Nups& & Cycle
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Involvement of the nuclear pore complexes in coordinating entry, progression and exit from mitosis

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Context of the project

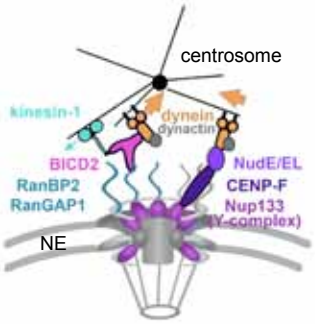
Nuclear Pore Complexes (NPCs) are elaborate structures embedded in the nuclear envelope (NE) and composed of multiple copies of about 30 different proteins termed nucleoporins (Nups). Our ANR project aimed at characterizing, beyond their well-established function in transport between the cytoplasm and the nucleus, **non-conventional functions of NPCs and nucleoporins during mitosis**. Two recent studies arising from this project are detailed below (see also talk from B. Palancade, V.Doye's lab for a 3rd study - Chadrin et al., 2010).

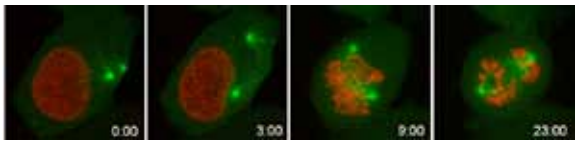
Nucleoporins tether centrosomes to the nuclear envelope in prophase

Our previous studies had revealed the key function of the vertebrate Nup107-160 complex (also termed the Y-complex) in **NPC re-assembly at mitotic exit** and its recruitment at **kinetochores**, where it is required for proper chromosome segregation.

We have recently demonstrated that in prophase, the Nup133 subunit of the Y-complex anchors at the NE a subset of proteins (CENP-F, NudE/EL, dynein), previously know to function at kinetochores in mitosis.

We further demonstrated that this network, along with the RanBP2/BicD2 pathway, tethers centrosomes to the NE in prophase and thus contributes to early stages of mitosis (Bohly et al., 2011).





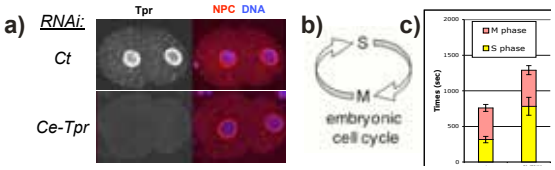
Time-lapse imaging of a cell entering mitosis in which the Nup133-dependent network is impaired. This cell expresses EB3-GFP (green, centrosomes and spindle) and H2B-mCherry (red, chromatin). Time is min:sec.

C. elegans Tpr, a component of nuclear pores intranuclear extensions, contributes to cell cycle progression in early embryos

In *Drosophila* and human cells, the **intranuclear NPC filaments made of Tpr** anchors the spindle assembly checkpoint (SAC) proteins at the NE in interphase. During mitosis, pores and NE are disassembled and the SAC delays metaphase until all kinetochores attach to microtubules. In tnese models,Tpr depletion decreases the level of SAC proteins at the NE and kinetochores, leads to a loss of function of the SAC and shorten mitosis.

We have shown **that NE localization of SAC components similarly relies on Tpr in *C. elegans***. Surprisingly however, we observed that Tpr depletion slows down *C. elegans* embryo development. This delay occurs during S phase, in a DNA repair/replication checkpoint independent way, and is suppressed upon SAC component depletion, revealing **a role of the SAC outside mitosis**.

We are currently testing how this function could encounter specific developmental defects that we observed.



a) Tpr is efficiently depleted in RNAi treated embryos. **b)** early embryonic cell divisions consists in consecutive S and M phases without Gap phases. **c)** RNAi depletion of Tpr extends early embryonic cell cycle duration especially in S phase.

Publications issued from this project:

•Wozniak R, Burke B, Doye V. (2010) Nuclear transport and the mitotic apparatus: an evolving relationship Cell Mol Life Sci. 67:2215-30.

* Chadrin A, Hess B, San Roman M, Gatti X, Lombard B, Loew D, Barral Y, Palancade B, Doye V. (2010) Pom33, a novel transmembrane nucleoporin required for proper nuclear pore complex distribution. J Cell Biol. 189:795-811 (see talk from B. Palancade).

* Bolhy S, Bouhlel I, Dultz E, Nayak T, Zuccolo M, Gatti X, Vallee R, Ellenberg J, Doye V. *A Nup133-dependent NPC-anchored network tethers centrosomes to the nuclear envelope in prophase*. J Cell Biol. 2011 Mar 7;192(5):855-71

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