

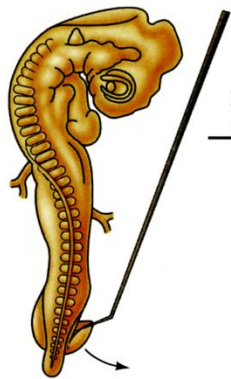
Définition d'un facteur neurotrophique

TROPHE = Nourriture

- 1) Les neurones ont besoin d'une quantité minimale de FN pour leur survie et pour maintenir leur connexions.**
- 2) Les tissus cibles synthétisent les FN et les mettent à disposition des neurones en développement**
- 3) En quantité limitée d'où compétition entre neurones.**

(A)

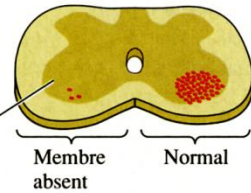
Ablation d'un bourgeon de membre



1 semaine plus tard

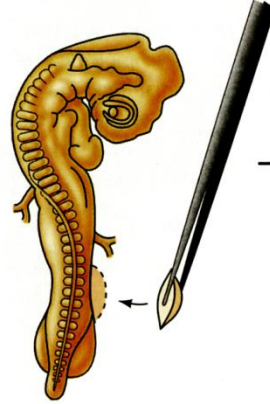
(B)

Coupe de la moelle



(C)

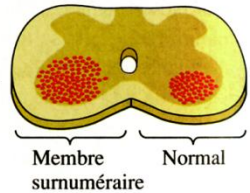
Greffe d'un bourgeon de membre surnuméraire

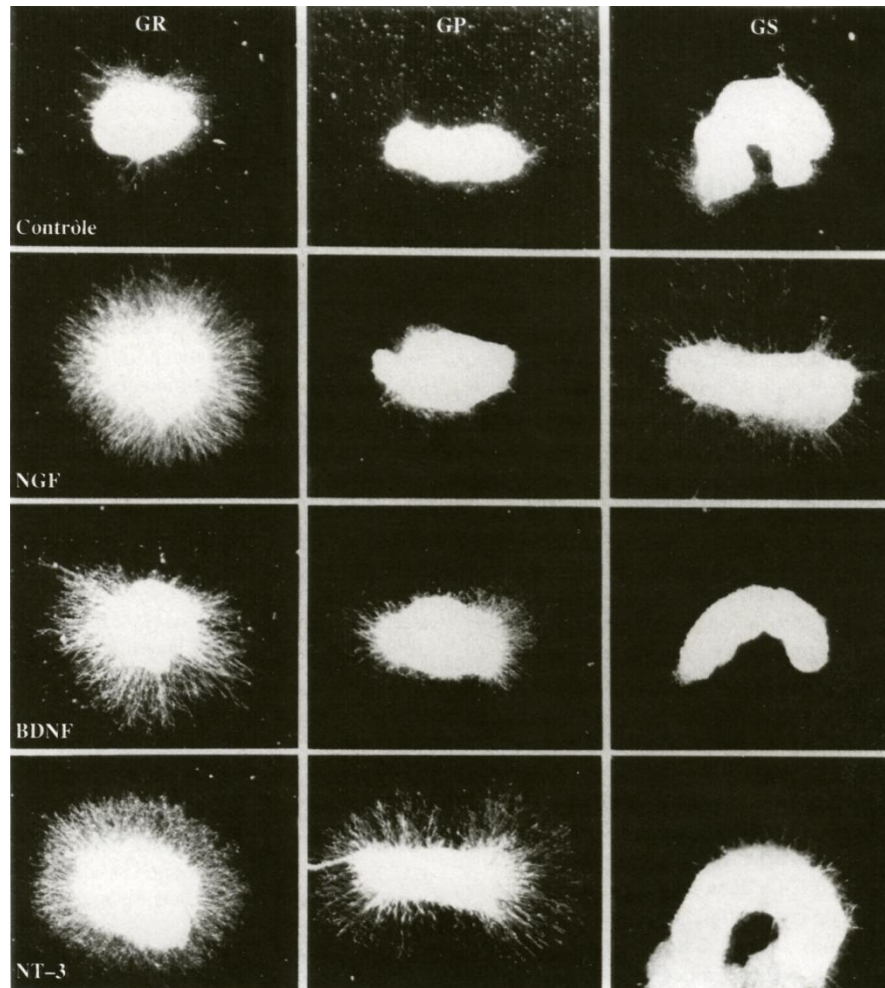


1 semaine plus tard

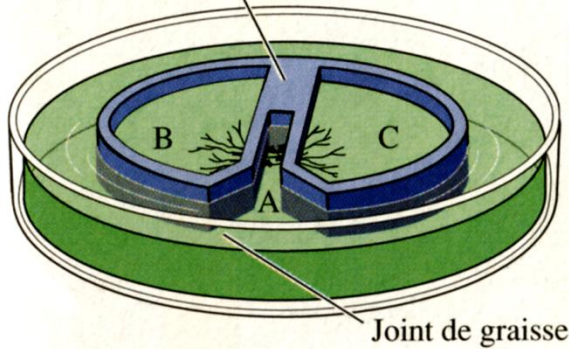
(D)

Coupe de la moelle



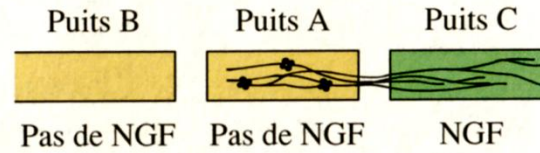
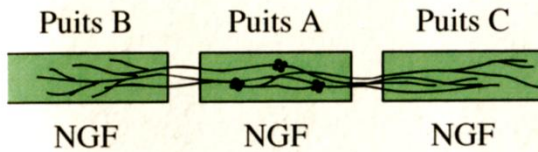
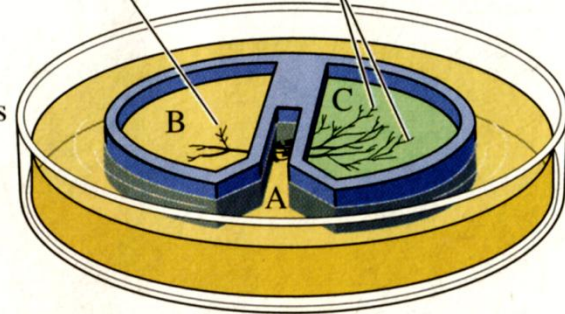


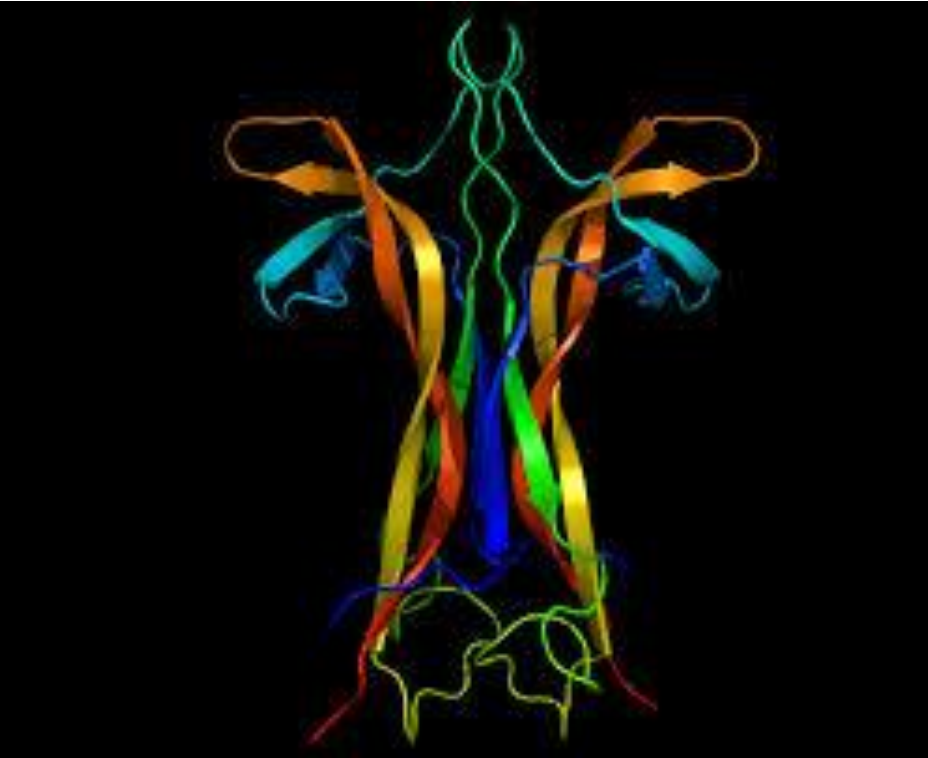
Des cloisons de téflon séparent les compartiments A, B et C



Le NGF est supprimé dans les compartiments A et B

Régression des neurites
NGF maintenu dans le compartiment ; la prolifération des ramifications se poursuit

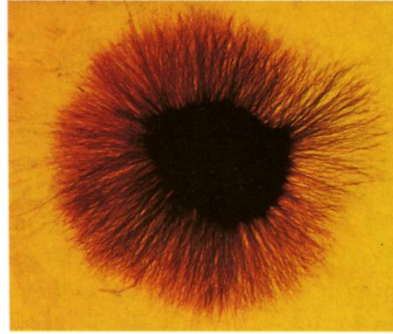




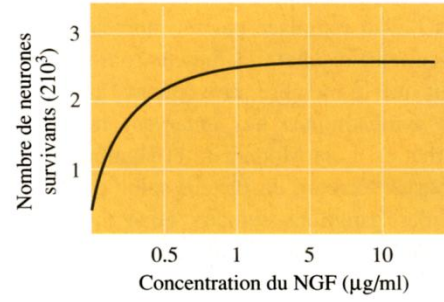
(A)



(B)



(C)

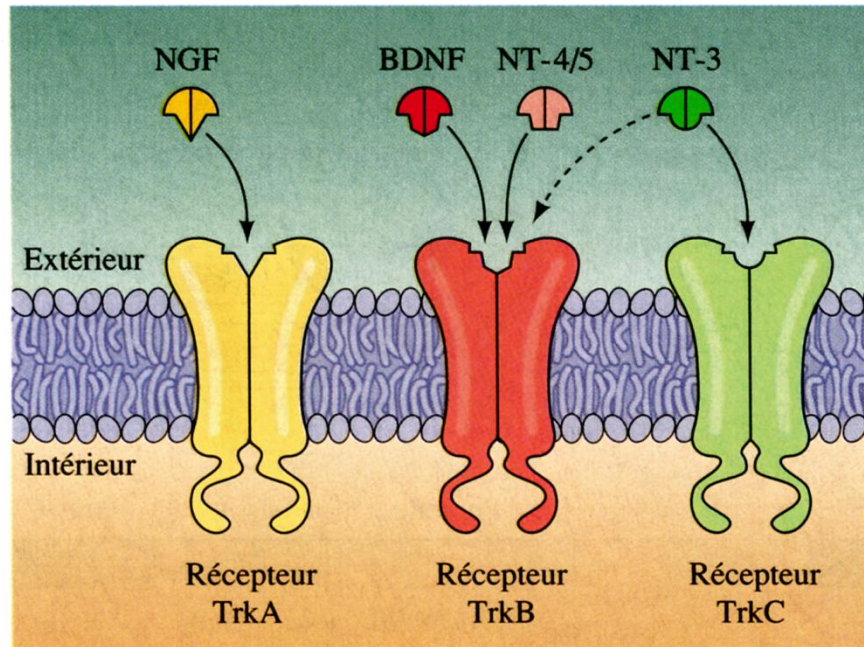


(D)

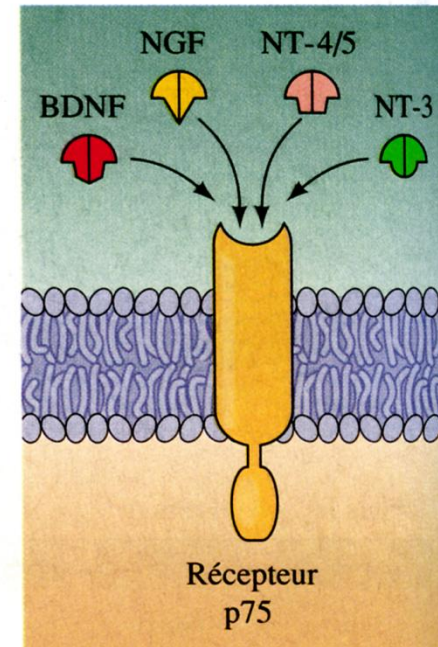


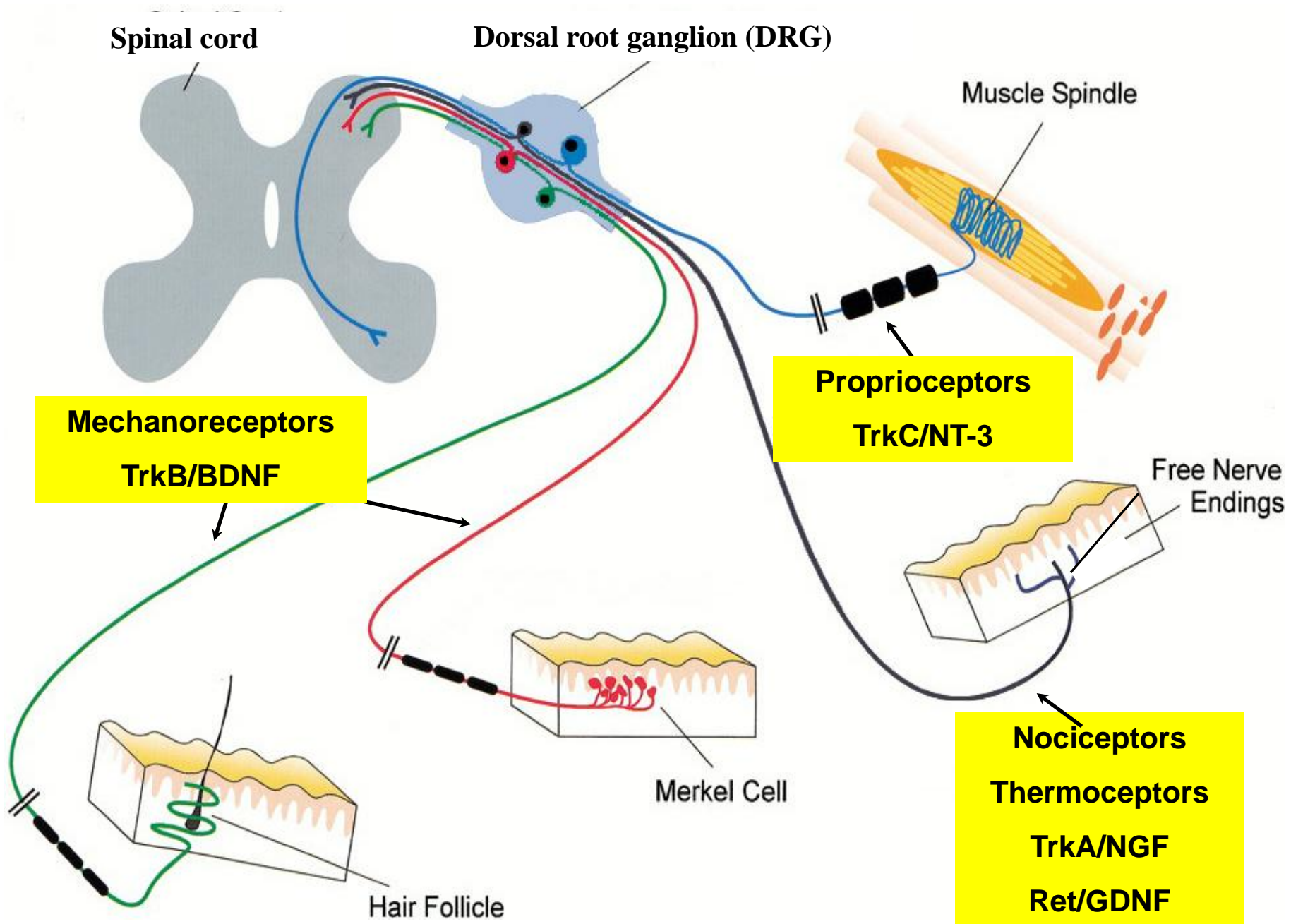
Class	Examples	Structural Features of Class
I	EGF receptor, NEU/HER2, HER3	cysteine-rich sequences
II	insulin receptor, IGF-1 receptor	cysteine-rich sequences; characterized by disulfide-linked heterotetramers
III	PDGF receptors, c-Kit	contain 5 immunoglobulin-like domains; contain the kinase insert
IV	FGF receptors	contain 3 immunoglobulin-like domains as well as the kinase insert; acidic domain
V	vascular endothelial cell growth factor (VEGF) receptor	contain 7 immunoglobulin-like domains as well as the kinase insert domain
VI	hepatocyte growth factor (HGF) and scatter factor (SC) receptors	heterodimeric like the class II receptors except that one of the two protein subunits is completely extracellular. The HGF receptor is a proto-oncogene that was originally identified as the Met oncogene
VII	neurotrophin receptor family (trkA, trkB, trkC) and NGF receptor	contain no or few cysteine-rich domains; NGFR has leucine rich domain

(A)

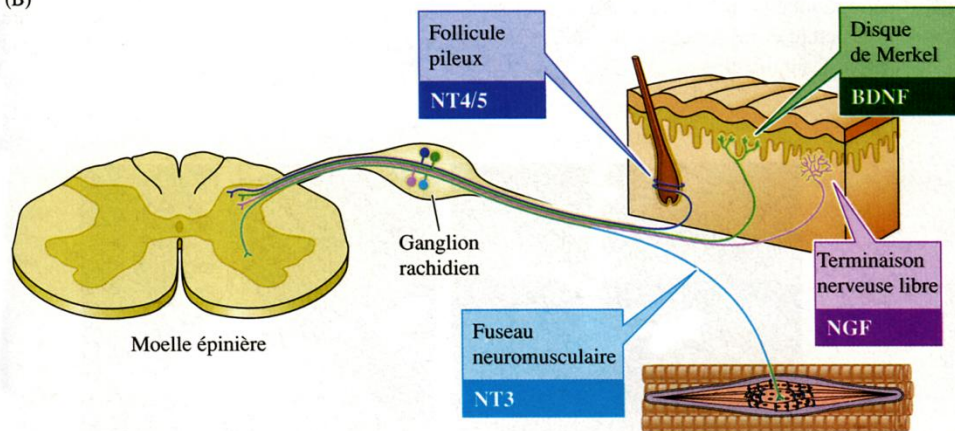


(B)

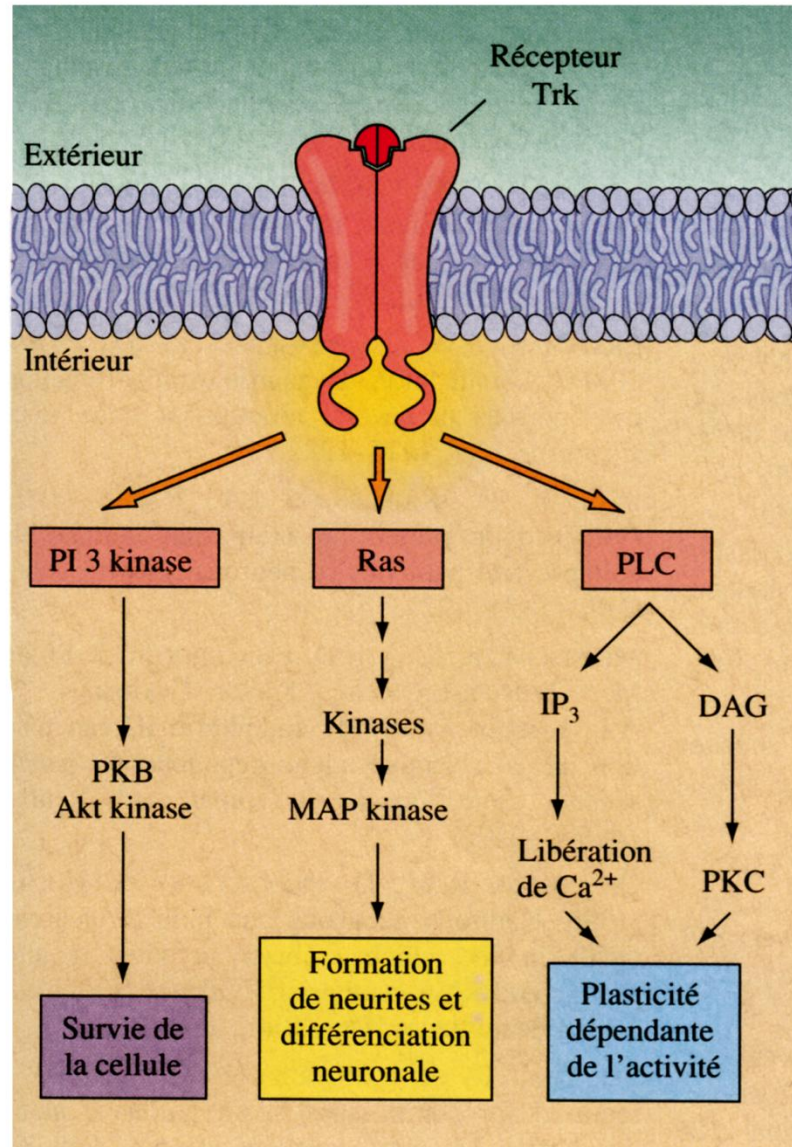


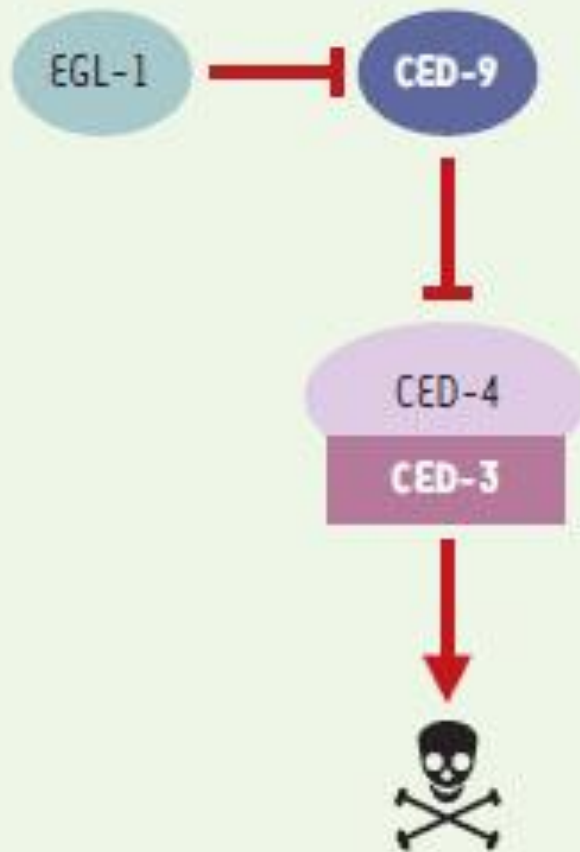


(B)

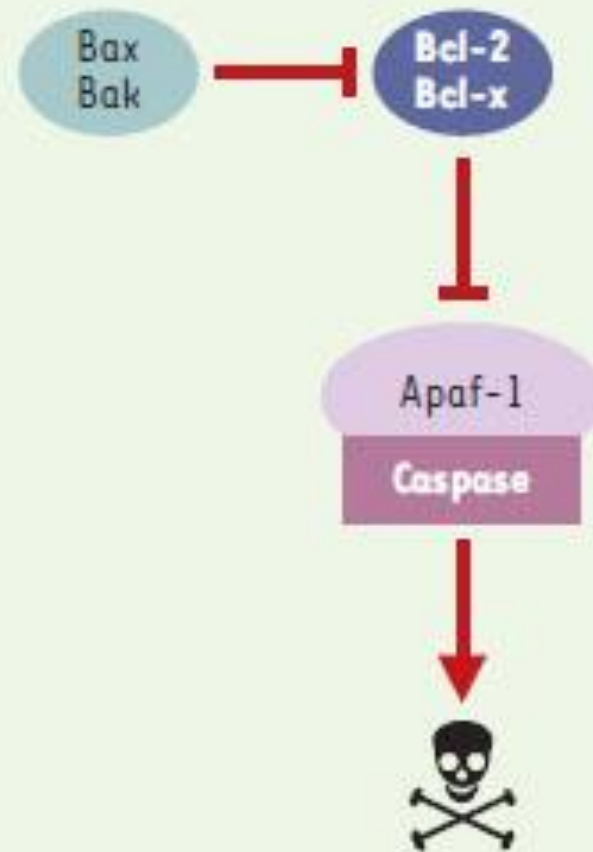


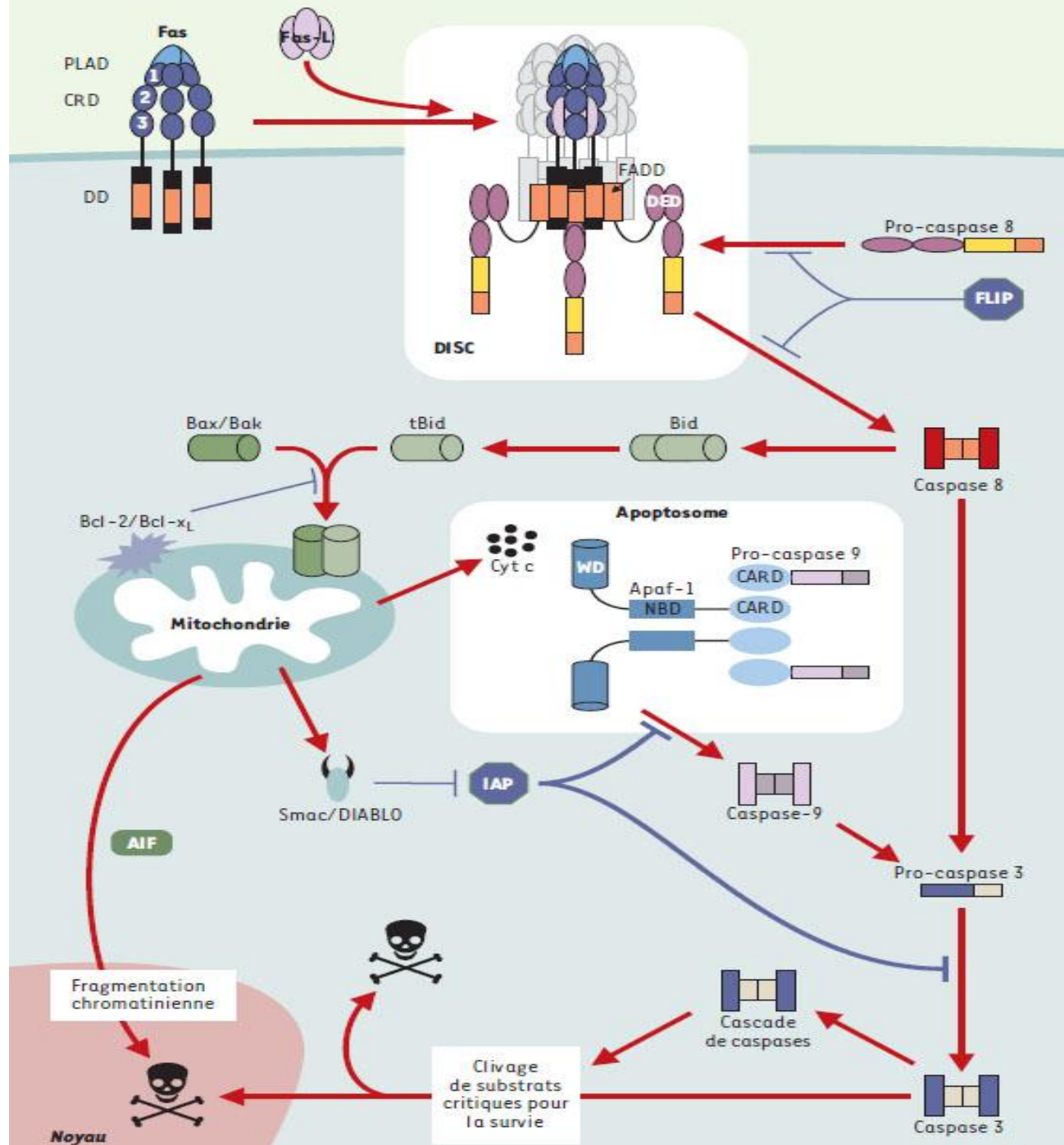
(A)

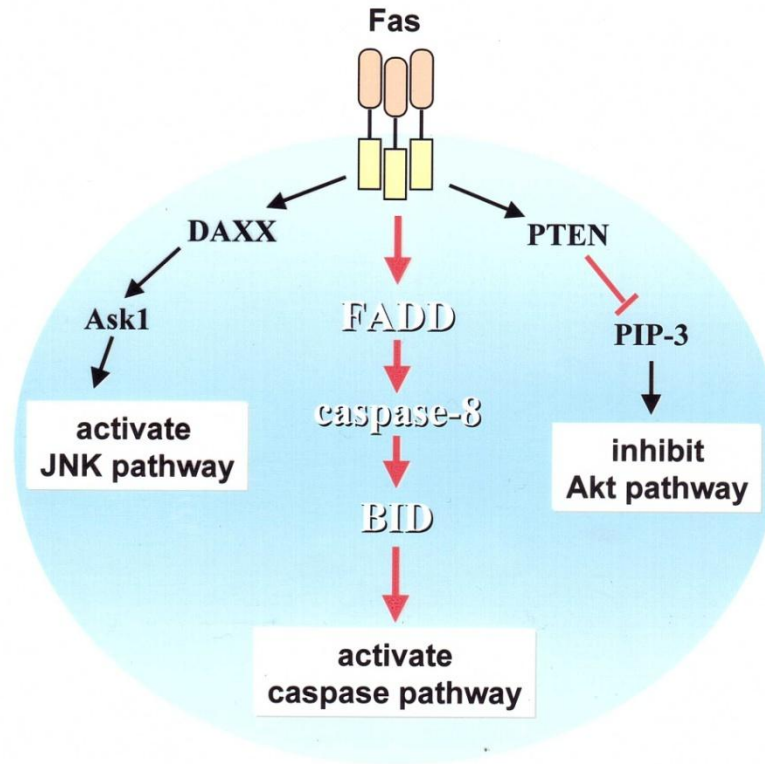


A*C. elegans***B**

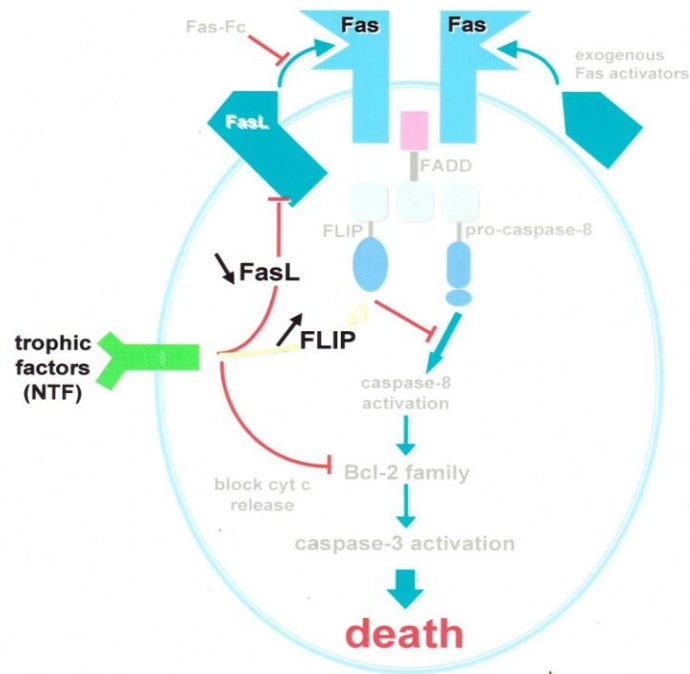
Mammifères



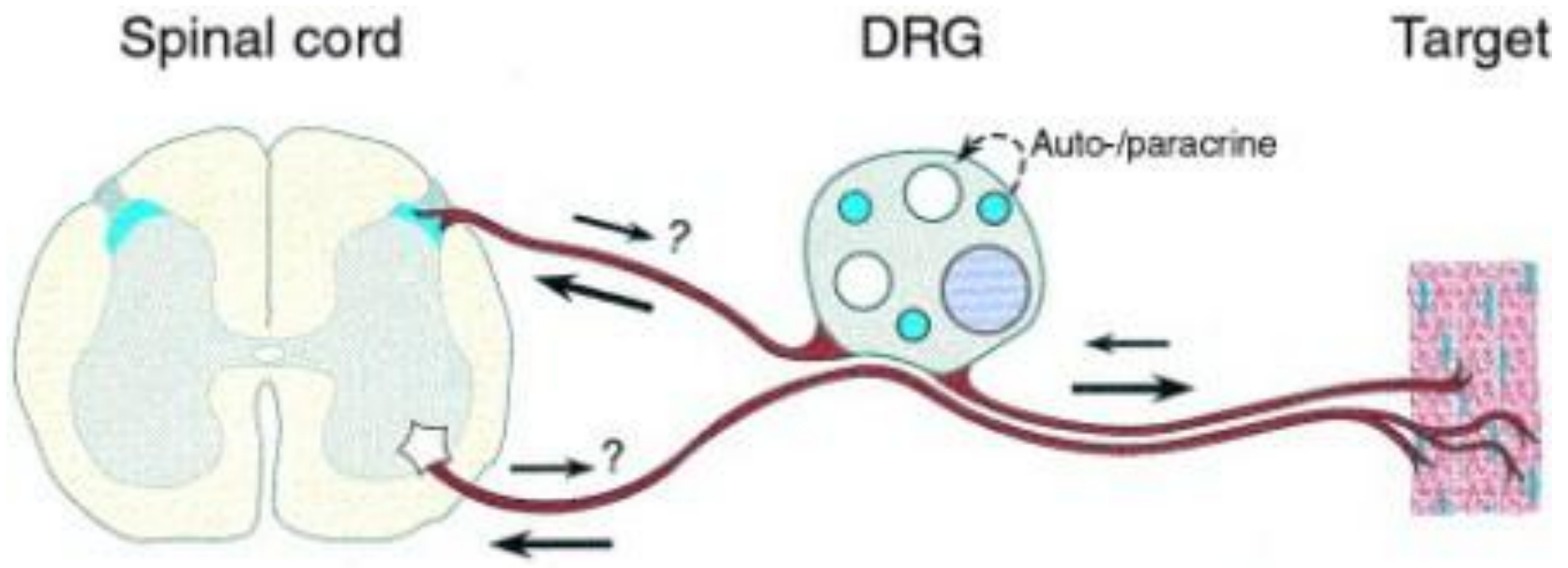




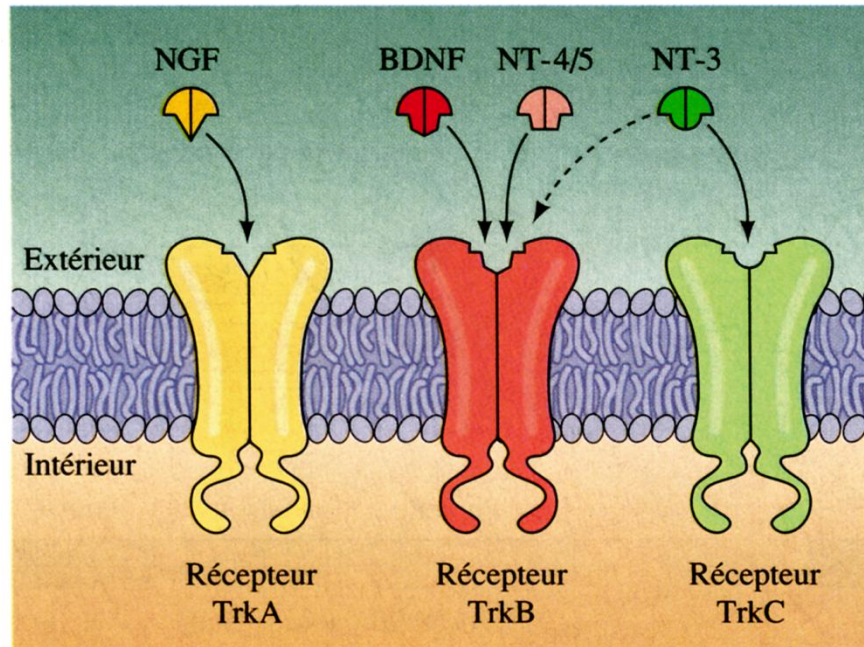
Raoul et al. Fig. 1



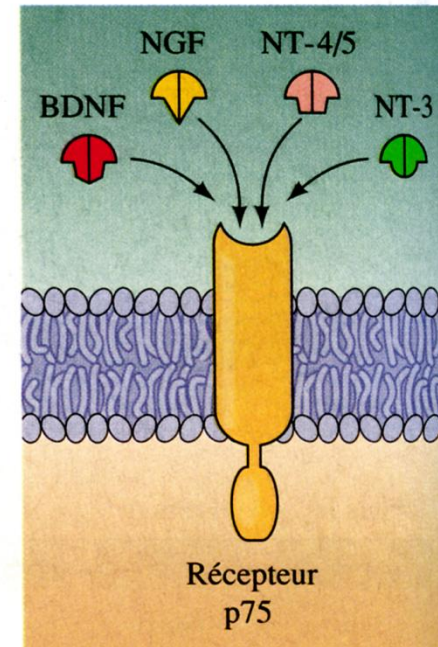
Raoul et al. Fig. 3



(A)

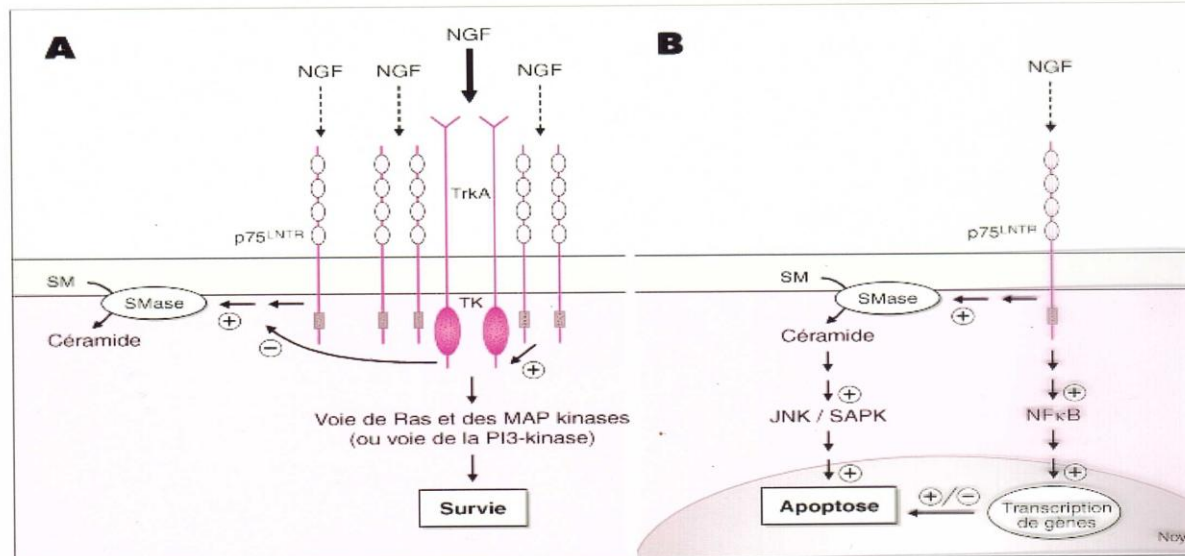


(B)



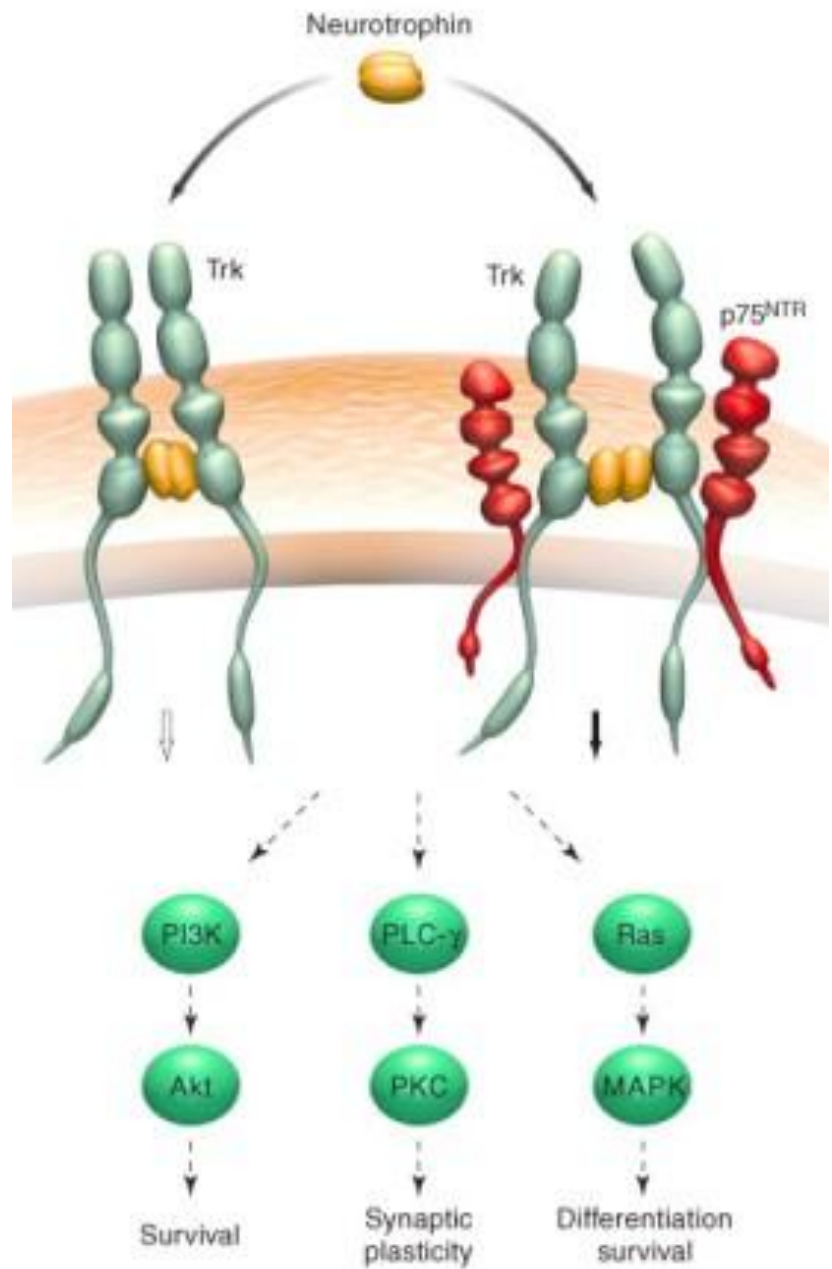
Le récepteur p75

- 1) p75 est nécessaire pour que le trkA est un site de haute affinité pour le NGF, en facilitant la dimérisation de trkA lorsqu'il se lie au NGF.**
- 2) p75 augmente la spécificité du NGF pour trkA vis-à-vis du NT3 par exemple.**
- 3) p75 augmente la vitesse d'association du NGF avec trkA.**
- 4) P75 module la signalisation intracellulaire du trkA.**

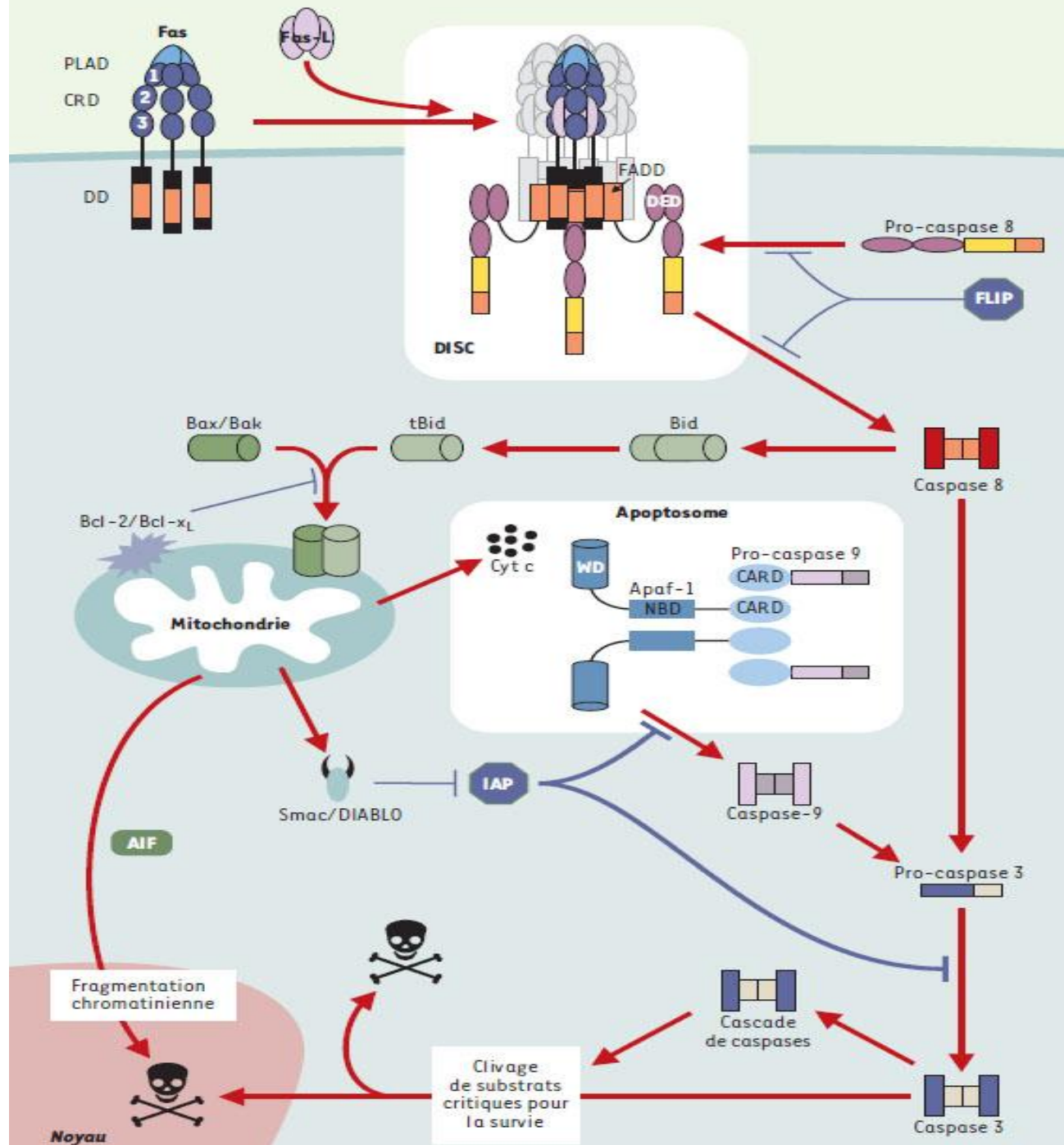


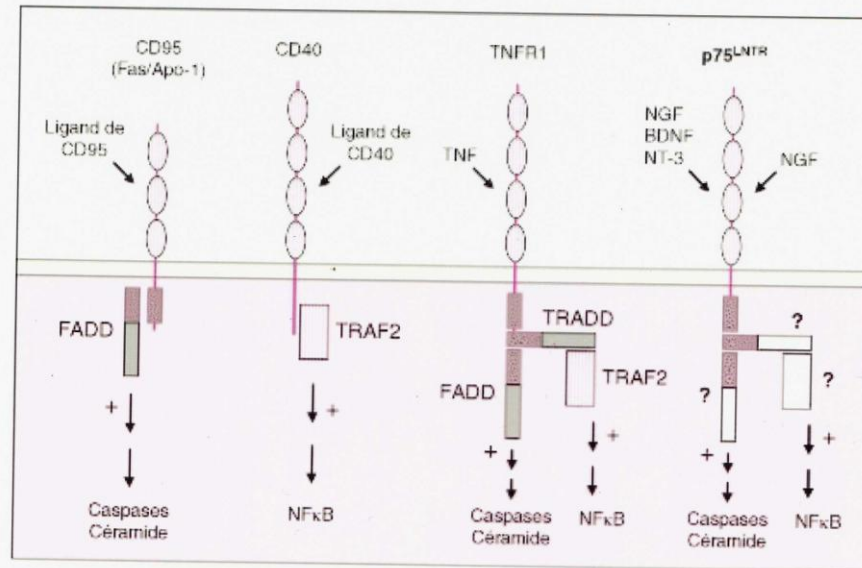
Le récepteur p75

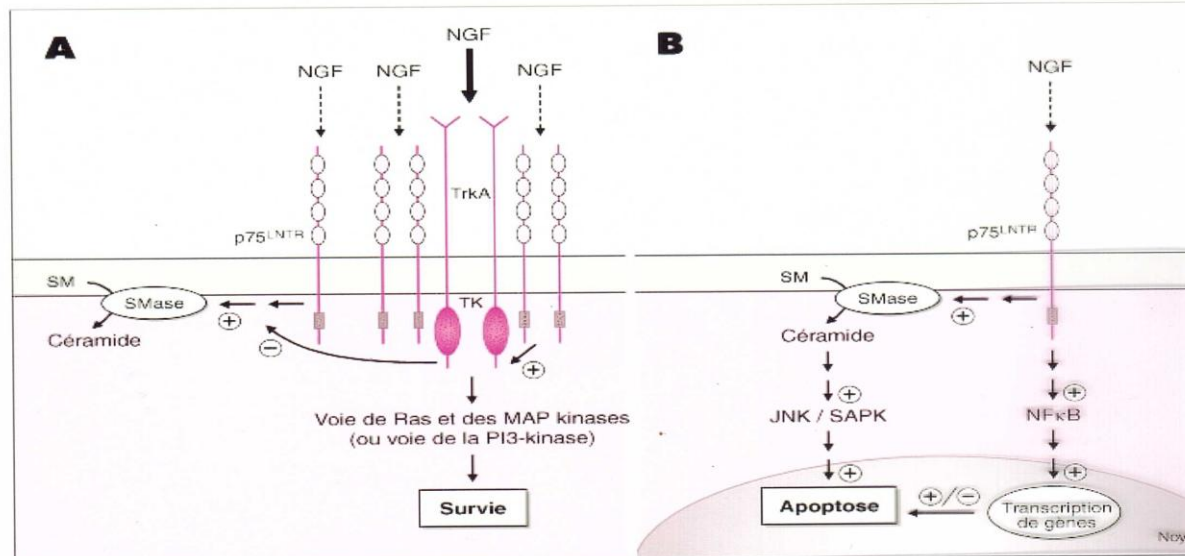
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- 2) p75 augmente la spécificité du NGF pour trkA vis-à-vis du NT3 par exemple.**
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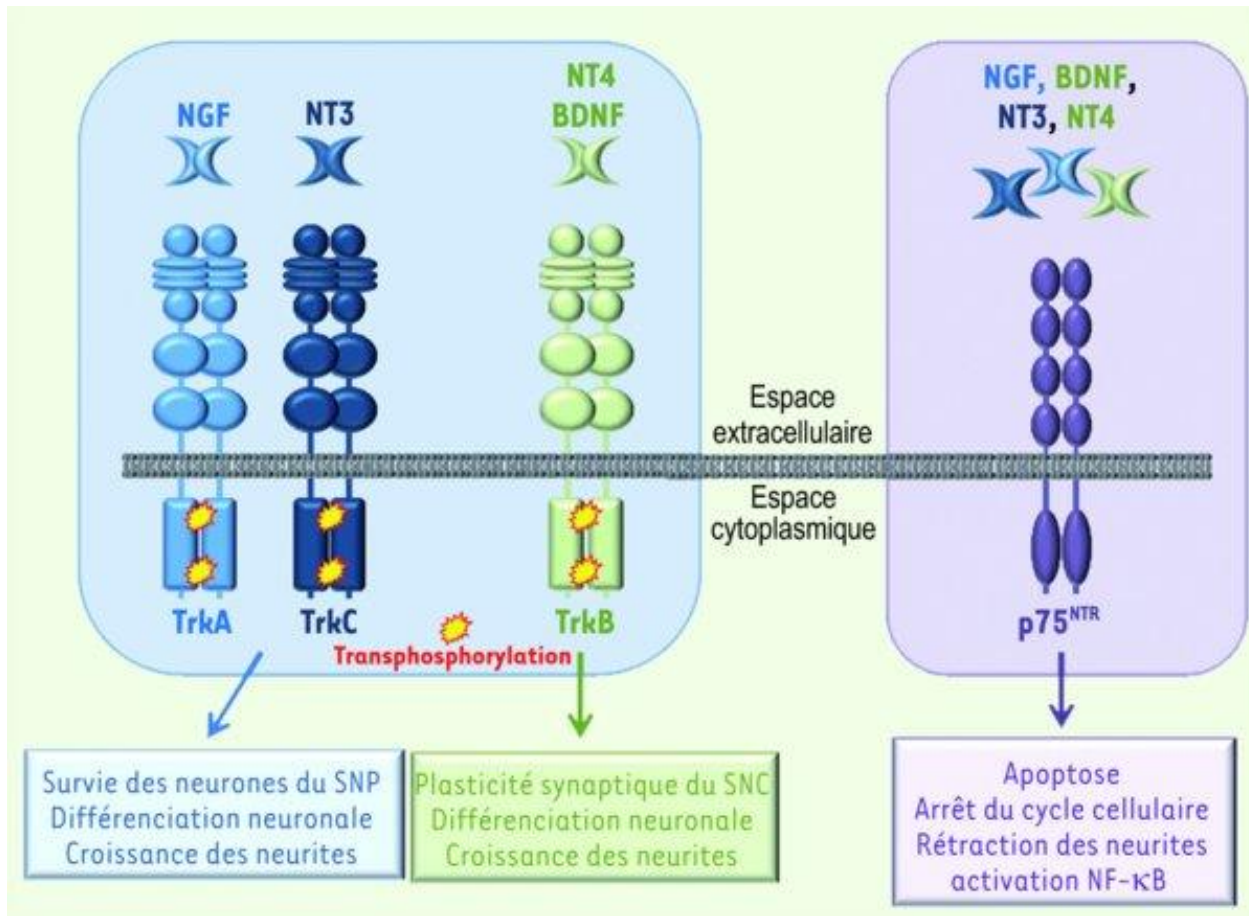


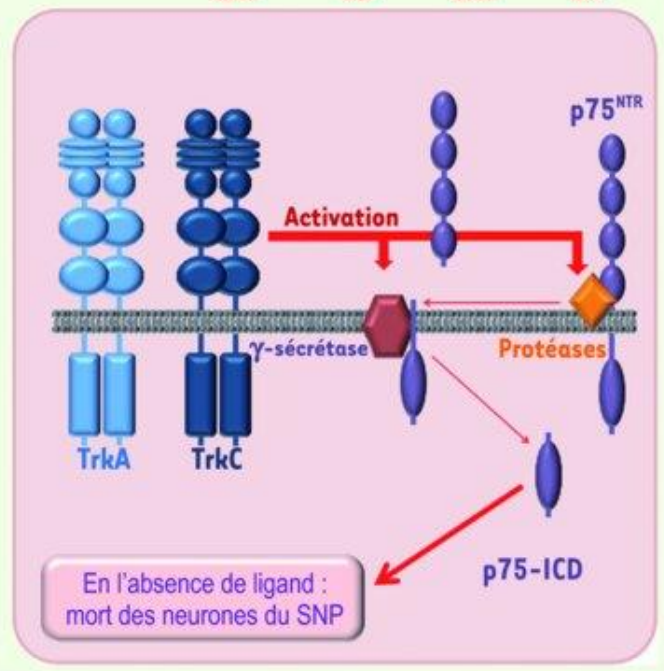
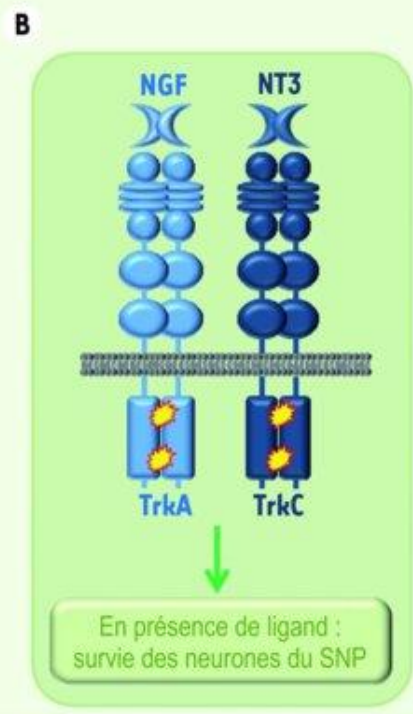
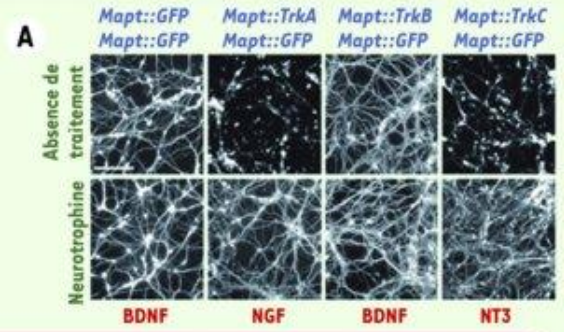
NGF	Trk	P75		EFFET	
++	++	++		++	Contrôle
++	-/-	++		-	
-/-	++	++		-	
++	++	-/-		+	
+++	++	-/-		++	
+++	++	++		+	
++++	++	+++		-	

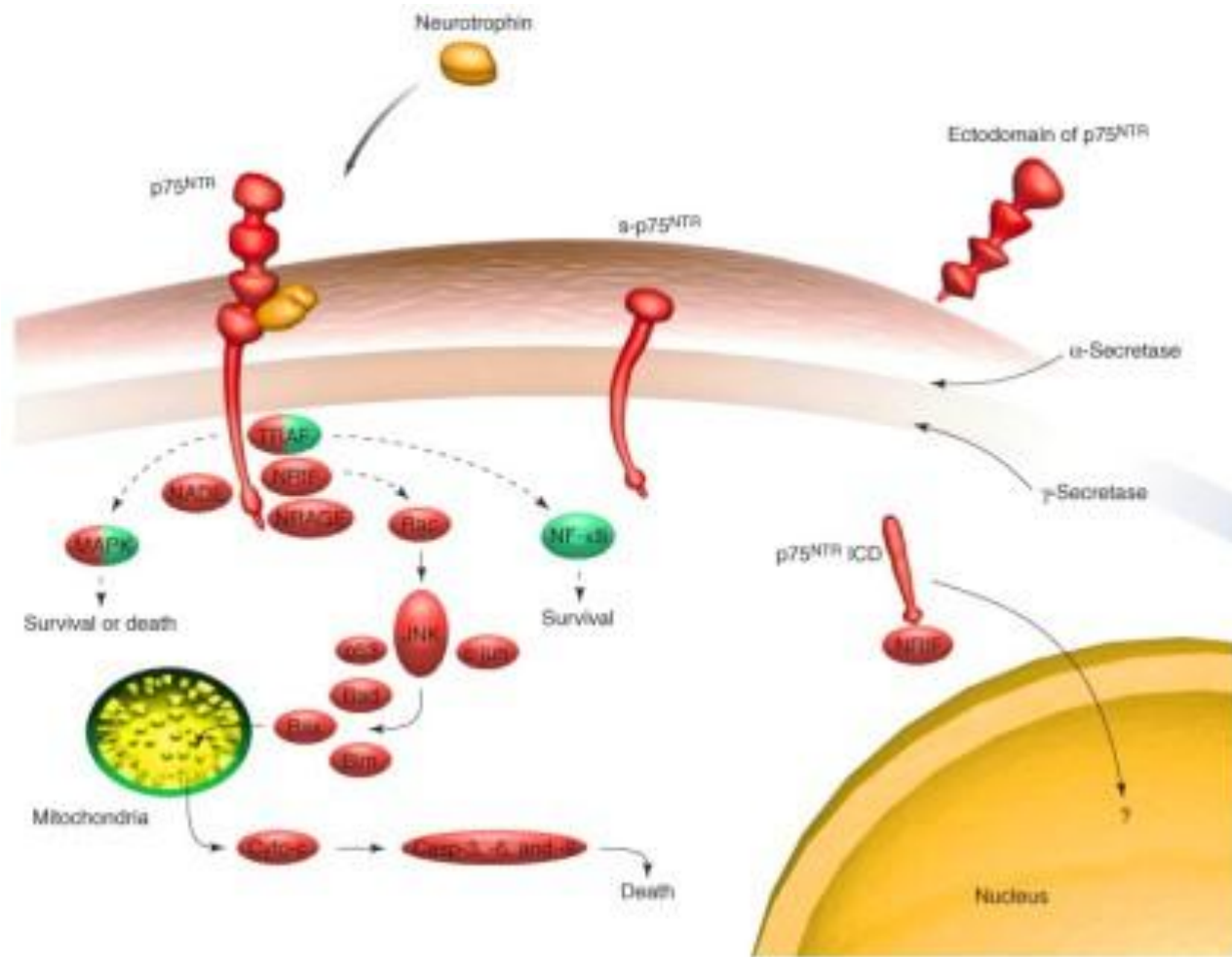


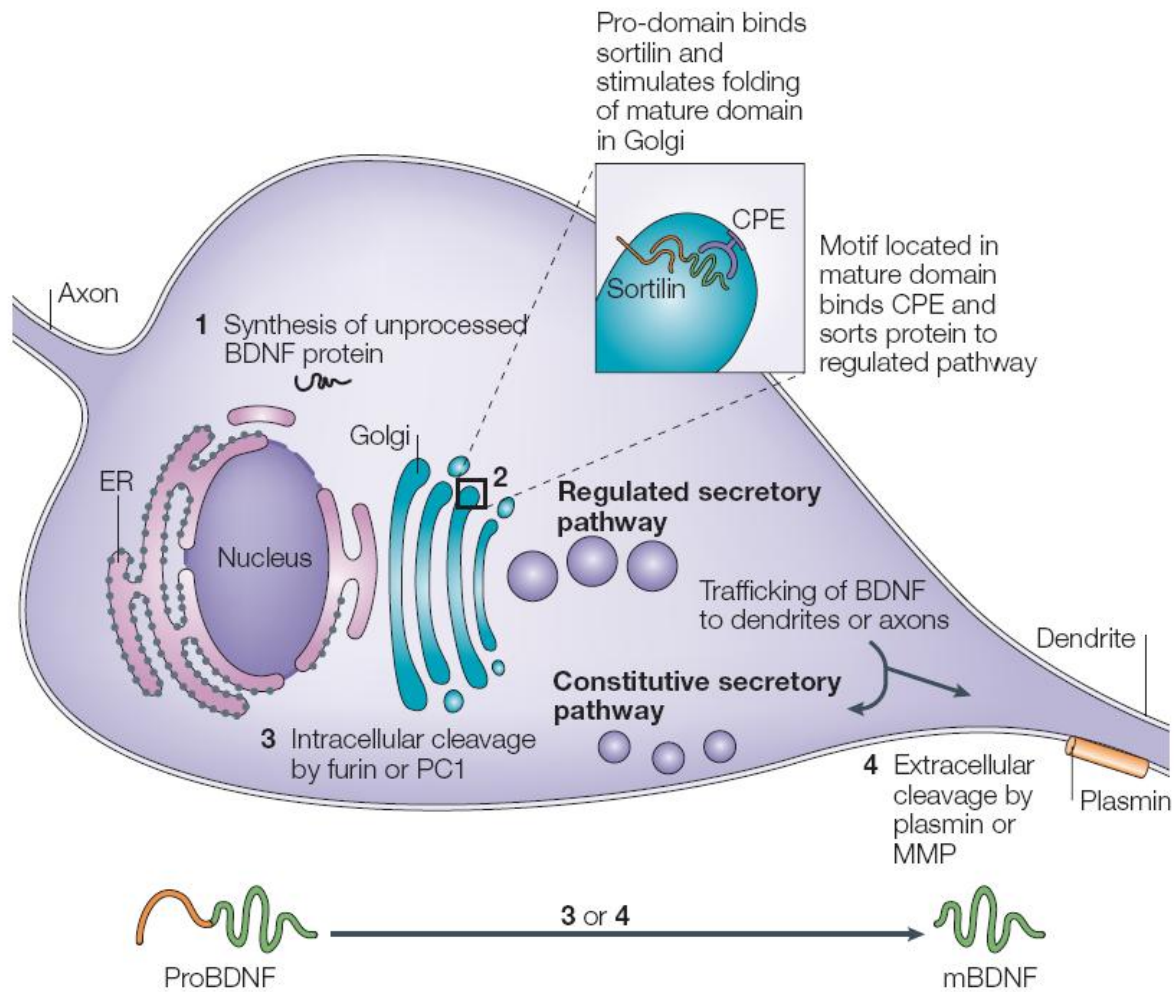


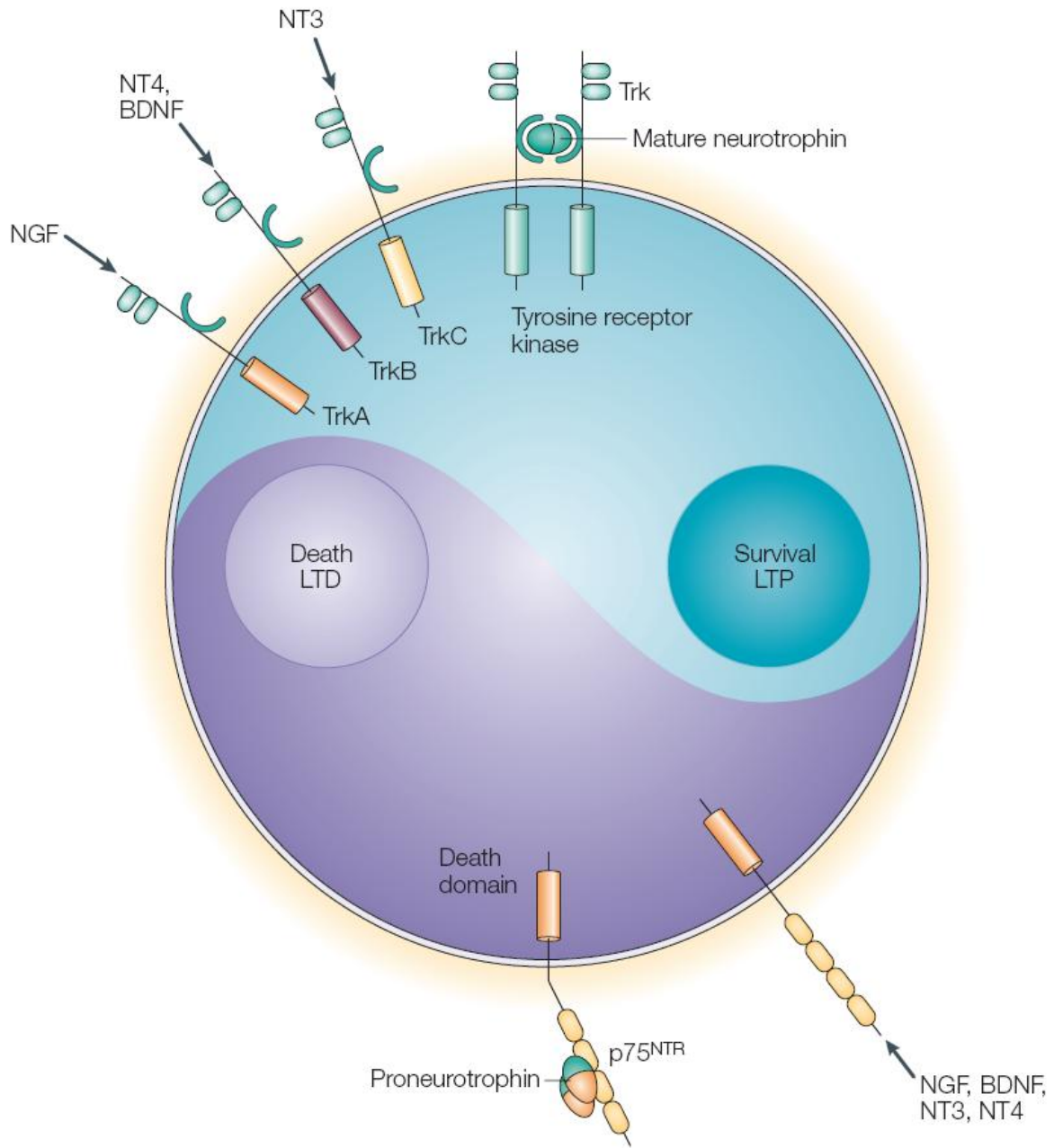




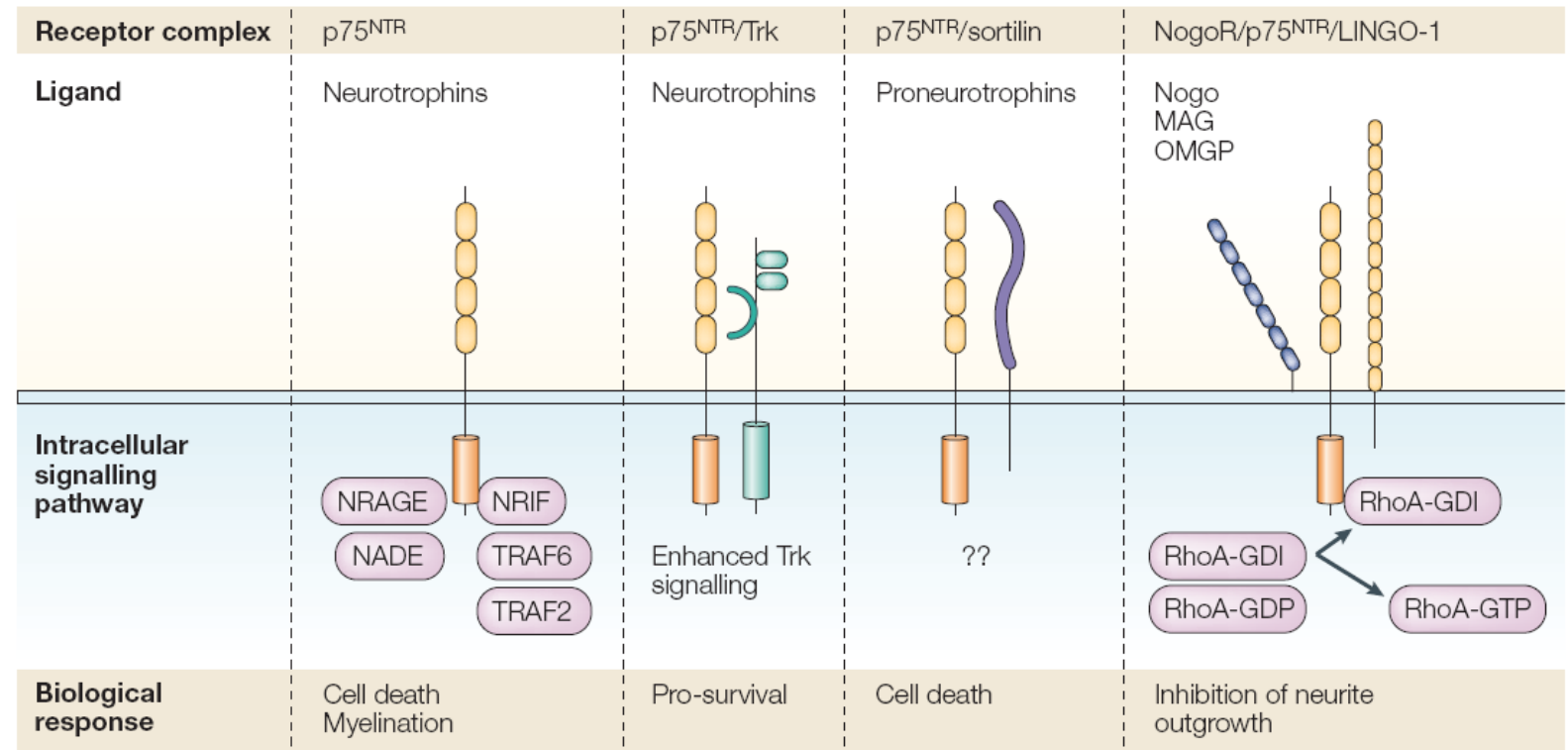


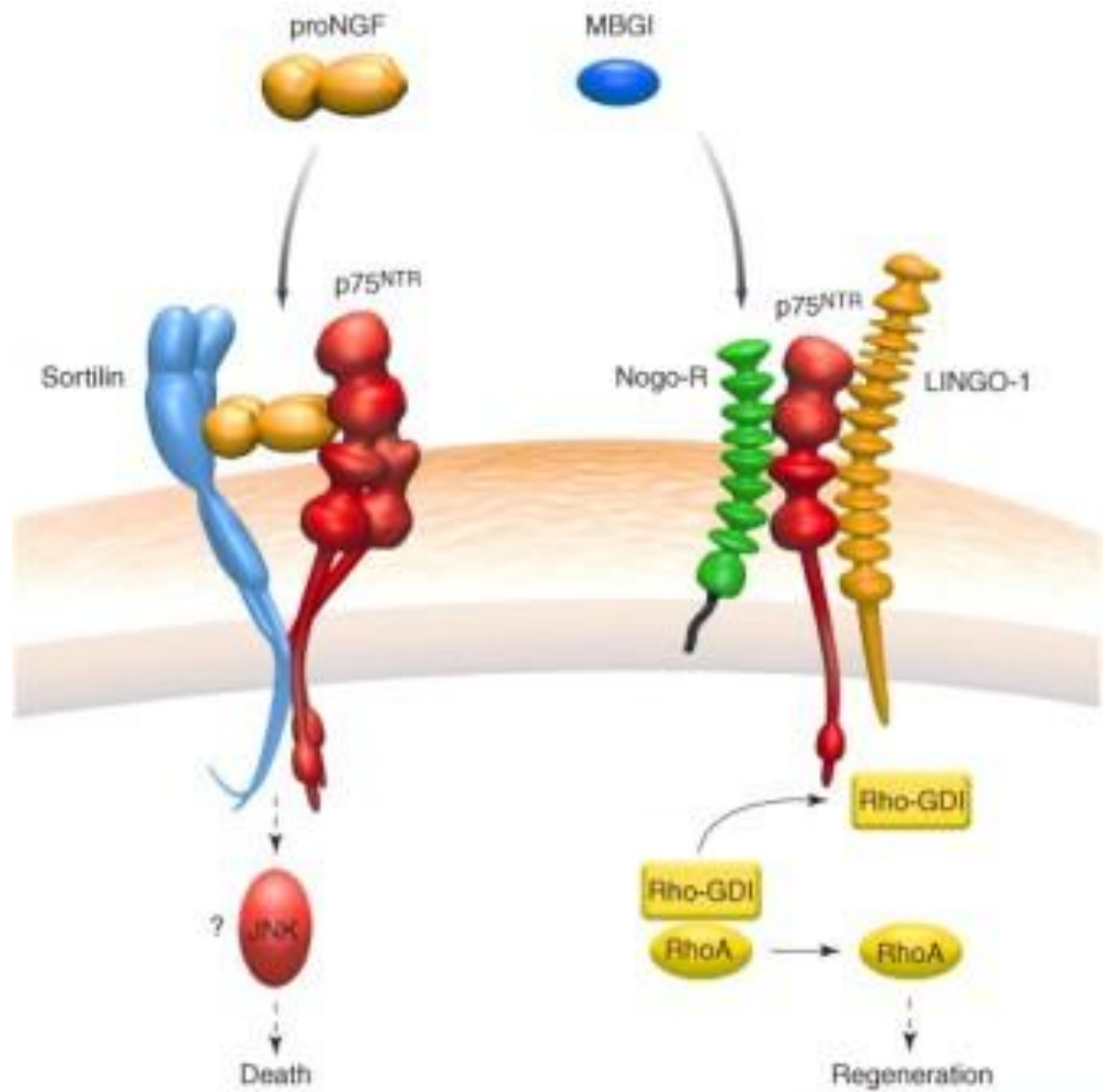






Box 1 | Multiple partners of p75^{NTR}





Récepteur	mNGF	proNGF
TrKA	Survie +	
p75/trkA	Survie +++	
P75	Apoptose +	Apoptose +++
P75/Sortiline		Apoptose +++

Table 1 | **Induction of p75 receptor expression after injury**

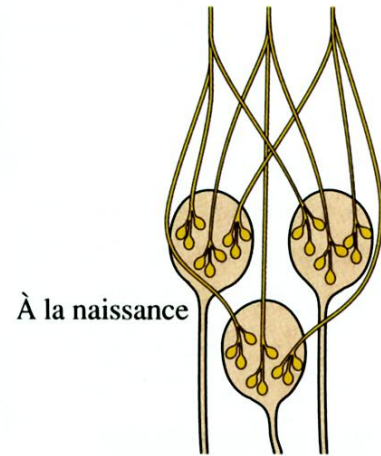
Cell type	Injury
Motor neurons	Axotomy, regeneration ¹³⁹⁻¹⁴¹
Purkinje neurons	Traumatic injury ¹⁴²
Entorhinal neurons	Seizure ⁴¹
Hippocampal neurons	Primary culture ¹⁴³
Striatal neurons	Ischaemia ¹⁴⁴
Cortical neurons	Zinc, ischaemia ¹⁴⁵ , Alzheimer's disease ¹⁴⁶
Schwann cells	Axotomy ^{147,148}
Oligodendrocytes	Spinal cord injury ⁴² , multiple sclerosis lesions ^{40,149}

p75 expression is also induced in experimental allergic encephalomyelitis^{150,151} and Alzheimer's disease¹⁵².

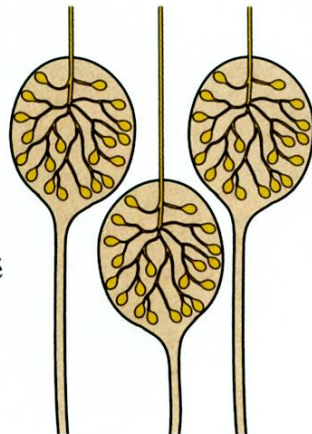
Propriétés neuronales régulées par les Neurotrophines

- Prolifération et survie des précurseurs (NT3)
- Mort cellulaire programmée
- Pousse axonale
- Synaptogenèse
- Différenciation (enzyme de synthèse, peptides, calcium binding protéin, etc...
- Efficacité et réarrangement synaptique
- Arborisation et réarrangement dendritique

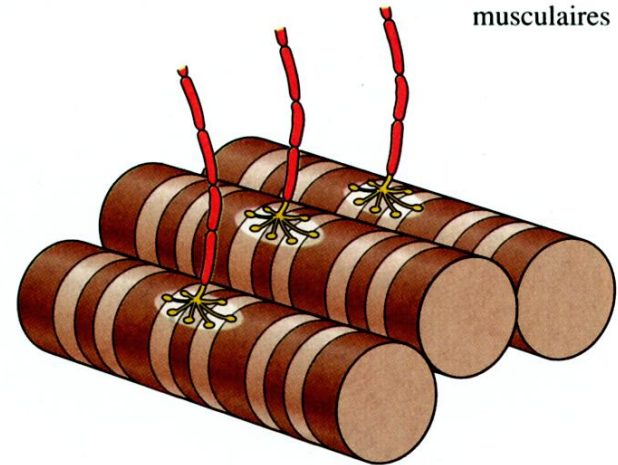
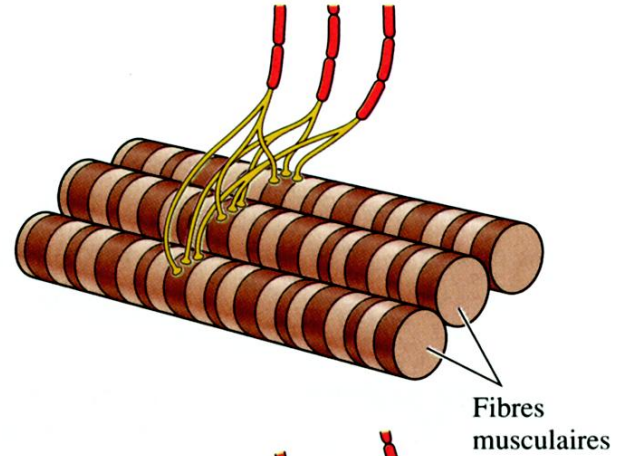
(A) Cellules ganglionnaires



À maturité



(B) Cellules musculaires



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