

BIOGRAPHICAL SKETCH

NAME: Gianluigi Zanusso, M.D., Ph.D.

POSITION TITLE: Associate Professor of Neurology, University of Verona

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Verona	Medicine and Surgery	1990	Medicine and Surgery
University of Verona	Specialization	1994	Neurology
University of Verona	Doctor of Philosophy	2000	Neurosciences

A. Personal Statement

Long-dated experience in clinical, neuropathologic and biochemical aspects of prion human disorders and other neurodegenerative disorders diagnostics. Main focus of our studies has been the involvement of olfactory system in neurodegeneration. I invented and set up olfactory swabbing (OS), a procedure which allows to collect primary olfactory neurons from the nasal vault. We applied Real-Time Quaking Inducing Conversion Assay (RT-QuIC), a specific and ultra-sensitive prion assay, to OS obtained from patients with Creutzfeldt-Jakob Disease allowing an *intravital* diagnosis of prion disorder with a diagnostic accuracy nearly to 100%. We are currently adapting this approach to the detection of pathological misfolded proteins of other neurodegenerative diseases such as Parkinson's disease, Dementia with Lewy bodies, Multiple system atrophy and idiopathic REM sleep behavior disorder.

B. Positions

1982-90	Student at the Faculty of Medicine and Surgery, University of Verona Graduated cum laude
1990	Licensed to practice Medicine
1994	Post-graduate degree, Neurology Residency, University of Verona Final graduation cum laude
1995-1998	Case Western Reserve University, Laboratory of Neuropathology, Cleveland OH, USA: Research Assistant
2002-2014	Assistant Professor, University of Verona, Italy
2014	Associate Professor of Neurology, University of Verona
2018- at present	Coordinator of the PhD course in Neuroscience, Psychological, Psychiatric and Movement Sciences University of Verona
2012-at present	Academic Editor, <i>PLoS ONE</i>
2002-2007	Member of the "Task force on transmissible spongiform encephalopathies", Ministry of health, Italy
2003-2009	Member of the Network of excellence Neuroprion;
2009-at present	Member of the Neuroprion Association.

C. Honors

NAID top 20 research advance FY 2014: Orrù et al. New Engl J Med 2014 371 (6): 519-29.
Prion 2016 Tokyo Best Poster Award
Aspen Italia Prize 2019

D. Top contribution to Science

Identification of the sporadic form of bovine spongiform encephalopathy

Casalone C*, Zanusso G*, Acutis P, Ferrari S, Capucci L, Tagliavini F, Monaco S, Caramelli M. Identification of a second bovine amyloidotic spongiform encephalopathy: Molecular similarities with sporadic Creutzfeldt-Jakob disease. *Proc Natl Acad Sci U S A* 2004;101:3065-70 *First authors

The first demonstration of olfactory system involvement in human prion disorders

Zanusso G, Ferrari S, Cardone F, Zampieri P, Gelati M, Fiorini M, Farinazzo A, Gardiman M, Cavallaro T, Bentivoglio M, Righetti PG, Pocchiari M, Rizzuto N, Monaco S. Detection of pathologic prion protein in the olfactory epithelium in sporadic Creutzfeldt-Jakob disease *N Engl J Med* 2003; 348:711-9

First application of nasal brushing as a diagnostic test in Creutzfeldt-Jakob disease

Christina D. Orrù, Matilde Bongianni, Giovanni Tonoli, Sergio Ferrari, Andrew G. Hughson, Bradley R. Groveman, Michele Fiorini, Maurizio Pocchiari, Salvatore Monaco, Byron Caughey, Gianluigi Zanusso. A test for Creutzfeldt-Jakob disease using nasal brushings. *N Engl J Med* 2014;371:519-29

Zanusso G, Monaco S, Pocchiari M, Caughey. Advanced tests for early and accurate diagnosis of Creutzfeldt-Jakob disease. *Nat Rev Neurol* 2016;12:427

Bongianni M, Orrù C, Groveman BR, Sacchetto L, Fiorini M, Tonoli G, Triva G, Capaldi S, Testi S, Ferrari S, Cagnin A, Ladogana A, Poleggi A, Colaizzo E, Tiple D, Vaianella L, Castriciano S, Marchioni D, Hughson AG, Imperiale D, Cattaruzza T, Fabrizi GM, Pocchiari M, Monaco S, Caughey B, Zanusso G. Diagnosis of Human Prion Disease Using Real-Time Quaking-Induced Conversion Testing of Olfactory Mucosa and Cerebrospinal Fluid Samples. *JAMA Neurol.* 2017;74:155-162.

Orrù CD, Groveman BR, Foutz A, Bongianni M, Cardone F, McKenzie N, Culeux A, Poleggi A, Grznarova K, Perra D, Fiorini M, Liu X, Ladogana A, Sbriccoli M, Hughson AG, Haik S, Green AJ, Geschwind MD, Pocchiari M, Safar JG, Zanusso G, Caughey B. Ring trial of 2nd generation RT-QuIC diagnostic tests for sporadic CJD. *Ann Clin Transl Neurol* 2020;7:2262-2271.

First transmission study on infectivity in nasal brushing, CSF and RT-QuIC products

Raymond GJ, Race B, Orrù CD, Raymond LD, Bongianni M, Fiorini M, Groveman BR, Ferrari S, Sacchetto L, Hughson AG, Monaco S, Pocchiari M, Zanusso G*, Caughey B*. Transmission of CJD from nasal brushings but not spinal fluid or RT-QuIC product. *Ann Clin Transl Neurol* 2020;7:932-944. *Corresponding authors.

First demonstration of normal proteins associated to neurodegeneration in nasal brushing of normal subjects

Brozzetti L, Sacchetto L, Cecchini MP, Avesani A, Perra D, Bongianni M, Portioli C, Scupoli M, Ghetti B, Monaco S, Buffelli M, Zanusso G. Neurodegeneration-Associated Proteins in Human Olfactory Neurons Collected by Nasal Brushing. *Front Neurosci* 2020;14:145.

First application of nasal brushing as a potential diagnostic approach for idiopathic REM sleep behavioral disorder, Parkinson's Disease and Dementia with Lewy bodies

Stefani A, Iranzo A, Holzknecht E, Perra D, Bongianni M, Gaig C, Heim B, Serradell M, Sacchetto L, Garrido A, Capaldi S, Sánchez-Gómez A, Cecchini MP, Mariotto S, Ferrari S, Fiorini M, Schmutzhard J, Cocchiara P, Vilaseca I, Brozzetti L, Monaco S, Jose Martí M, Seppi K, Tolosa E, Santamaria J, Högl B, Poewe W, Zanusso G; SINBAR (Sleep Innsbruck Barcelona) group. Alpha-synuclein seeds in olfactory mucosa of patients with isolated REM sleep behaviour disorder. *Brain* 2021; 144:1118-1126.

Perra D, Bongianni M, Novi G, Janes F, Bessi V, Capaldi S, Sacchetto L, Tagliapietra M, Schenone G, Morbelli S, Fiorini M, Cattaruzza T, Mazzon G, Orrù CD, Catalan M, Polverino P, Bernardini A, Pellitteri G, Valente M, Bertolotti C, Nacmias B, Maggiore G, Cavallaro T, Manganotti P, Gigli G, Monaco S, Nobili F, Zanusso G. Alpha-synuclein seeds in olfactory mucosa and cerebrospinal fluid of patients with dementia with Lewy bodies. *Brain Commun* 2021;3:fcab045.

Dementia with Lewy bodies and Alzheimer's Disease diagnosis by RT-QuIC in CSF

Bongianni M, Ladogana A, Capaldi S, Klotz S, Baiardi S, Cagnin A, Perra D, Fiorini M, Poleggi A, Legname G, Cattaruzza T, Janes F, Tabaton M, Ghetti B, Monaco S, Kovacs GG, Parchi P, Pocchiari M, Zanusso G. a-Synuclein RT-QuIC assay in cerebrospinal fluid of patients with dementia with Lewy bodies. *Ann Clin Transl Neurol.* 2019 Oct;6(10):2120-2126.

Pilotto A, Bongianni M, Tirloni C, Galli A, Padovani A, Zanusso G. CSF alpha-synuclein aggregates by seed amplification and clinical presentation of AD. *Alzheimer's Dement.* 2023 Apr 27. doi: 10.1002/alz.13109.

Dementia with Fronto-temporal Dementia diagnosis by RT-QuIC in CSF

Fontana E, Bongianni M, Benussi A, Bronzato E, Scialo C, Sacchetto L, Cagnin A, Castriciano S, Buratti E, Gardoni F, Italia M, Schreiber A, Ferracin C, Fiorini M, Newell KL, Cracco L, Garringer HJ, Cecchini MP, Polymenidou M, Padovani A, Monaco S, Legname G, Ghetti B, Borroni B, Zanusso G. Detection of TDP-43 seeding activity in the olfactory mucosa from patients with frontotemporal dementia. *Alzheimer's Dement.* 2023 Oct 31. doi: 10.1002/alz.13541.

E. Research Support

- MJFF 01/01/2021 – 31/12/2023.0 Multicentre assessment of nasal swabbing approach: α -syn RT-QuIC assay diagnostic performance in olfactory mucosa and cerebrospinal fluid in patients with prodromal PD, PD or PD with neurocognitive impairment. Principal investigator
- 2022 Target ALS Foundation 01/09/2022 – 31/08/2024 Ultrasensitive detection of TDP-43 pathology with RT-QuIC of nasal swabs. Partner
- 01/01/2025-31/12/2026. Multi-center assessment of olfactory swab procedure performed by non-otolaryngologists for improving and simplifying human prion disease diagnosis. Principal investigator
- 01/03/2025-29/02/2028. AriSLA. Detection of TDP-43 aggregates and TDP-43 misfolding in the olfactory mucosa of patients with Amyotrophic lateral sclerosis. Multicenter study Principal investigator
- 01/03/2025-29/02/2028. AriSLA. Detection of TDP-43 aggregates and TDP-43 misfolding in the olfactory mucosa of patients with Amyotrophic lateral sclerosis. Multicenter study Principal investigator
- 16/04/2024-31/03/2029 National Institutes of Health (NIH) RO1. Investigating the role of TDP-43 mislocalization, structure, and post-translational modifications in the neuropathologically heterogeneous TDP-43 proteinopathies. Partner
- 2024-2029 HORIZON-HLTH-2024-DISEASE-03-13-two-stage. Accelerating the Validation of Predictive Liquid Biomarkers for Frontotemporal Dementia Diagnosis and Subclassification. Partner

From Google Scholar:

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Prof. Gianluigi Zanusso