



# Société Francophone de Psychogériatrie et de Psychiatrie de la Personne Âgée

6 et 7  
JUN 2024  
MONTPELLIER

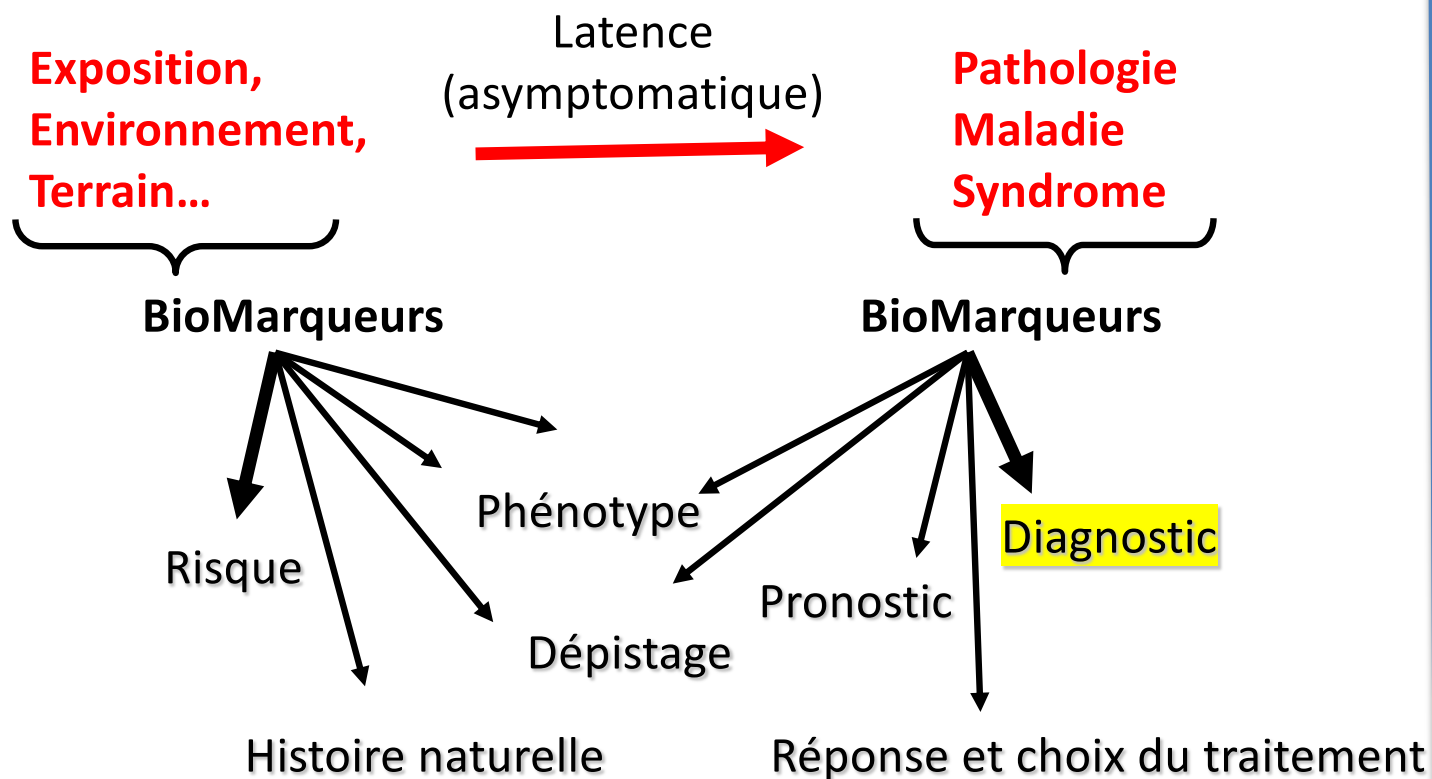


## Biomarqueurs de Troubles Neuro Cognitifs (TNC) en psychiatrie

Sylvain LEHMANN  
(INM/CHU, Montpellier)



## Place des biomarqueurs en médecine



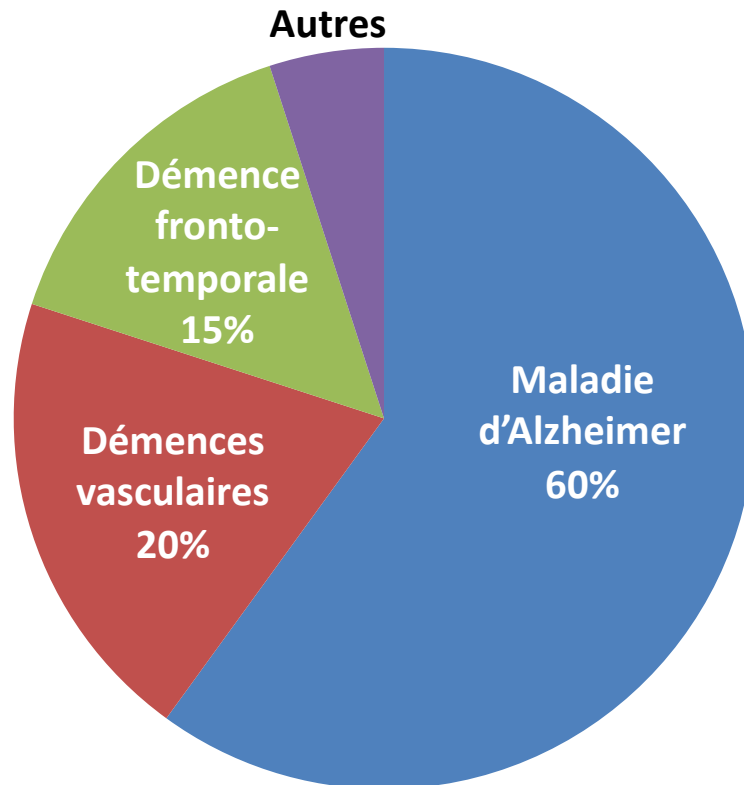
Différents types de biomarqueurs : MMSE, température, protéines dans les fluides biologiques, imagerie...

### Origine des biomarqueurs

- Impliqués dans les mécanismes pathologiques
- Biomarqueurs témoins / de substitution
- Liés à l'environnement / aux facteurs de risque
- Retour à l'homéostasie

## Etiologies des Troubles Neuro Cognitifs (TNC)

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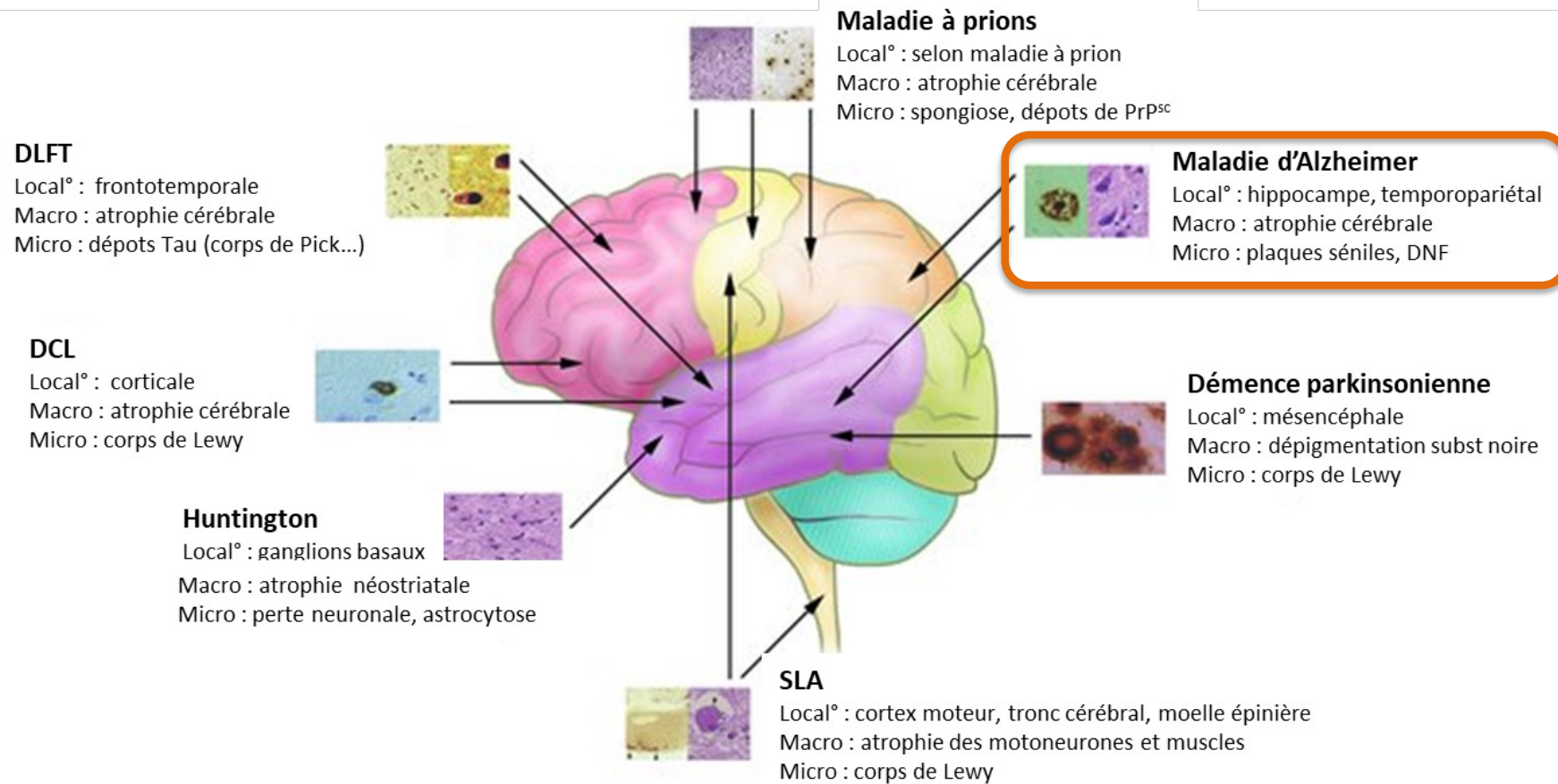


### Autres :

- Démence à corps de Lewy
- Démences Parkinsoniennes
- Hydrocéphalie à pression normale
- Infectieuses (VIH, Syphilis, ...)
- Maladie de Creutzfeldt-Jakob
- Huntington
- ...

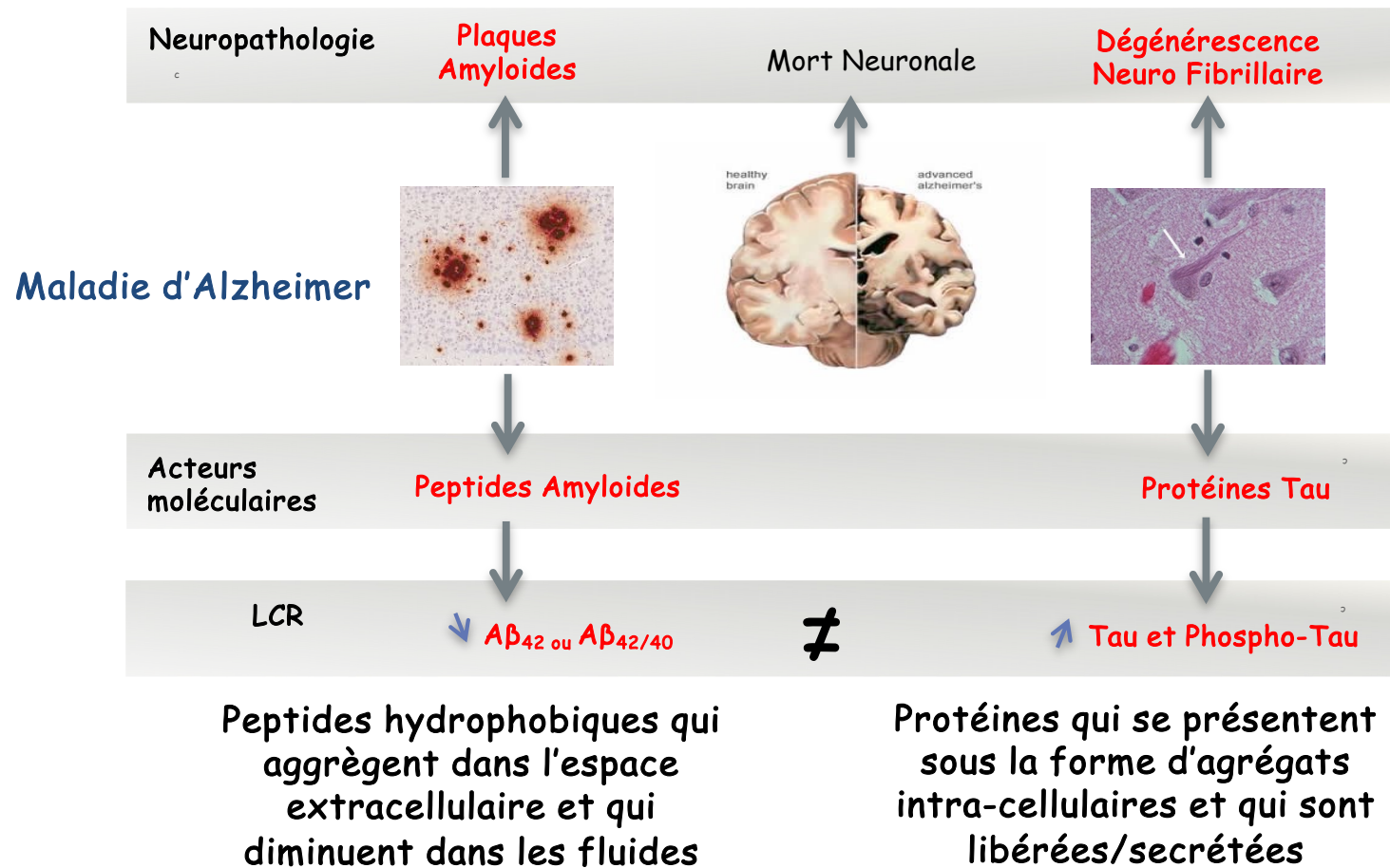
Centre Mémoire Lille - Bailleul (1992-2001) (n=4212)

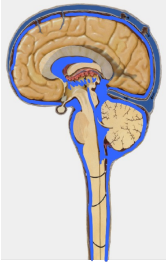
# Maladies neurodégénératives



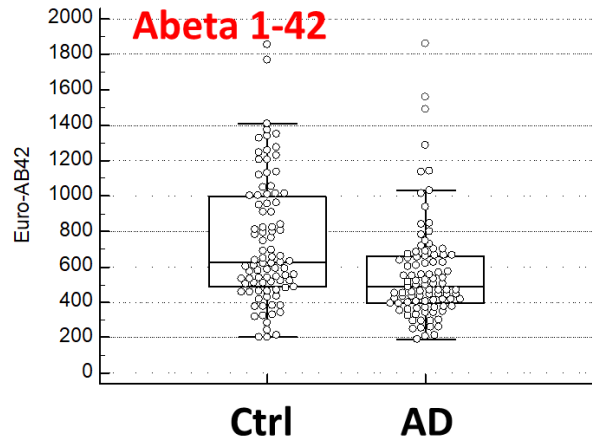
Adapté de Bertram and RE Tanzi, Fig 3  
The Journal of Clinical Investigation, 115(6): 1449-1457,2005.

## Marqueurs amyloïdes et tau: Alzheimer

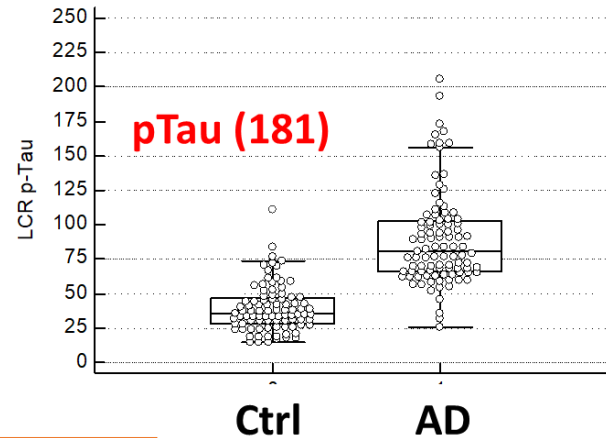




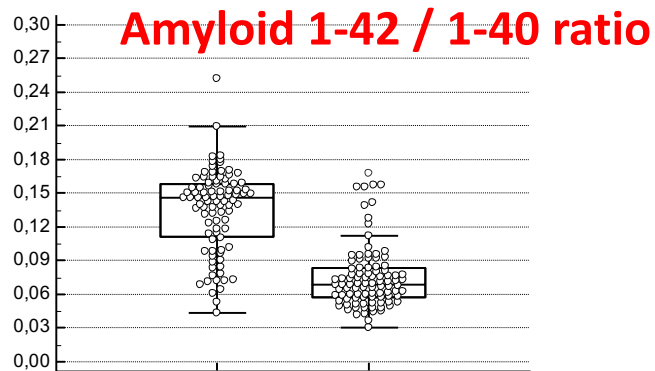
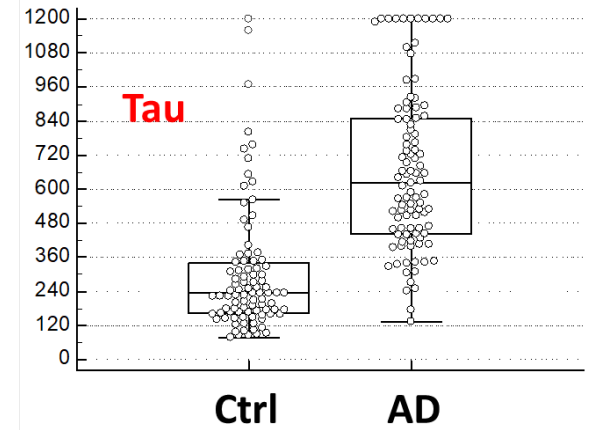
## Marqueurs amyloïdes et tau: Alzheimer



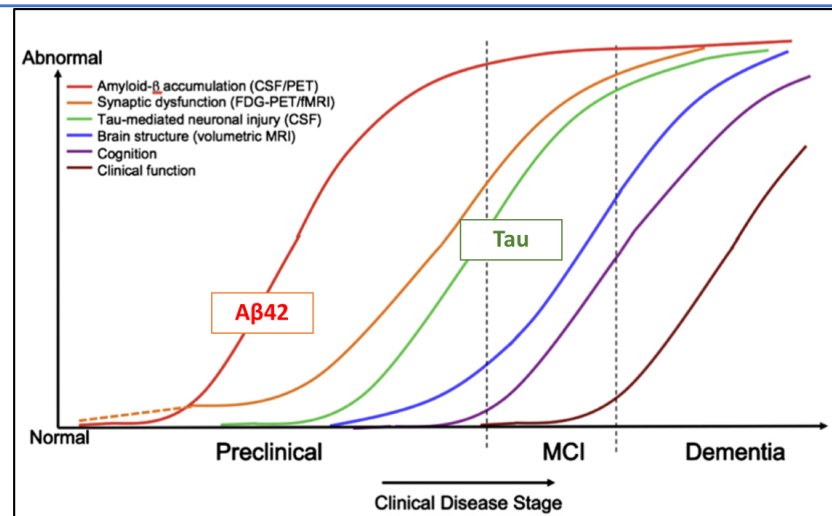
Decrease Aβ42 peptide : < 500 ou 700 ng/L



Increase Tau > 400 ng/L et p-Tau 181 > 60 ng/L



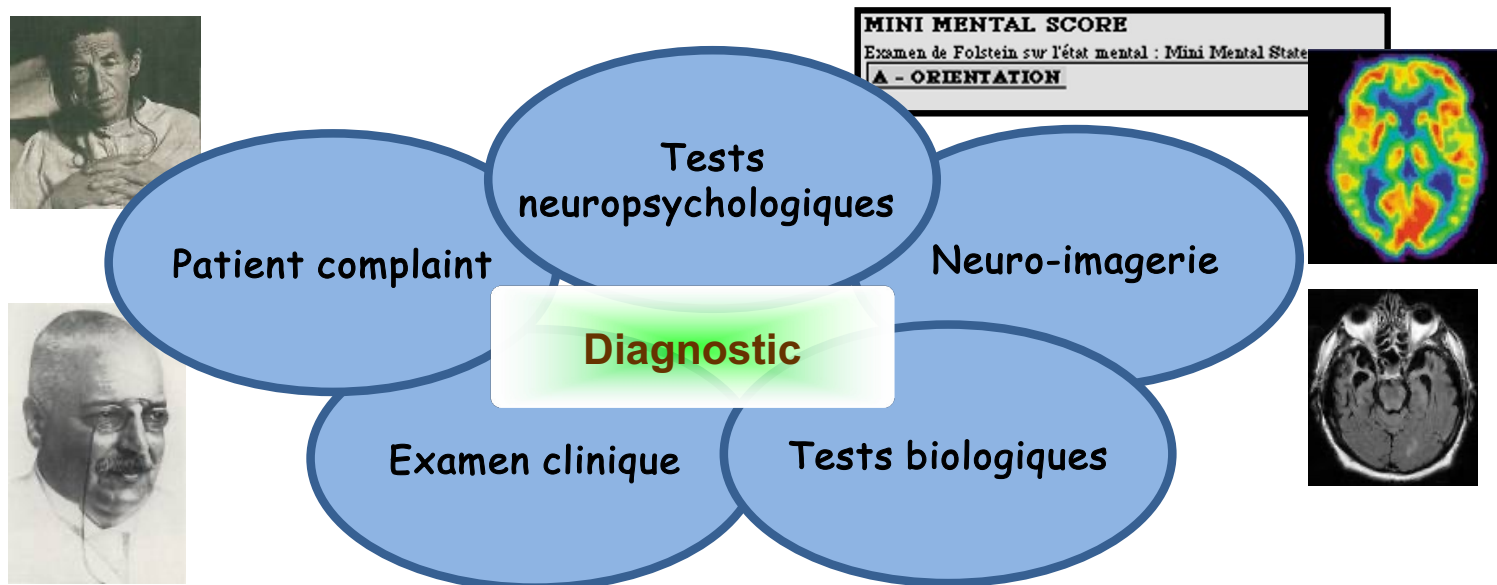
Ratio in CSF: < 0.1



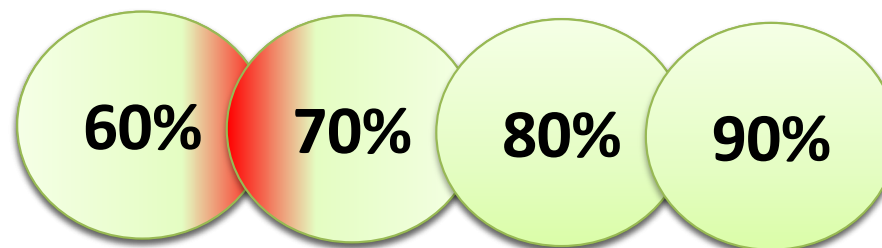
Sperling et al, 2011

Data and figures:  
CHU of Montpellier.

## Diagnostic de la maladie d'Alzheimer



Que pensez-vous de la précision  
du diagnostic de la maladie  
d'Alzheimer ?



## Diagnosis of Alzheimer's disease

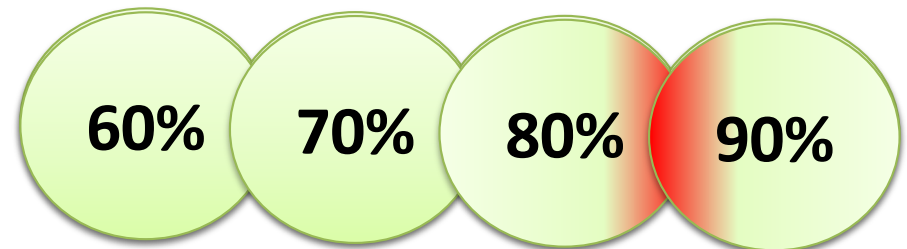
Published in The Medical clinics of North America 2013

### International Work Group criteria for the diagnosis of Alzheimer disease.

→ Marqueur A $\beta$  (LCR ou TEP) et marqueur tau (LCR ou TEP)

Table 1 Diagnosis recognized by the IWG criteria		
Disorder	Clinical Manifestations	Biomarker Required
AD risk state	None	Biomarker consistent with AD
Preclinical AD	None	Autosomal-dominant mutation causative of AD
Prodromal AD	Episodic memory loss or recognized atypical presentation; preserved ADL	Biomarker consistent with AD
AD dementia	Episodic memory loss or recognized atypical presentation; impaired ADL	Biomarker consistent with AD

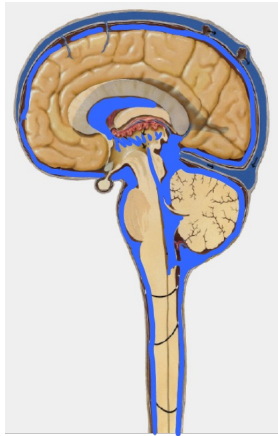
Que pensez-vous de la précision du diagnostic de la maladie d'Alzheimer ?





## Intérêt des dosages sanguins

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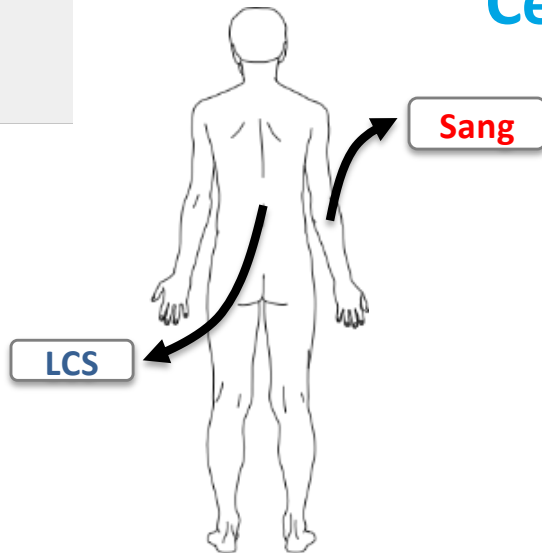


Liquide  
Cerebro  
Spinal

## Intérêt des dosages sanguins

- Intérêt car **moins invasif** que la ponction lombaire → possibilité d'utilisation en routine, à plus large échelle, pour le suivi...

## Cependant....



- Effet de « dilution » par rapport au LCS et d'autres origines que le cerveau (**baisse sensibilité et spécificité**)
- Nécessite souvent des méthodes innovantes, **ultrasensibles** et optimisées
- Risque d'interférence et de variabilités en lien avec des **comorbidités**...

# Détection des peptides amyloïdes dans le sang

Hirtz et al. *Alzheimer's Research & Therapy* (2023) 15:34  
<https://doi.org/10.1186/s13195-023-01188-8>

Alzheimer's  
 Research & Therapy

RESEARCH

Open Access



JAMA Neurology | Original Investigation

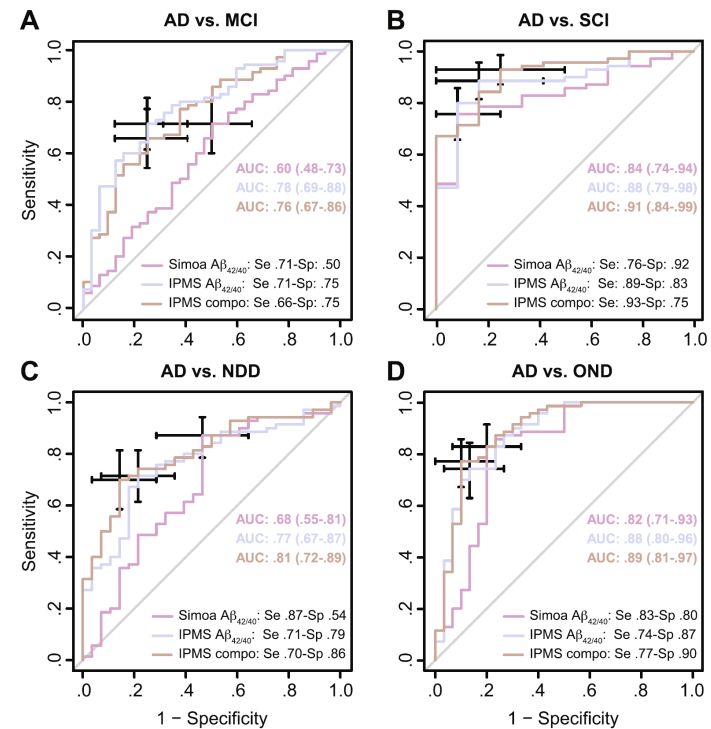
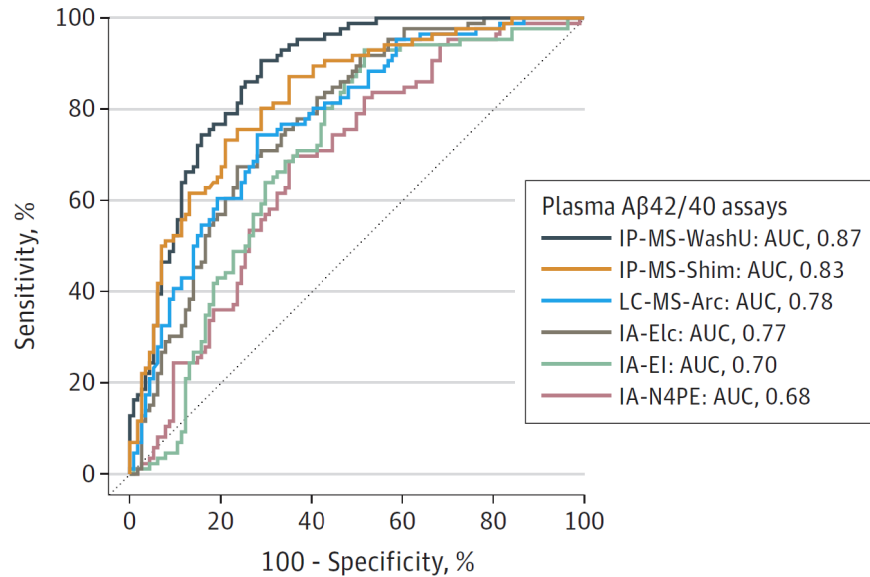
## Head-to-Head Comparison of 8 Plasma Amyloid- $\beta$ 42/40 Assays in Alzheimer Disease

Shorena Janelidze, PhD; Charlotte E. Teunissen, PhD; Henrik Zetterberg, MD, PhD; José Antonio Allué, PhD; Leticia Sarasa, PhD; Udo Eichenlaub, PhD; Tobias Bittner, PhD; Vitaliy Ovod, MSs; Inge M. W. Verberk, MSs; Kenji Toba, MD, PhD; Akinori Nakamura, MD, PhD; Randall J. Bateman, MD, PhD; Kaj Blennow, MD, PhD; Oskar Hansson, MD, PhD

## Comparison of ultrasensitive and mass spectrometry quantification of blood-based amyloid biomarkers for Alzheimer's disease diagnosis in a memory clinic cohort

Christophe Hirtz<sup>1†</sup>, Germain U. Busto<sup>2,3†</sup>, Karim Bennys<sup>2</sup>, Jana Kindermans<sup>1</sup>, Sophie Navucet<sup>2</sup>, Laurent Tiers<sup>1</sup>, Simone Lista<sup>2</sup>, Jérôme Vialaret<sup>1</sup>, Laure-Anne Gutierrez<sup>2</sup>, Yves Dauvilliers<sup>3,4</sup>, Claudine Berr<sup>2</sup>, Sylvain Lehmann<sup>1†\*</sup> and Audrey Gabelle<sup>2,3†</sup>

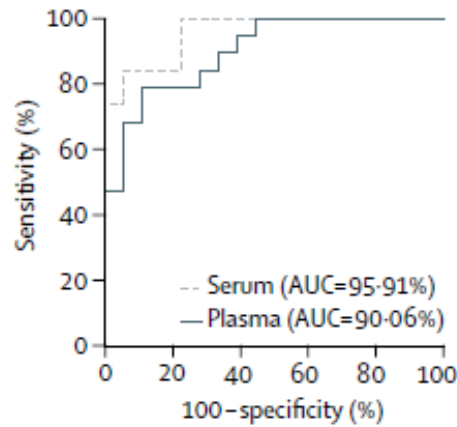
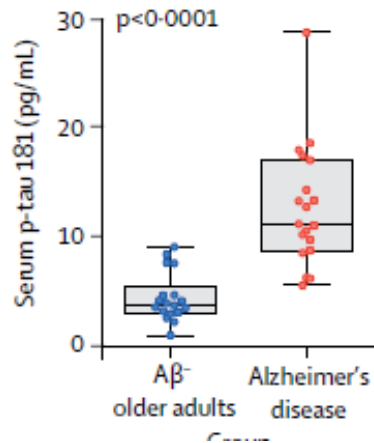
### (ROC) Analysis for Abnormal Cerebrospinal Fluid (CSF) Amyloid



# Détection de la protéine pTau dans le sang

## Blood phosphorylated tau 181 as a biomarker for Alzheimer's disease: a diagnostic performance and prediction modelling study using data from four prospective cohorts

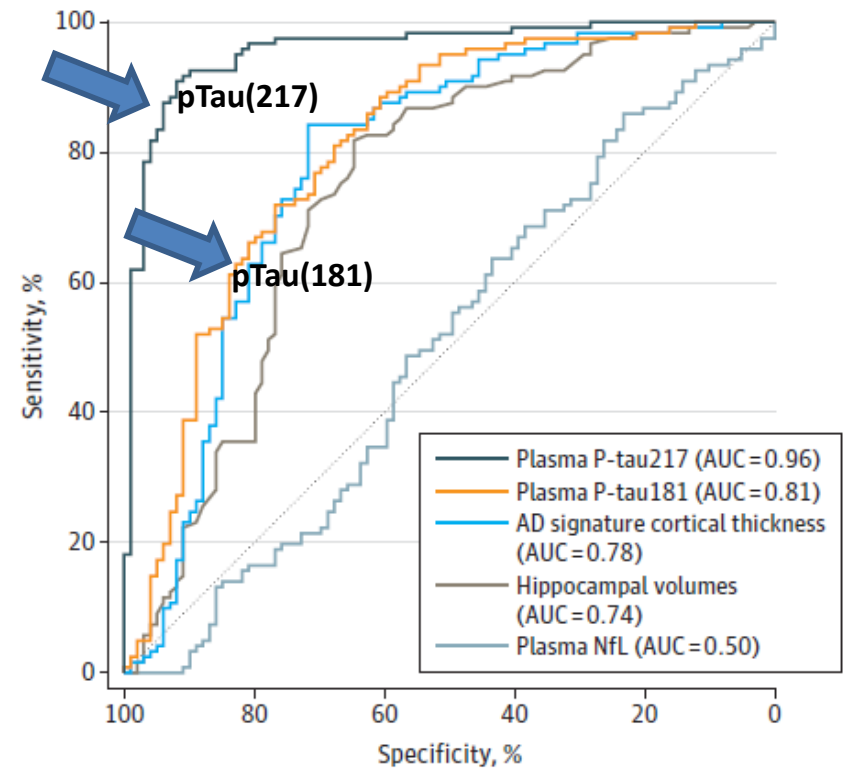
Thomas K Karikari\*, Tharick A Pascoal\*, Nicholas J Ashton, Shorena Janelidze, Andréa Lessa Benedet, Juan Lantero Rodriguez, Mira Chamoun, Melissa Savard, Min Su Kang, Joseph Theriault, Michael Schöll, Gassan Massarweh, Jean-Paul Soucy, Kina Höglund, Gunnar Brinkmalm, Niklas Mattsson, Sebastian Palmqvist, Serge Gauthier, Erik Stomrud, Henrik Zetterberg, Oskar Hansson†, Pedro Rosa-Neto†, Kaj Blennow†



JAMA | Original Investigation

## Discriminative Accuracy of Plasma Phospho-tau217 for Alzheimer Disease vs Other Neurodegenerative Disorders

Sebastian Palmqvist, MD, PhD; Shorena Janelidze, PhD; Yakeel T. Quiroz, PhD; Henrik Zetterberg, MD, PhD; Francisco Lopera, MD; Erik Stomrud, MD, PhD; Yi Su, PhD; Yinghua Chen, MSc; Geidy E. Serrano, PhD; Antoine Leuzy, PhD; Niklas Mattsson-Carlgen, MD, PhD; Olof Strandberg, PhD; Ruben Smith, MD, PhD; Andres Villegas, MD; Diego Sepulveda-Falla, MD; Xiyun Chai, MD; Nicholas K. Proctor, BS; Thomas G. Beach, MD, PhD; Kaj Blennow, MD, PhD; Jeffrey L. Dage, PhD; Eric M. Reiman, MD; Oskar Hansson, MD, PhD



# Détection de la protéine pTau dans le sang : PHRC Baltazar

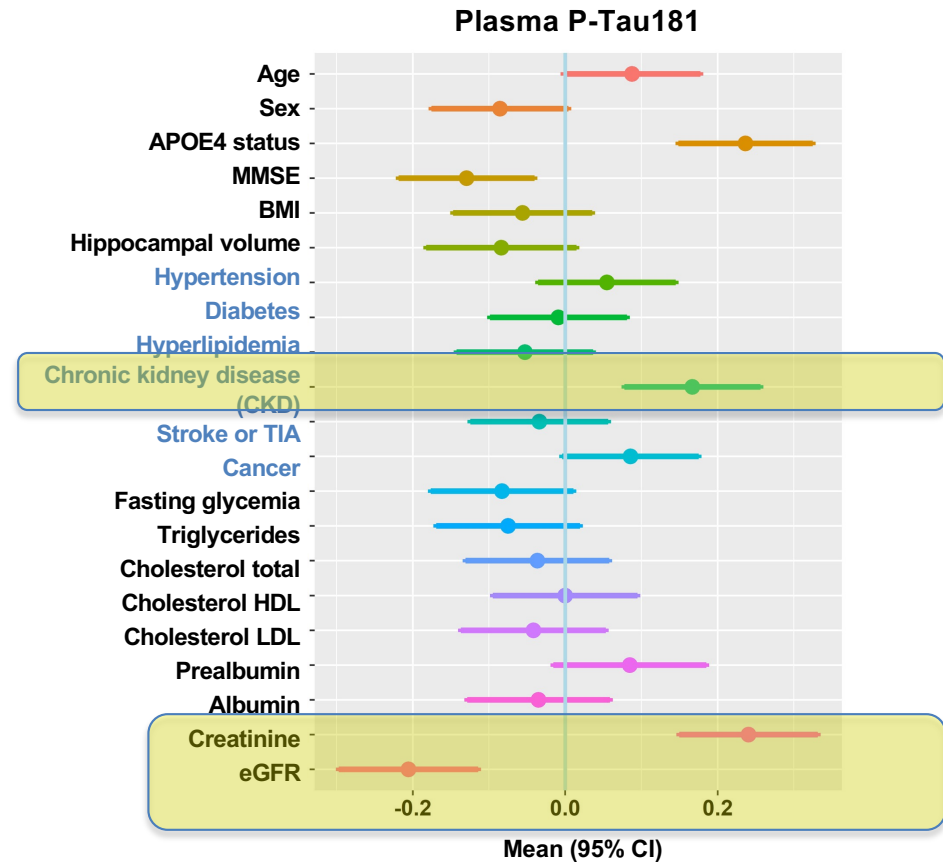
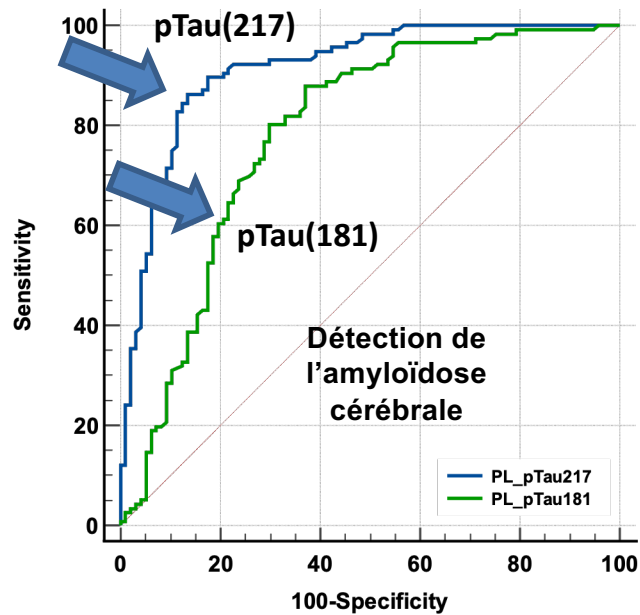
## Neurodegeneration

Original research

Plasma phosphorylated tau 181 predicts amyloid status and conversion to dementia stage dependent on renal function

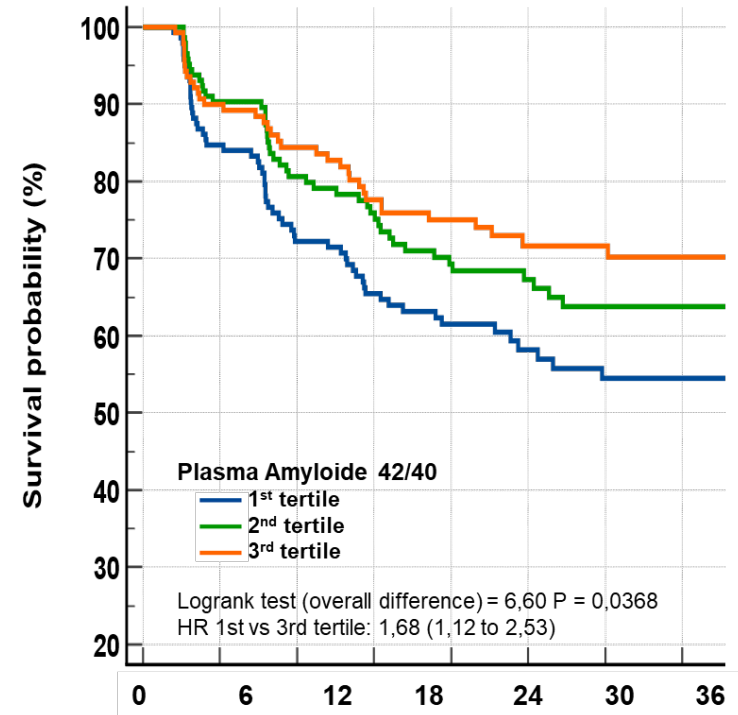
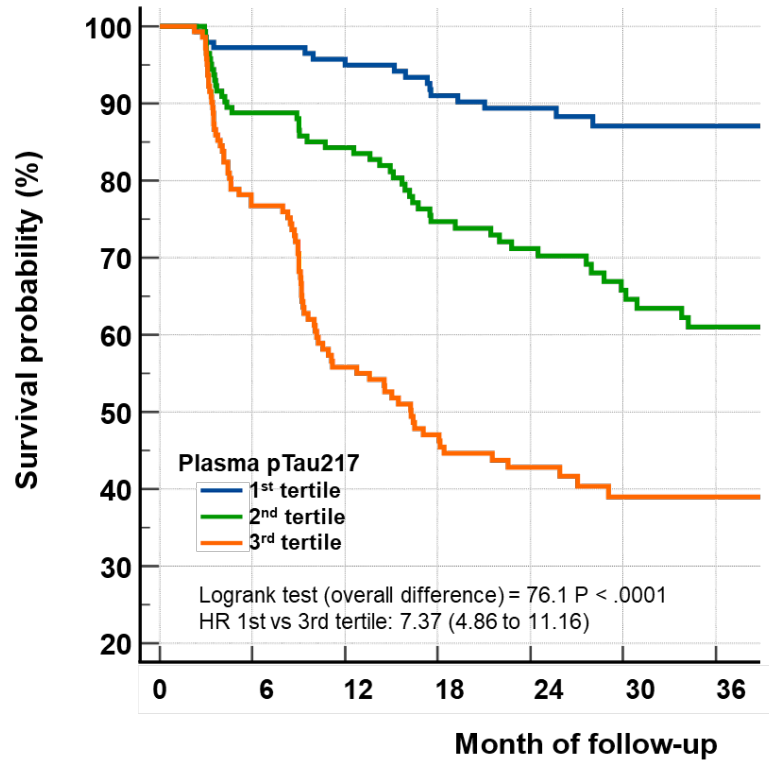
Sylvain Lehmann <sup>1</sup>, Susanna Schraen-Maschke <sup>2</sup>, Jean-Sébastien Vidal <sup>3</sup>,  
 Constance Delaby <sup>1,4</sup>, Frédéric Blanc <sup>5</sup>, Claire Paquet <sup>6</sup>, Bernadette Allinquant <sup>7</sup>,  
 Stéphanie Bombois <sup>2,8</sup>, Audrey Gabelle <sup>9</sup>, Olivier Hanon <sup>3</sup>

Lehmann S, et al. *J Neurol Neurosurg Psychiatry* 2023;0:1–9. doi:10.1136/jnnp-2022-330540

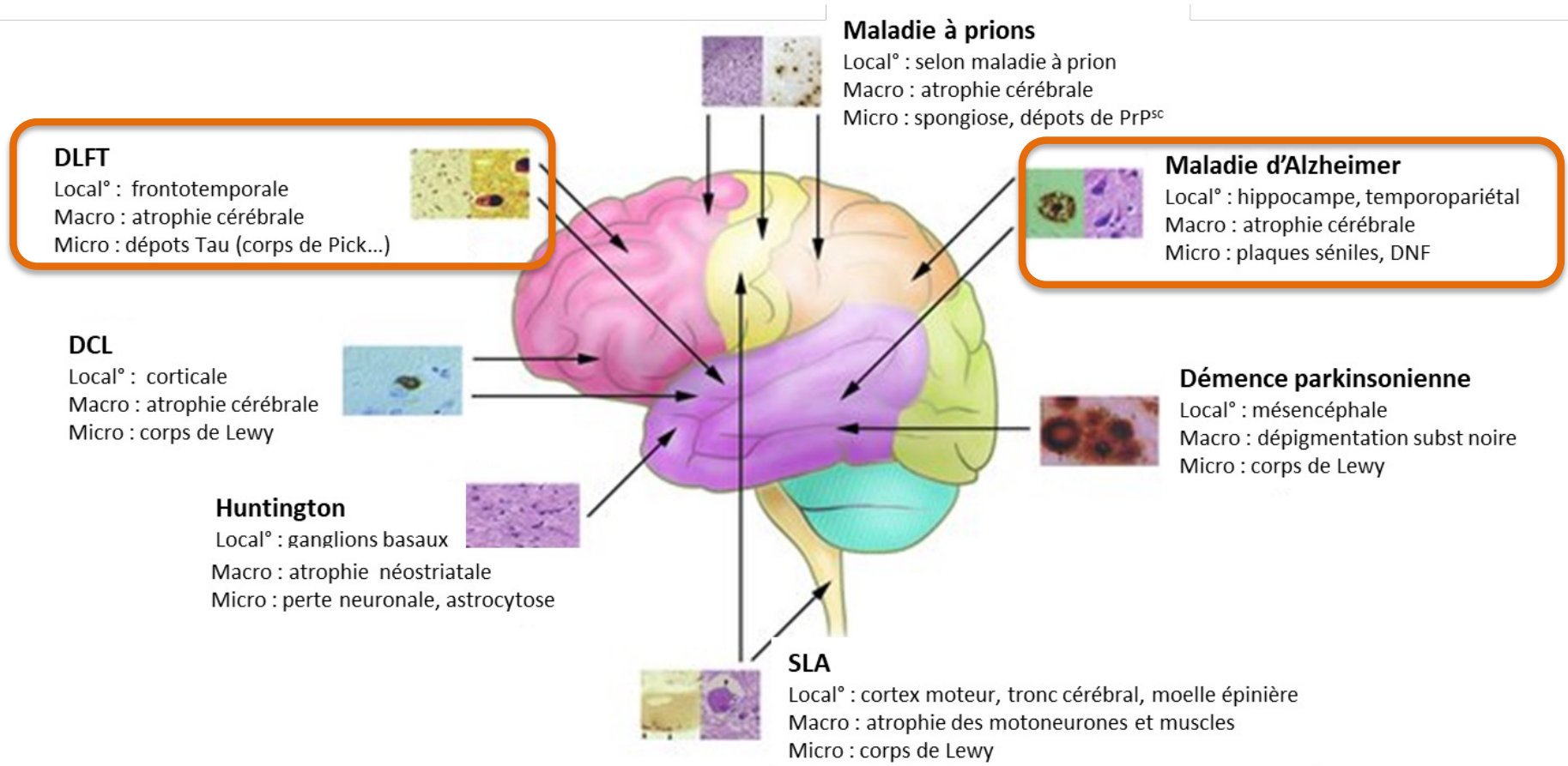


## Détection de la protéine pTau dans le sang : PHRC Baltazar

### Conversion en démence des patients MCI (mild cognitive impairment)



# Maladies neurodégénératives



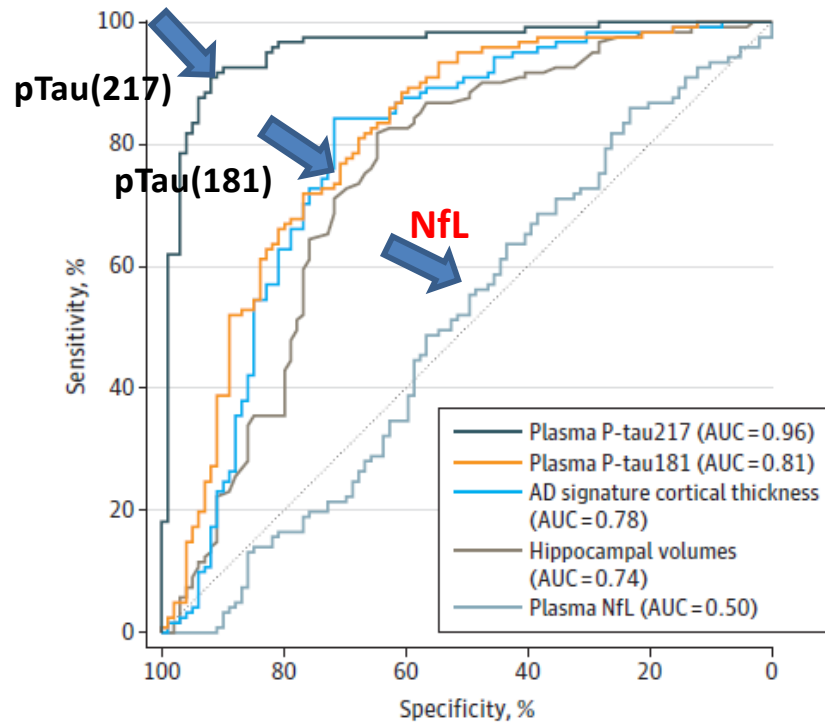
Adapté de Bertram and RE Tanzi, Fig 3  
The Journal of Clinical Investigation, 115(6): 1449-1457,2005.

# Détection des Neurofilaments

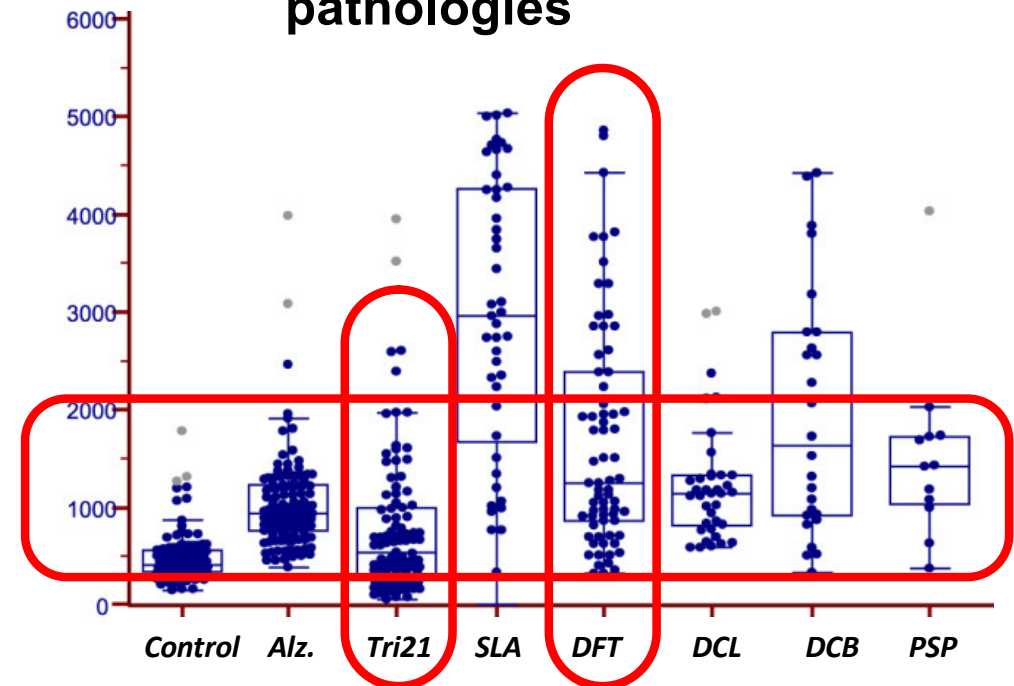
JAMA | Original Investigation

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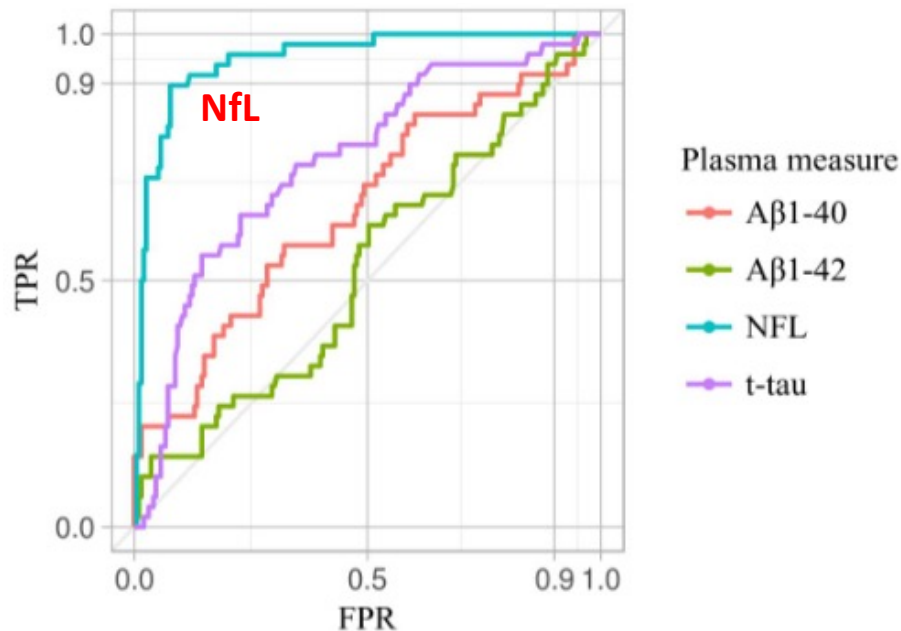
## NfL dans différentes pathologies



## Détection des Neurofilaments

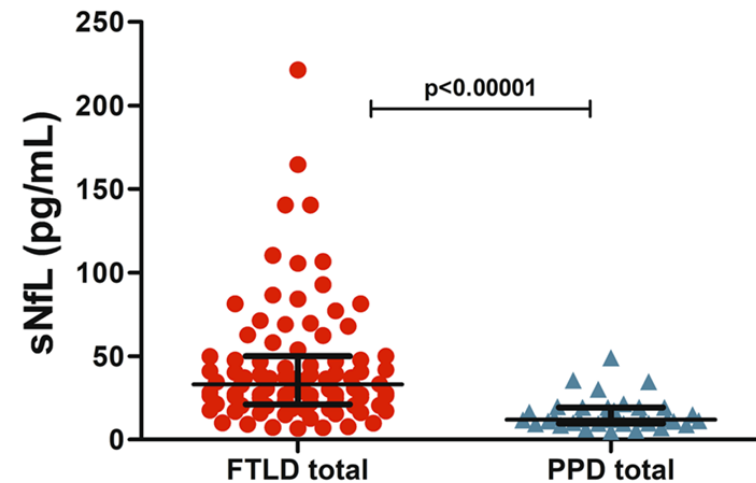
Plasma and CSF biomarkers for the diagnosis of Alzheimer's disease in adults with Down syndrome: a cross-sectional study

Juan Fortea, María Carmona-Iragui, Bessy Benejam, Susana Fernández, Laura Videla, Isabel Barroeta, Daniel Alcolea, Jordi Pegueroles, Laia Muñoz, Olivia Babin, Mony J de Leon, Aleksandra Maleska Macieski, Christophe Hirtz, Jordi Clarimón, Sebastián Videla, Constance Delaby, Sylvain Lehmann, Rafael Blesa\*, Alberto Lleó\*



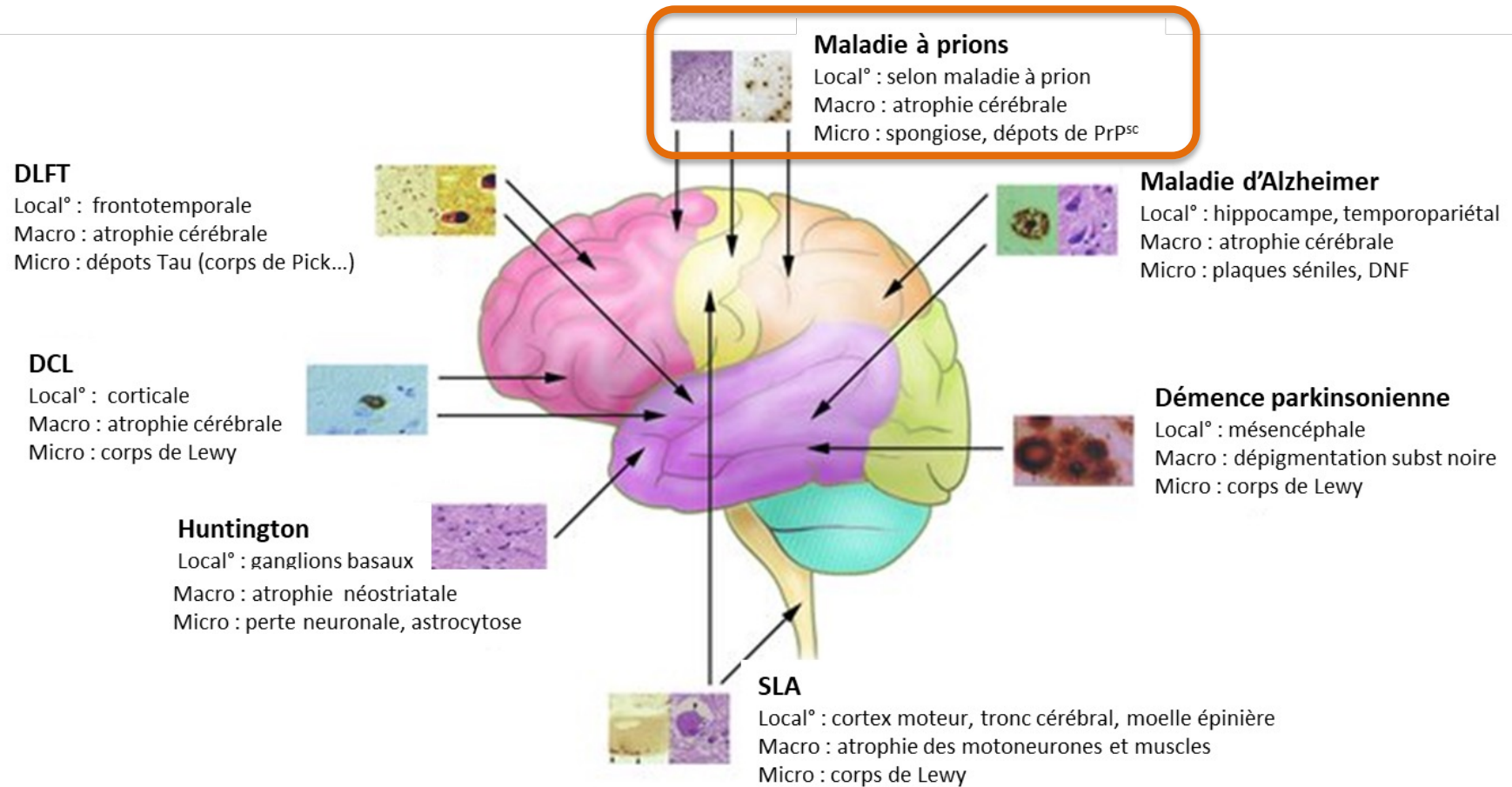
La chaîne légère du neurofilament sérique est un biomarqueur discriminant entre la dégénérescence lobaire frontotemporale et les troubles psychiatriques primaires

Katisko et al (2020) *J Neurol*. 2020 Jan;267(1):162-167





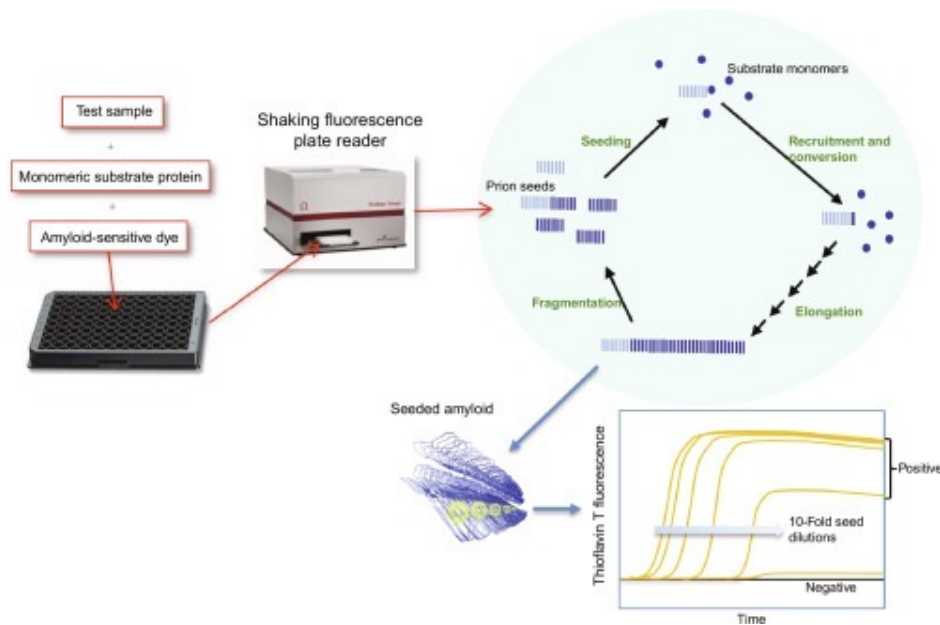
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Adapté de Bertram and RE Tanzi, Fig 3  
The Journal of Clinical Investigation, 115(6): 1449-1457,2005.

# Maladies à prion / Maladie de Creutzfeldt-Jakob

## RT-Quic assay




## Article

### Tau protein and 14-3-3 protein in the differential diagnosis of Creutzfeldt-Jakob disease

February 2002 · *Neurology* 58(2):192-7

DOI: [10.1212/WNL.58.2.192](https://doi.org/10.1212/WNL.58.2.192)

Source · [PubMed](#)

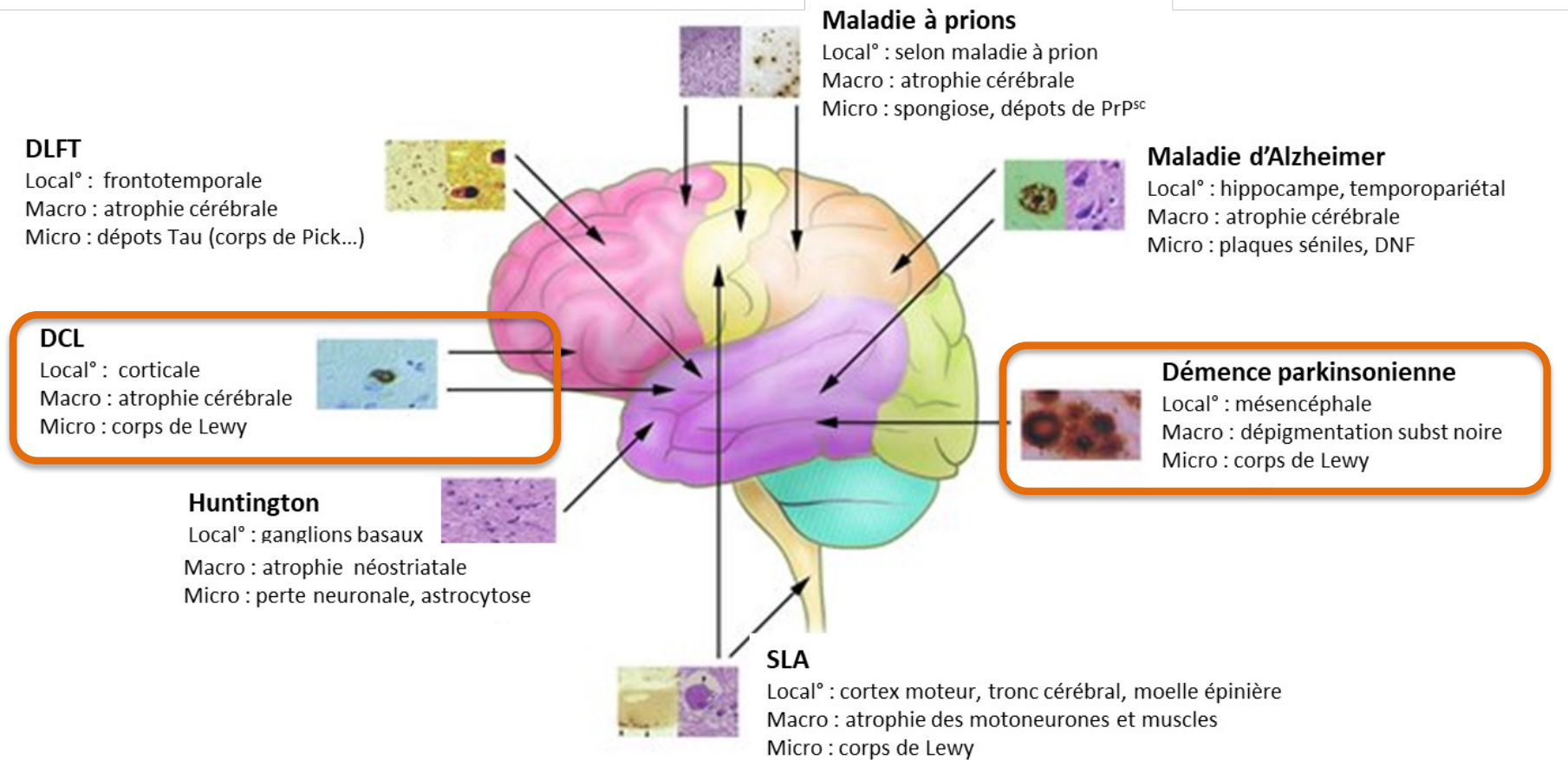
M Otto ·  Jens Wiltfang · L Cepek · [Show all 10 authors](#) · S Poser

> *J Neural Transm (Vienna)*. 2022 Feb;129(2):133-139. doi: 10.1007/s00702-021-02443-8. Epub 2022 Jan 18.

### Comparison of cerebrospinal fluid tau, ptau(181), synuclein, and 14-3-3 for the detection of Creutzfeldt-Jakob disease in clinical practice

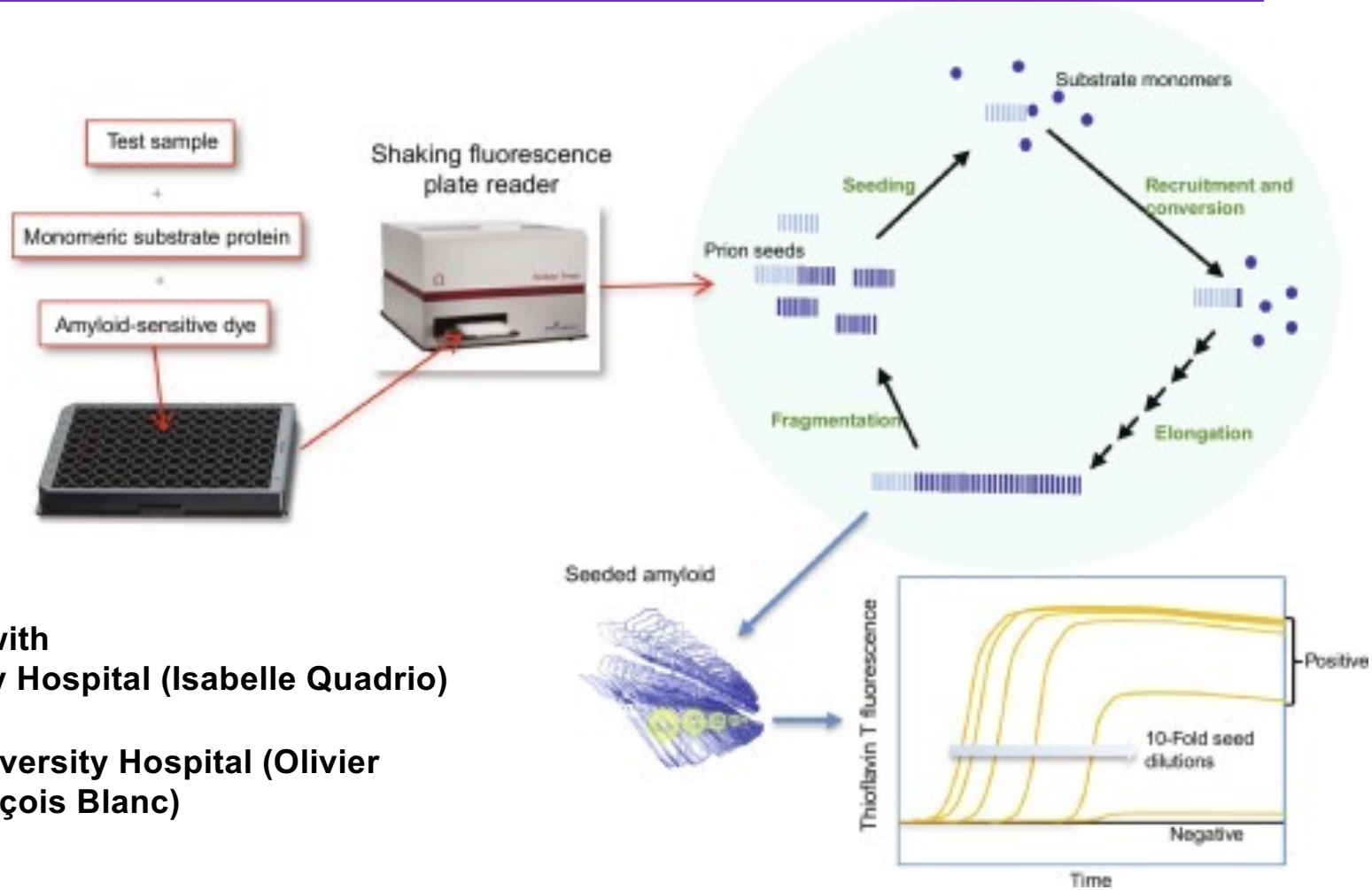
Martin Fayolle <sup>1</sup>, Sylvain Lehmann <sup>2</sup>, Constance Delaby <sup>1 3</sup>

# Maladies neurodégénératives



Adapté de Bertram and RE Tanzi, Fig 3  
The Journal of Clinical Investigation, 115(6): 1449-1457,2005.

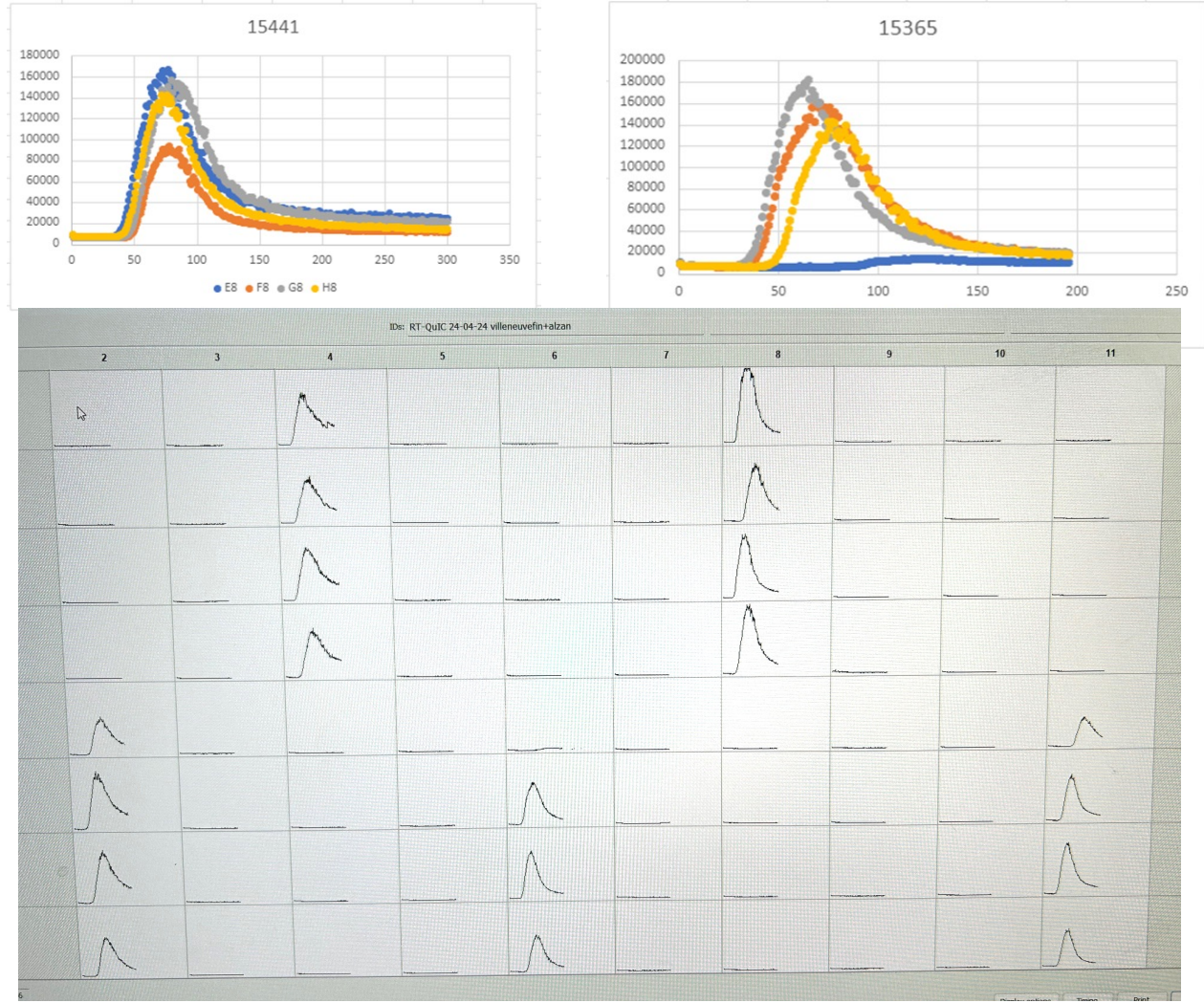
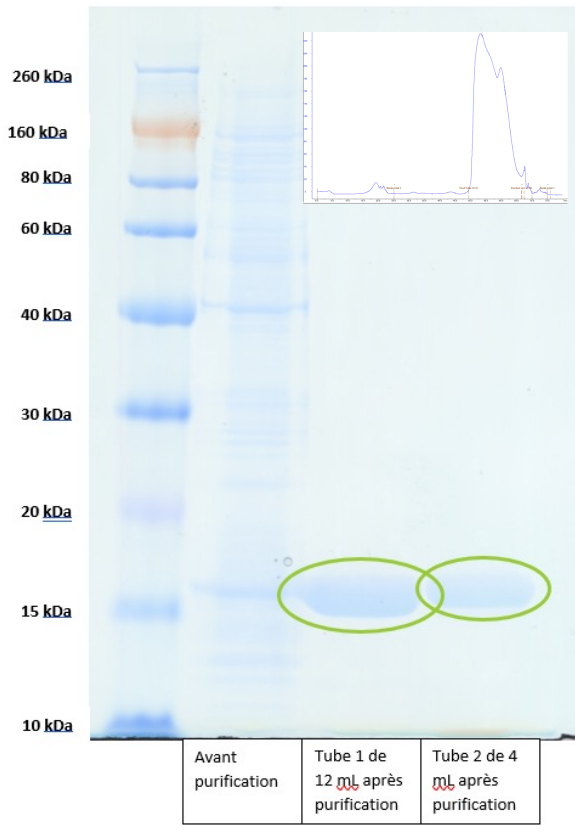
# RT-Quic pour la synucléine



**Collaboration with  
Lyon University Hospital (Isabelle Quadrio)  
and  
Strasbourg University Hospital (Olivier  
Bousiges, François Blanc)**

# RT-Quic pour la synucléine

## Production recombinant synuclein



## Blood biomarkers of Alzheimer's: what for

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Biomarqueurs	intérêt	Utilisation
Peptides A $\beta$ + Tau + pTau du LCR	Amyloïdose cérébrale et pathologie tau	Détection Alzheimer, Thérapie, Prise en charge
Peptides A $\beta$ + Tau + pTau sanguin	Amyloïdose cérébrale et pathologie tau	Evaluation en cours...
NfL (Sang et LCR)	Neurodégénérescence	Marqueurs de suivi / sévérité, différentiel: DFT vs PPD / Trisomie 21
Synucléine (LCR)	Synucléinopathies	Diagnostic, co-pathologies



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