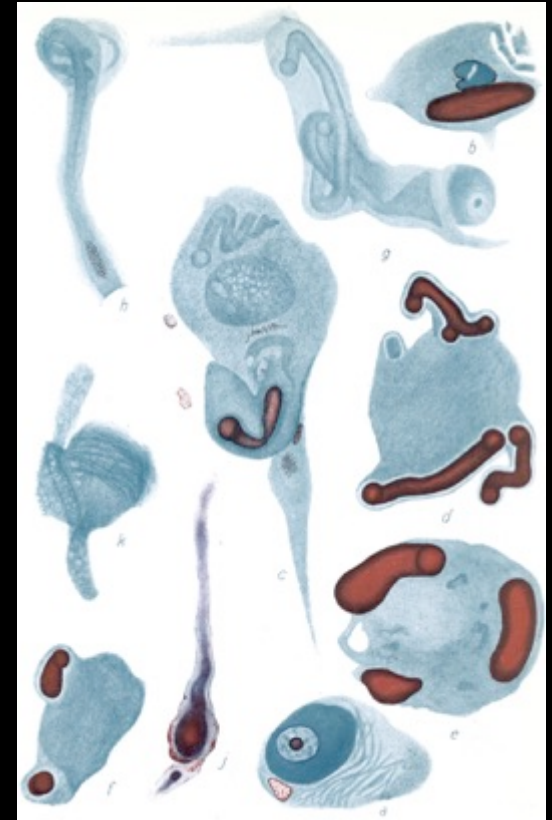


Tauopathie et synucléinopathie

Corps de Lewy



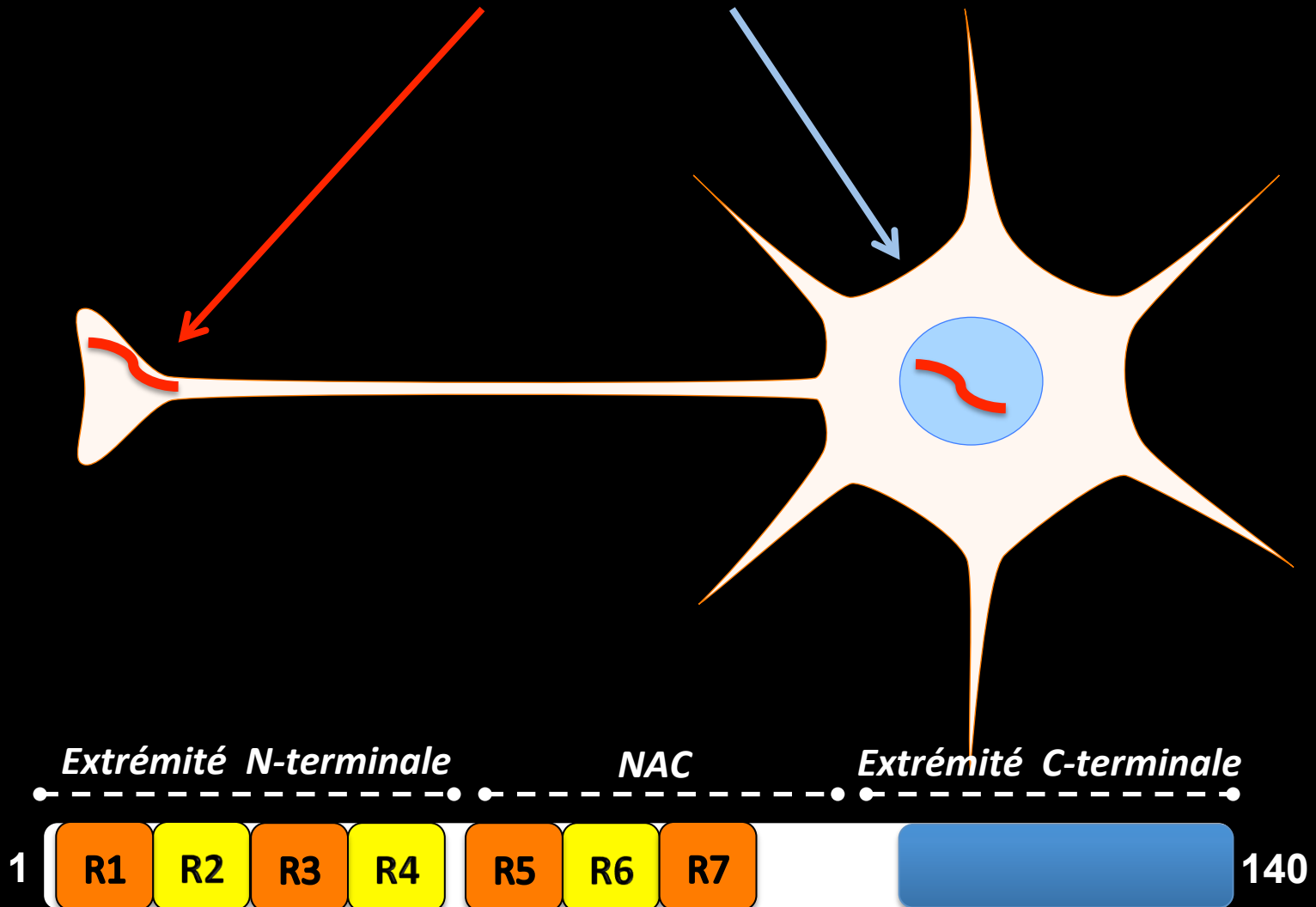
Members of Alois Alzheimer's research group at the Royal Psychiatric Clinic of the University of Munich, Germany in 1910



Lewy, F. H. Die Lehre vom Tonus und der Bewegung 1923

**Mais qu'il y a t-il dans les corps de
Lewy?**

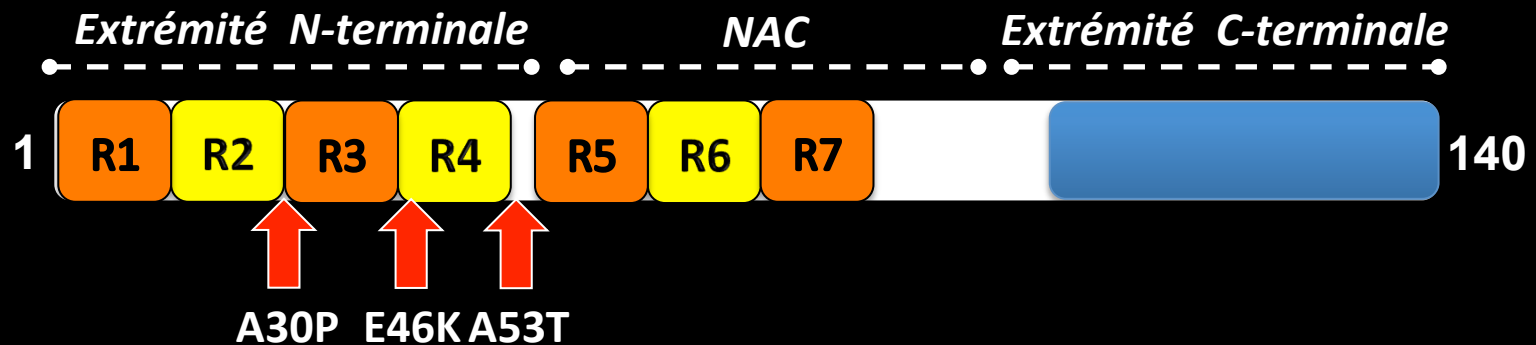
Alpha-synucléine: 1988



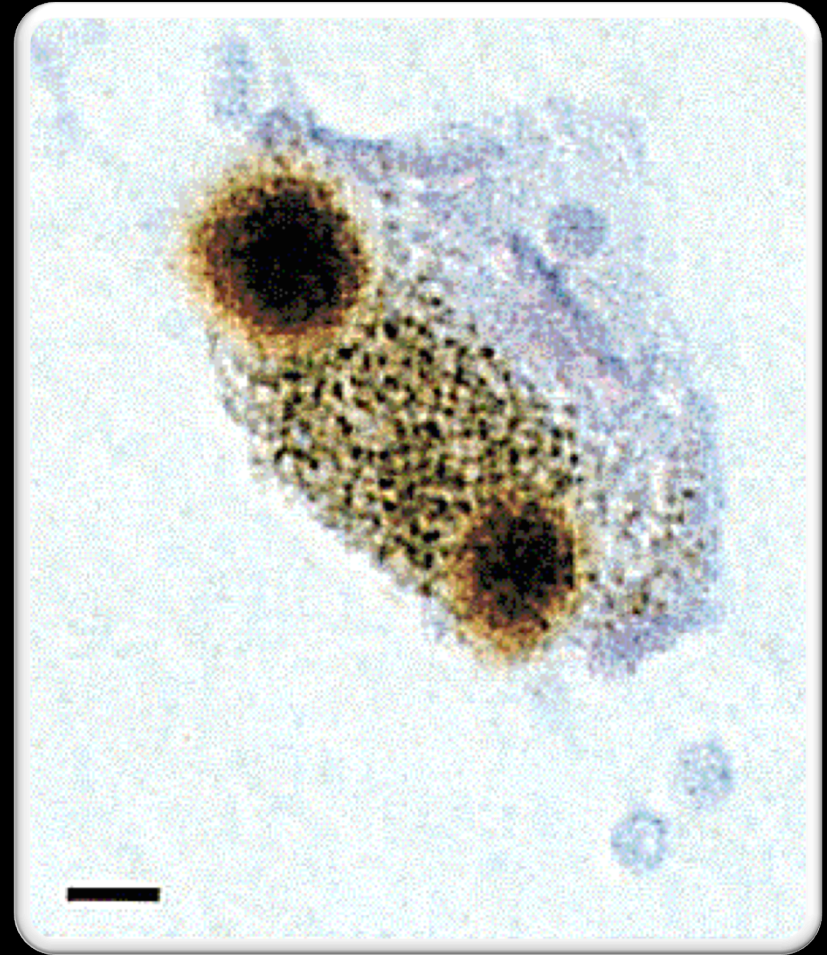
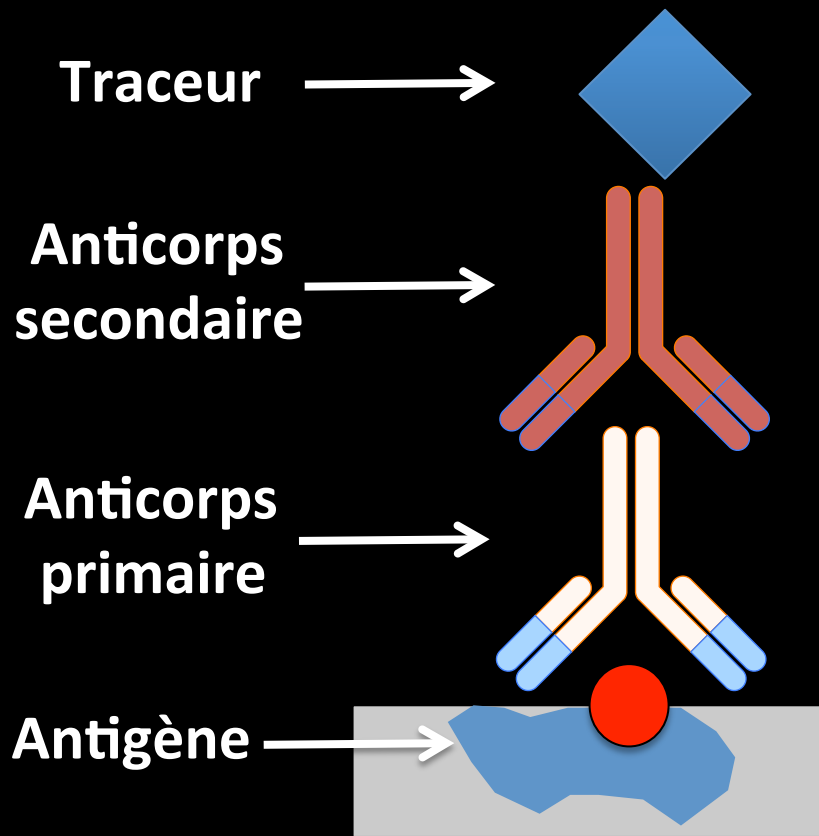
Alpha-synucléine: 1997

Mutation in the α -Synuclein Gene Identified in Families with Parkinson's Disease

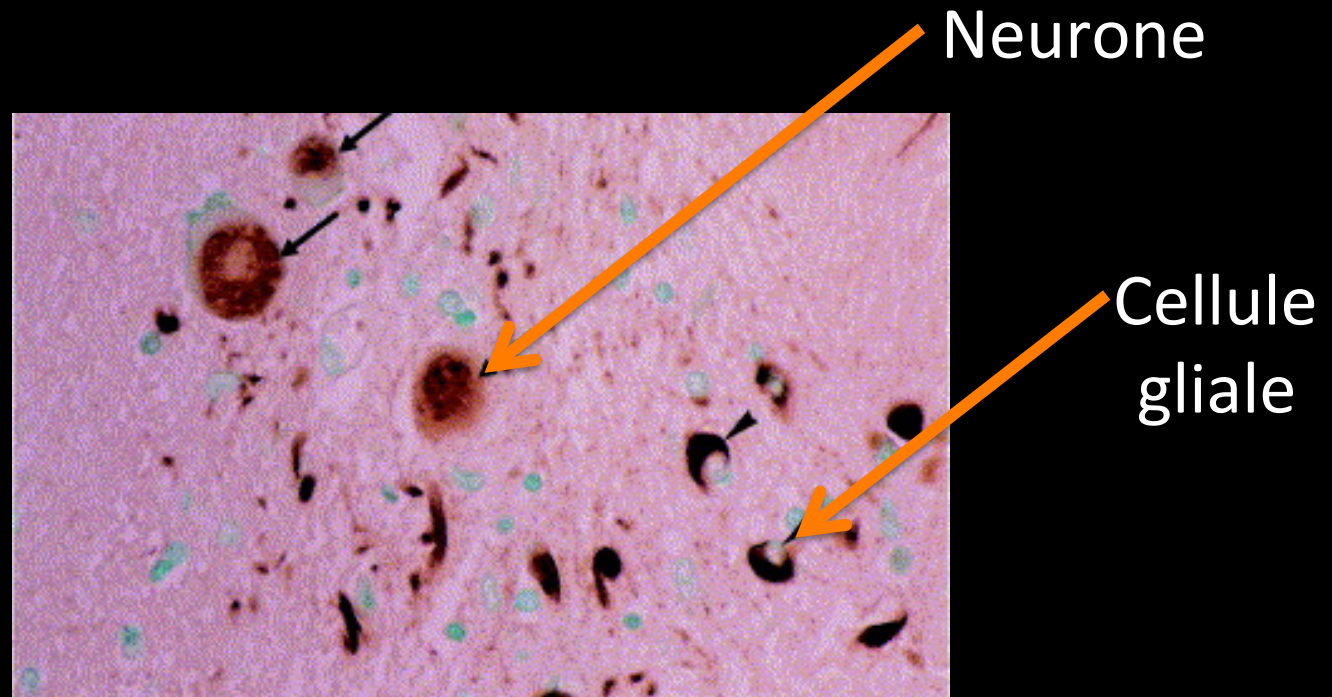
Polymeropoulos et al., Science 1997



Alpha-synucléine 1997, principal composant des corps de Lewy



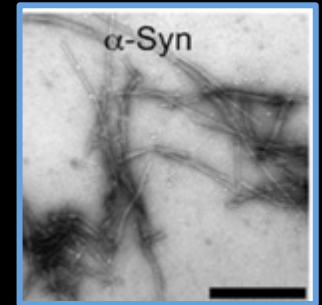
Les lésions d'AMS sont aussi positives pour l' α -synucléine



Synucleinopathies

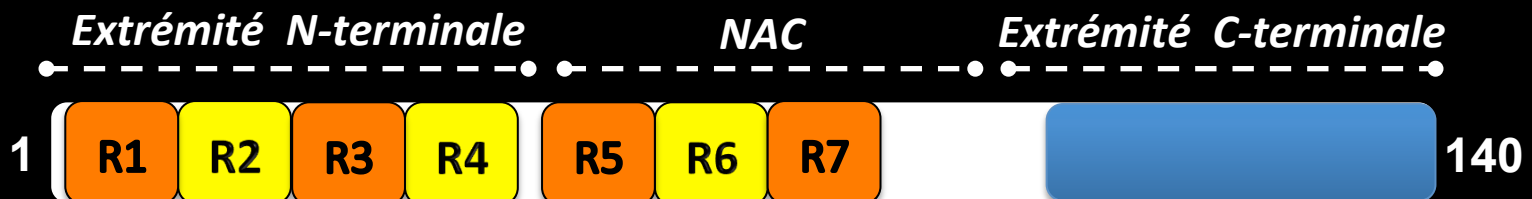
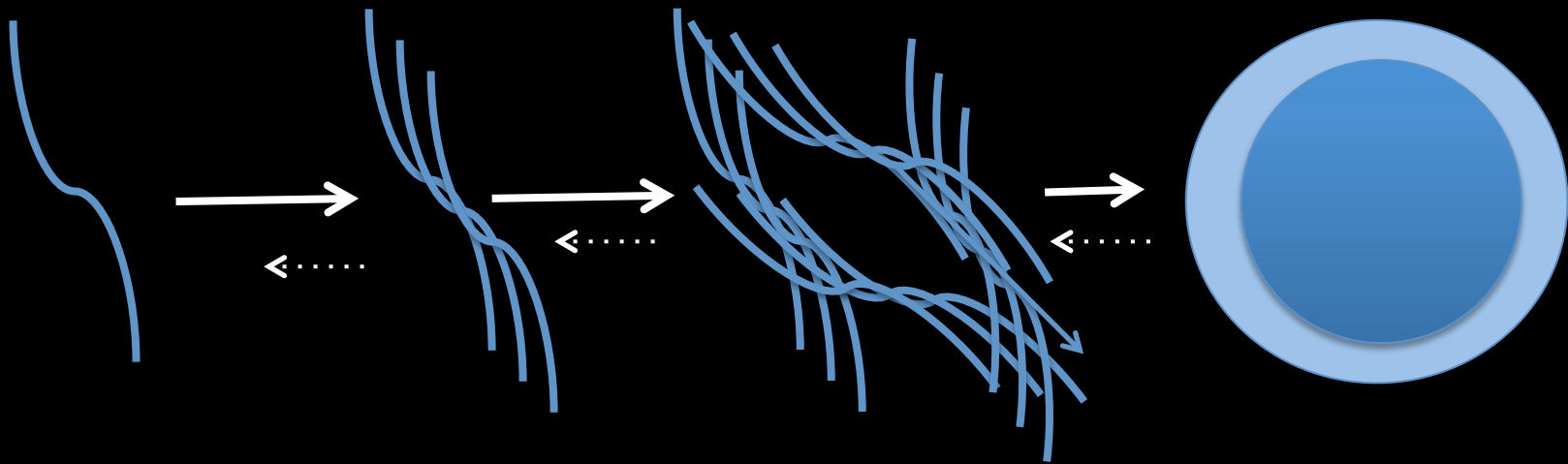
- Maladie de Parkinson
- Atrophie multi-systématisée
- Maladie à corps de Lewy diffus

Alpha-synucléine: une tendance naturelle à s'agréger



Winner et al. PNAS 2011

Monomère Oligomère Fibrille Corps de Lewy

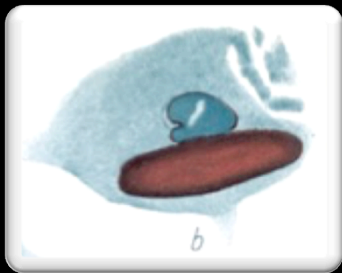


Progrès en neuropathologie pour la détection de la pathologie de Lewy

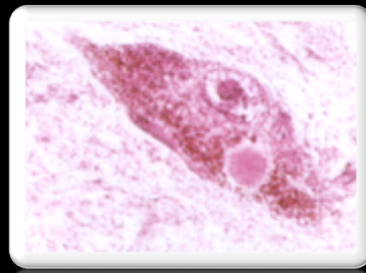
**Fritz Heinrich
Lewy**

1912

Histochemistry, Hematein/Eosin



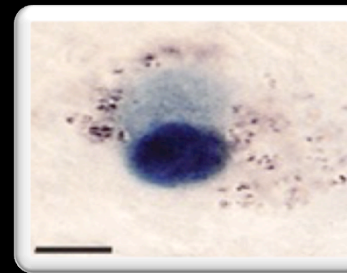
1988



**Spillantini and
Goedert**

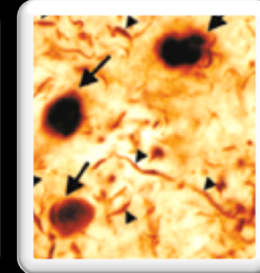
1997

Synuclein IHC



Fujiwara

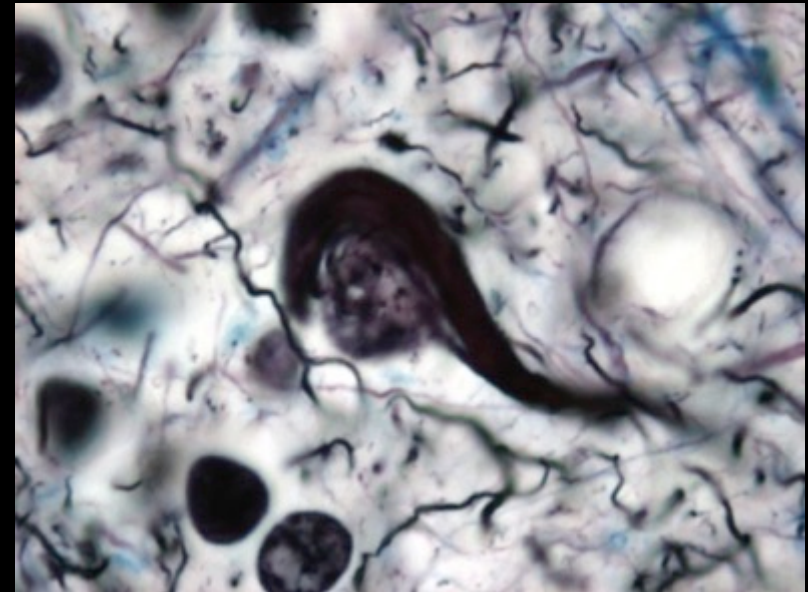
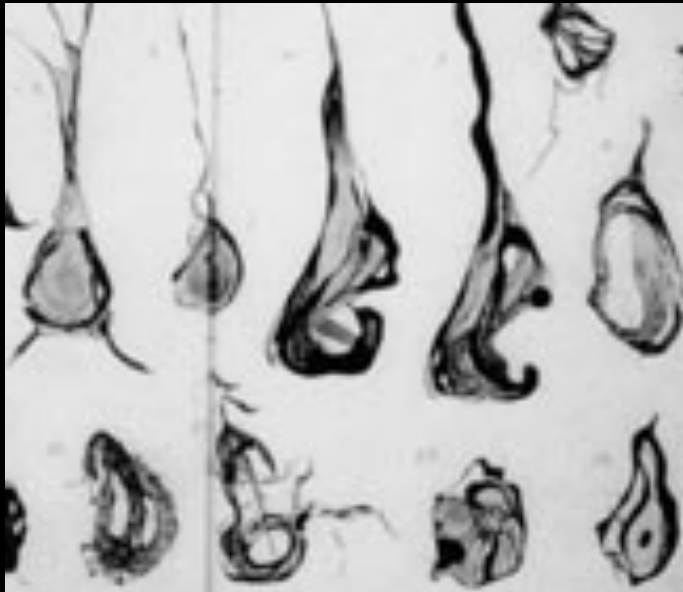
2002



Spillantini et al., PNAS 1997

Fujiwara et al., Nat Cell Biol 2002

Dégénérescence neurofibrillaire



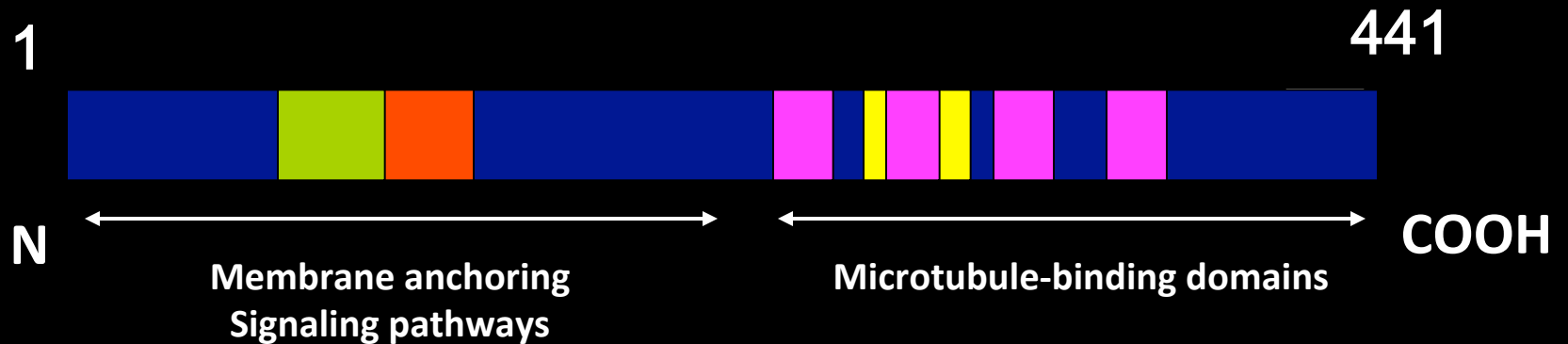
DNF, dessins originaux d'Alzheimer

Coloration argentique

Protéine tau

Tubulin-associated unit

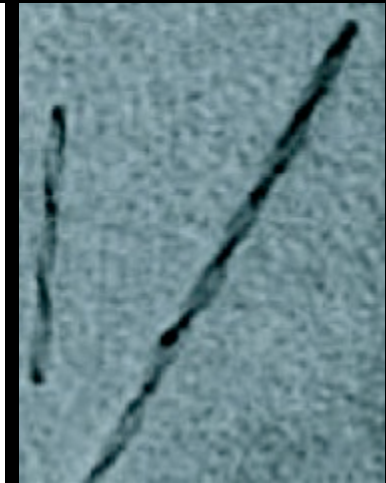
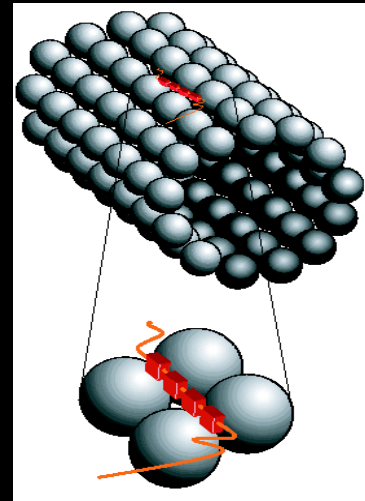
Microtubule-associated protein



Microtubule-binding domains

Protéine tau

- Une protéine associée aux microtubules
- 3 ou 4 domaines de liaison aux microtubules selon l'épissage alternatif de l'exon 10
- Région amyloïdogénique

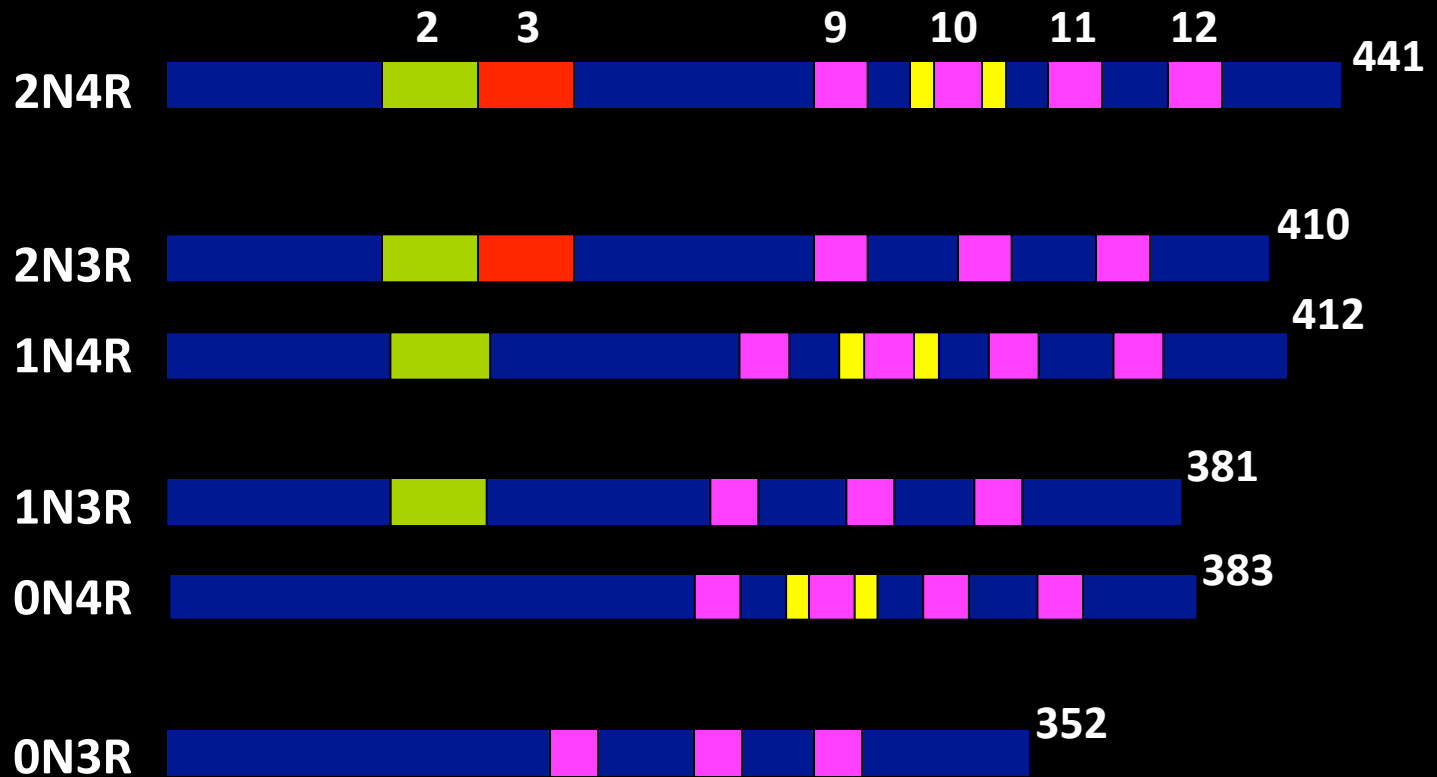


Isoforme	Exons	N	C	acides aminés
2N4R	2+3+10+			441
1N4R	2+3-10+			412
0N4R	2-3-10+			383
2N3R	2+3+10-			410
1N3R	2+3-10-			381
0N3R	2-3-10-			352

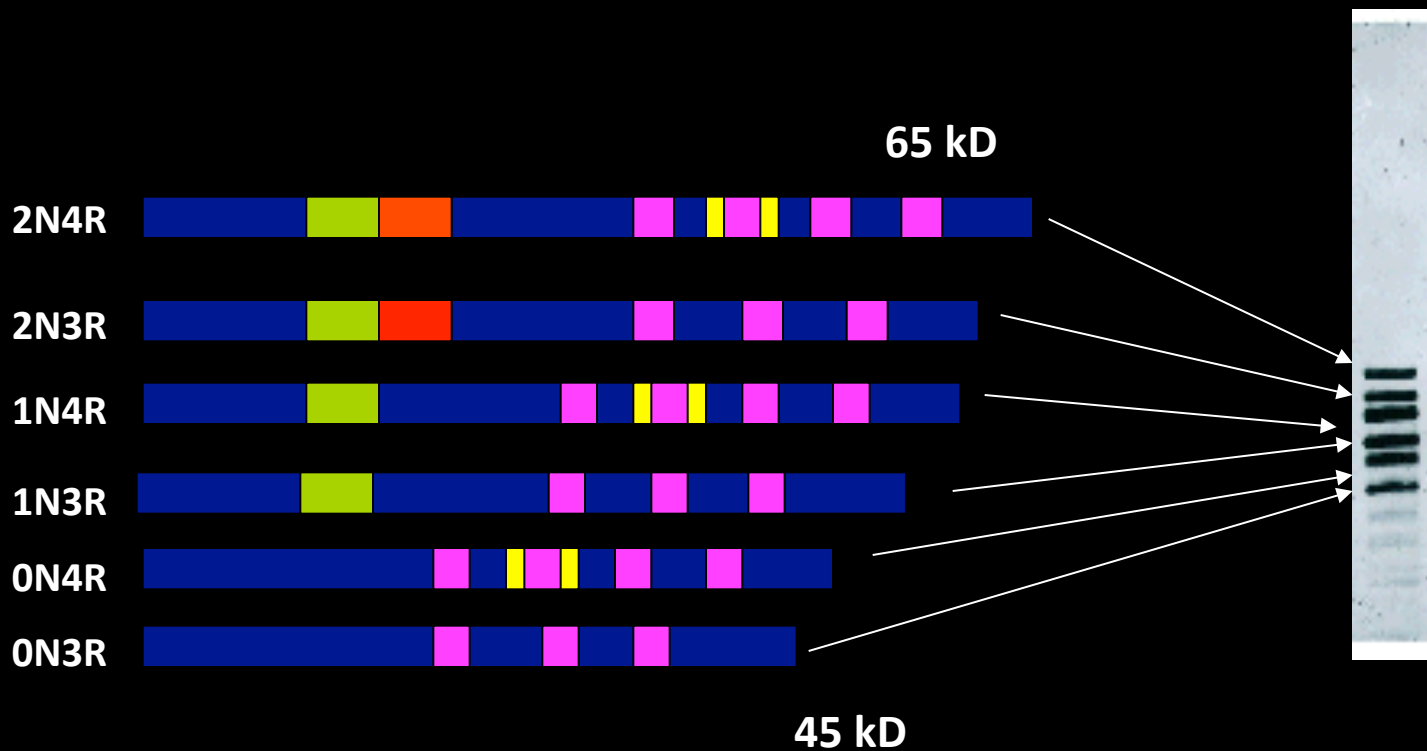
Tau 4R

Tau 3R

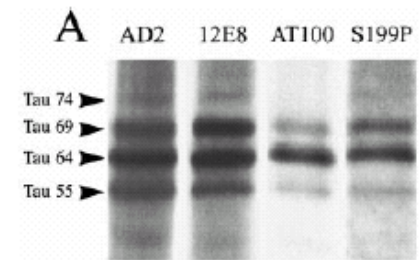
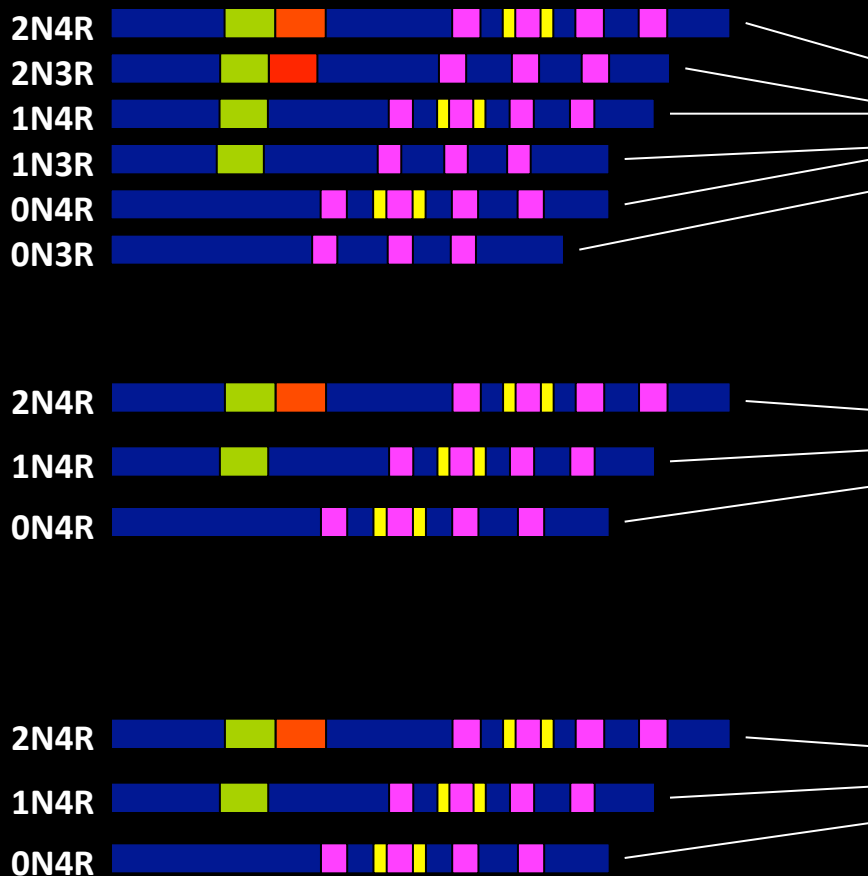
Isoformes de la protéine tau



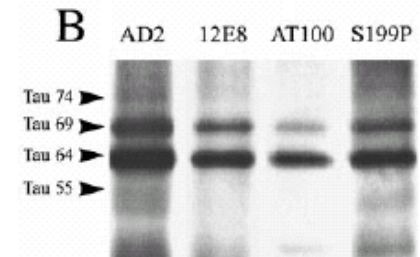
Profil électrophorétique des isoformes de la protéine tau



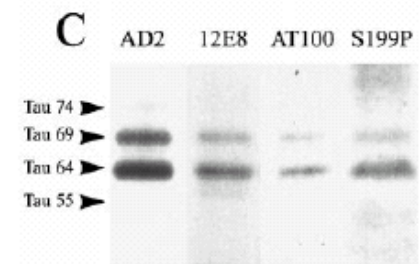
Un profil spécifique pour chaque tauopathie



AD



CBD



PSP

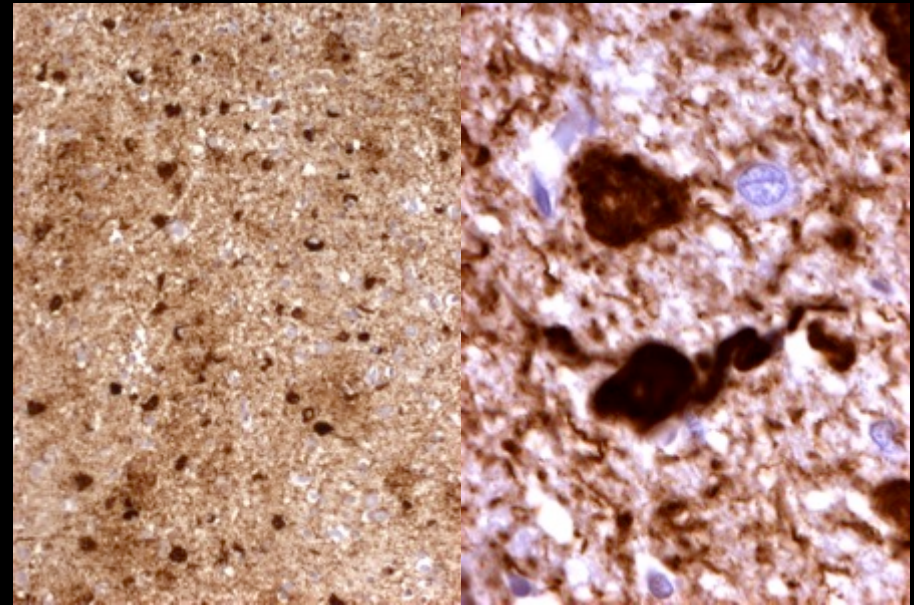
Tauopathies

- **Taupathies 3R**
 - Maladie de Pick
- **Taupathies 4R**
 - Paralyse supranucléaire progressive (PSP)
 - Dégénérescence cortico-basale (DCB)
- **Taupathies mixtes**
 - Maladie d'Alzheimer
- **DLFT-17** (3R, 4R ou mixtes)

Protéine tau et taupathies

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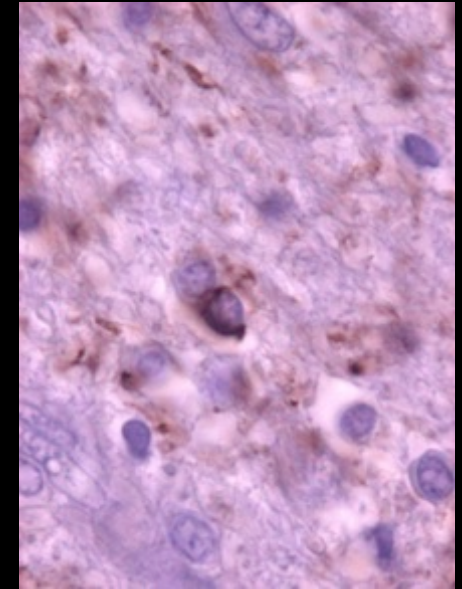
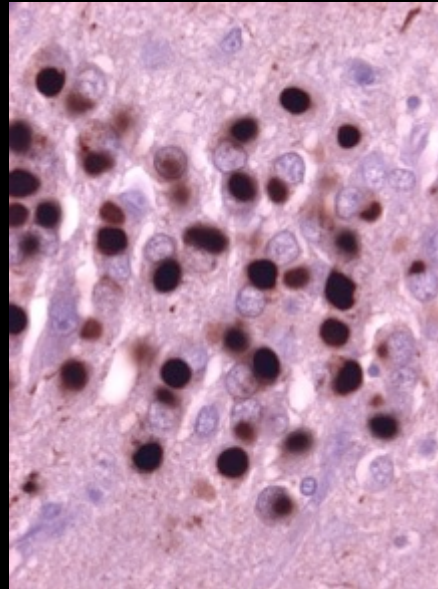


Dégénérescences neurofibrillaires isocorticales dans la maladie d'Alzheimer

Protéine tau et taupathies

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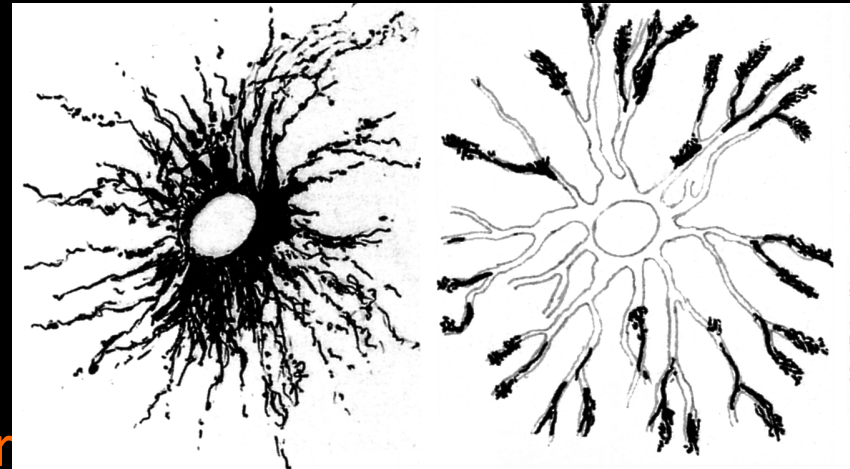


Corps de Pick du gyrus dentelé et corps bobinés (coiled threads) dans la maladie de Pick

Protéine tau et taupathies

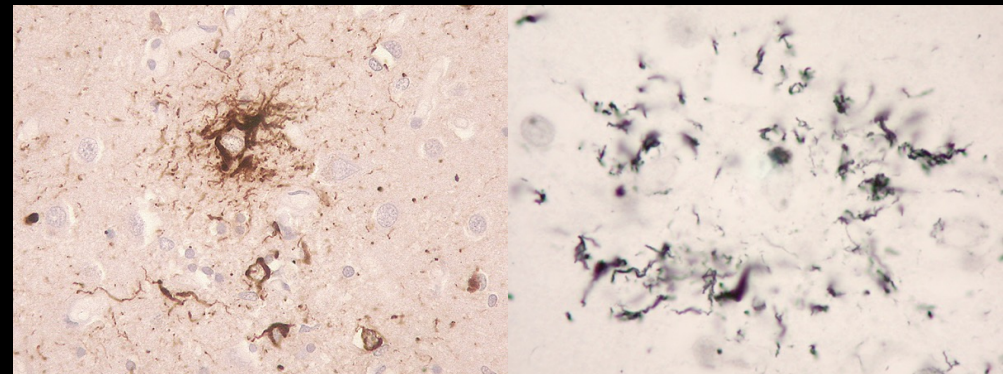
Taupathies

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- **DLFT-17 (3R, 4R ou mixtes)**



PSP

DCB



Touffe gliale (tufted astrocyte) dans la PSP

Plaque astrocytaire (astrocytic plaque) dans la DCB

Lien direct entre tau et pathologie neurodégénérative

Proc. Natl. Acad. Sci. USA
Vol. 95, pp. 13103–13107, October 1998
Genetics

Pathogenic implications of mutations in the tau gene in pallido-ponto-nigral degeneration and related neurodegenerative disorders linked to chromosome 17

(frontotemporal dementia and Parkinsonism/tauopathies/glia and neuronal tangles/microtubule associated proteins/Alzheimer's disease)

LORRAINE N. CLARK^{a,b}, PARVONEH POORKAJ^{b,c,d}, ZBIGNIEW WSZOLEK^e, DANIEL H. GESCHWIND^f, ZIAD S. NASREDDINE^g, BRUCE MILLER^{b,f}, DIANE LI^f, HAYDEH PAYAMI^b, FRE AWERTⁱ, KATERINA MARKOPOULOU^e, ATHENA ANDREADIS^l, IAN D'SOUZA^{c,d}, VIRGINIA M.-Y. LEE^k, LEE REED^k, JOHN Q. TROJANOWSKI^k, VICTORIA ZHUKAREVA^k, THOMAS BIRD^{c,l}, GERARD SCHELLENBERG^{b,c,d,l,m}, AND KIRK C. WILHELMSSEN^{a,b,n}

- Frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17)
 - Démence comportementale
 - Atrophie fronto-temporale
 - Agrégats intraneuronaux ou intragliaux de protéine tau

Un rôle dans la diffusion de la pathologie

