Project Title: Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

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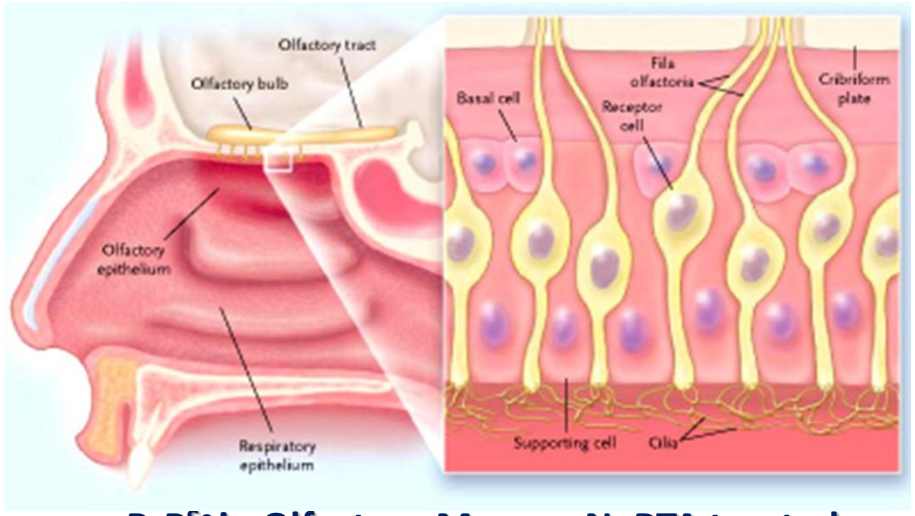
Dr. Stephane Haik, *Paris Brain Institute and AP-HP Cellule Nationale de Référence des MCJ, Salpêtrière Hospital, Paris, France*

Drs. Anna Ladogana, Anna Poleggi, *Istituto Superiore di Sanità, Rome, Italy*

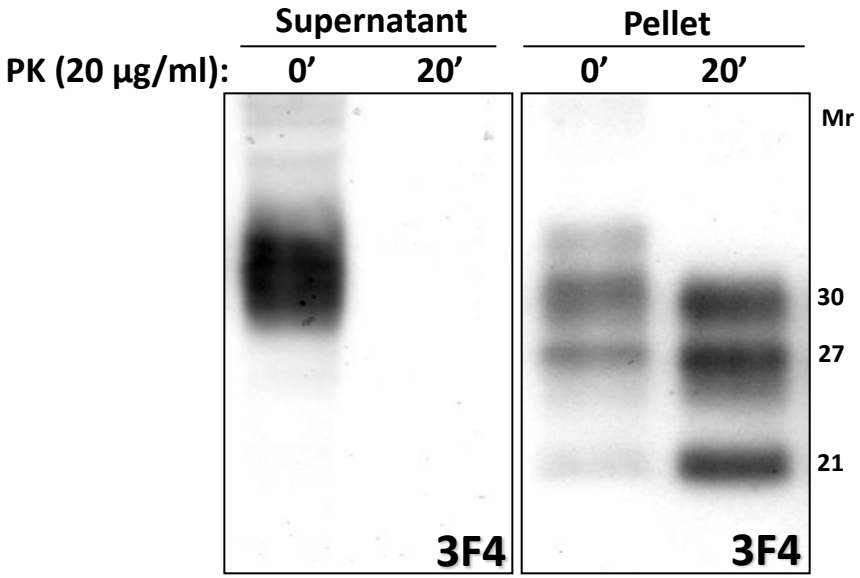
2026 Family Conference, Mariott Chicago O'Hare, Chicago, Illinois, July 10-12, 2026

Detection of PrP^{Sc} in the Olfactory Neuroepithelium of sCJD

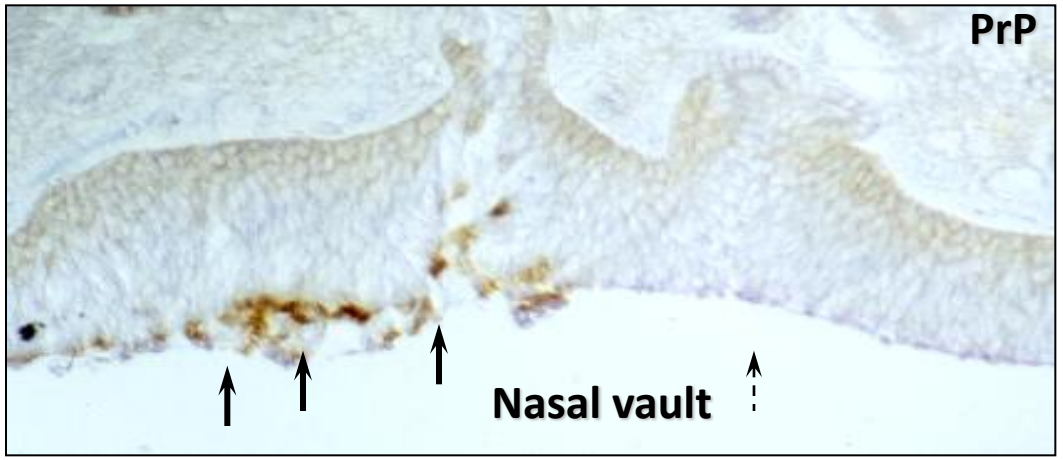


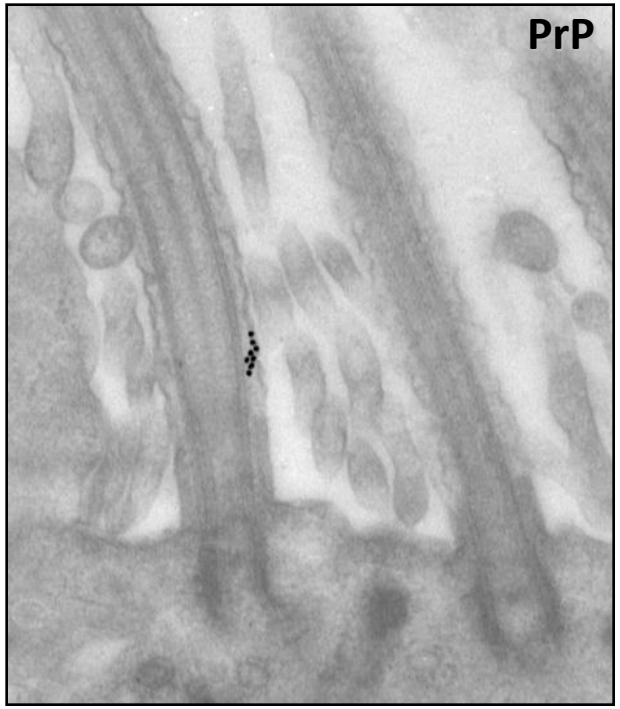
PrP^{Sc} in Olfactory Mucosa NaPTA treated

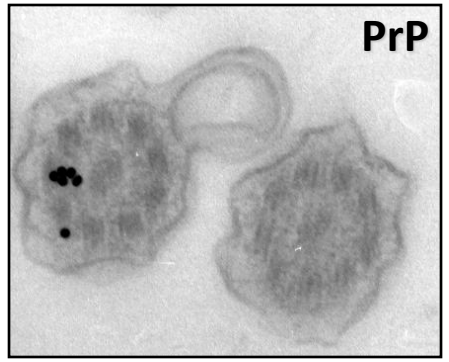
(from 100 mg or wet tissue)

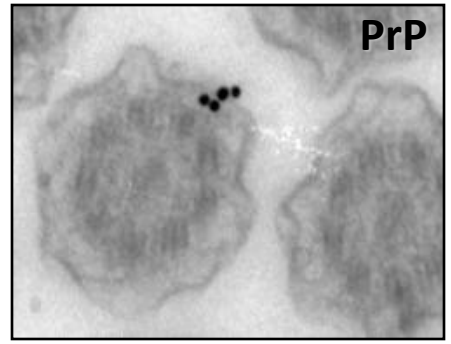


PrP^{Sc} deposition in olfactory neuroepithelium









Zanusso et a. NEJM 2003

The NEW ENGLAND JOURNAL of MEDICINE 2014;371:519-29

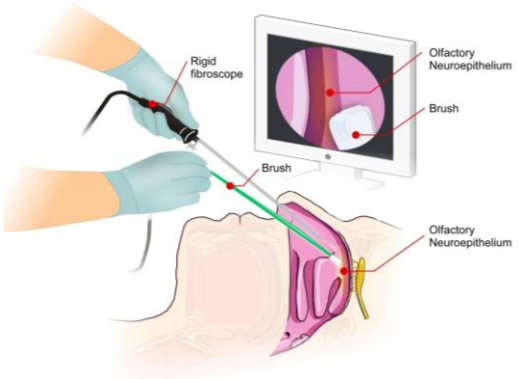
ORIGINAL ARTICLE

A Test for Creutzfeldt–Jakob Disease Using Nasal Brushings

Christina D. Orrú, Ph.D., Matilde Bongianni, Ph.D., Giovanni Tonoli, M.D., Sergio Ferrari, M.D., Andrew G. Hughson, M.S., Bradley R. Groveman, Ph.D., Michele Fiorini, Ph.D., Maurizio Pocchiari, M.D., Salvatore Monaco, M.D., Byron Caughey, Ph.D., and Gianluigi Zanusso, M.D., Ph.D.

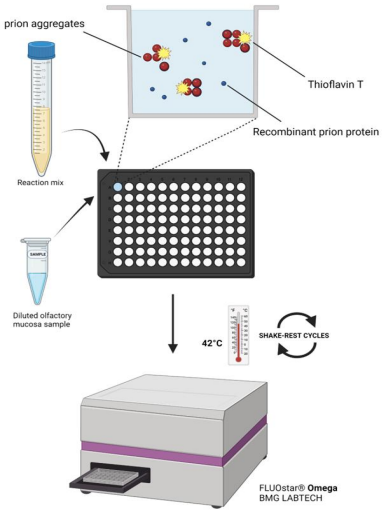
Major Pitfalls

Complexity of olfactory swab procedure



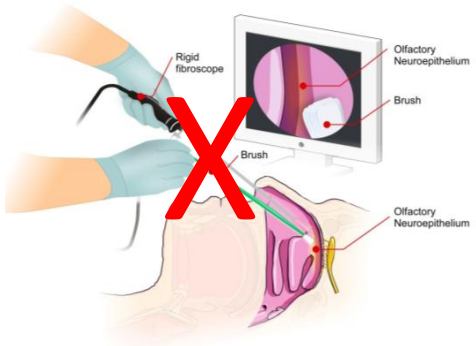
Olfactory swab sample preparation and delivery

Reproducibility of RT-QuIC assay among laboratories



Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

Aim 1: To perform OS by non-ENT trained by a tutorial video without using endoscopes in a large cohort of patients referred to each center with a clinical diagnosis of suspected prion disorder



VIDEO

Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

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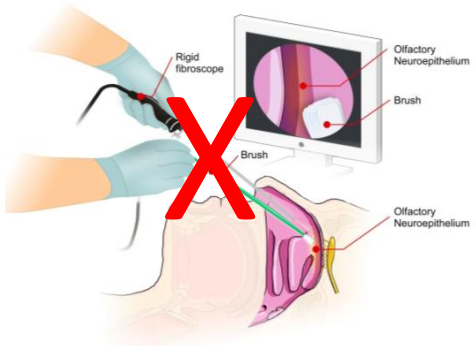
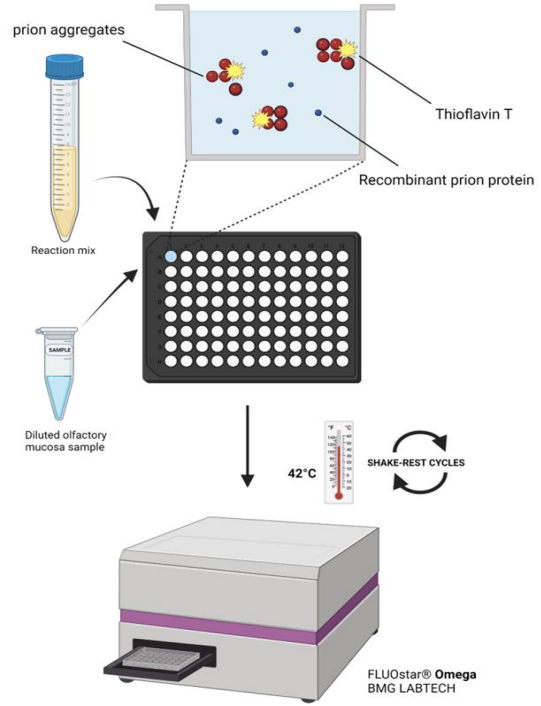


Aim 2: To analyze OS samples by RT-QuIC in each laboratory and evaluate RT-QuIC diagnostic sensitivity and specificity

Prion Detection by RT-QuIC



Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

Sensitivity of Olfactory swab in patients with sporadic CJD

Unit	Patients	RT-QuIC OM positive	Sensitivity	Probable/Definite Prion Diseases
UNIVR	88	76/87	87.3%	55/33
ISS	41	34/41	82.9%	17/24
Goettingen*	2	2/2	100%	2/0
Paris*	-	-	-	-

* Ongoing collection

Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

Sensitivity of Olfactory Swab in patients with Genetic Prion disorders

Unit	E200K - V210I	P102L	FFI
UNIVR	5/5 - 2/2	0/2	0/2
ISS	1/0	1/1	-
Goettingen	-	1/3	1/2

Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

Specificity of olfactory swabs in patients with non-prion disorders

Unit	Number of patients with Non-Prion Disease	RT-QuIC OM positive	Confirmed Prion Diseases	Specificity
UNIVR	69	0/69	None	100%
ISS	14	0/14	None	100%
Goettingen*	6	0/6	None	100%
Paris*	-	-	-	

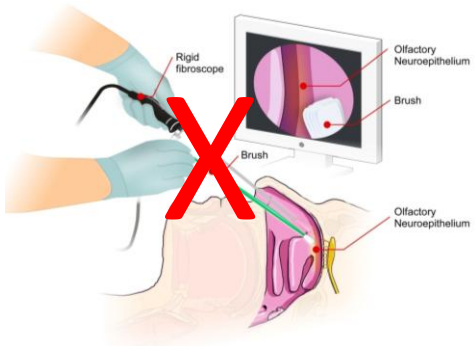
* Ongoing collection

Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

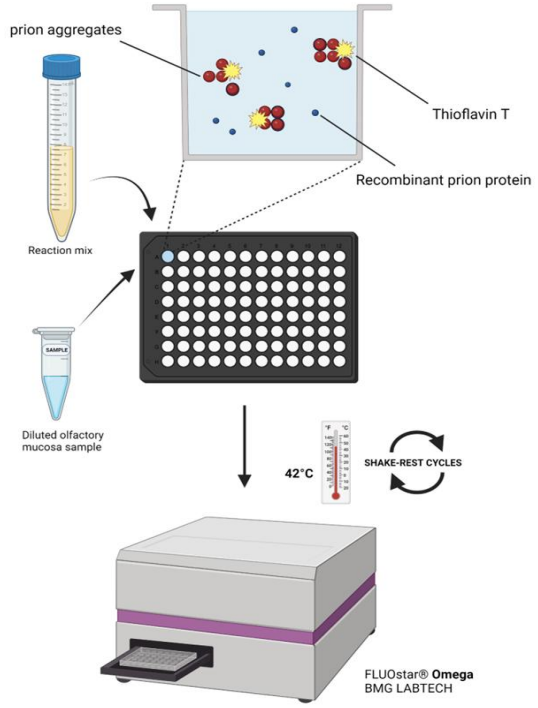
Aim 1: To perform OS by non-ENT trained by a tutorial video without using endoscopes in a large cohort of patients referred to each center with a clinical diagnosis of suspected prion disorder

Aim 2: To analyze OS samples by RT-QuIC in each laboratory and evaluate RT-QuIC diagnostic sensitivity and specificity

Aim 3: To define the interlaboratory concordance of RT-QuIC in OS in a preliminary ring trial



Prion Detection by RT-QuIC



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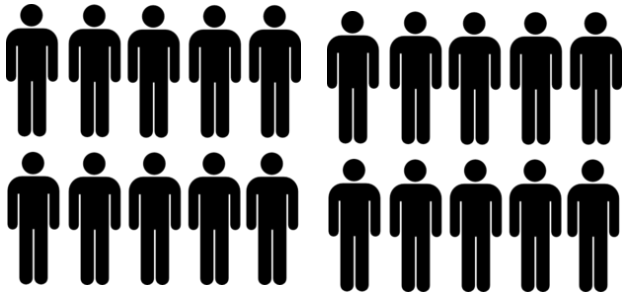
Aim 3: To define the interlaboratory concordance of RT-QuIC in olfactory swab in a preliminary ring trial (still ongoing)

Olfactory swabs obtained at UNIVR
From 20 patients affected
with prion disease
From 20 individuals
with non-prion diseases



Sent to different labs
For blinded
RT-QuIC analysis

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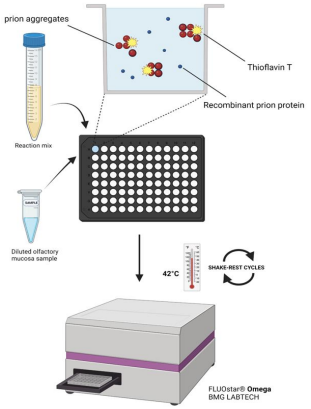
RT-QuIC analysis



Data analysis
Final results

Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

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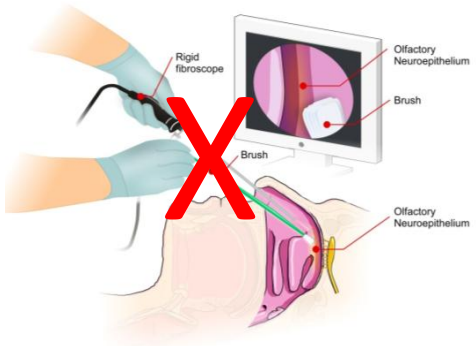

Aim 2: To analyze OS samples by RT-QuIC in each laboratory and evaluate RT-QuIC diagnostic sensitivity and specificity

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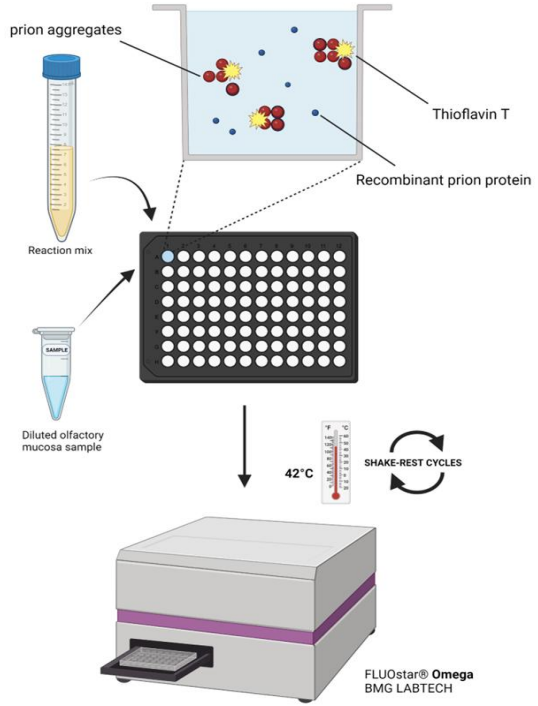
Prion Detection by RT-QuIC



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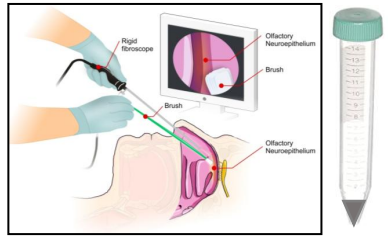
Aim 4: To assess the diagnostic accuracy of RT-QuIC assay in CSF and OS from the same patient and in combination

Cerebrospinal Fluid

Olfactory Swab



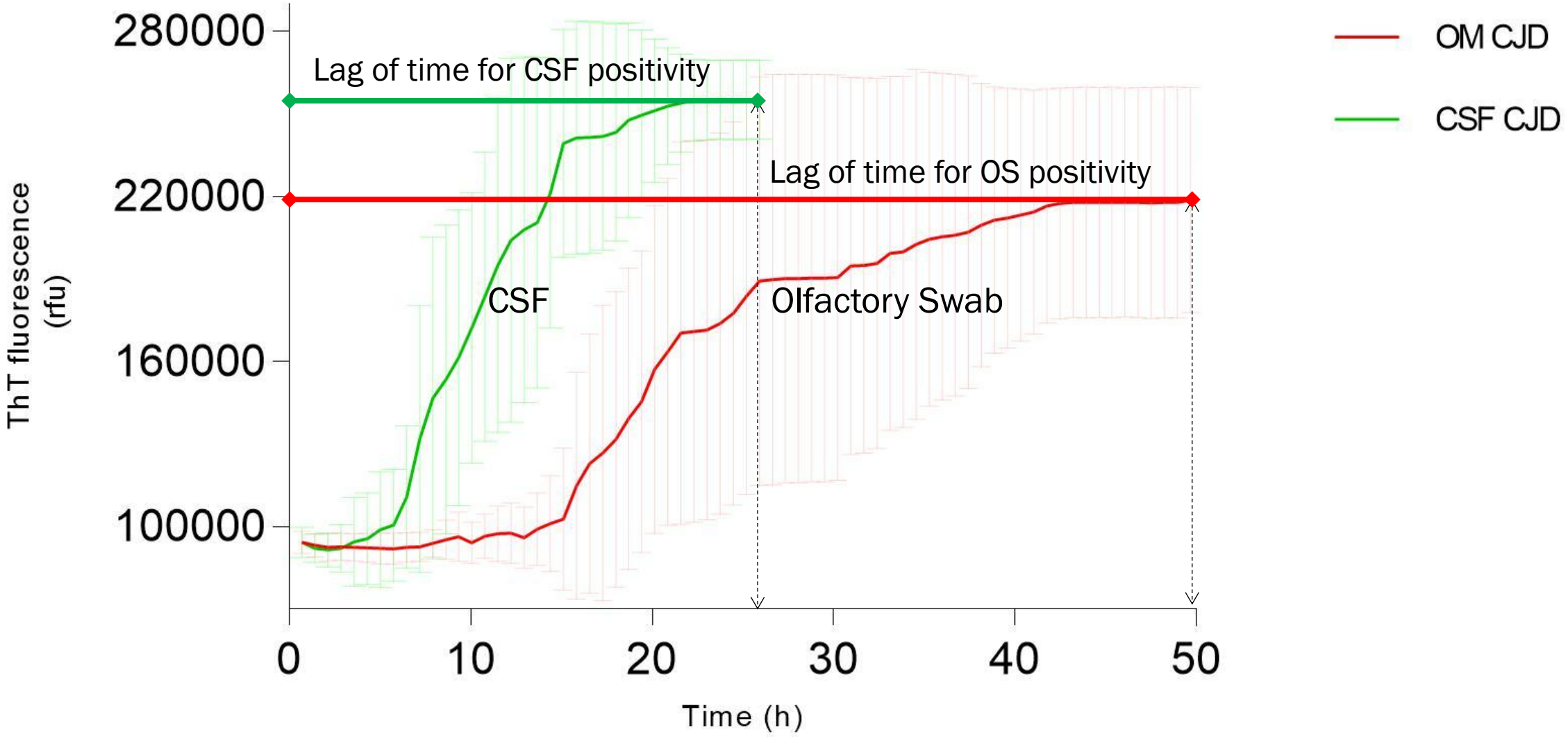
Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis

Diagnostic Sensitivity of Olfactory swab and CSF in the same patients

Unit	Number of patients	RT-QuIC OM positive	RT-QuIC CSF positive	RT-QuIC CSF sensitivity	RT-QuIC OM positive in patients with no CSF collaction**	Final diagnostic accuracy of combined CSF and OM analyses
UNIVR	88	76/87	57/61	93.4%	26/26	100%
ISS	41	34/41	33/37	89.1%	4/4	100%
Goettingen*	2	2/2	ND	-	ND	ND
Paris*	-	-	-	-	-	-

*Ongoing collection;
** unpracticable lumbar puncture: patients with behavioral disturbances, spine arthrosis, anticoagulant intake, cost of LP, etc.

RT-QuIC assay in CSF and Olfactory swab in patients with sporadic CJD



Implications of our study and what TBD

- ✓ Olfactory swab is a simple and non-invasive procedure. Same as COVID-19 test, it can be performed in any environment by a healthcare professional, **simplifying the diagnosis of human prion disorders;**

- ✓ Diagnostic sensitivity of RT-QuIC assay in olfactory swab is nearly to 90% and the specificity of 100%. RT-QuIC in olfactory swabs can be independently tested with high fidelity in each laboratory;

- ✓ The interlaboratory assessment of RT-QuIC in OS is ongoing (TBD);

- ✓ Diagnostic sensitivity of RT-QuIC assay in CSF is also nearly to 90% and the specificity of 100% but when in the same patient both olfactory swab and CSF are available, **the diagnosis of prion disorder is provided in nearly 100% of patients**

- ✓ **Practical implications include:**
  - A short lag of time for reaching an accurate prion disease diagnosis
  - A reduced number of additional investigations and useless therapies
  - Prompt communication of prion diagnosis to the family, shortening the anguish of uncertainty
  - The short time (in 48 hours) for the diagnosis of prion disorder allows to start with therapies to be started in the early stage of the disease
  - In treated patients serial olfactory swab sampling allows to monitor therapy efficacy

We are extremely grateful to:

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The Strides for CJD Grant, contributed by the Families of the CJD Foundation

for the support of our research study, which has helped to advance our knowledge for recognizing and defeating human prion disorders