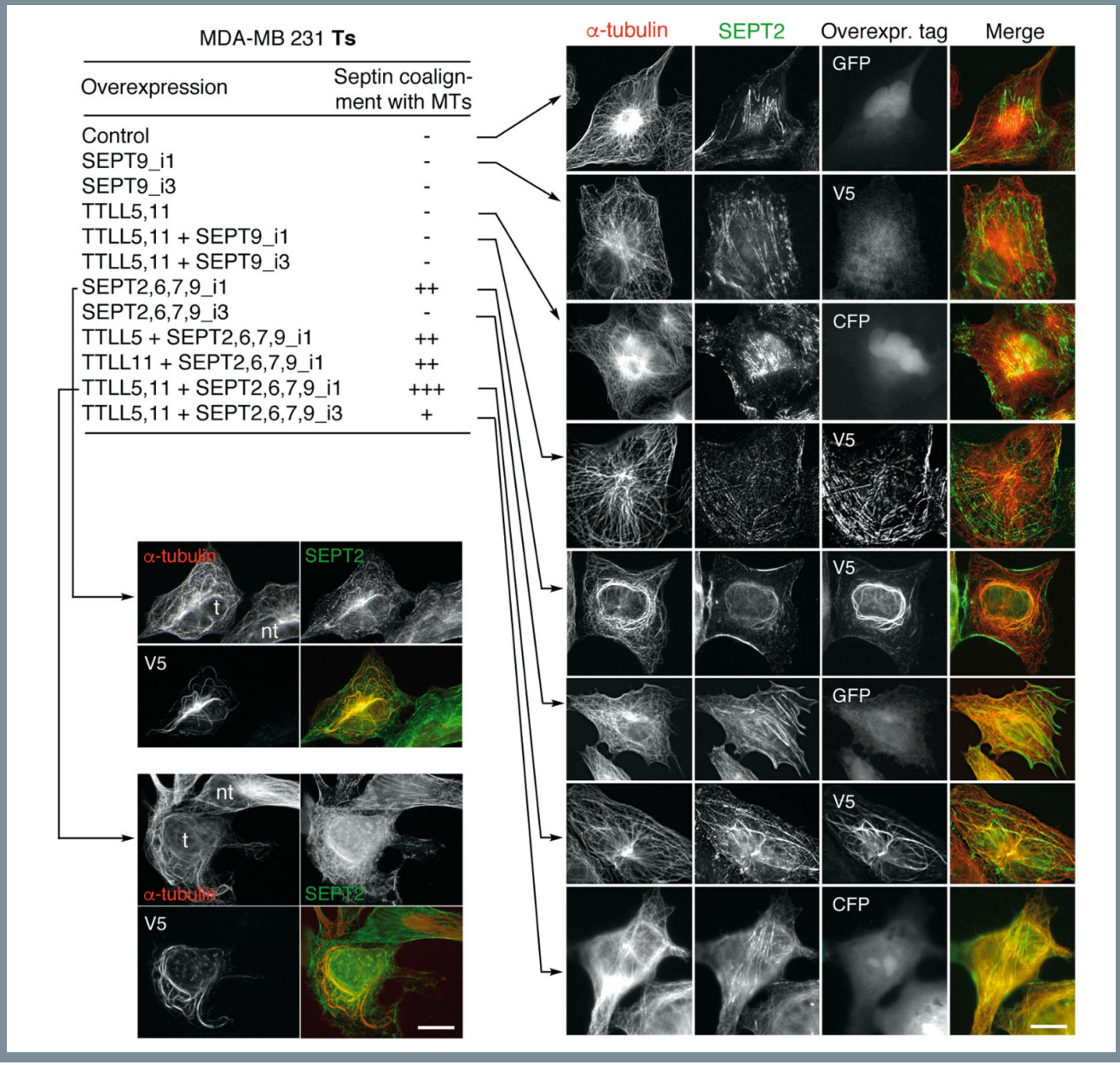

Targa et al. *Cell Death and Disease* (2019)10:54
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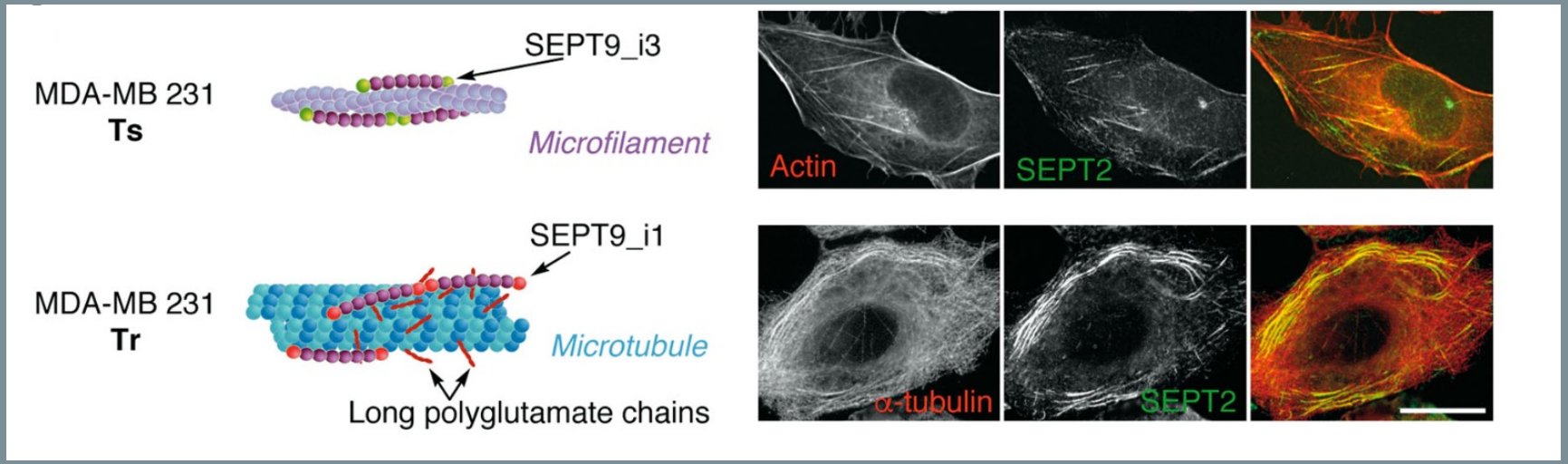

Change in the expression of SEPT9 isoforms

Increase of long polyglutamate chains on microtubules

Targa et al. *Cell Death and Disease* (2019)10:54
https://doi.org/10.1038/s41419-019-1318-6

Cell Death & Disease

ARTICLE Open Access

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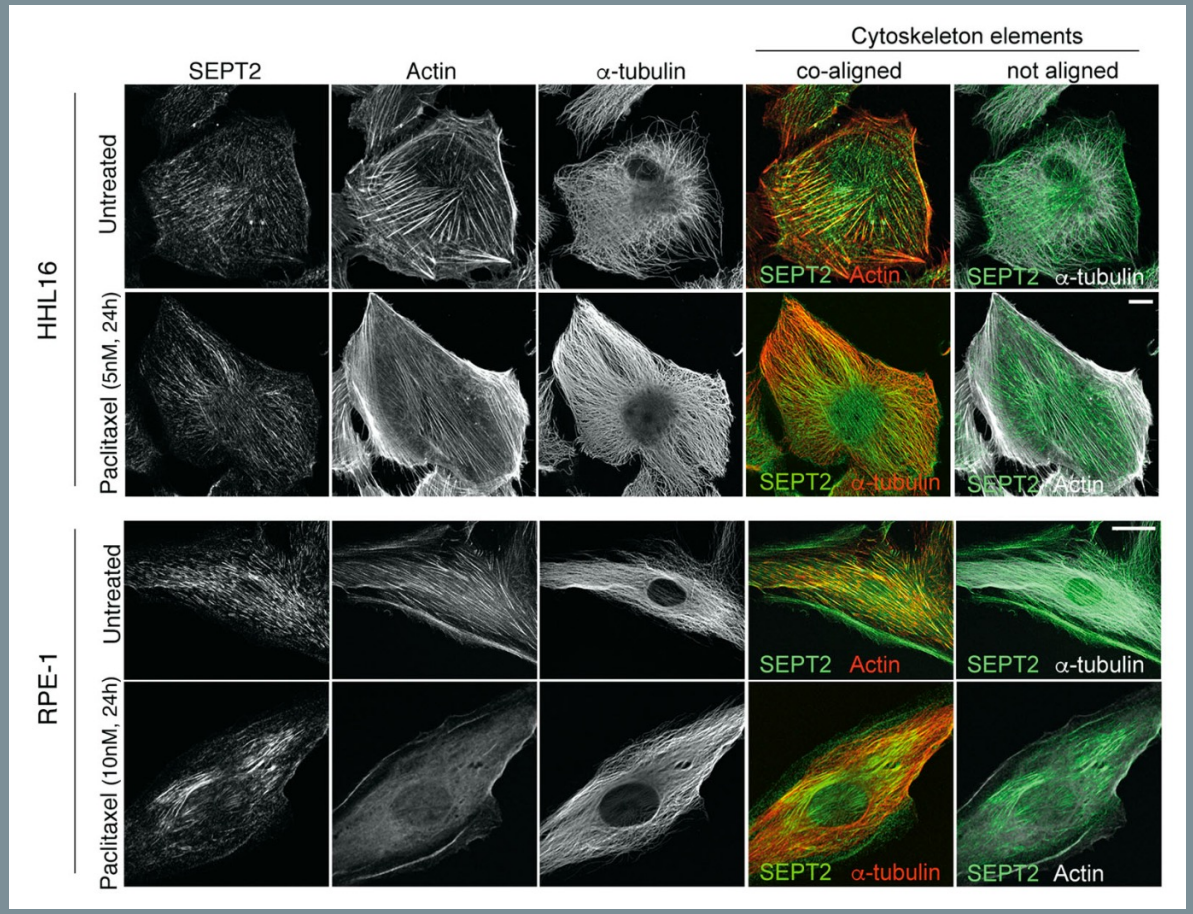
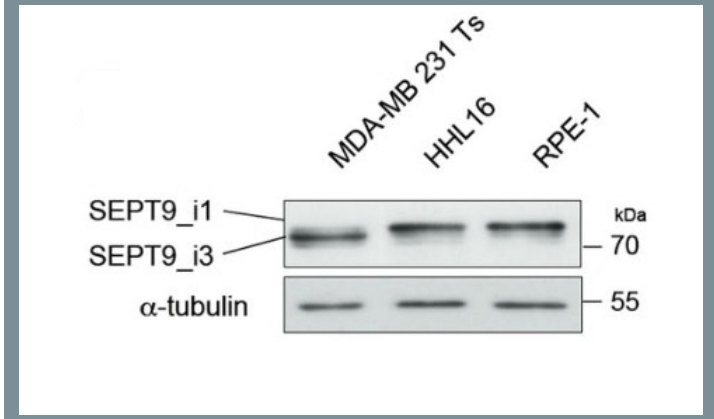
General mechanism



Early feature as long as SEPT9_i1 is expressed



Current Biology

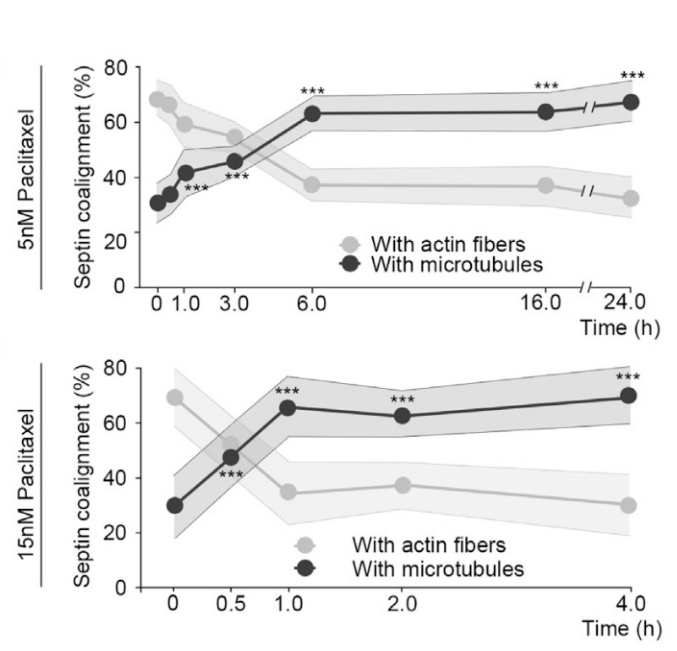
CellPress

Article

Cdc42 and its BORG2 and BORG3 effectors control the subcellular localization of septins between actin stress fibers and microtubules

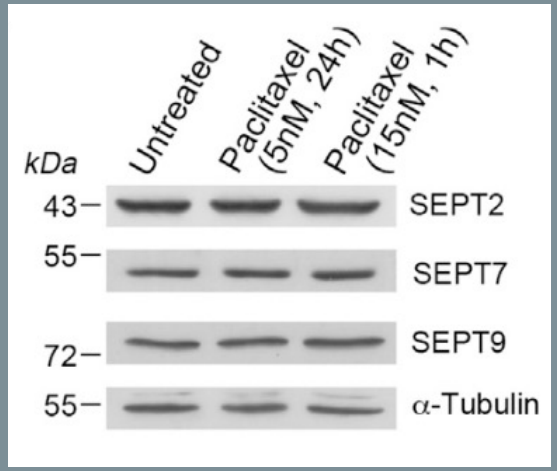
Joëlle Salameh,[1,3] Isabelle Cantaloube,[1,3] Béatrice Benoit,[1] Christian Poüs,[1,2,4,*] and Anita Baillet[1,*]

Immortalized hepatocytes HHL16

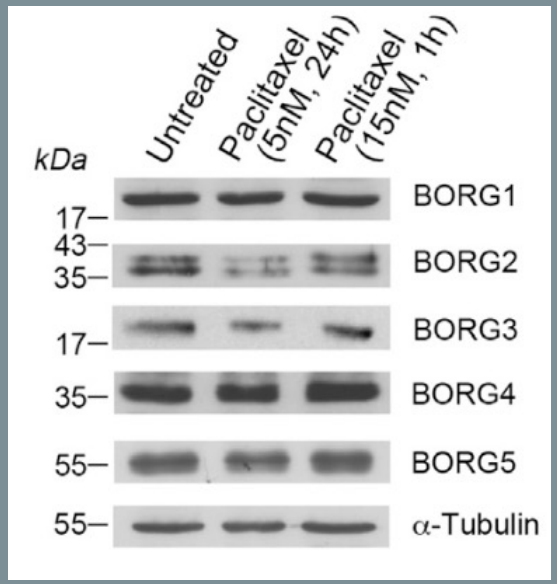


Septin relocalization is an early event

in cells expressing SEPT9_i1



Septin expression is not modified



BORG proteins are deregulated

BORG = Cdc42 effector proteins

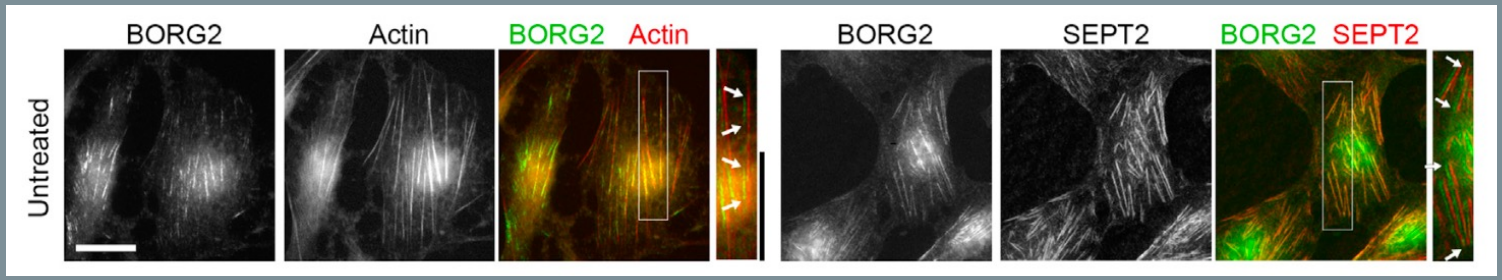
Current Biology

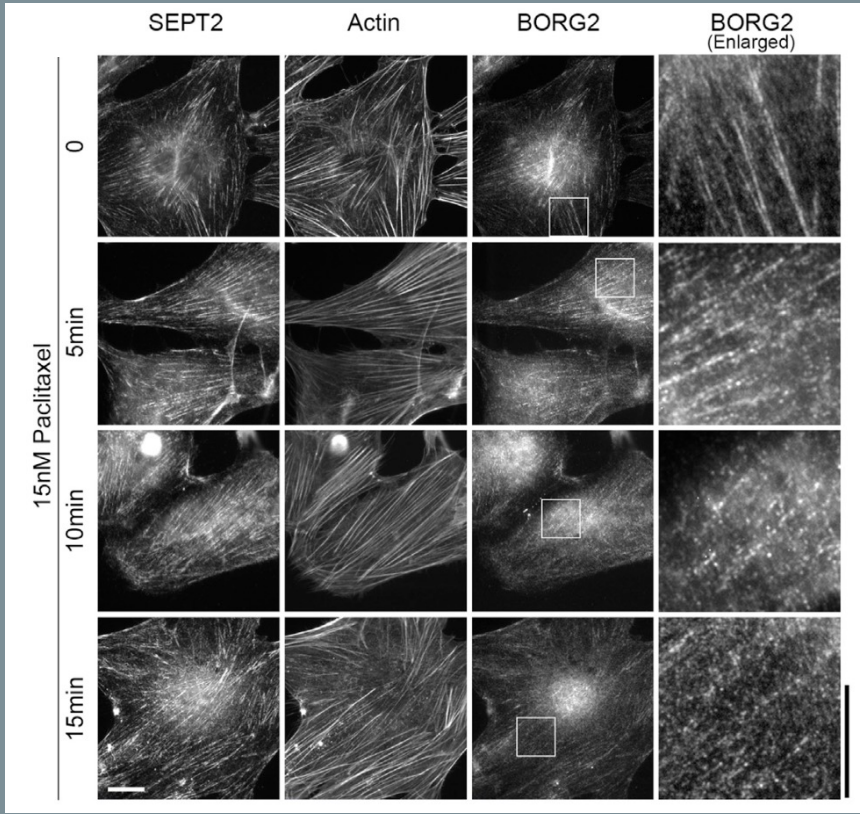
CellPress

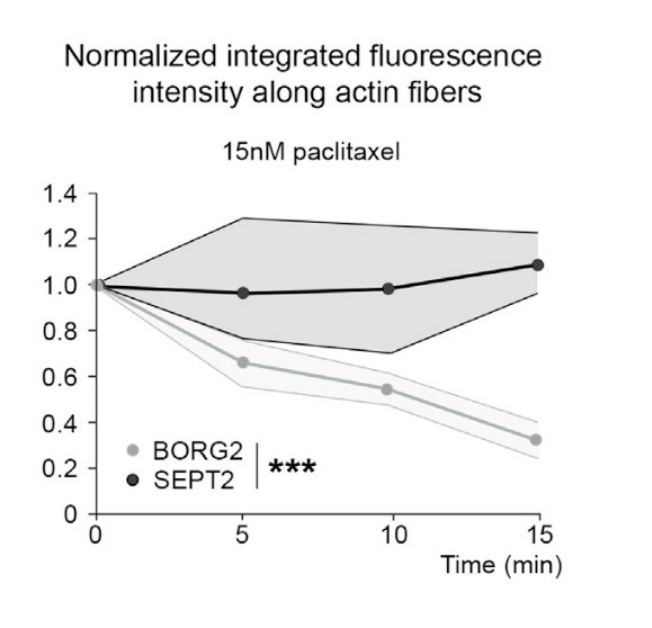
Article

Cdc42 and its BORG2 and BORG3 effectors control the subcellular localization of septins between actin stress fibers and microtubules

Joëlle Salameh,[1,3] Isabelle Cantaloube,[1,3] Béatrice Benoit,[1] Christian Poüs,[1,2,4,*] and Anita Baillet[1,*]







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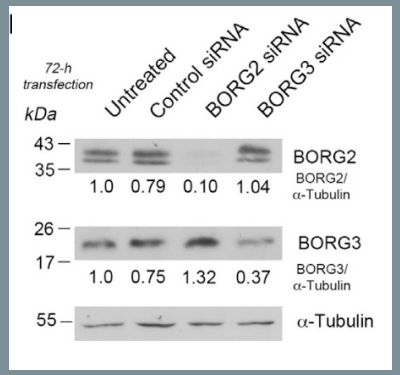
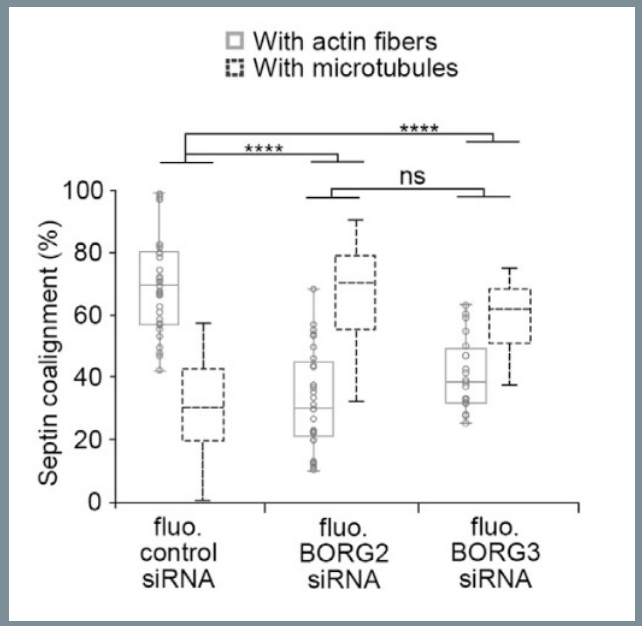
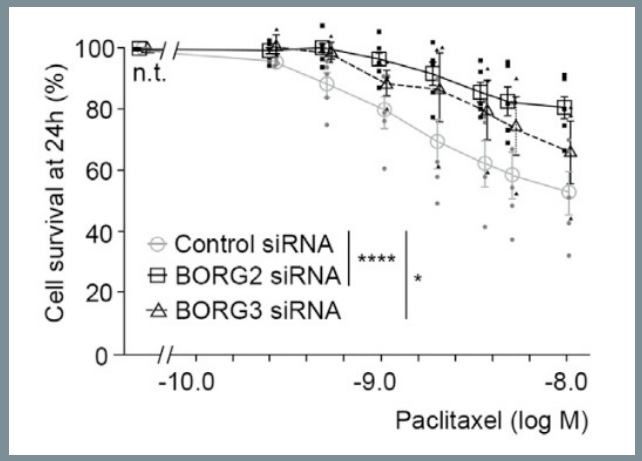
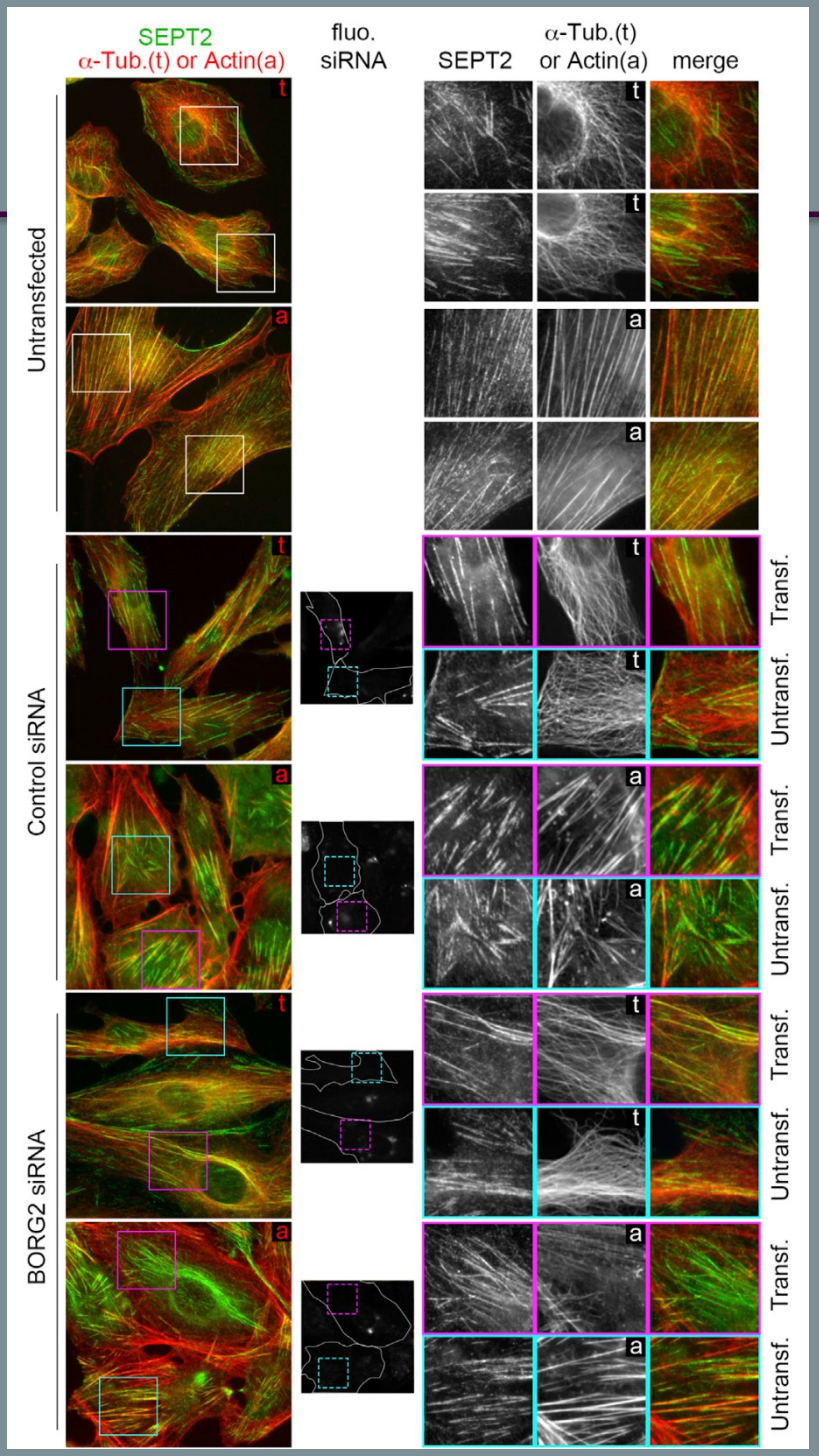




Inhibiting BORG proteins induces septin relocalization and chemoresistance





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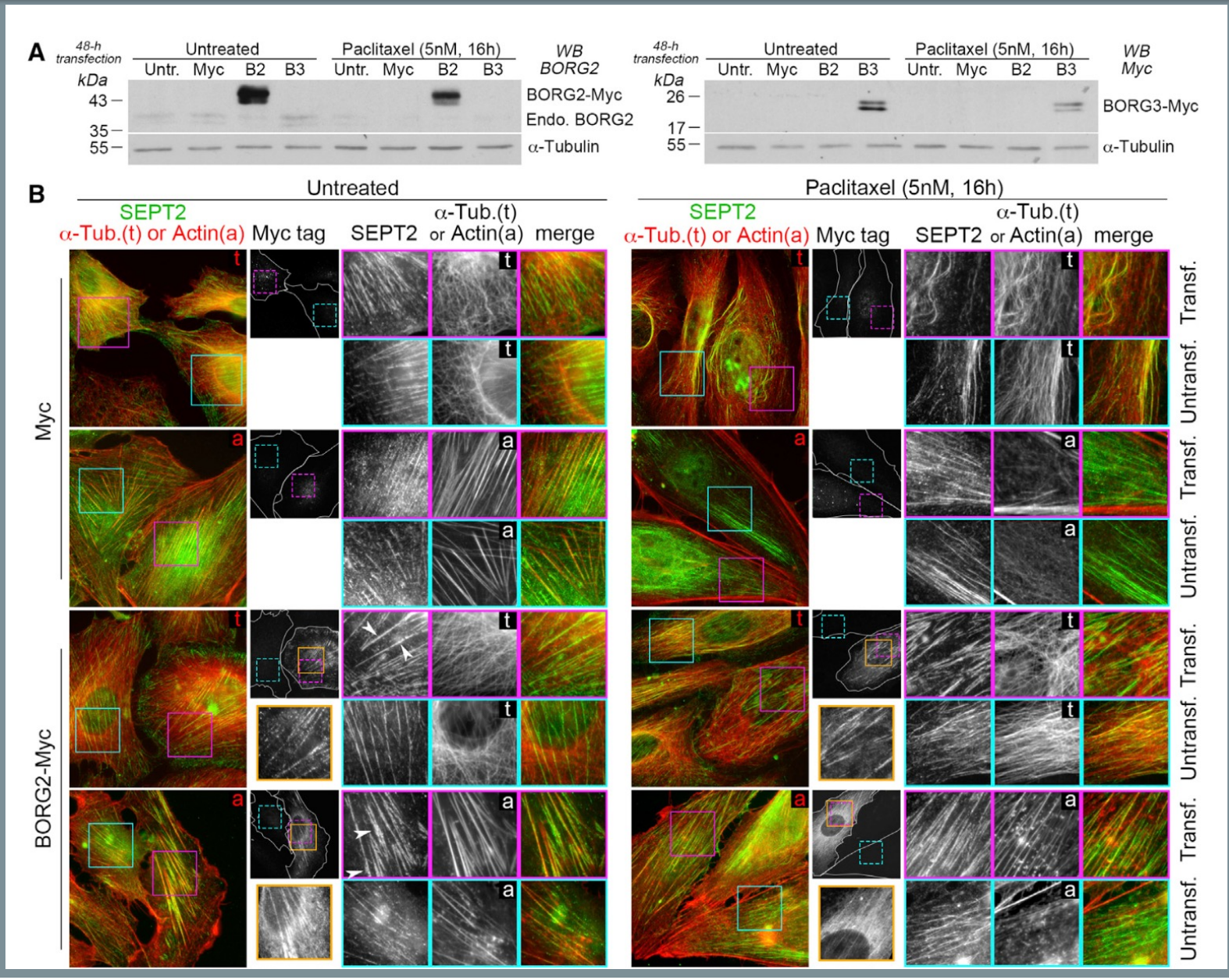
And conversely



Current Biology

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Cdc42 and its BORG2 and BORG3 effectors control the subcellular localization of septins between actin stress fibers and microtubules

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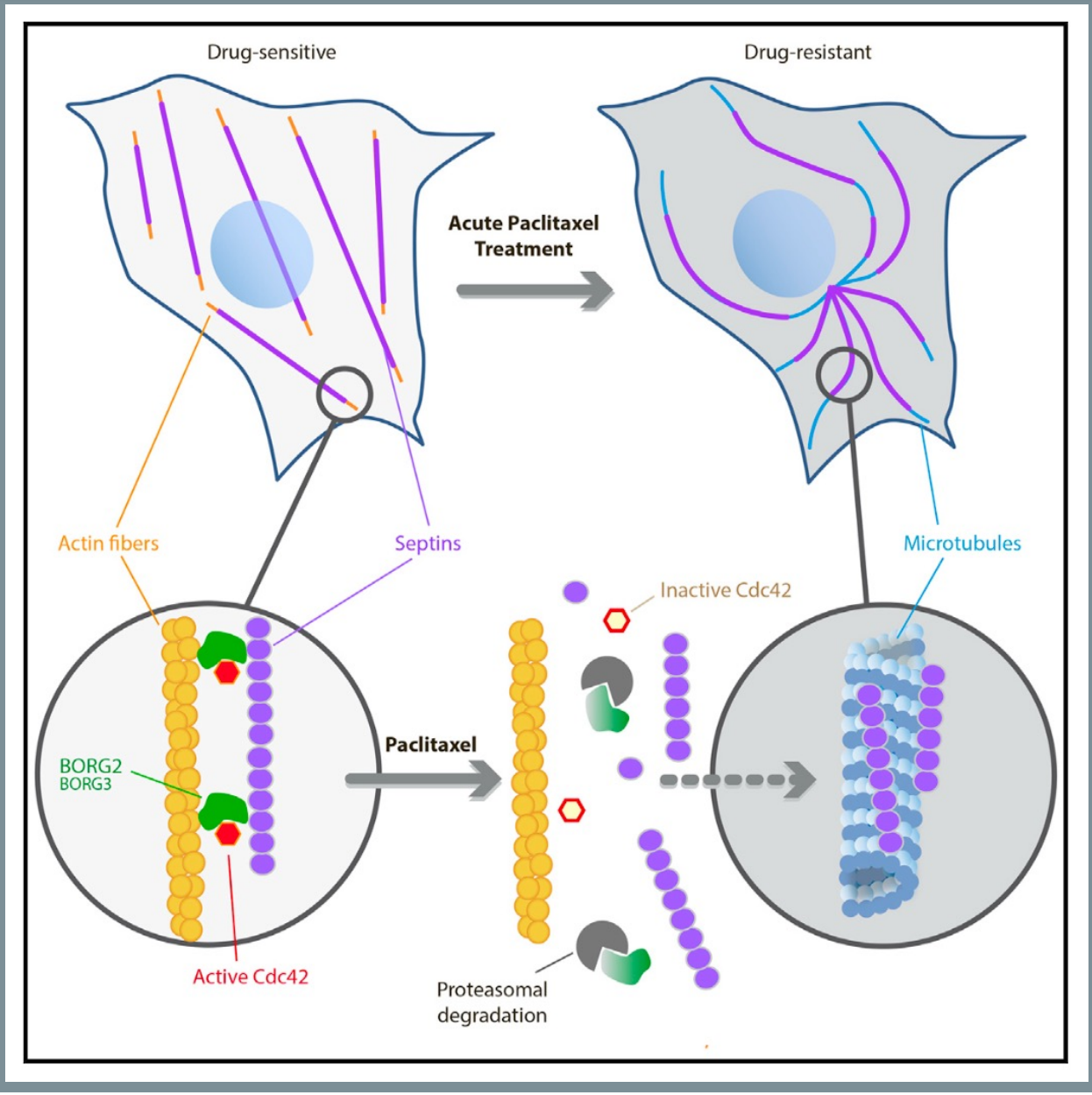
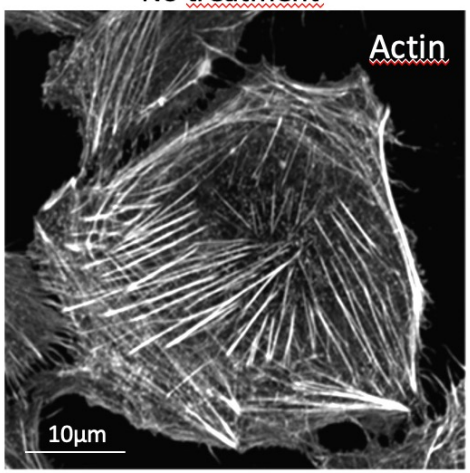


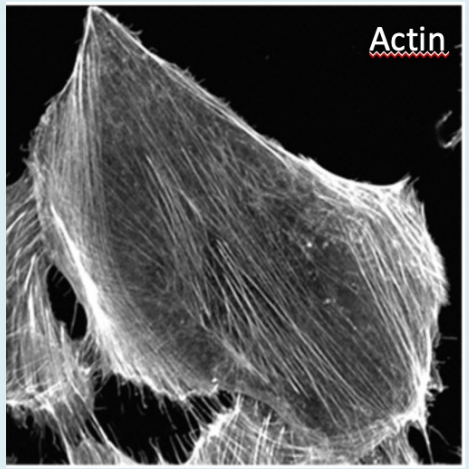
Why to get interested in mechanotransduction ?

HHL16 cells

Human immortalized hepatocytes

No treatment





5nM Paclitaxel, 24h

Reorganization of the cytoskeleton

Change in septin localization

⬇

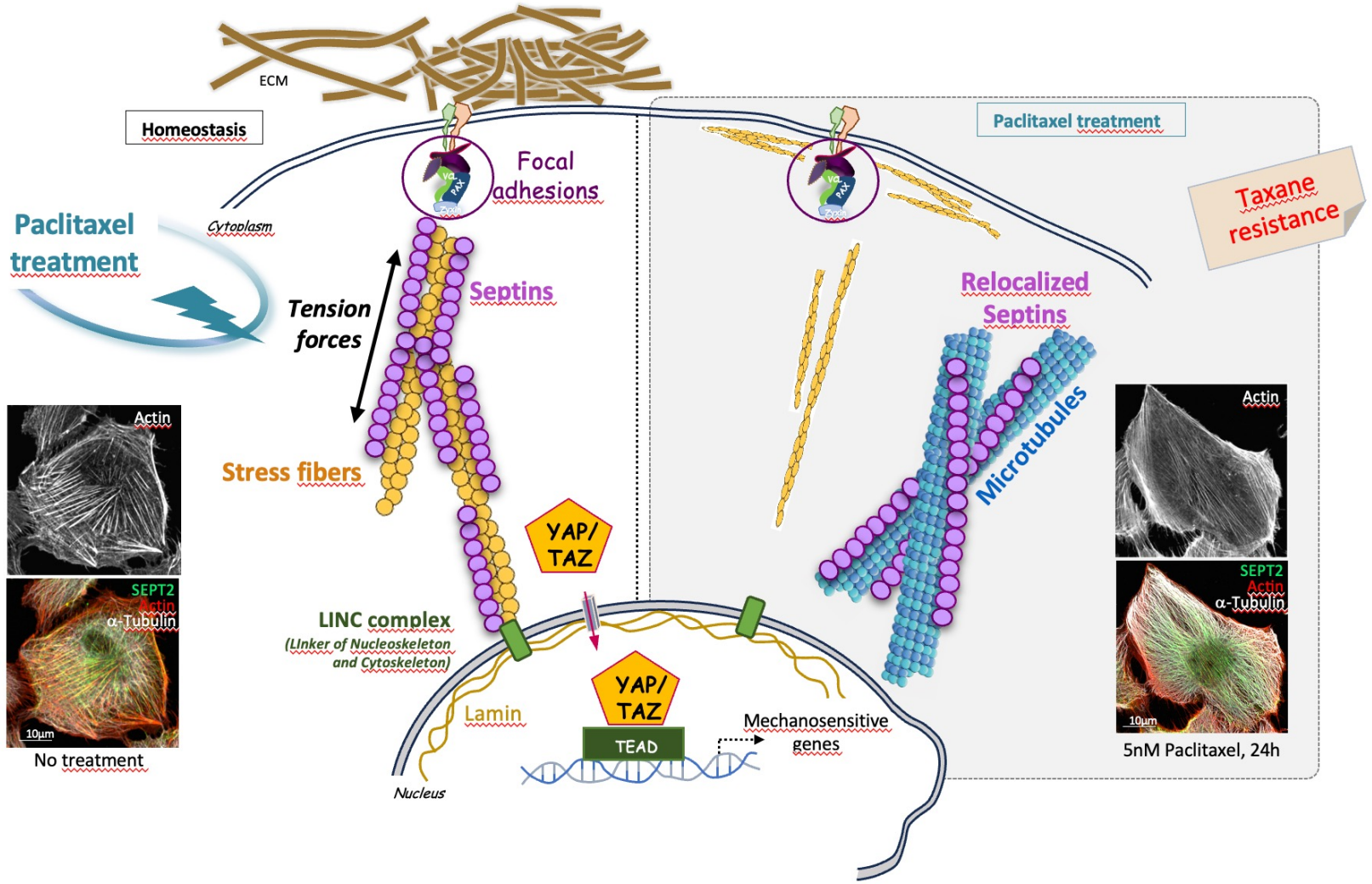
i) Thining and loss of thick stress fibers

ii) Repositioning of stress fibers at the cell periphery

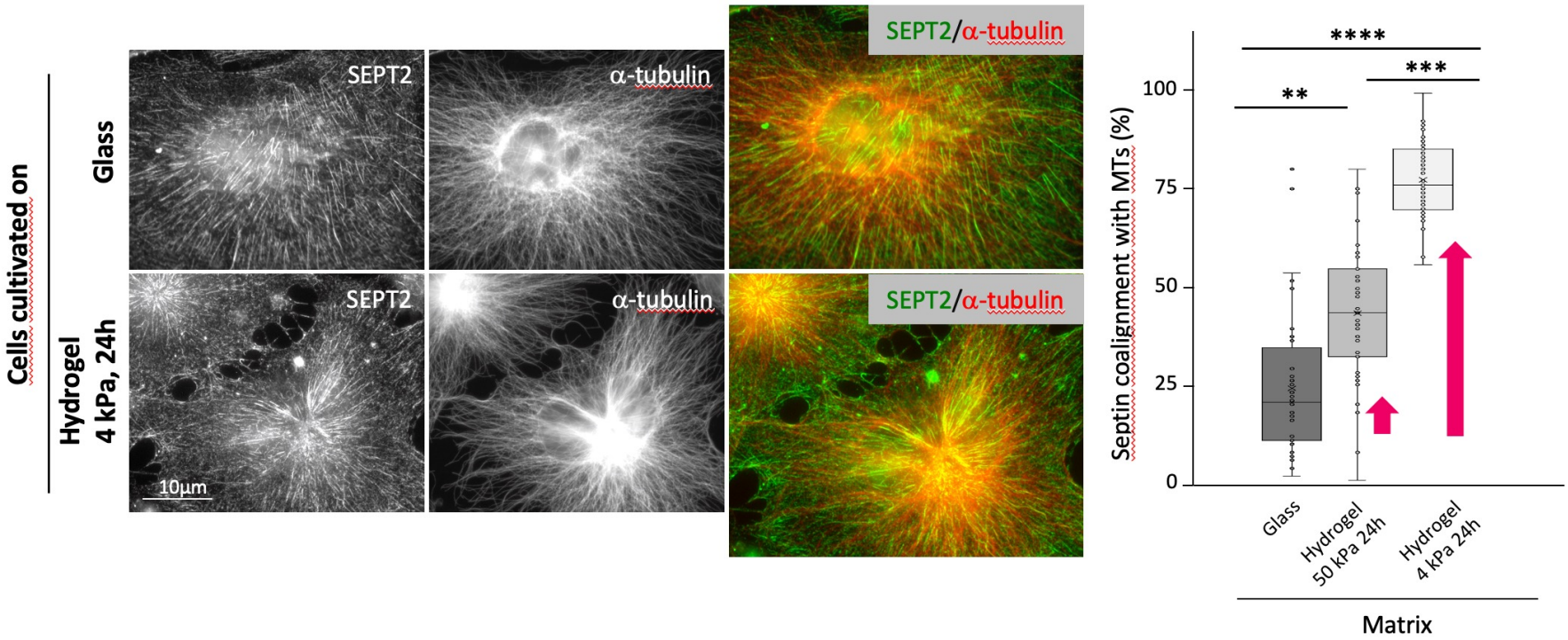
⬇ **??**

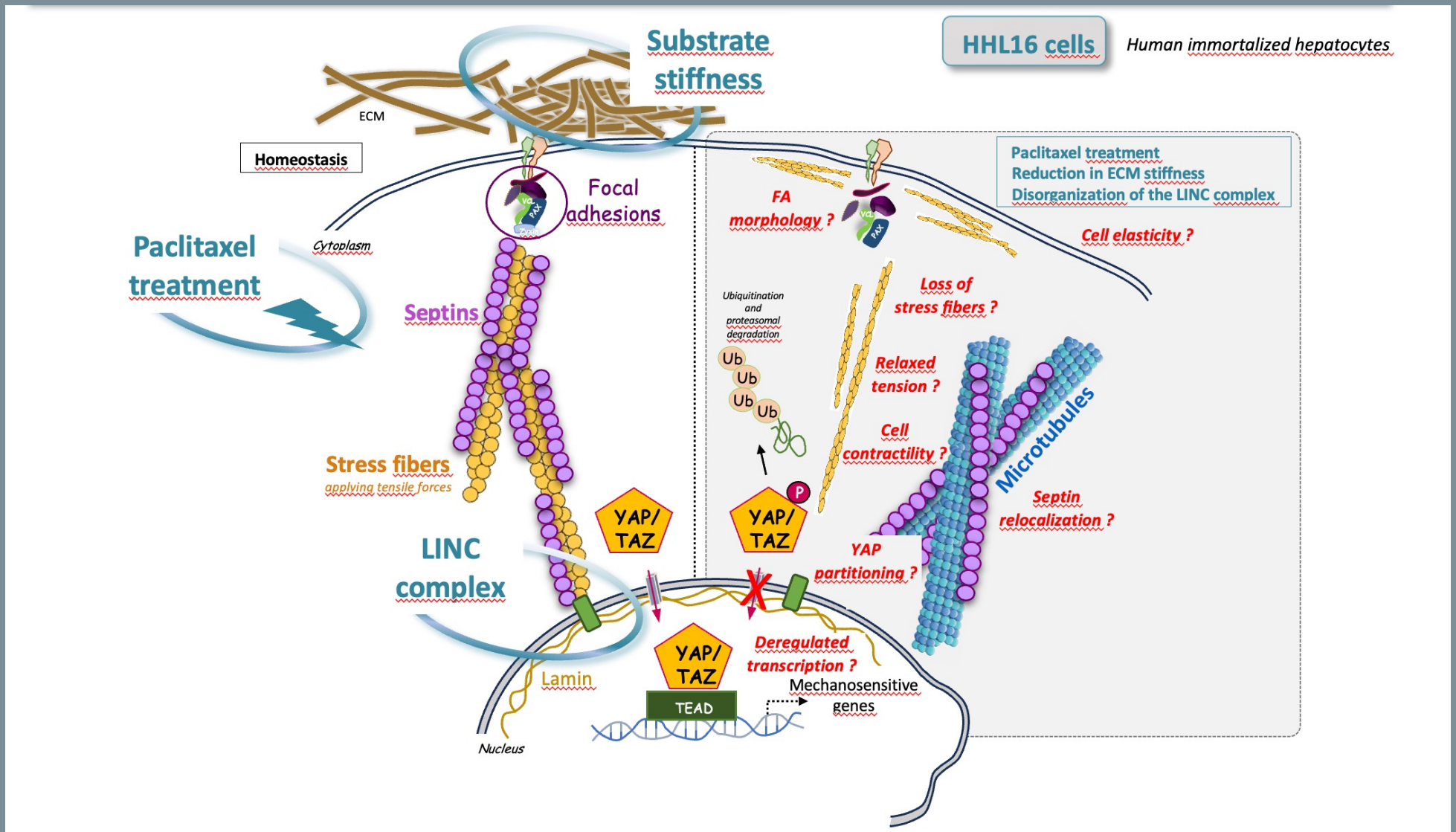
Altered mechanotransduction

Paclitaxel induces the remodeling of the cytoskeleton

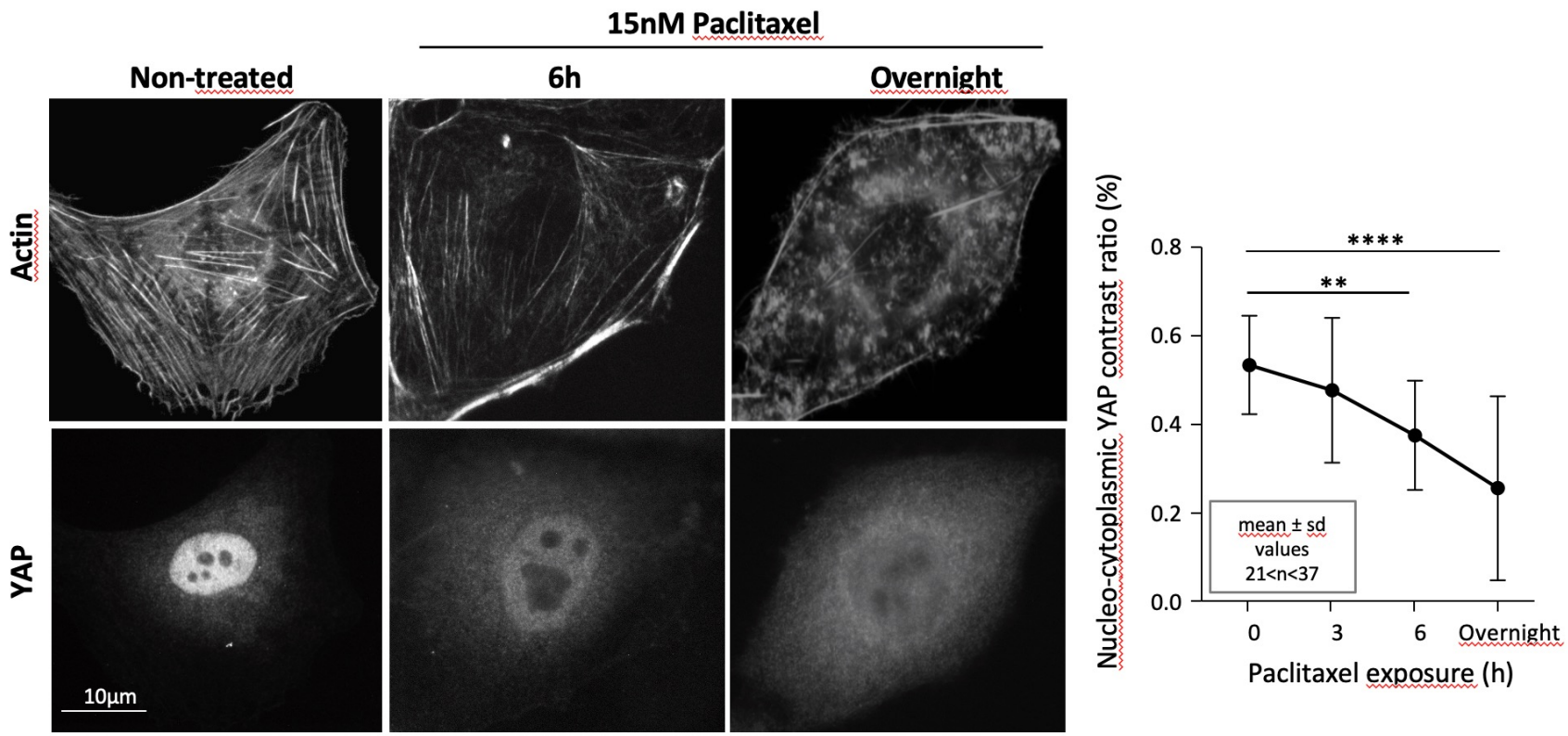


Lowering matrix stiffness mimics the Paclitaxel effect on septin localization

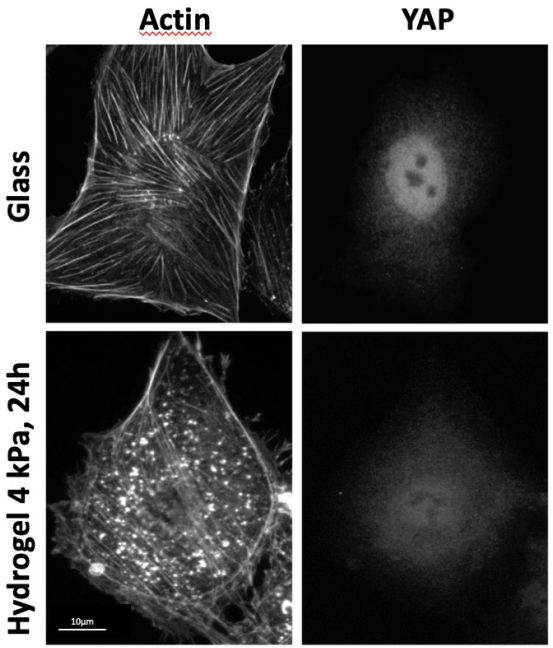


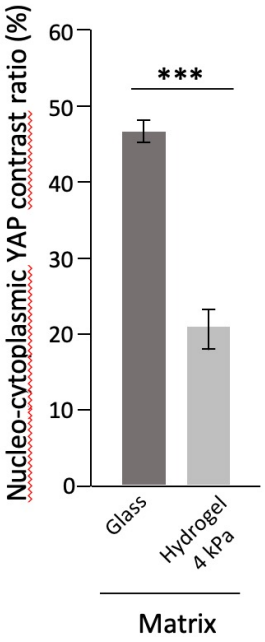

HHL16 cells
Human immortalized hepatocytes
Substrate stiffness
ECM
Homeostasis
Focal adhesions
Paclitaxel treatment
Cytoplasm
Septins
Stress fibers
applying tensile forces
LINC complex
Lamin
Nucleus
YAP/ TAZ
TEAD
Mechanosensitive genes
Paclitaxel treatment
Reduction in ECM stiffness
Disorganization of the LINC complex
FA morphology ?
Cell elasticity ?
Ubiquitination and proteasomal degradation
Ub
Loss of stress fibers ?
Relaxed tension ?
Cell contractility ?
Microtubules
Septin relocalization ?
YAP partitioning ?
Deregulated transcription ?

Paclitaxel treatment results in decreased YAP nuclear localization…



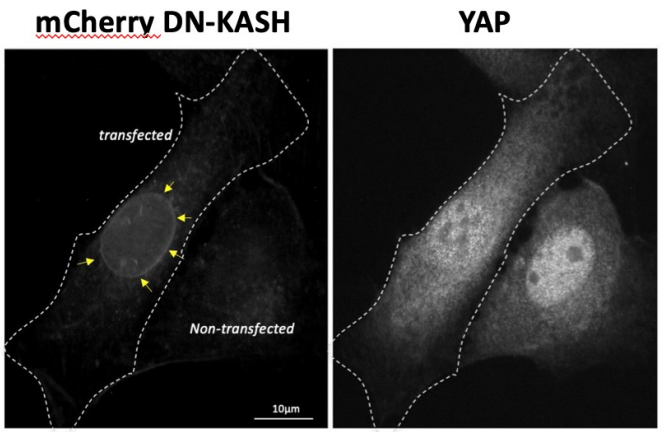
… like when reducing substrate stiffness or perturbing the LINC complex

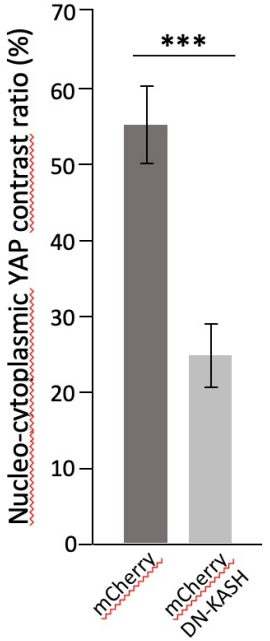




Modifying substrate stiffness

Perturbing the LINC complex organization





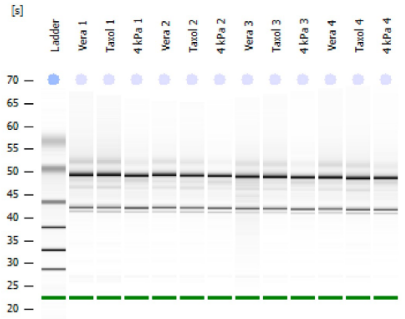
Identification of differentially expressed genes following Paclitaxel treatment

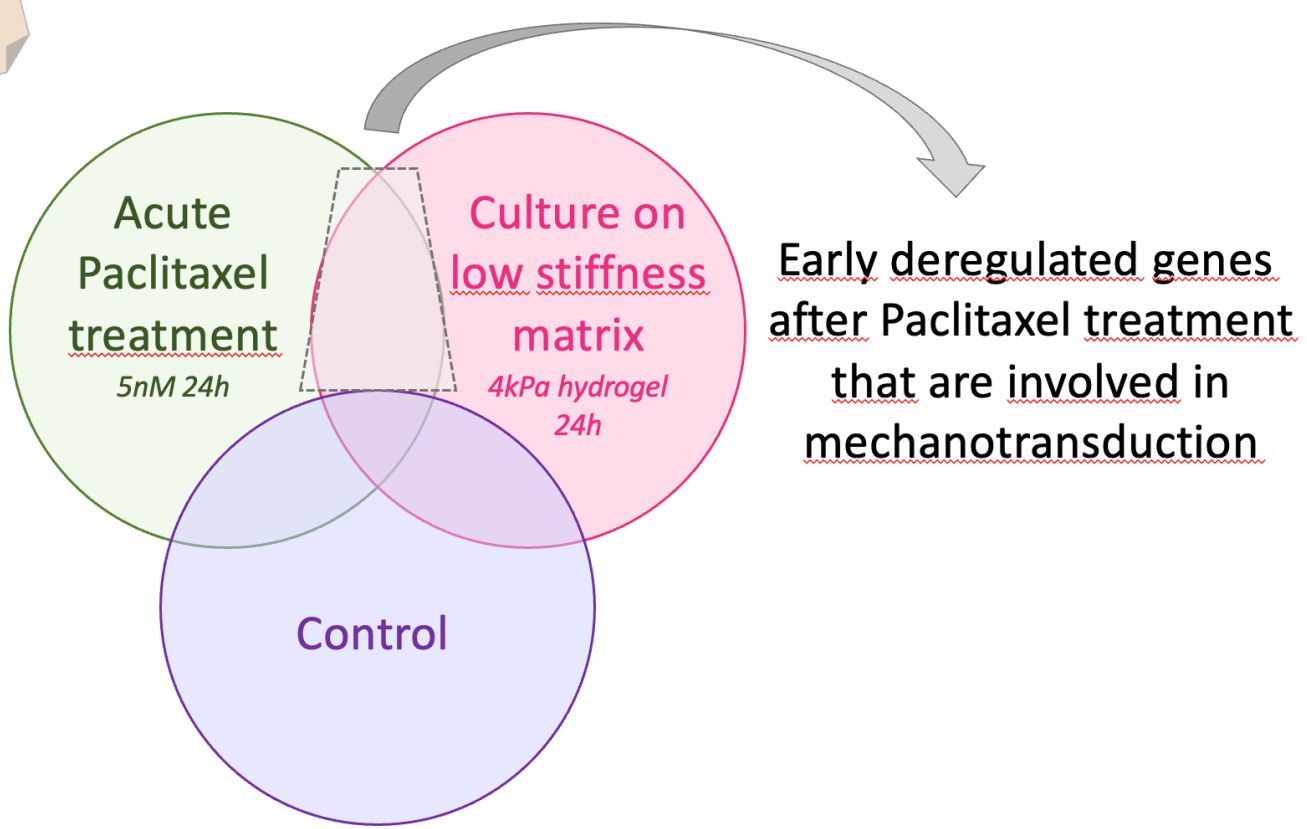
RNA SEQUENCING

I2BC

ACTAGen

Ongoing

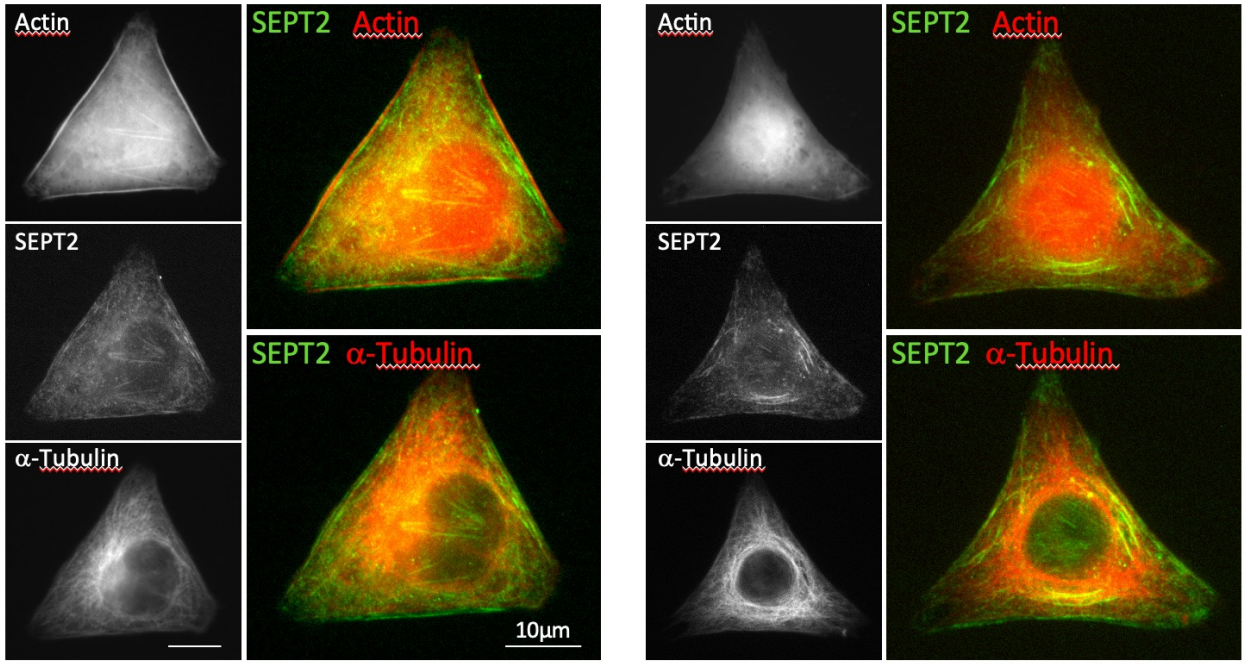


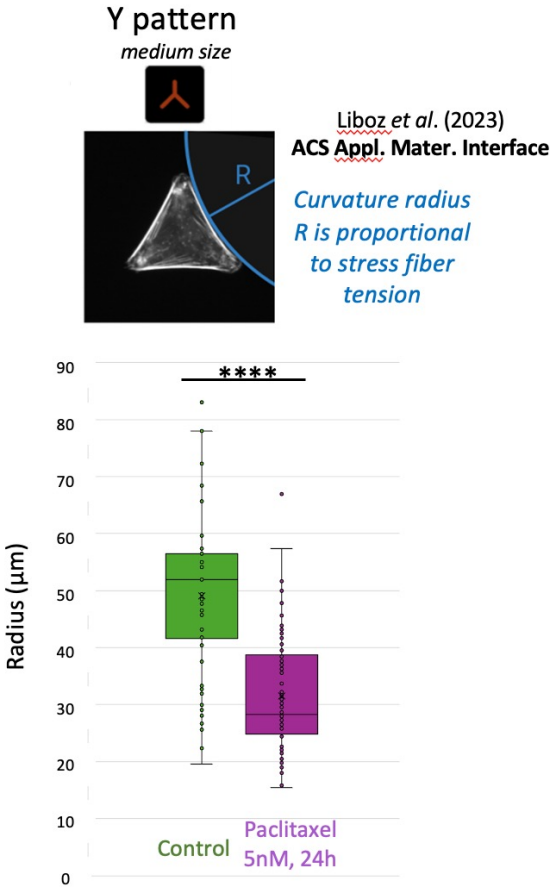


Early deregulated genes after Paclitaxel treatment that are involved in mechanotransduction

Paclitaxel treatment results in reduced intracellular tension

CONSTRAINED CELL GROWTH ON MICROPATTERNS

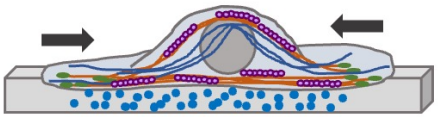




Traction Force Microscopy (TFM) to assess actin contractility

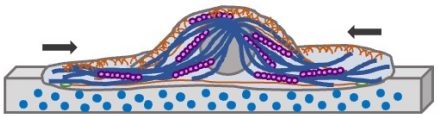
TRACTION FORCE MICROSCOPY

No treatment

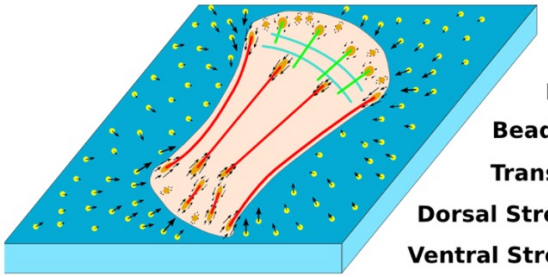


Hydrogel with fluorescent microbeads

5nM Paclitaxel, 24h



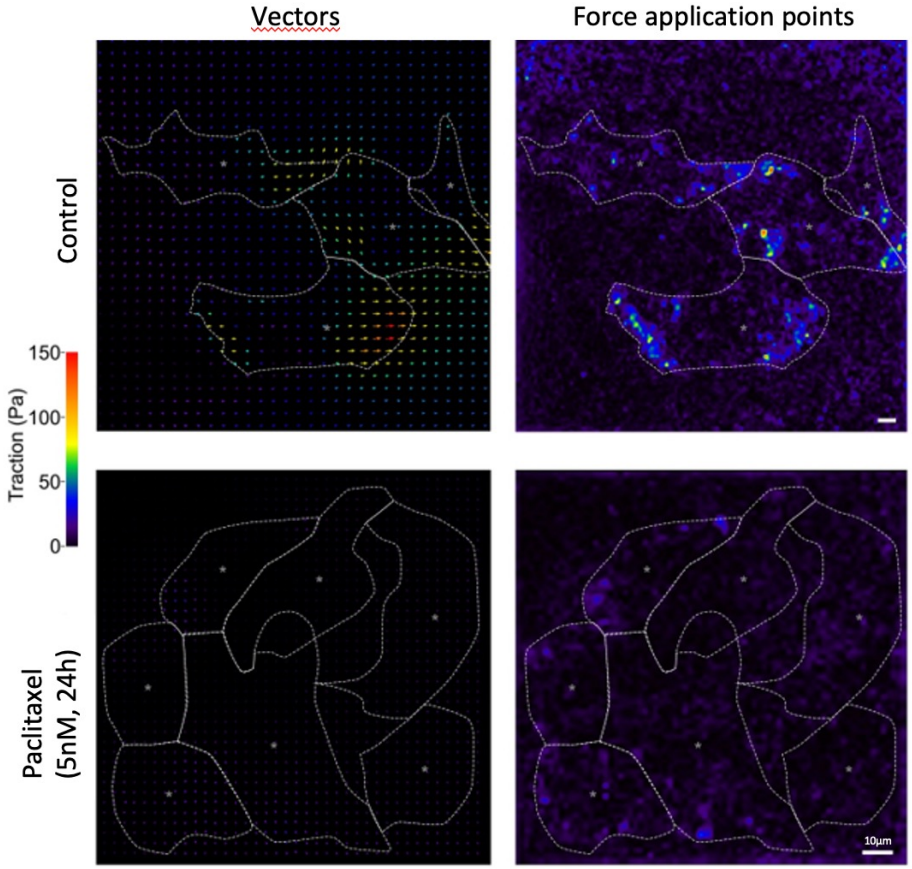
Septin
Microtubule
Actin
Focal adhesion

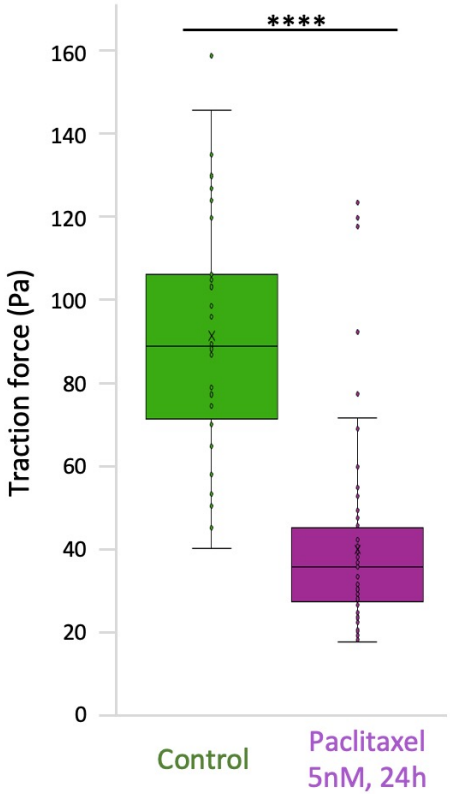


Focal Adhesion
Bead Displacement
Transverse Arc (TA)
Dorsal Stress Fiber (DSF)
Ventral Stress Fiber (VSF)

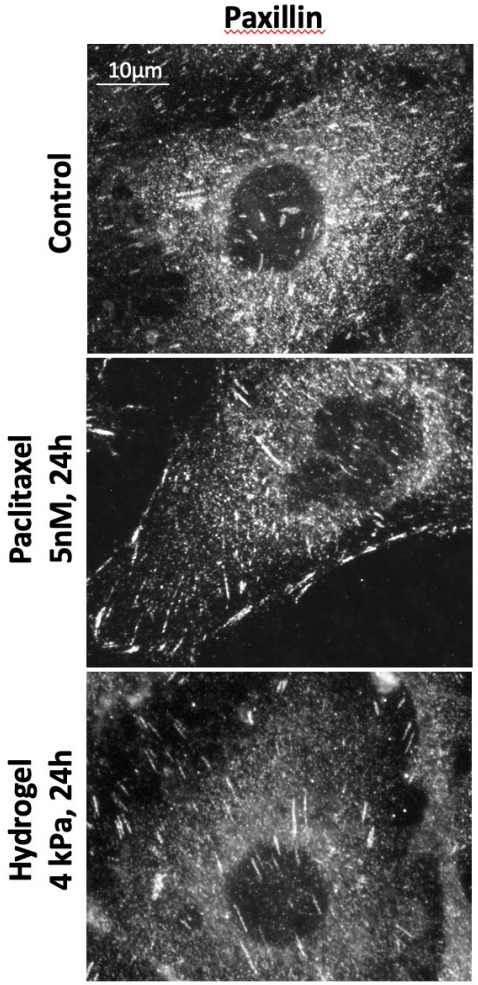
Soiné et al., PLOS Computational Biology (2015)

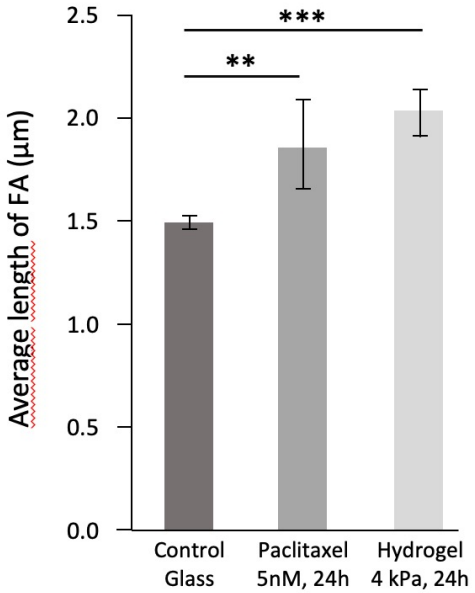
Paclitaxel treatment results in a reduced actin contractility

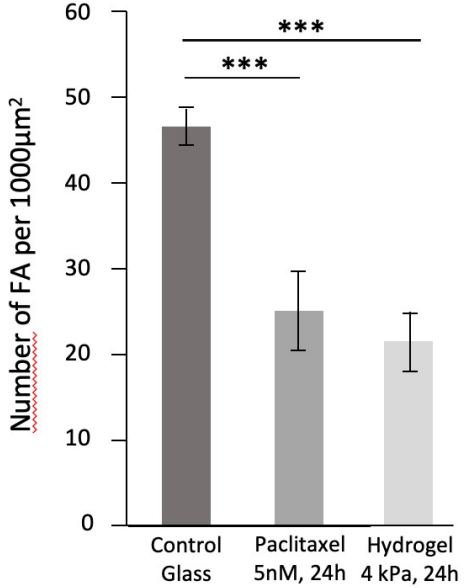




Paclitaxel and soft matrix make focal adhesions longer and less abundant…





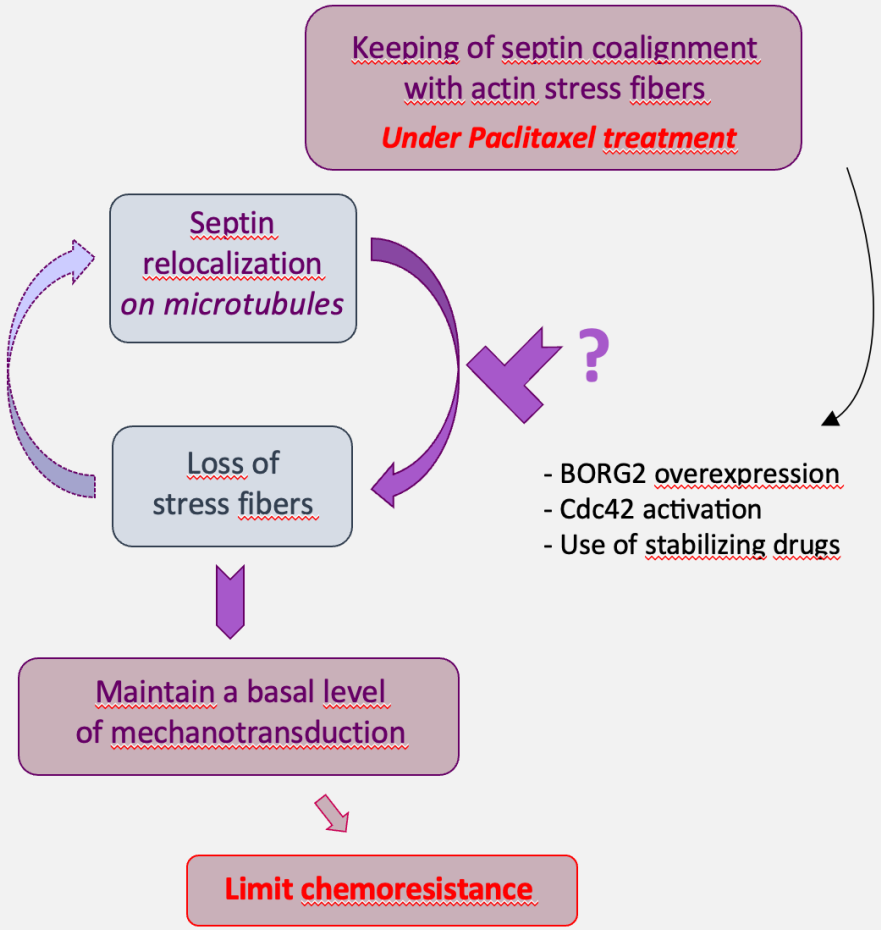


Conclusions and Future prospects

- Septins associate with actin stress fibers in a mechanosensitive manner

- Paclitaxel has the same tension-releasing effect than lowering matrix stiffness or disorganizing the LINC complex:
  - ⇨ *Septin relocalization to microtubules*
  - ⇨ *Disappearance of thick stress fibers*
  - ⇨ *Reduced actin contractility*
  - ⇨ *Reduced nuclear translocation of YAP*

- Altered mechanotransduction early induced by Paclitaxel treatment is likely to contribute to the acquisition of the resistant phenotype



FIN