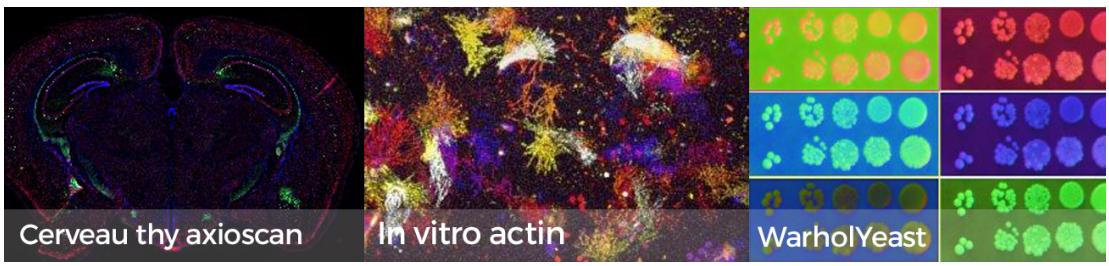
Team "Physiopathologies of the Cytoskeleton"

Director: Annie ANDRIEUX

Understand the intrinsic properties of microtubules, one of the constituents of the cytoskeleton, and their effectors; analyze their functions in the organization and operating of the central nervous system.
The team "Physiopathologies of the Cytoskeleton" investigates cytoskeletal microtubules, a major component of neuronal cells.



Research themes and techniques used

The team "Physiopathologies of the Cytoskeleton" investigates cytoskeletal microtubules, a major component of neuronal cells. Hundreds of effectors influence the microtubules' structure or function in various neuronal processes, e.g. proliferation of neuronal progenitors, neuronal differentiation, neuronal network maturation, synaptic plasticity, etc. Our team focuses more specifically on Microtubule-Associated Proteins of the MAP6 family on the one hand and enzymes that modify the C-terminal amino acid of tubulins (tyrosination/detyrosination cycle) on the other hand.
These microtubular effectors are studied at various levels in the team "Physiopathologies of the Cytoskeleton", from structure to whole organisms, in order to understand the various levels of microtubules' regulation:

Tubulin: characterize the importance of specific C-terminal amino acids in the assembly of tubulin dimers, the formation of microtubules and their function in the yeast.

Tubulin-modifying enzymes: describe the physiological impact of post-translational modifications of tubulin, such as C-terminal tyrosination / detyrosination of alpha-tubulin, on neuronal differentiation and neuronal plasticity in the adult.

Regulation of microtubules' dynamics *in vitro*: analyze how MAP6 proteins and their partners influence the dynamic properties of microtubules and actin, in cell-free systems.

Neuronal differentiation and microtubule-associated protein 6 (MAP6): understand the contribution of these proteins and their partners in neuronal development and synaptic connectivity.

Development of neuronal networks and defective neuronal connectivity: study the anatomical and physiological consequences of the absence of specific MAPs in model mice.

Techniques used:

Molecular biology: plasmid constructions, cloning and sub-cloning, PCR, expression of recombinant proteins, lentivirus, CRISPR/Cas9

Biochemistry: purification of proteins and antibodies, interaction of protein partners, yeast two-hybrid screening, immunoprecipitation, TIRF imaging, electronic microscopy

Cellular biology: cell lines and primary cultures of neurons, classical or confocal fluorescence imaging, videomicroscopy, FRAP and STORM high resolution imaging

Animal models: production of transgenic or conditional knockout mice, phenotypic assessment (anatomy, tractography using DTI and behavioral studies)

Publications

Major publications since 2012

Evidence for new C-terminally truncated variants of ?- and ?-tubulins. **Aillaud C**, **Bosc C**, **Saoudi Y**, **Denarier E**, **Peris L**, Sago L, Taulet N, Cieren A, Tort O, Magiera M, Janke C, Redeker V, **Andrieux A**, **Moutin MJ**. Mol Biol Cell 2016, Feb 15;27(4):640-53.

Microtubule-associated protein 6 mediates neuronal connectivity through Semaphorin 3E-dependent signalling for axonal growth. **Deloulme JC**, **Gory-Fauré S**, Mauconduit F, Chauvet S, **Jonckheere J**, **Boulan B**, Mire E, Xue J, **Jany M**, **Maucler C**, **Deparis AA**, Montigon O, Daoust A, Barbier EL, **Bosc C**, Deglon N, **Brocard J**, **Denarier E**, **Le Brun I**, Pernet-Gallay K, Vilgrain I, Robinson PJ, Lahrech H, Mann F, **Andrieux A**. Nat Commun. 2015 Jun 3;6:7246.

The cytosolic carboxypeptidases CCP2 and CCP3 catalyze posttranslational removal of acidic amino acids. Tort O, Tanco S, Rocha C, Bièche I, Seixas C, **Bosc C**, **Andrieux A**, **Moutin MJ**, Avilés FX, Lorenzo J, Janke C. Mol Biol Cell. 2014 Oct 1;25(19):3017-27.

Neuronal transport defects of the MAP6 KO mouse - a model of schizophrenia - and alleviation by Epothilone D treatment, as observed using MEMRI. Daoust A, Bohic S, **Saoudi Y**, Debacker C, **Gory-Fauré S**, **Andrieux A**, Barbier EL, **Deloulme JC**. Neuroimage. 2014 Aug 1;96:133-42.

Mutations in TUBG1, DYNC1H1, KIF5C and KIF2A cause malformations of cortical development and microcephaly. Poirier K, Lebrun N, Broix L, Tian G, Saillour Y, **Boscheron C**, Parrini E, Valence S, Pierre BS, Oger M, Lacombe D, Geneviève D, Fontana E, Darra F, Cances C, Barth M, Bonneau D, Bernadina BD, N'guyen S, Gitiaux C, Parent P, des Portes V, Pedespan JM, Legrez V, Castelnau-Ptakine L, Nitschke P, Hieu T, Masson C, Zelenika D, **Andrieux A**, Francis F, Guerrini R, Cowan NJ, Bahi-Buisson N, Chelly J. Nat Genet. 2013 Jun;45(6):639-47.

MAP6-F is a temperature sensor that directly binds to and protects microtubules from cold-induced depolymerization. **Delphin C**, Bouvier D, **Seggio M, Couriol E**, **Saoudi Y, Denarier E, Bosc C, Valiron O, Bisbal M,** Arnal I, **Andrieux A** . J Biol Chem. 2012 Oct 12;287(42):35127-38.

>> All the publications of Dr Annie Andrieux

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Keywords

Cytoskeleton, microtubules, tubulin, tubulin-modifying enzymes, MAP6, neurodevelopment, neuropsychiatric diseases, cerebral plasticity.

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