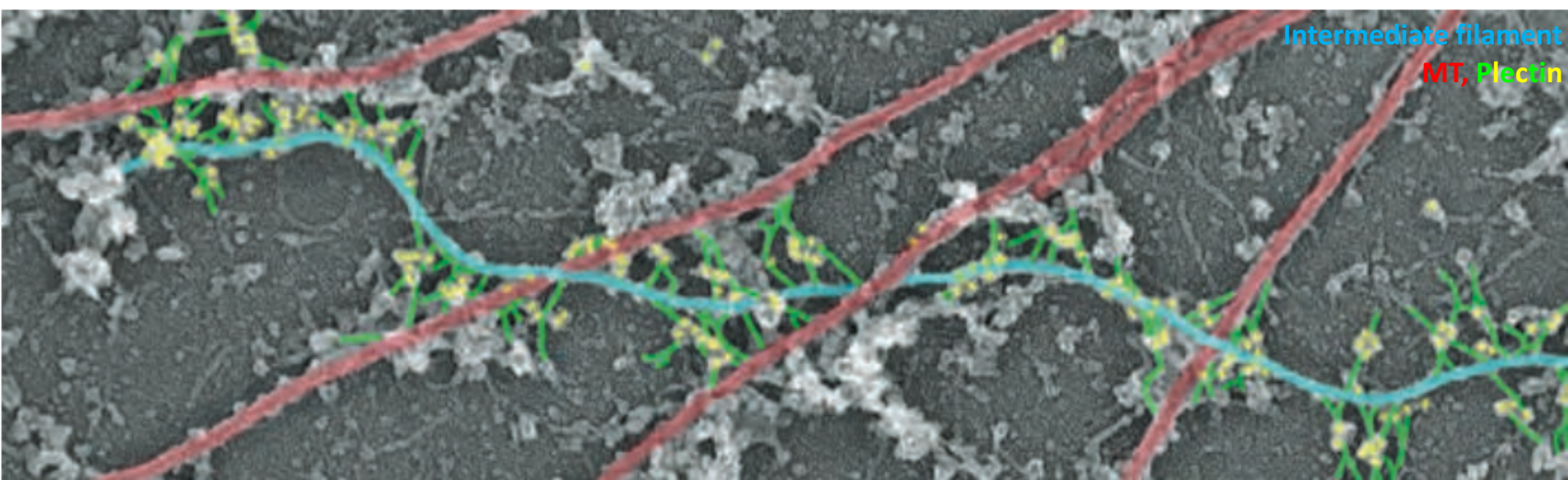


Filaments intermédiaires



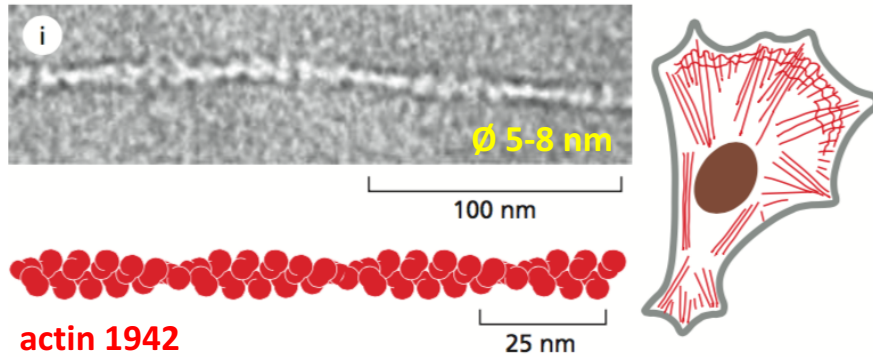
M1 Sciences des médicaments et des produits de Santé

université
PARIS-SACLAY

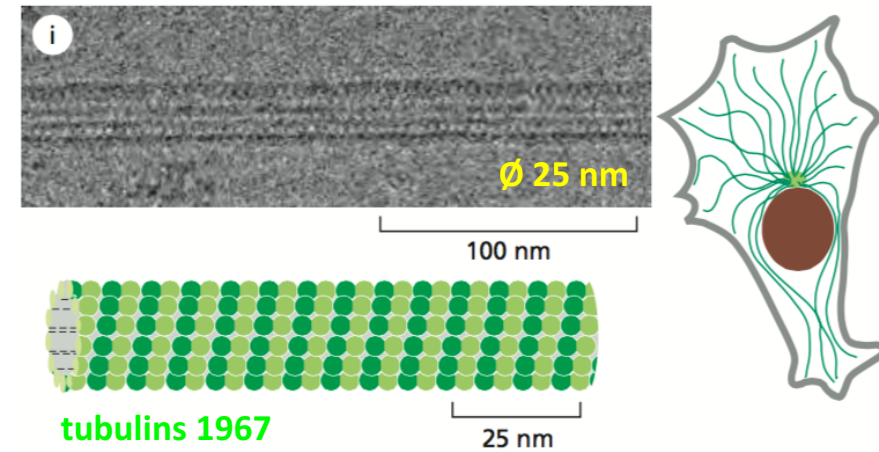
FACULTÉ DE
PHARMACIE

Cell cytoskeleton

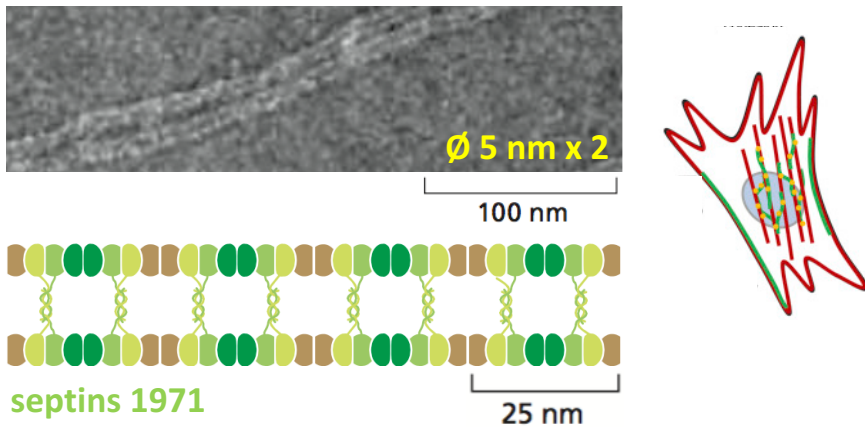
ACTIN FILAMENTS



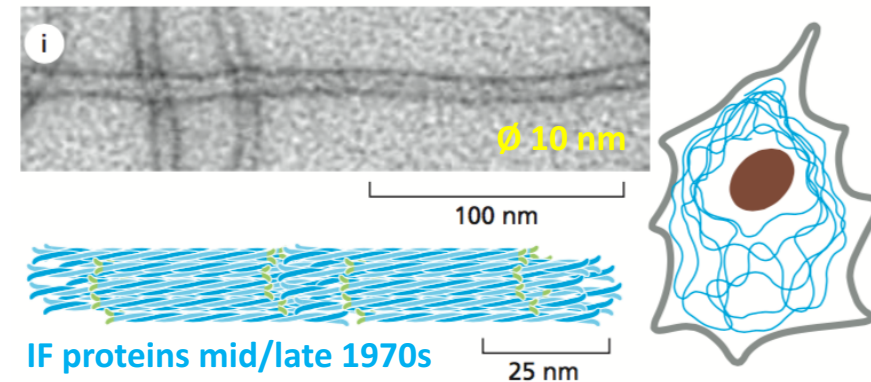
MICROTUBULES



SEPTIN FILAMENTS



INTERMEDIATE FILAMENTS

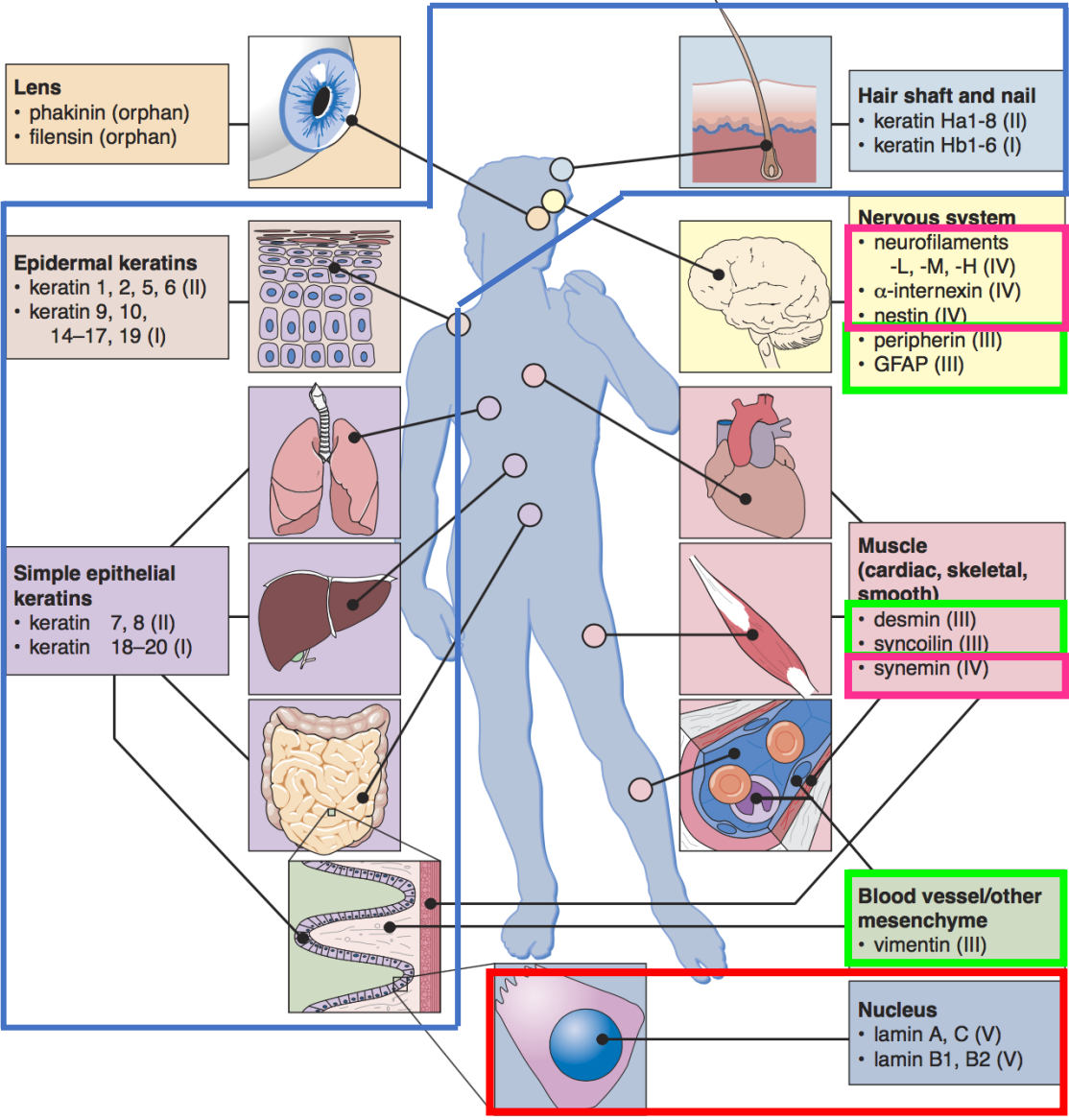


Calvo et al., Cell reports, 2015

Adapted from panel 16-1 & fig 74, Molecular Biology of the Cell 6th

Diversity of IFs (70 genes) : cell specificity

Orphan VI



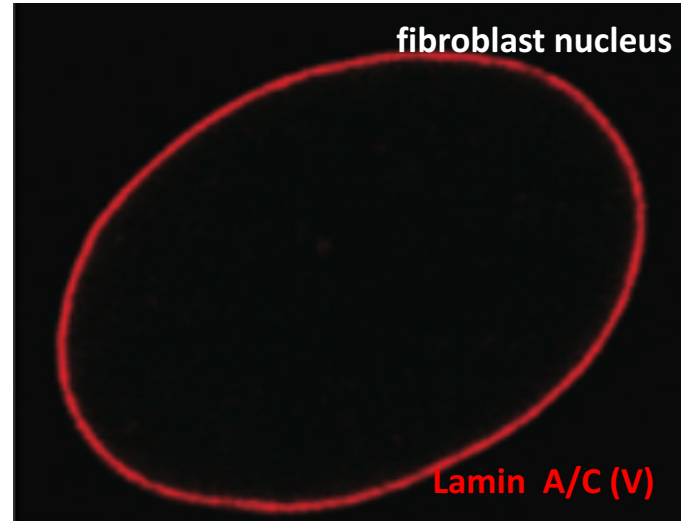
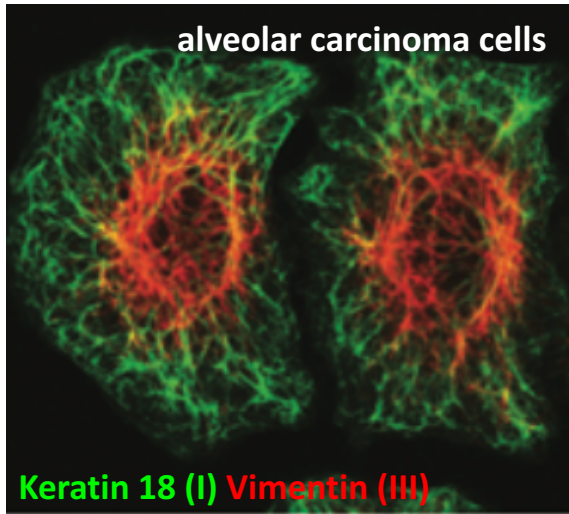
Keratins
I (acid), II (neutral, basic)

Neurofilaments IV

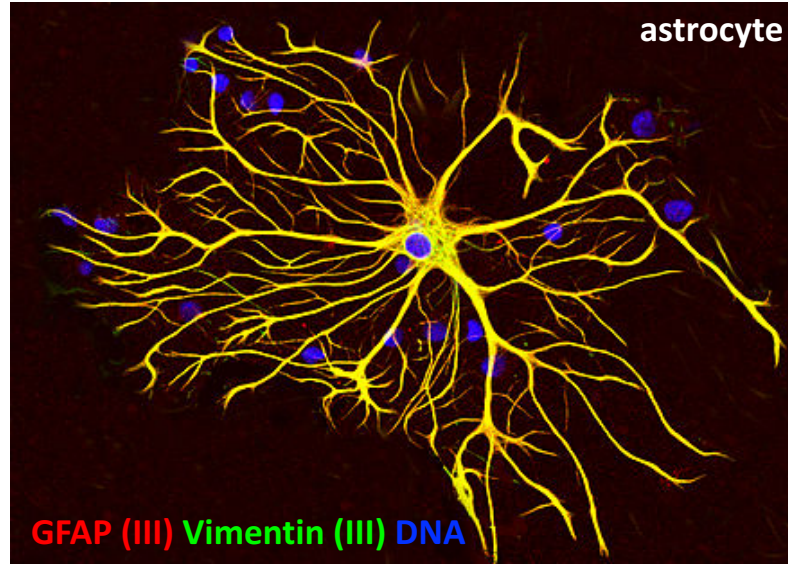
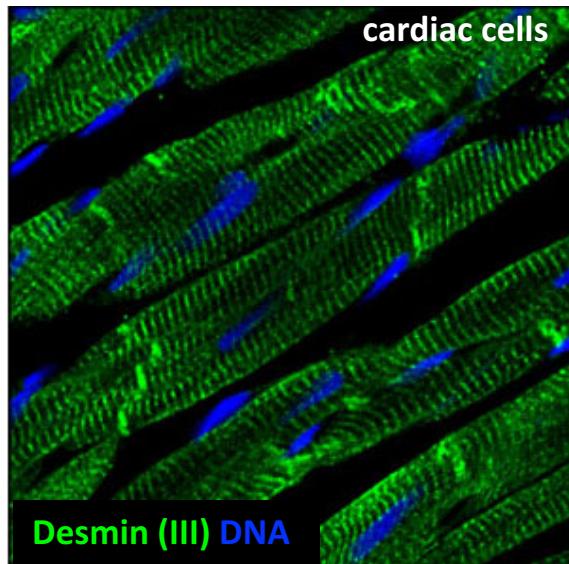
Vimentin-like III
Desmin, GFAP, peripherin

Lamins V

Intermediate filaments networks



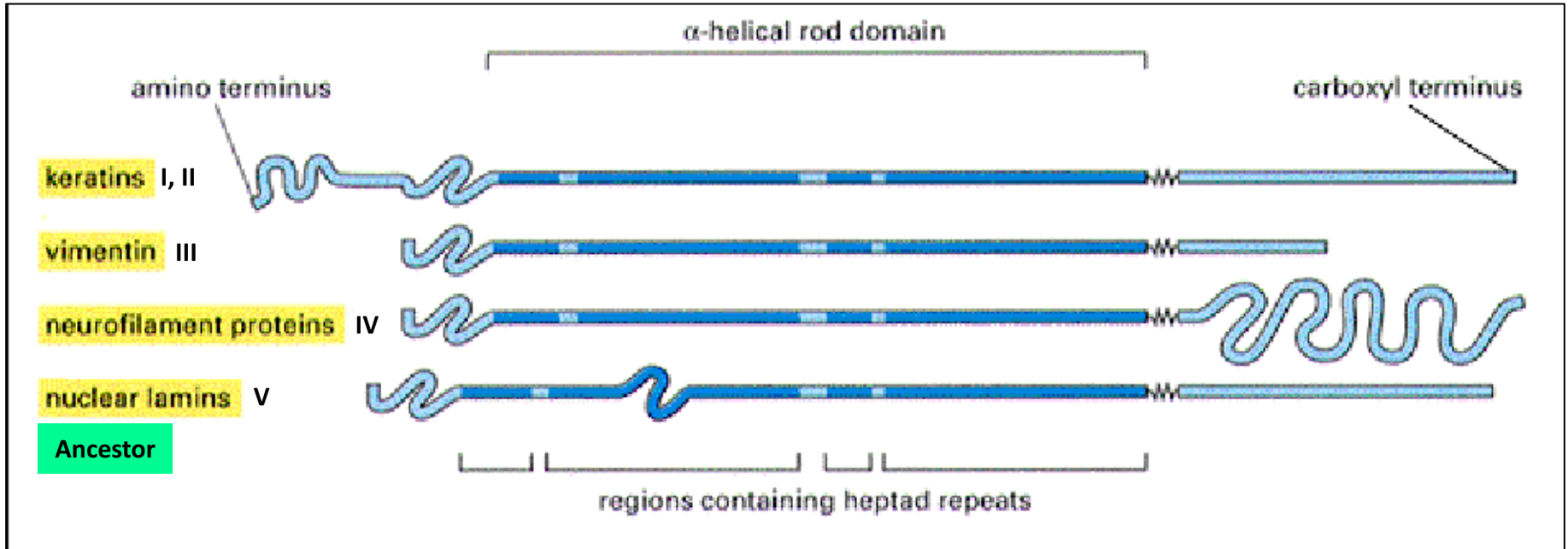
immunofluorescence



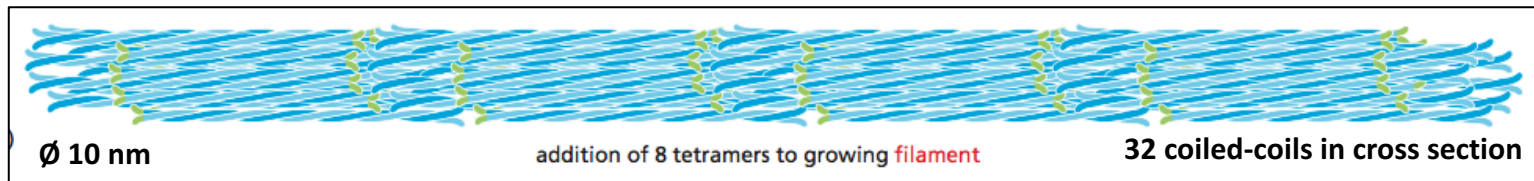
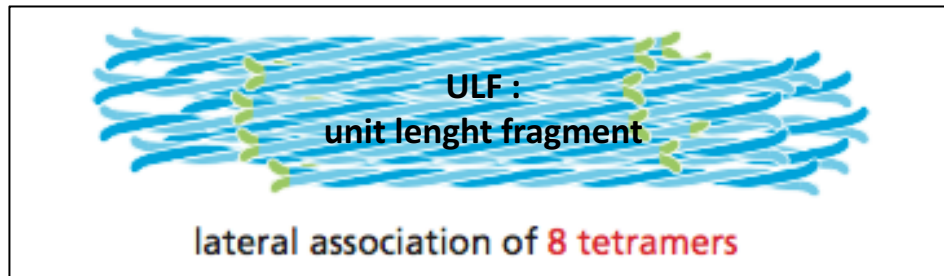
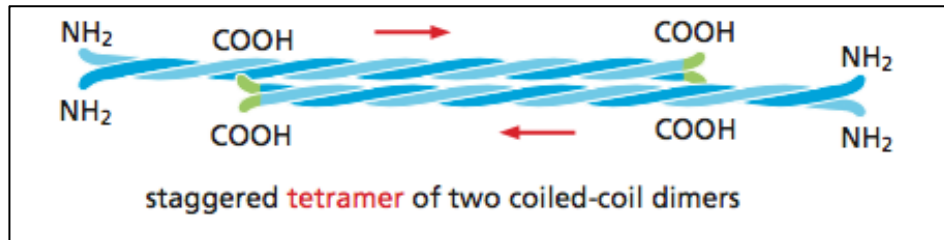
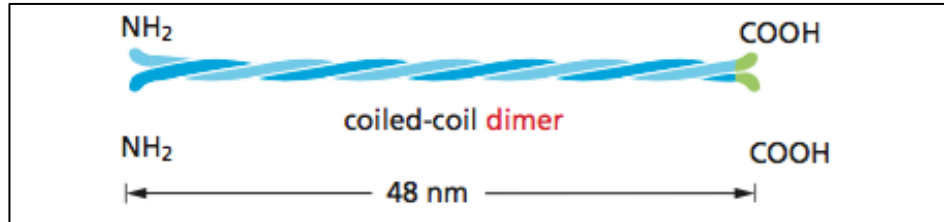
Cell Signaling Technology ; EnCor Biotec Inc

Eriksson et al., J. Clin. Inv., 2009; Wöll et al., Eur J Cell Biol, 2005

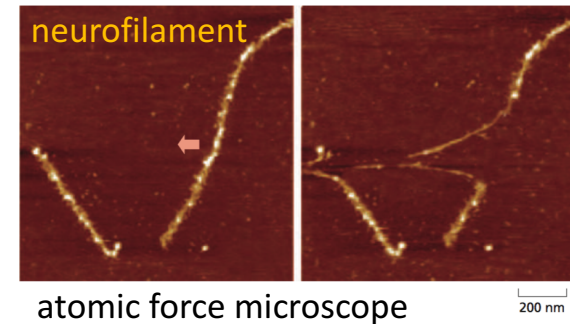
Intermediate filament protein subdomains



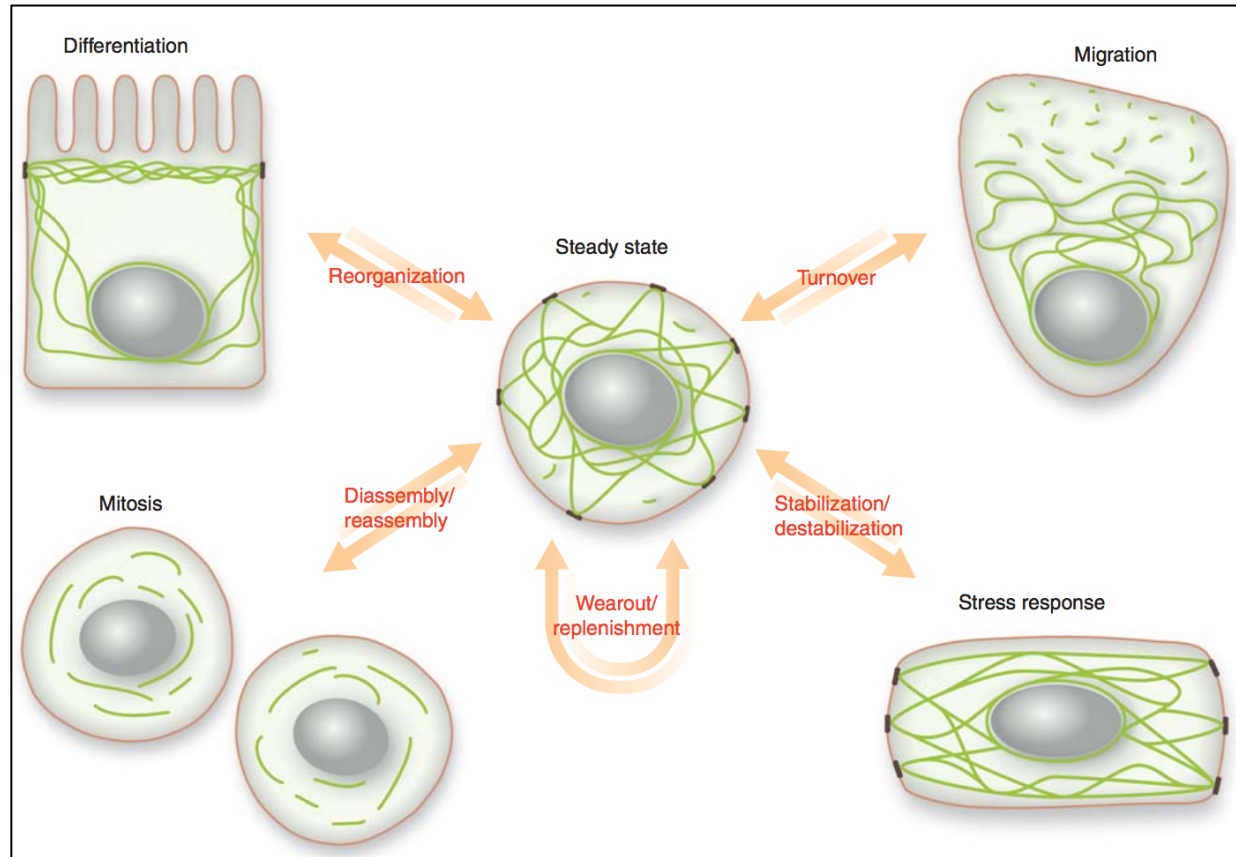
Intermediate filament structure



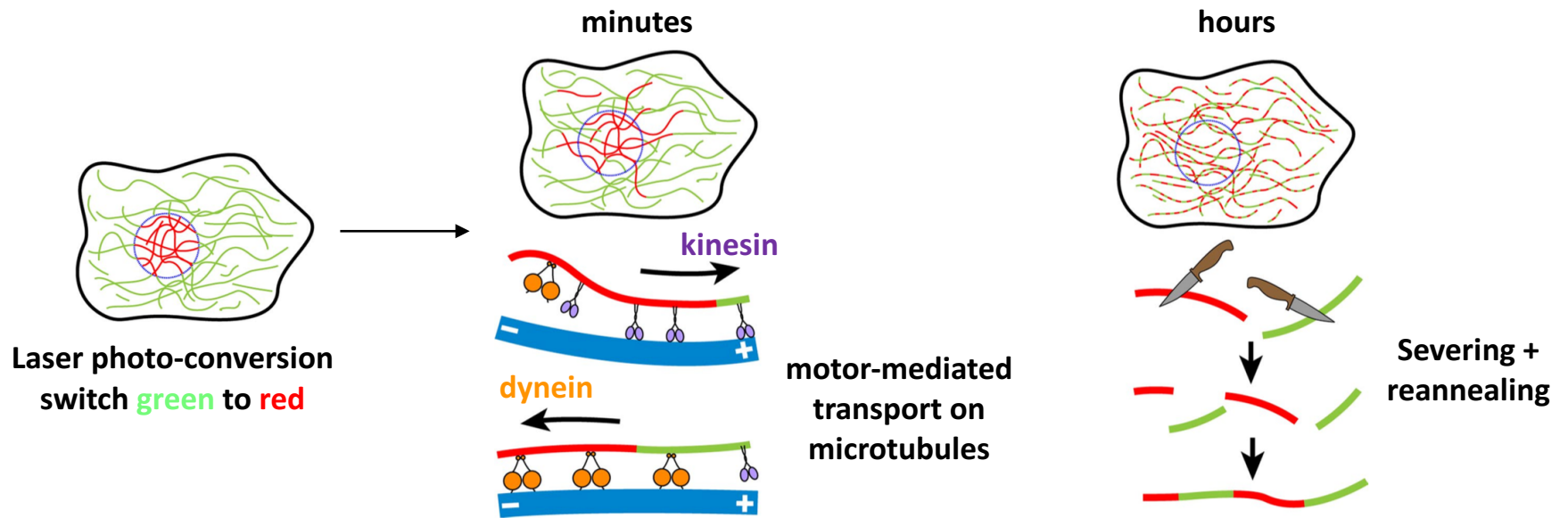
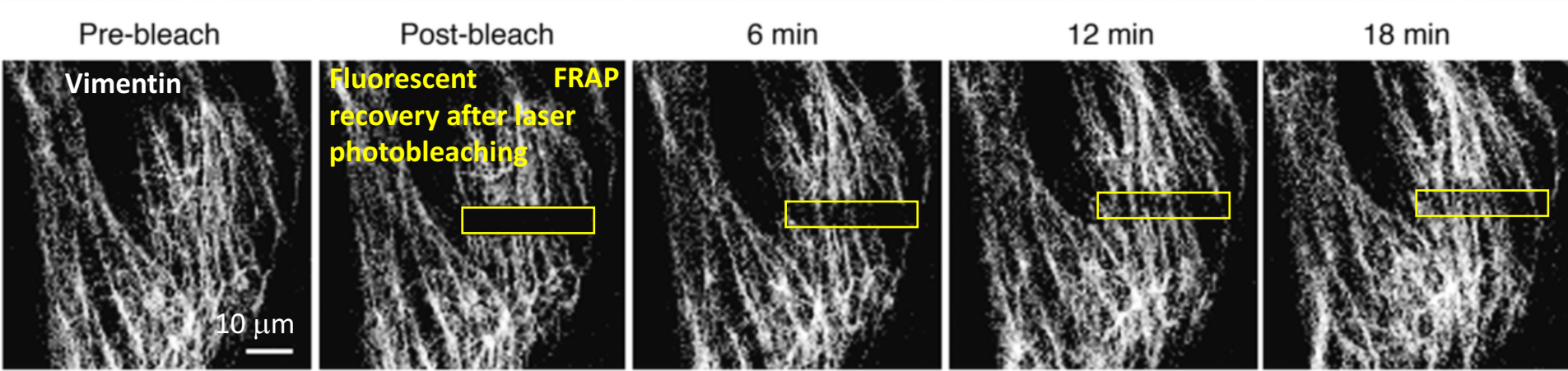
- no polarity (no motor)
- no need of ATP, GTP
- low solubility (salt, detergent)
- elastic structure difficult to break
- binding partners not well known



Intermediate filament dynamic restructuring

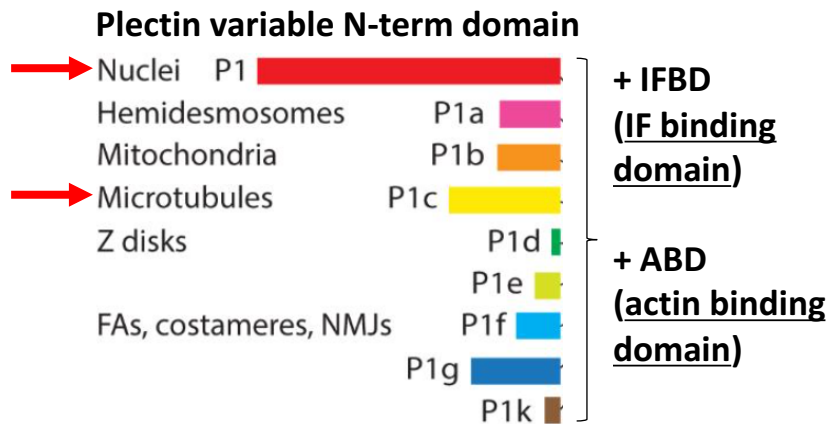
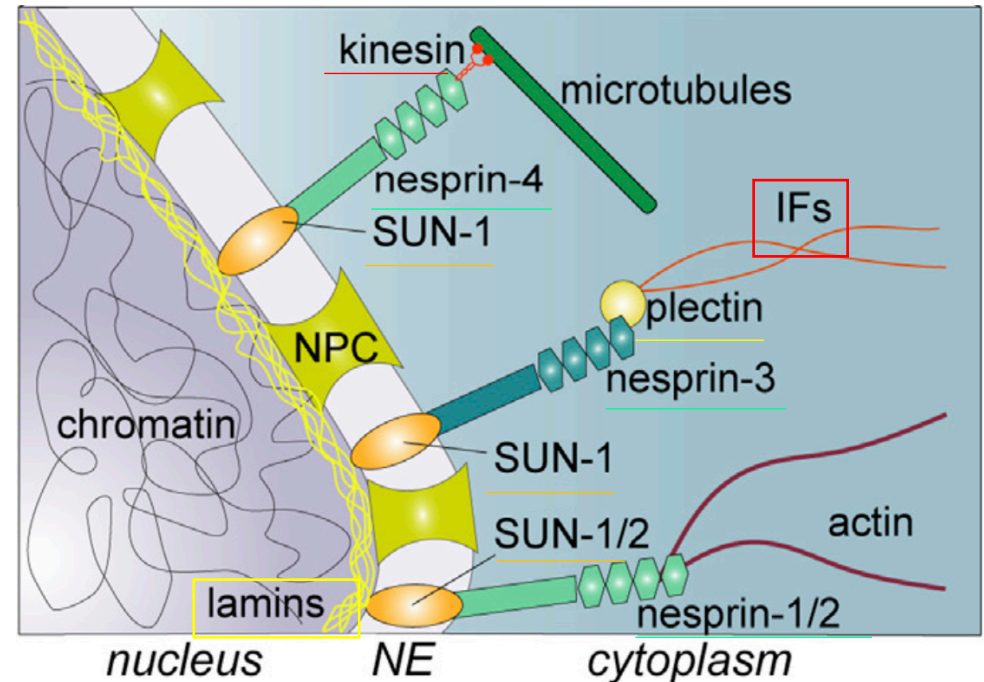
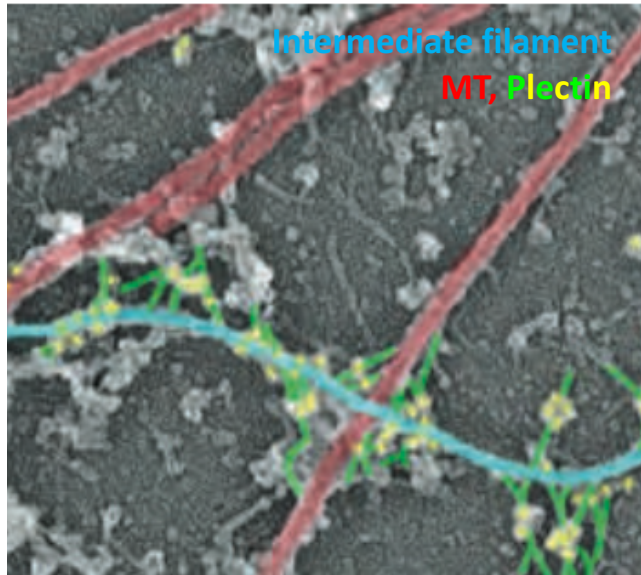


Intermediate filament dynamics



Intermediate filament-associated proteins (IFAPs)

linkers : plectin, SUNs, nesprin



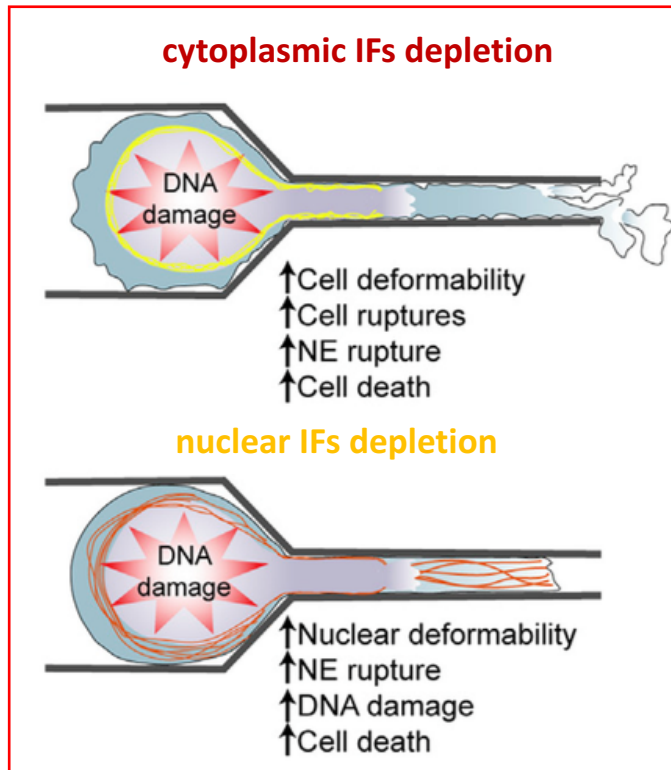
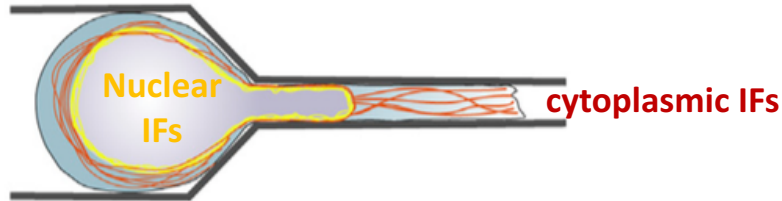
Roles in cell adhesion, migration, division

Svitkina et al., JCB, 1996, Wiche, Cells, 2021

Infante & Etienne-Manneville, Front. Cell Dev. Biol., 2022

Intermediate filament cellular functions

Cell migrating through confined space

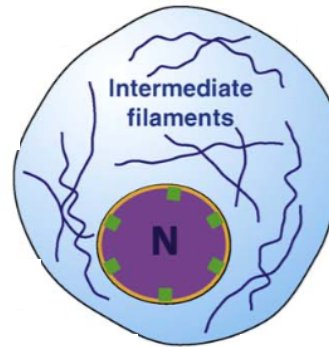
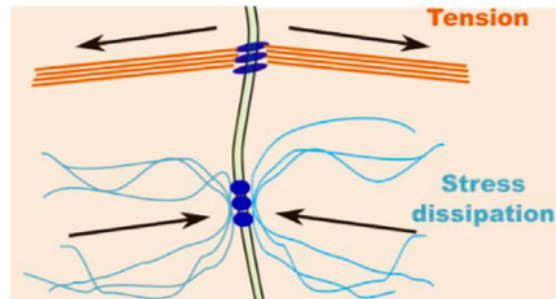
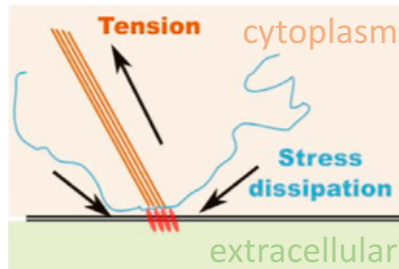
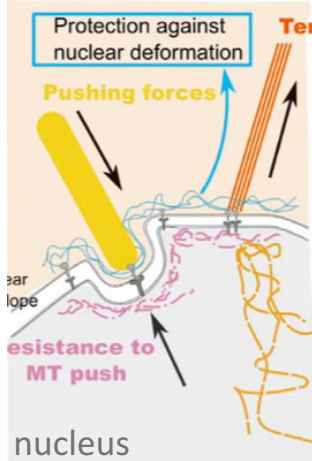
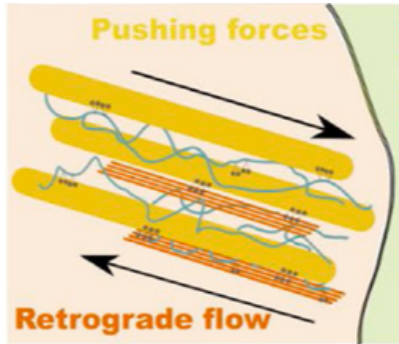


Roles in
maintenance of cell shape
DNA integrity
structural integrity (organelle positioning)
migration
adhesion
division
...

IFs in cell-stress response

Plasma membrane

Nuclear membrane



Stress

Mechanic (tension, shear, compression)

Intermediate filament (cytoplasm)

Intermediate filament (nucleus)

Actin

Microtubule

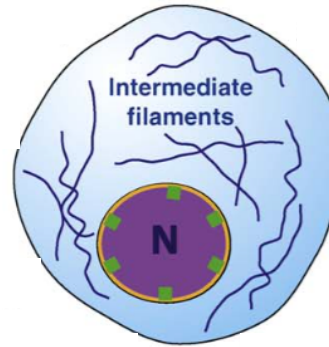
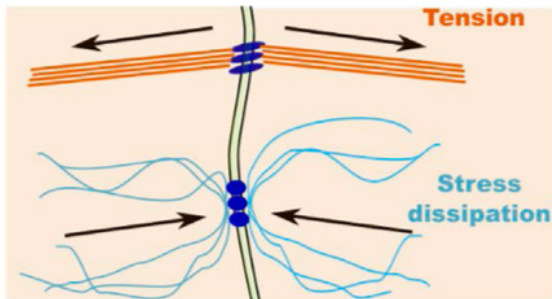
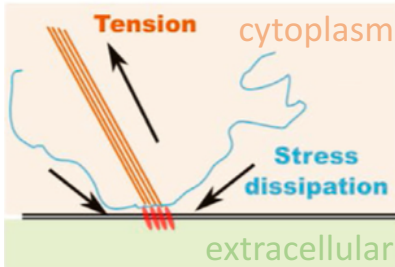
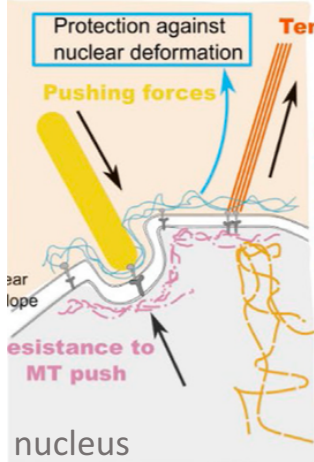
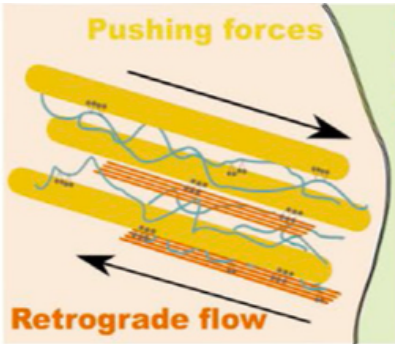
Ndiaye et al., *Front. Cell Dev. Biol.*, 2022

Adapted from Toivoila et al., *Trends Cell Biol.*, 2010

IFs in cell-stress response

Plasma membrane

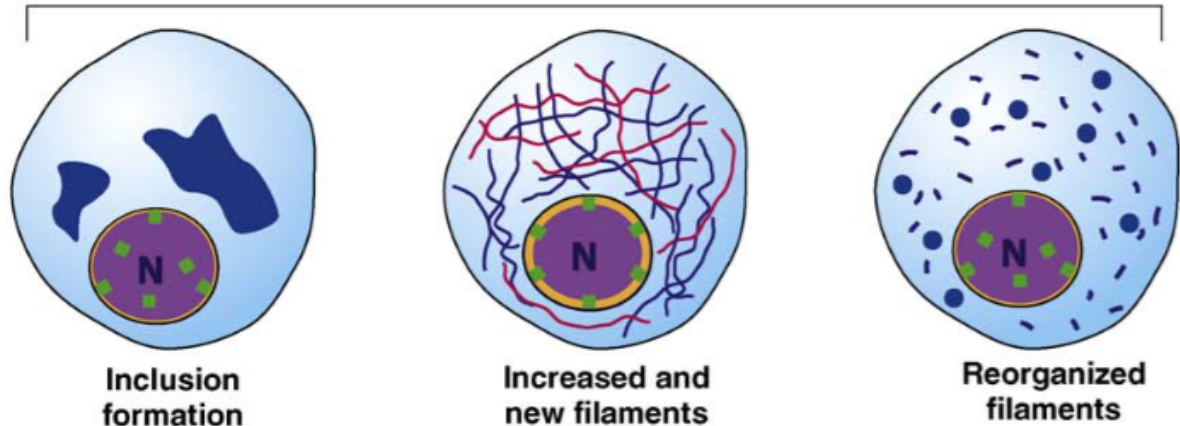
Nuclear membrane



Stress

- Mechanic (tension, shear, compression)
- Wound closure
- Hypoxia
- Osmotic, oxidative
- Protein misfolding
- Toxin, radiation
- DNA damage
- Pathogens (virus, bacteria)
- Heat

Response depends on stress type and duration



Intermediate filament (cytoplasm)

Intermediate filament (nucleus)

Actin

Microtubule

Ndiaye et al., *Front. Cell Dev. Biol.*, 2022

Adapted from Toivoila et al., *Trends Cell Biol.*, 2010

IFs orchestrate organelles positioning

Organelle/ compartment	IF (context)	Wild-type IF	Absent/mutant IF
Mitochondria	<ul style="list-style-type: none"> • Desmin (muscle) • Keratins (liver, skin) • Neurofilaments (cell culture) 		
Golgi	<ul style="list-style-type: none"> • Keratins (cell culture) • Vimentin (cell culture) • Neurofilaments (cell culture) 		
Lysosomes	<ul style="list-style-type: none"> • Vimentin (cell culture) 		
Membrane-associated proteins	<ul style="list-style-type: none"> • Keratins (intestine, liver, cell culture) • Lamins/desmin (heart) • Vimentin (cell culture) 		
Nucleus	<ul style="list-style-type: none"> • Lamins (tissues, cell culture) • Cytoplasmic IF (tissues, cell culture) 		

IFs and diseases

Keratins I, II : skin diseases (epidermolysis bullosa simplex EBS), predisposition for liver diseases (steatosis), cancer markers

Vimentin-like III : myopathies, Alexander disease, cataract, metastasis

Neurofilaments IV : neuropsychiatric diseases (Charcot-Marie-Tooth, Alzheimer, amyotrophic lateral sclerosis, Parkinson)

Lamins V : laminopathies (progeria/ precocious aging)

Orphan VI : cataract

Ashwagandha *Withania somnifera*



wikipedia

withaferin A :

Disrupts Vimentin, Keratin, NF networks

Grin et al., PLOS ONE, 2012

Phase I trial osteosarcoma

Pires et al., J. A. Int. Med, 2020

statin (simvastatin) :

anti-cholesterol / chemotherapy

Disrupts Vimentin network

Trogden et al., Faseb J, 2018

Phase II trial (combination therapy) in progress