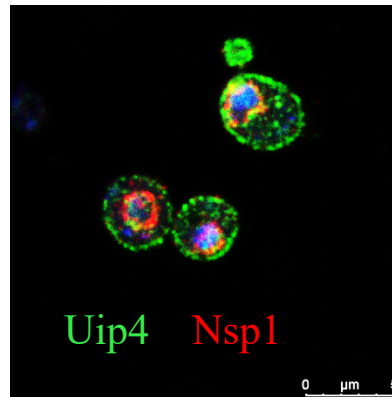


Uip4, a novel endoplasmic reticulum protein, maintains nuclear shape and cellular homeostasis in *S. cerevisiae*

Ms Pallavi Deolal , Dr Krishnaveni Mishra

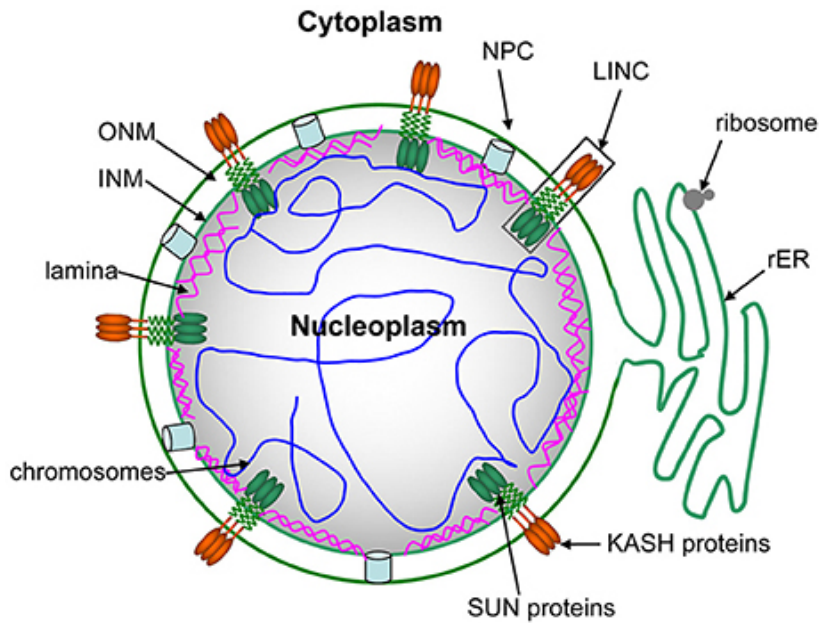


Supervisor: Prof. Krishnaveni Mishra

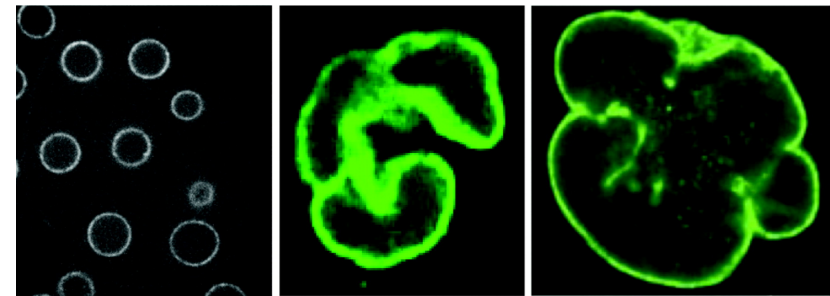
University of Hyderabad, Hyderabad

India

Nuclear Morphology



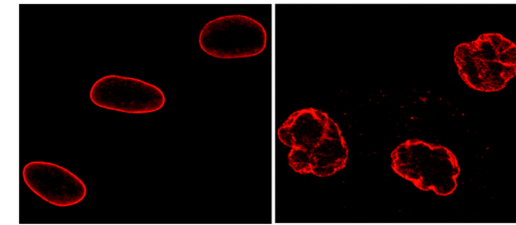
Zeng X. *et al* Front. Cell Dev. Biol., 2018



A *C. elegans*

B Neutrophil

C HGPS



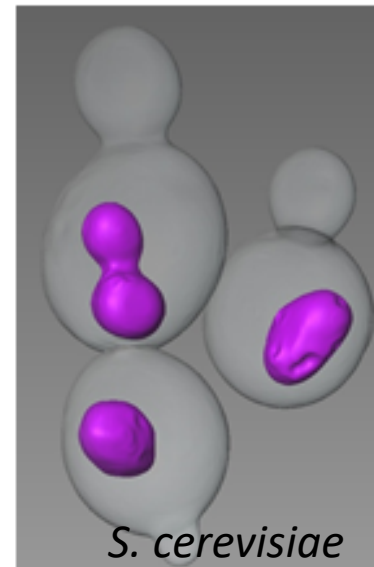
9-year old

96-year old

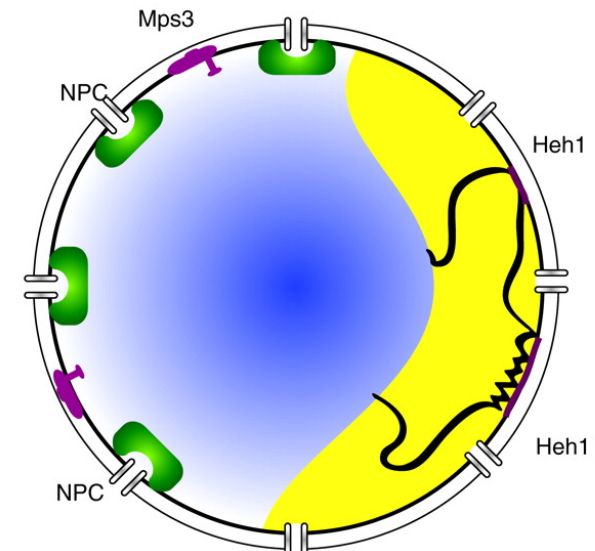
D Aging

Webster M. *et al*
JCS 2009

Nucleus is one of the most prominent cellular organelles and changes in the structural organization of nucleus are known to be associated with aging, several laminopathies and muscular diseases.

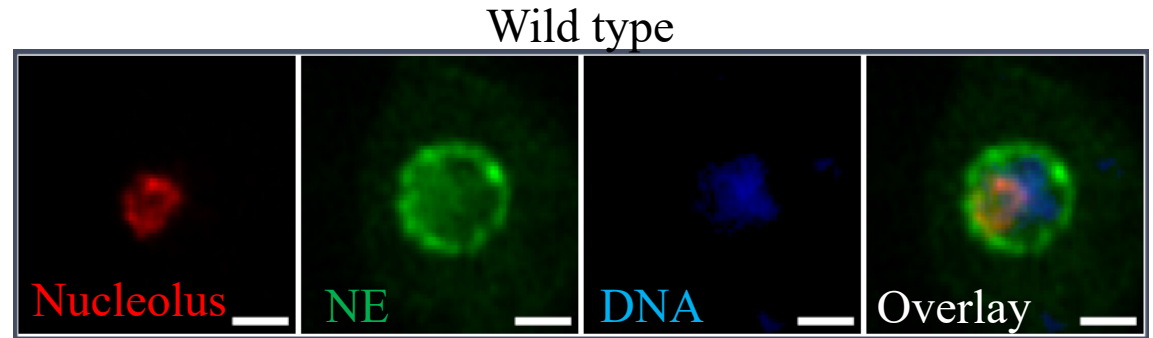
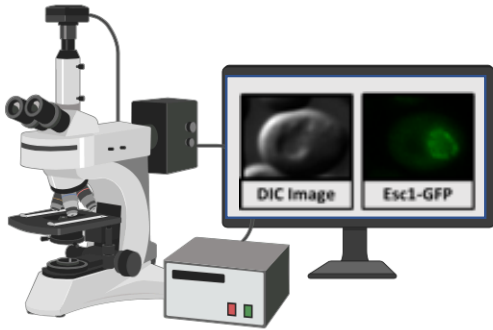


S. cerevisiae

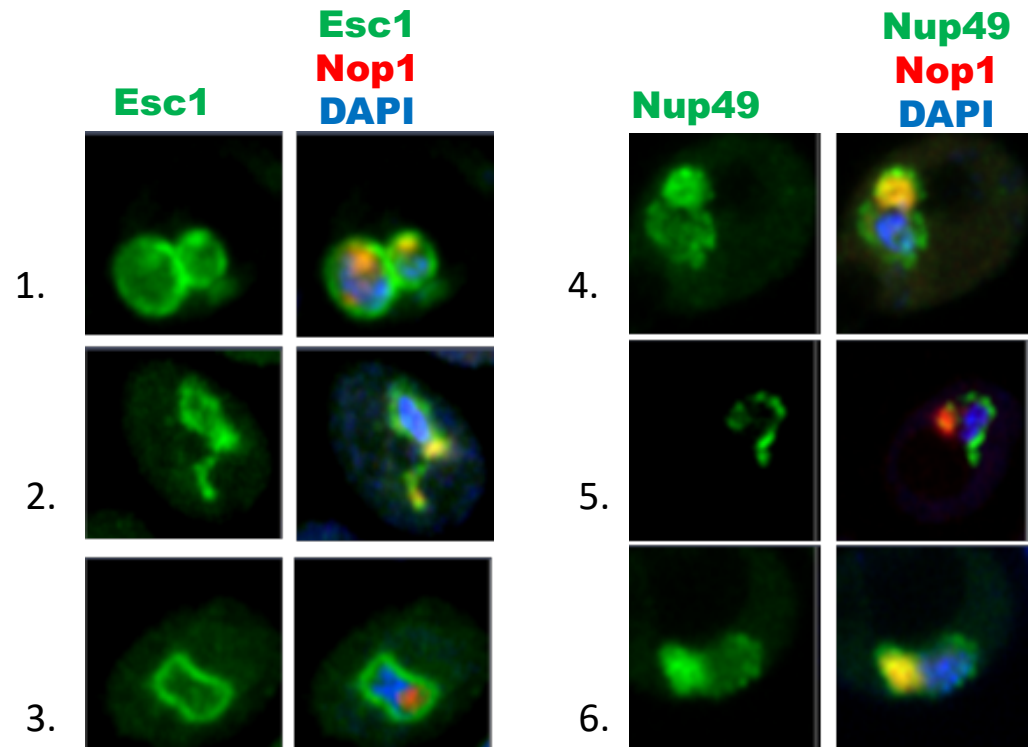
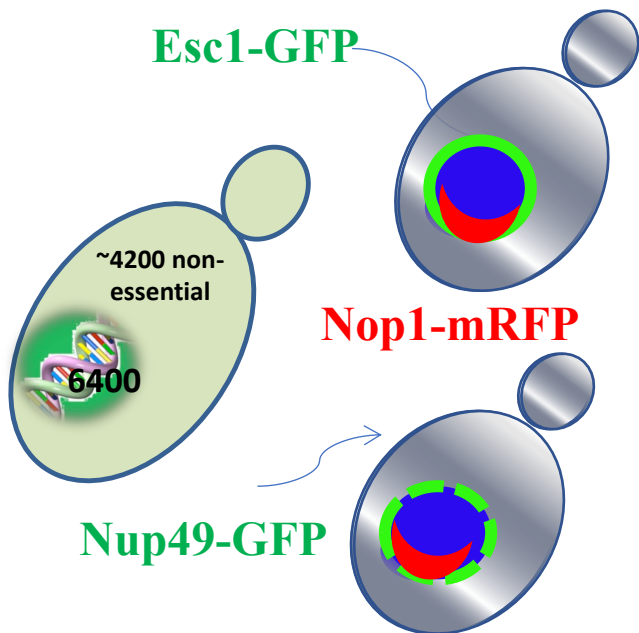


Taddei A. *et al* CSHPB 2010

Identify factors important for maintaining nuclear organization



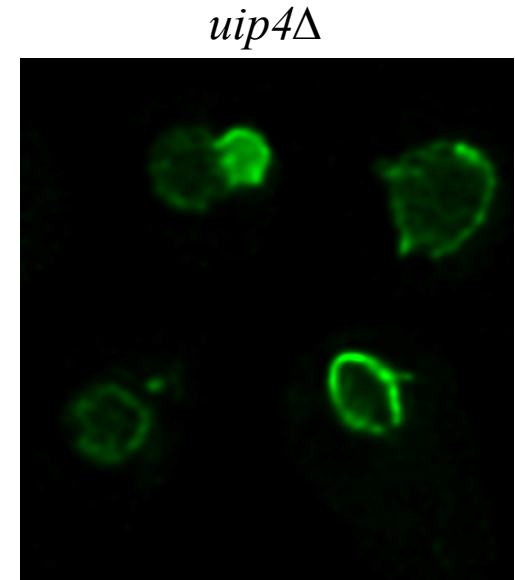
A genome-wide approach



Scale-1 μ m

Nuclear morphology in the absence of Ulp1 interacting proteins

	Gene name(ORF)	Reported localization	Function
1	<i>UIP1/NUP42</i>	NPC	Nucleocytoplasmic transport
2	<i>UIP2/SYN8</i>	Unknown	Unknown
3	<i>UIP3/YAR027W</i>	Nuclear envelope, plasma membrane*	Unknown
4	<i>UIP4/YPL186c</i>	Nuclear envelope, ER*	Unknown
5	<i>UIP5/YKR044w</i>	Nuclear envelope	Unknown



Esc1-GFP

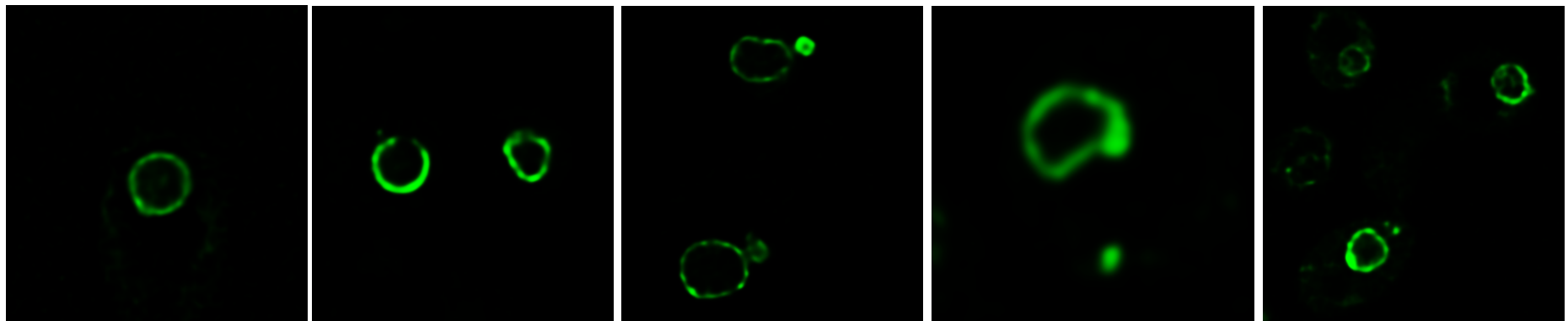
Wild type

uip1Δ

uip2Δ

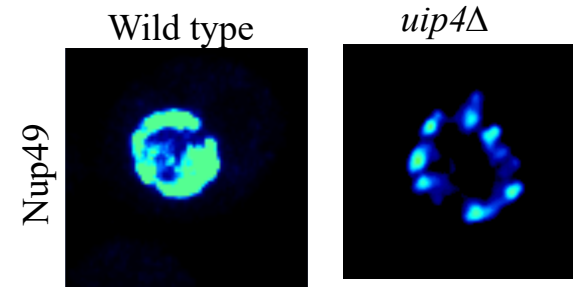
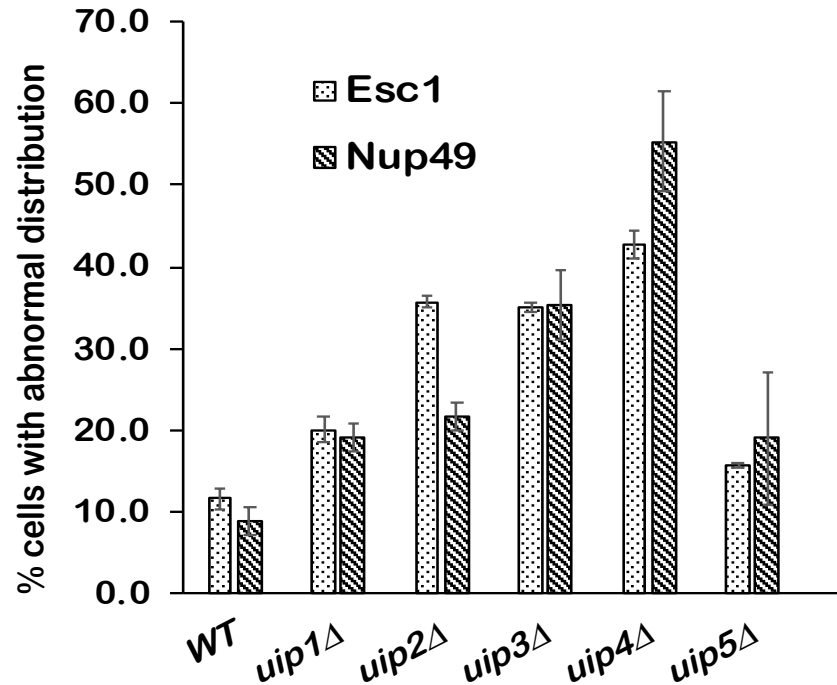
uip3Δ

uip5Δ



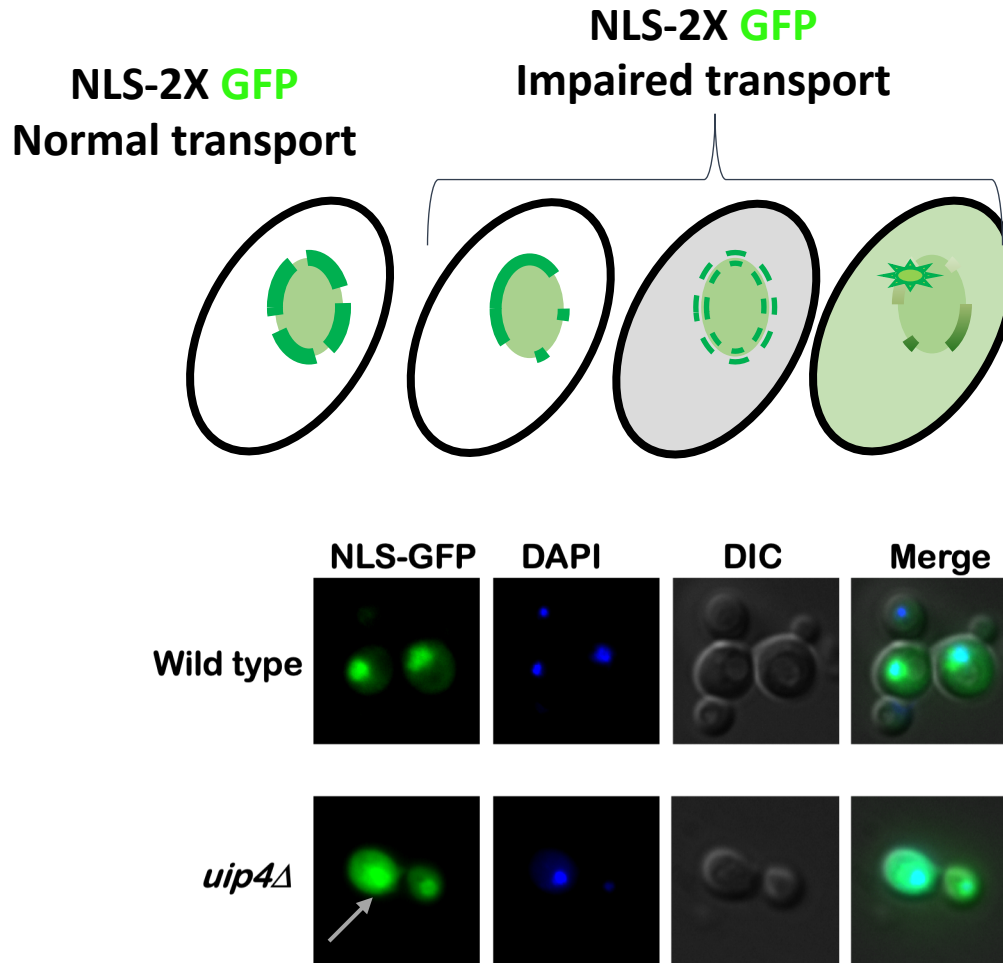
*high throughput

Nuclear morphology in the absence of Ulp1 interacting proteins



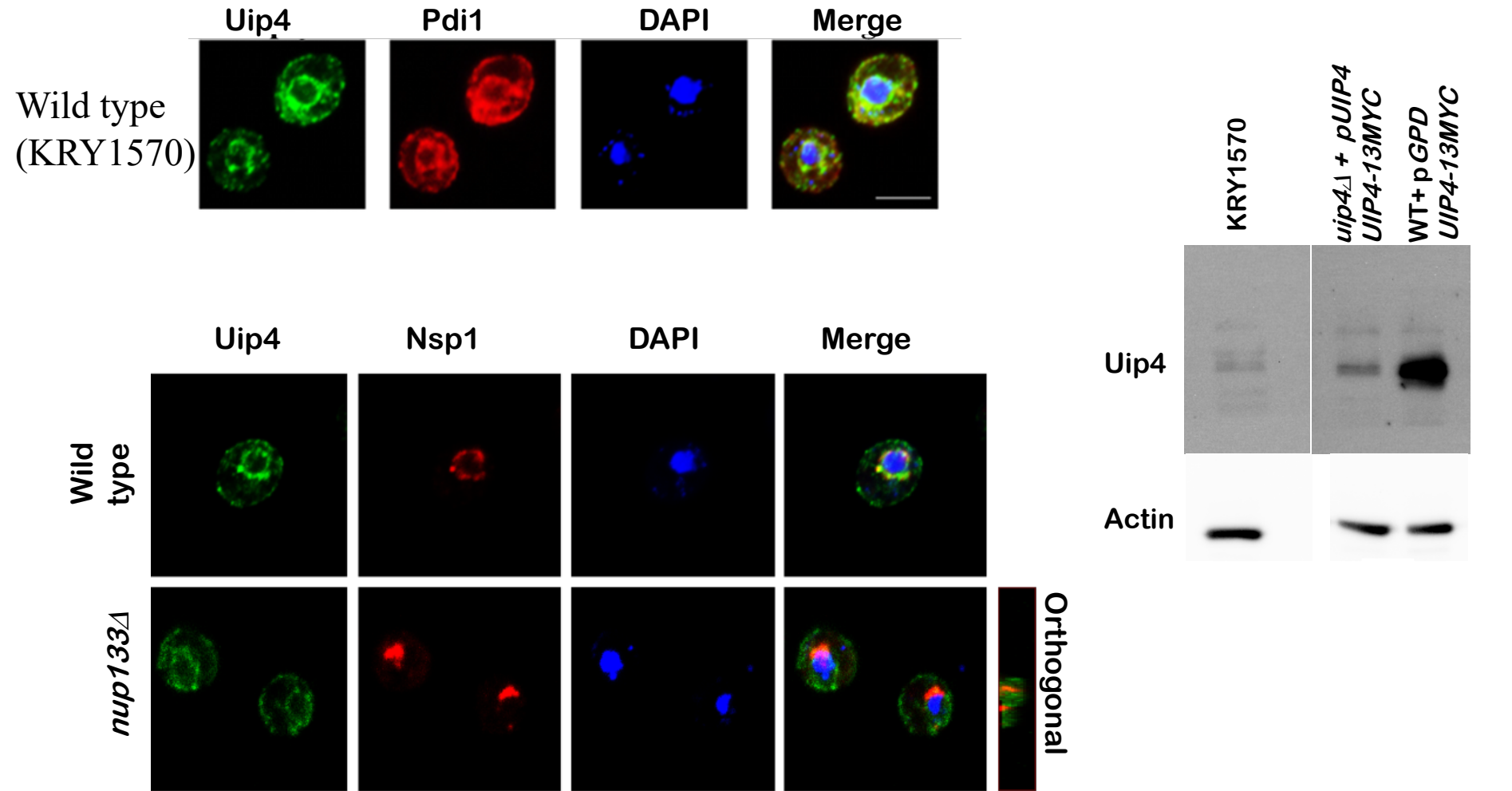
Loss of Ulp1 interacting proteins leads to nuclear shape distortions

Assessing nucleocytoplasmic transport upon compromised NPC distribution



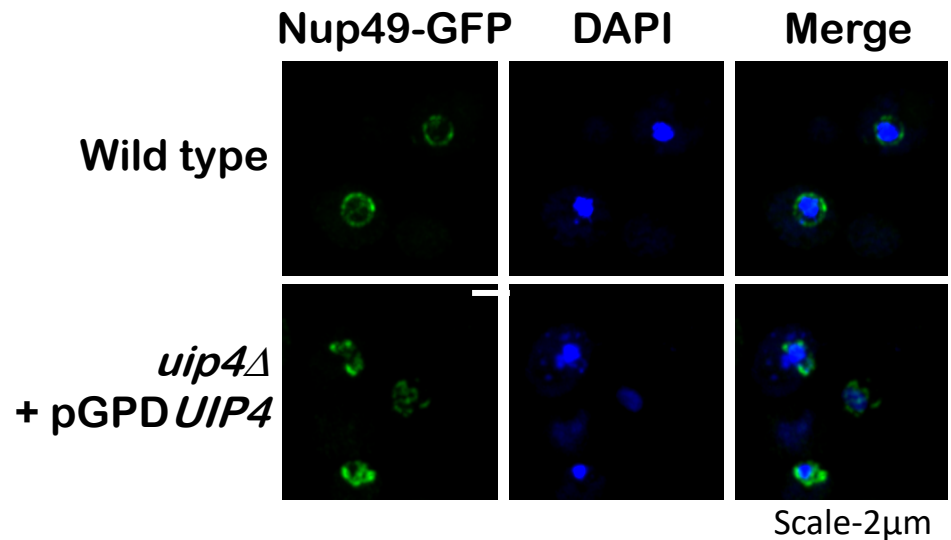
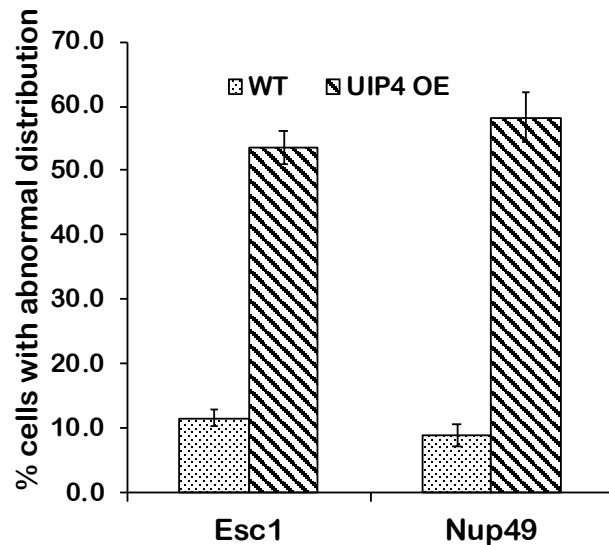
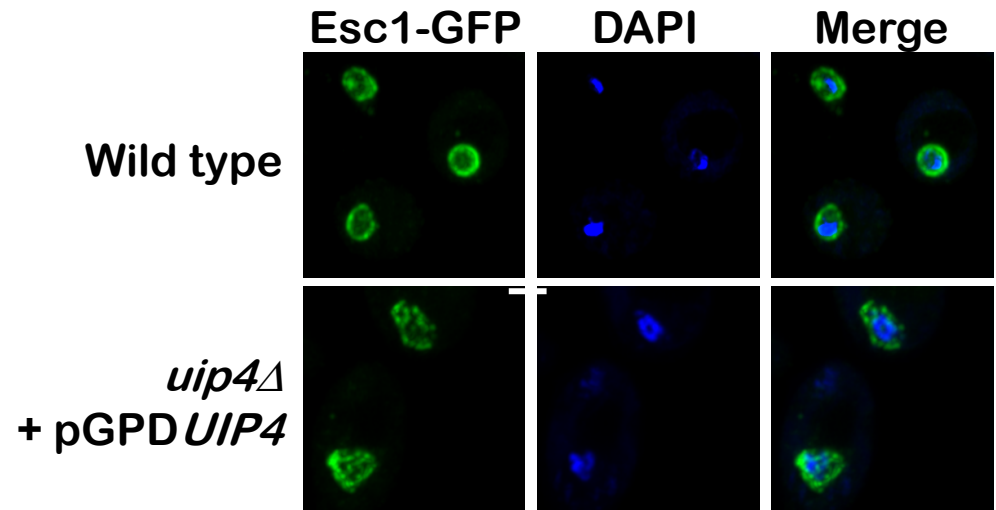
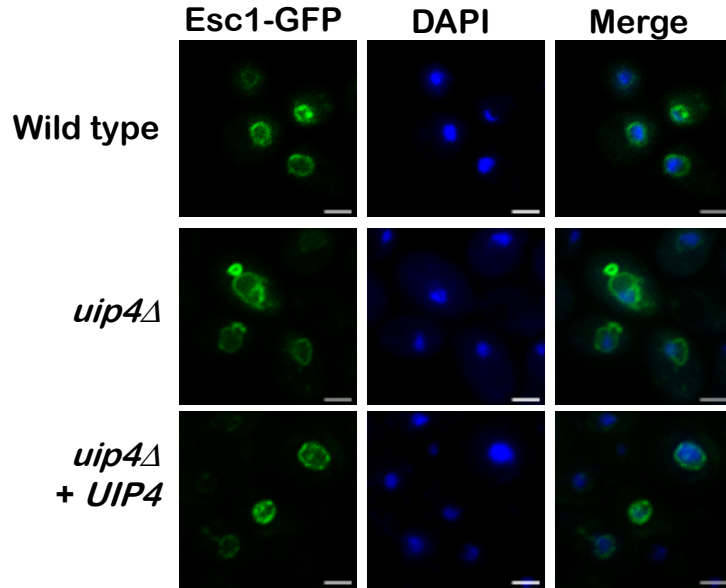
Loss of Uip4p leads to nuclear import defect

Localization and expression of Uip4p



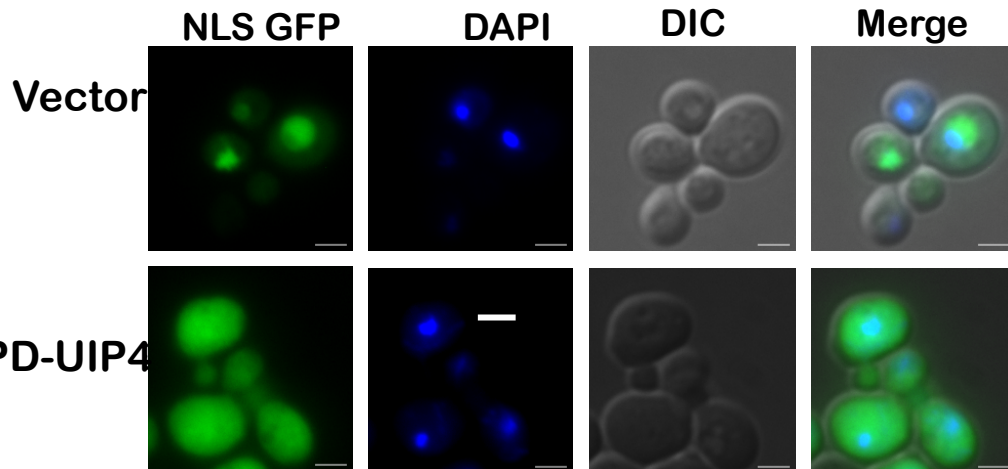
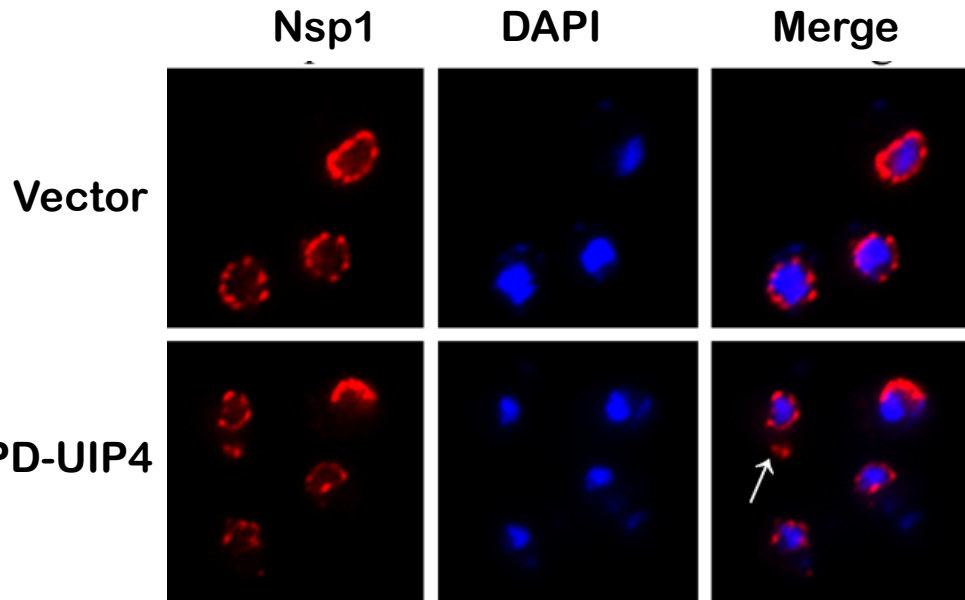
Uip4p localizes to NE/ER but does not associate with NPCs

Perturbing Uip4p level

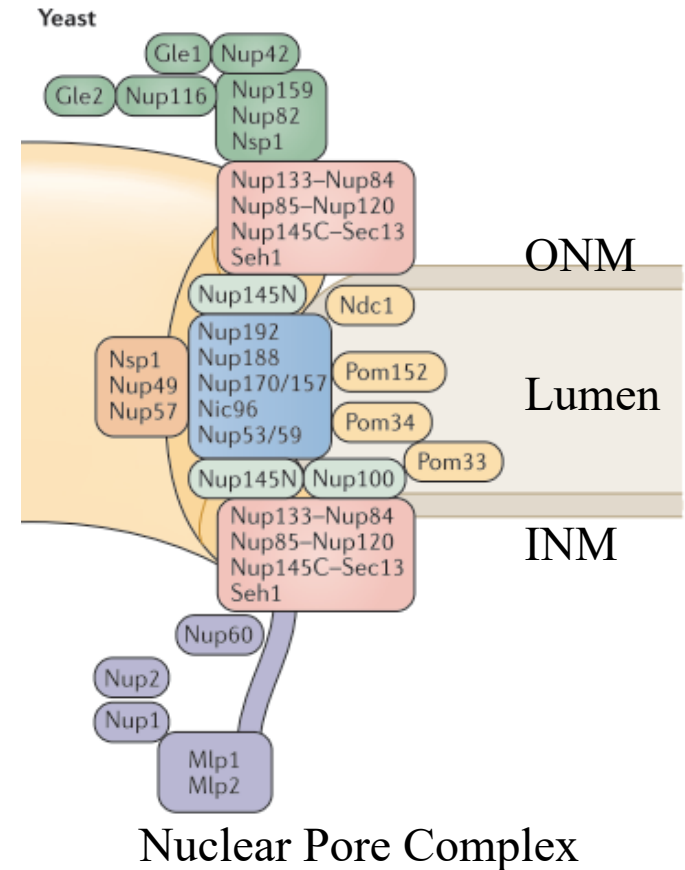


Overexpression of Uip4 exacerbates the nuclear shape defects

Perturbing Uip4p level

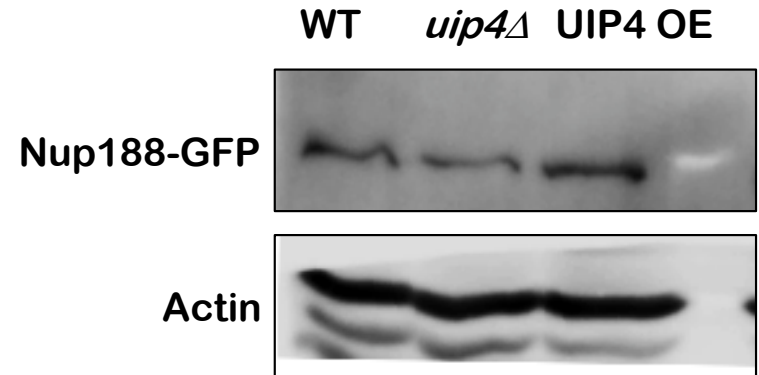
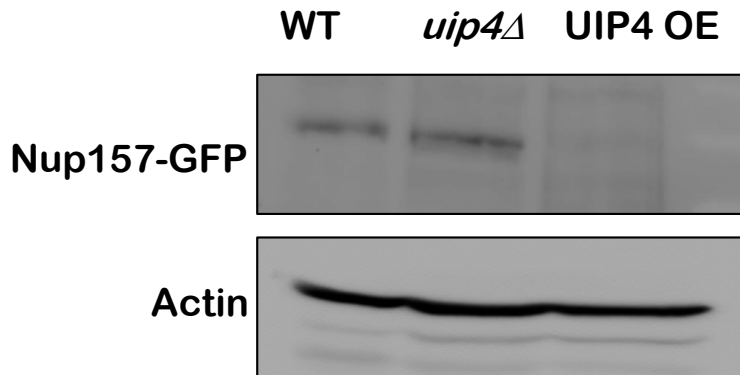
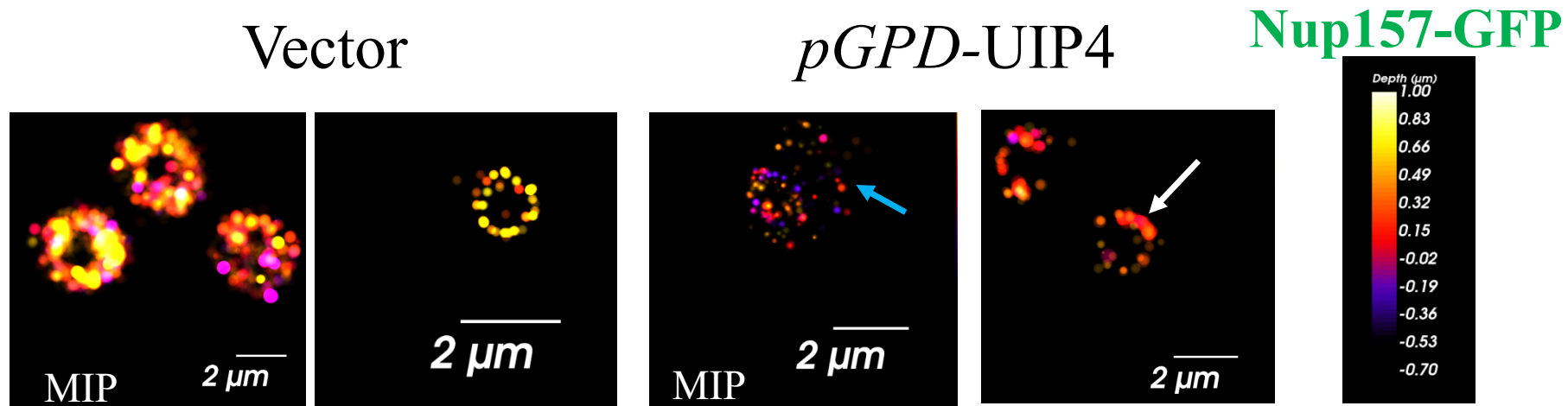


Scale-2μm



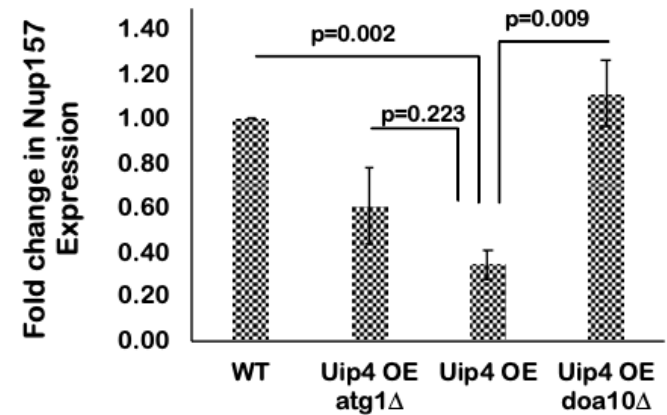
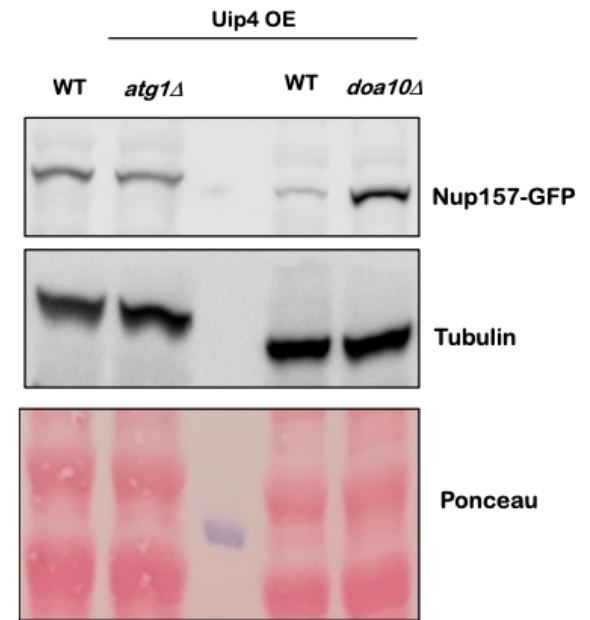
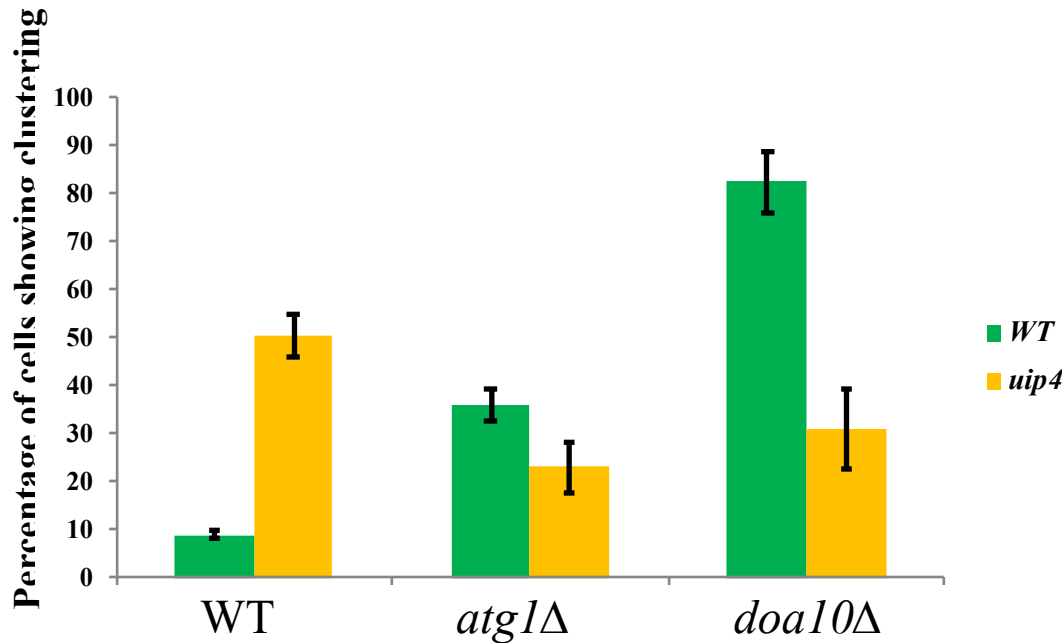
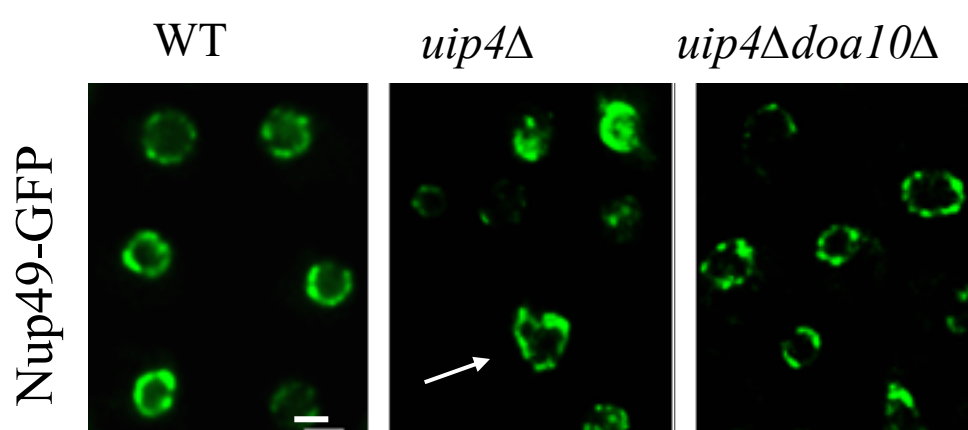
Overexpression of Uip4 compromises NE quality

Effect of Uip4 OE on Nup157p



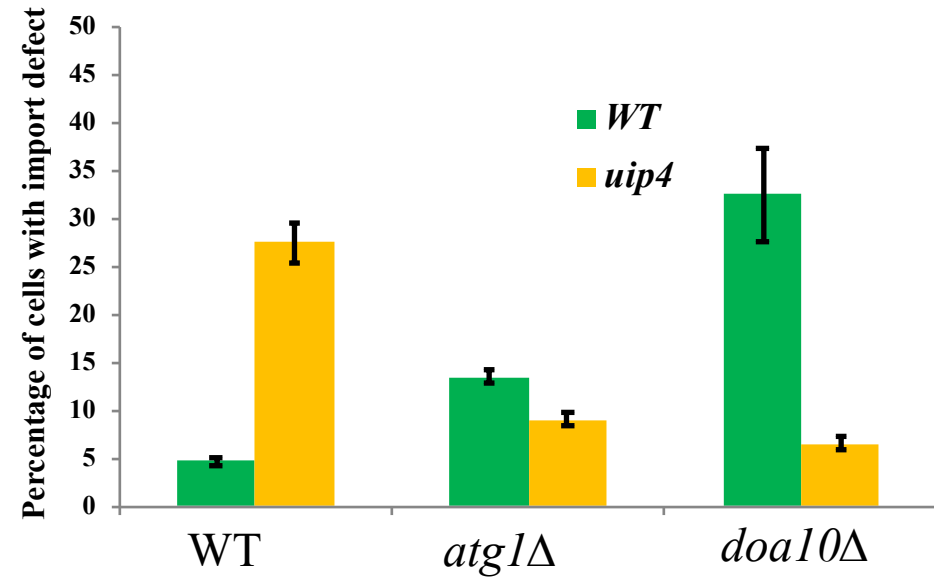
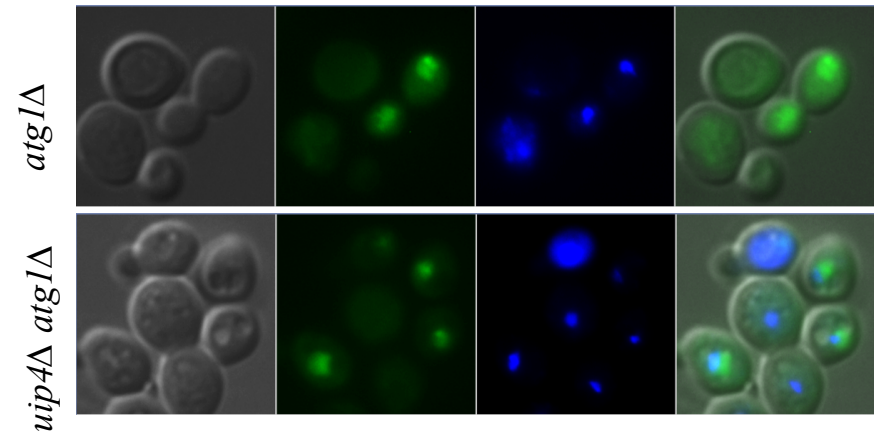
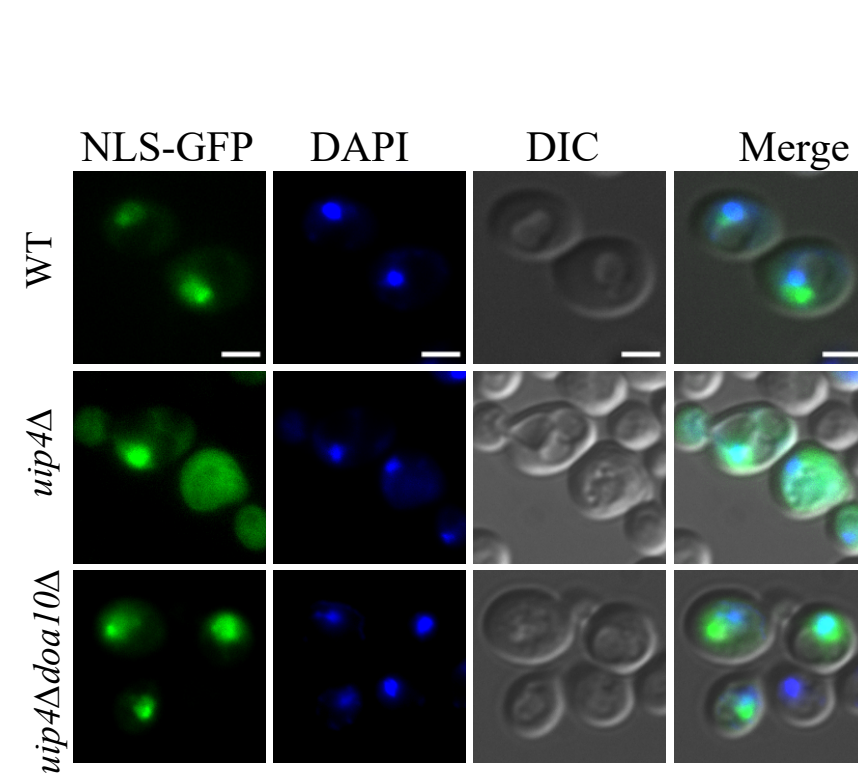
Overexpression of Uip4 leads to reduction of Nup157 levels

NPC distribution in the absence of clearance pathways



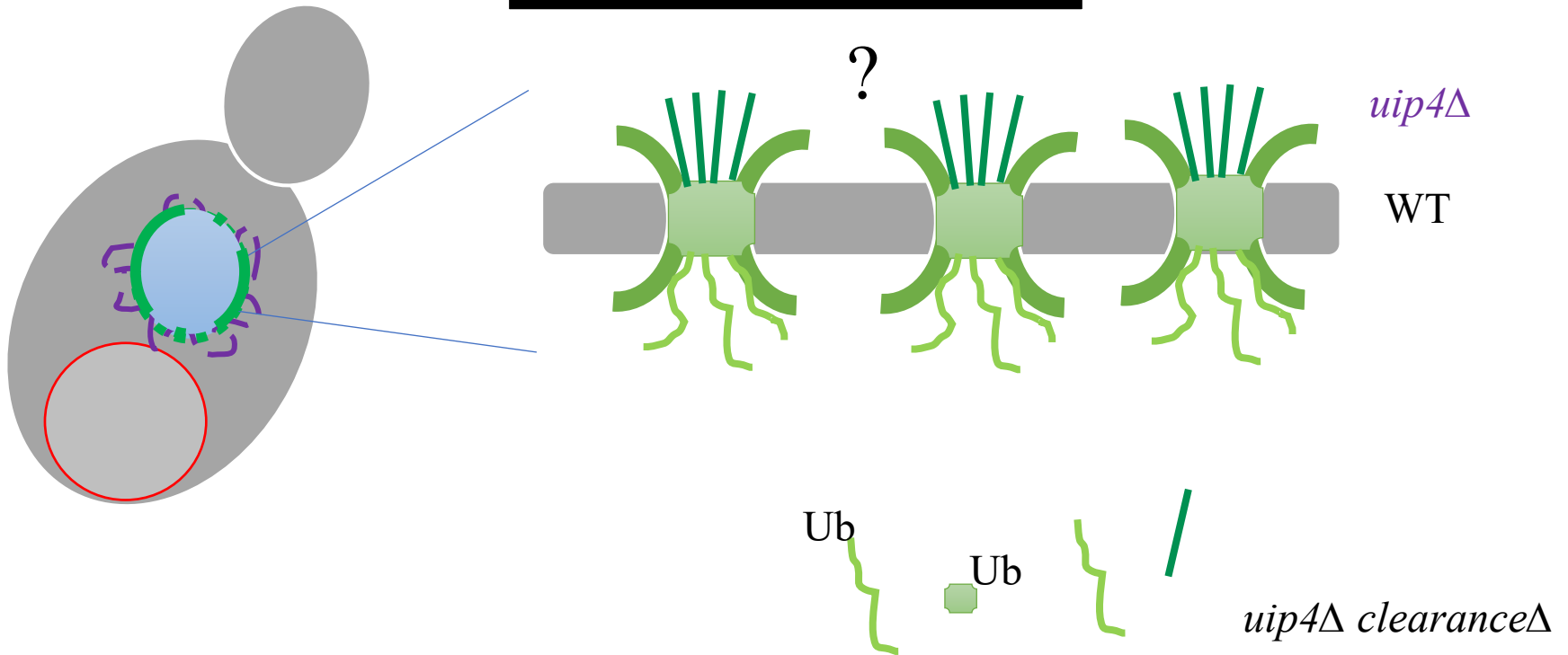
NPC clustering is rescued when substrates are not degraded upon altered Uip4 expression

Nuclear import in the absence of clearance pathways



Transport defect is rescued when Nups are not marked for degradation in the absence of Uip4

Working hypothesis



Open questions:

Role of Uip4 at the NE

Specific interactors/ regulators

NPC quality check

Approaches undertaken:

Time lapse live cell

Super Resolution Microscopy

Identification of interactors (MS, Y2H screen)

Biochemical/Biophysical characterisation

Acknowledgement

Supervisor:

Prof. Krishnaveni Mishra

Lab members

Organizer



Funding



Facilities

