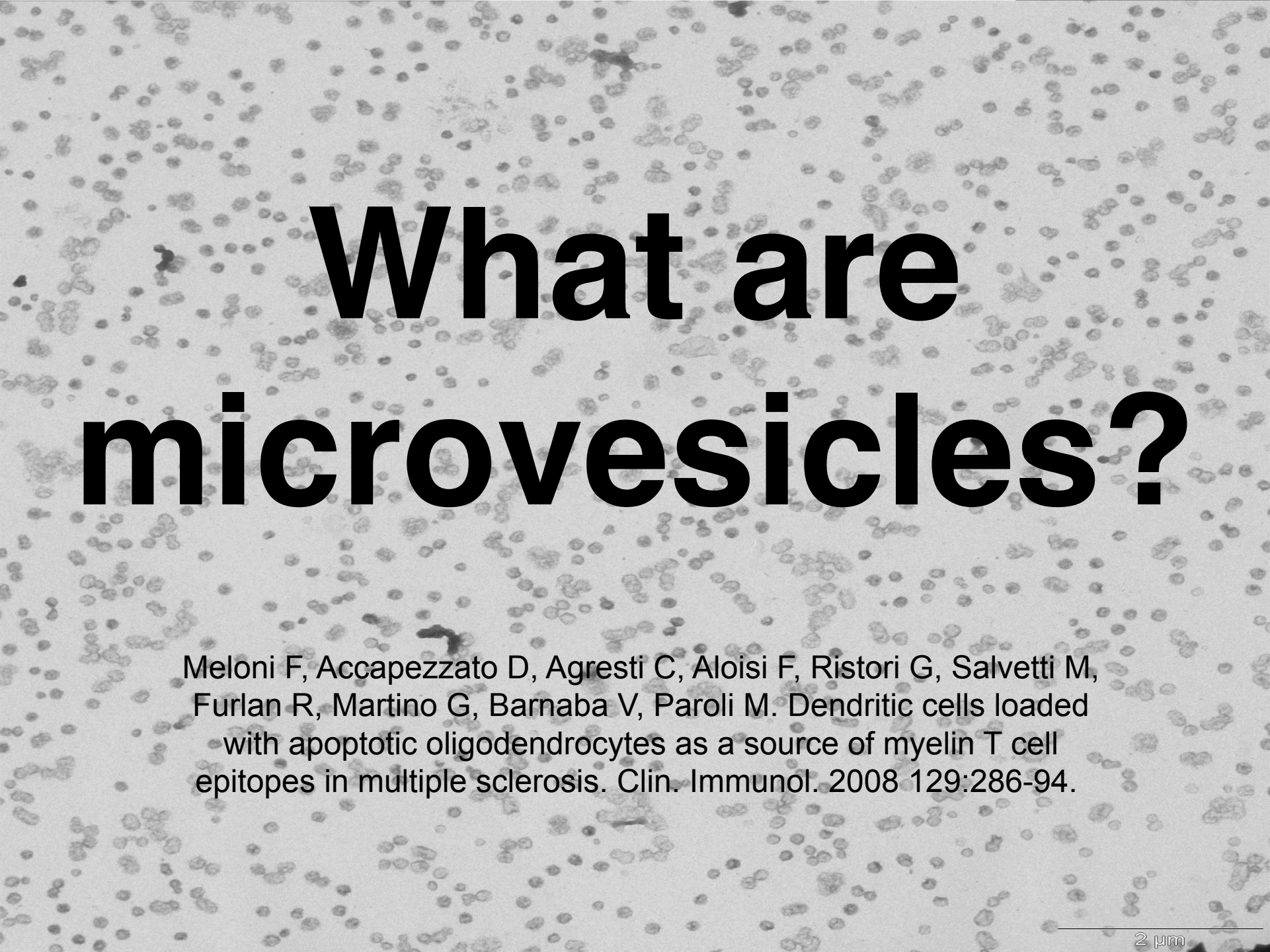
OSPEDALE SAN RAFFAELE

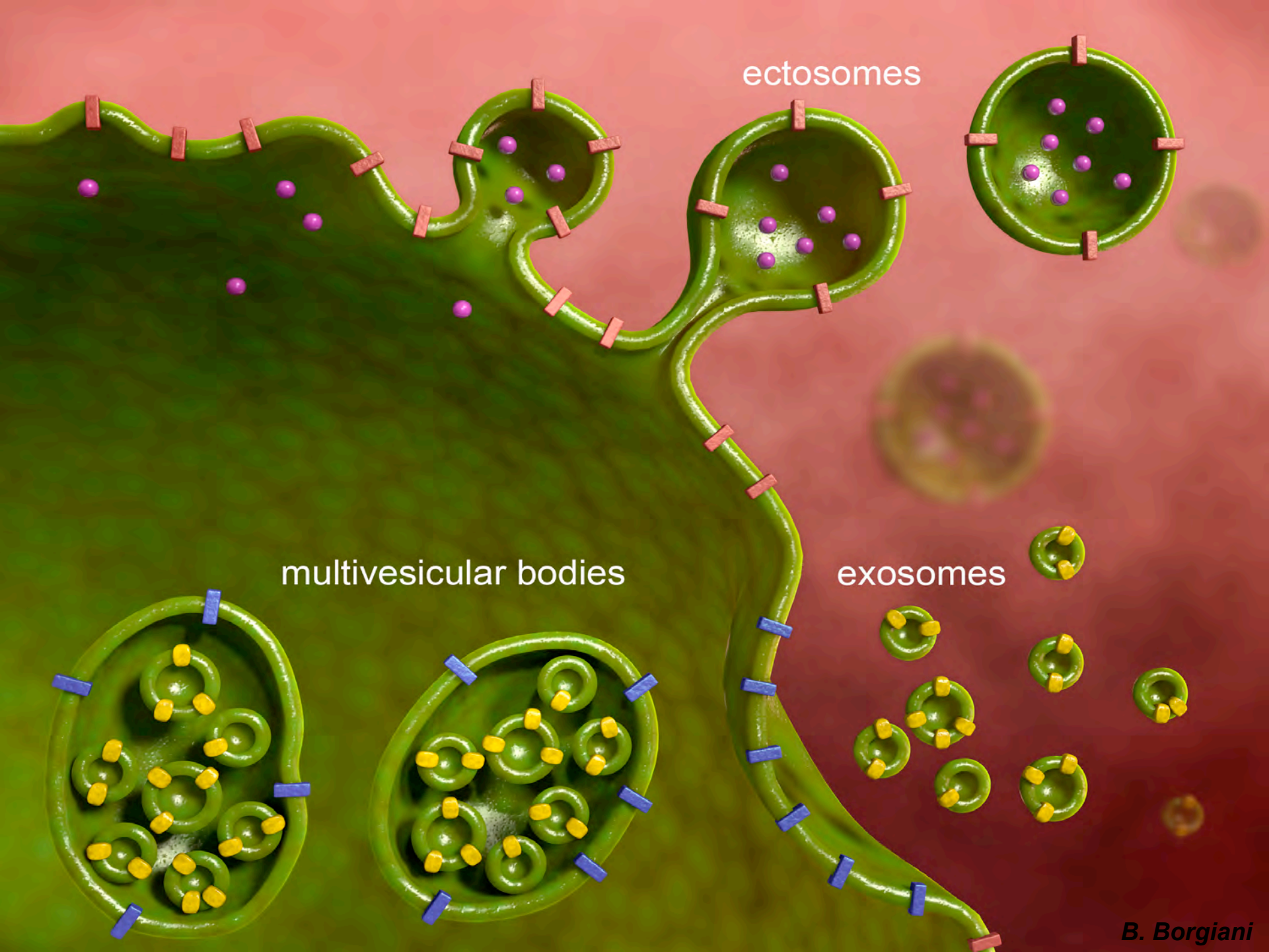
- **Le microvescicole: un nuovo modo**
- **di comunicazione intercellulare**
- Roberto Furlan

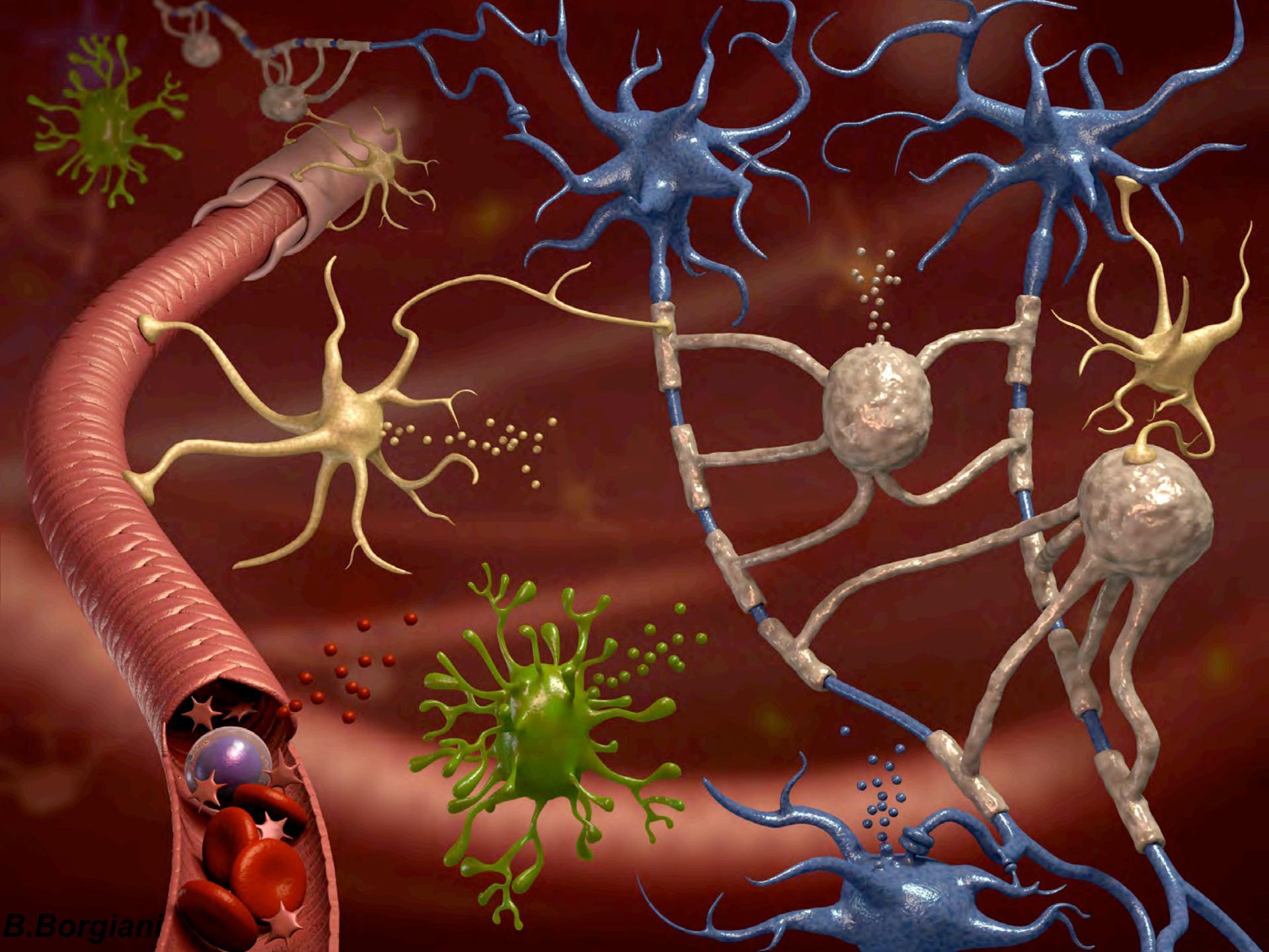
Monza, 10 giugno, 2015

What are microvesicles?

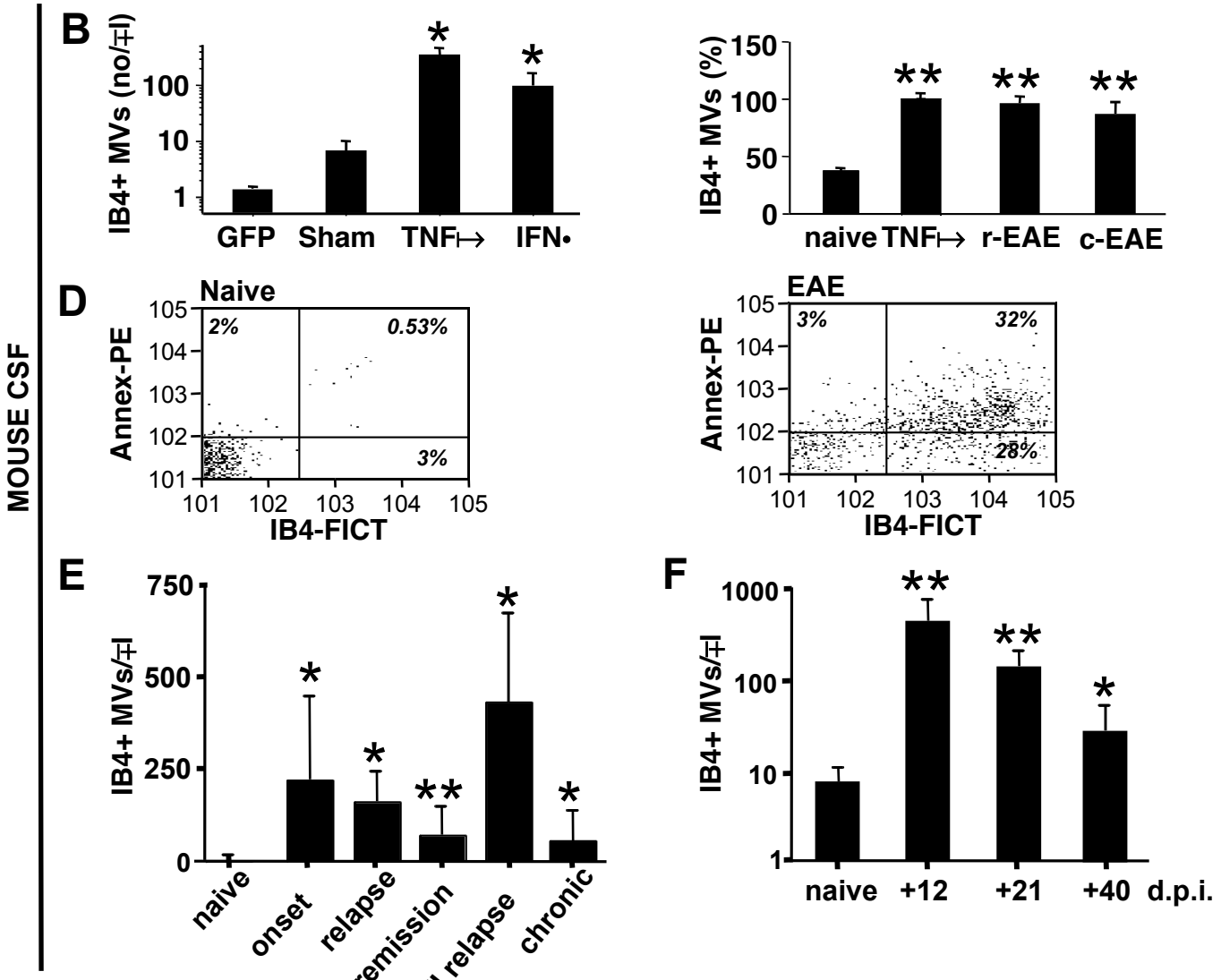
Meloni F, Accapezzato D, Agresti C, Aloisi F, Ristori G, Salvetti M, Furlan R, Martino G, Barnaba V, Paroli M. Dendritic cells loaded with apoptotic oligodendrocytes as a source of myelin T cell epitopes in multiple sclerosis. Clin. Immunol. 2008 129:286-94.



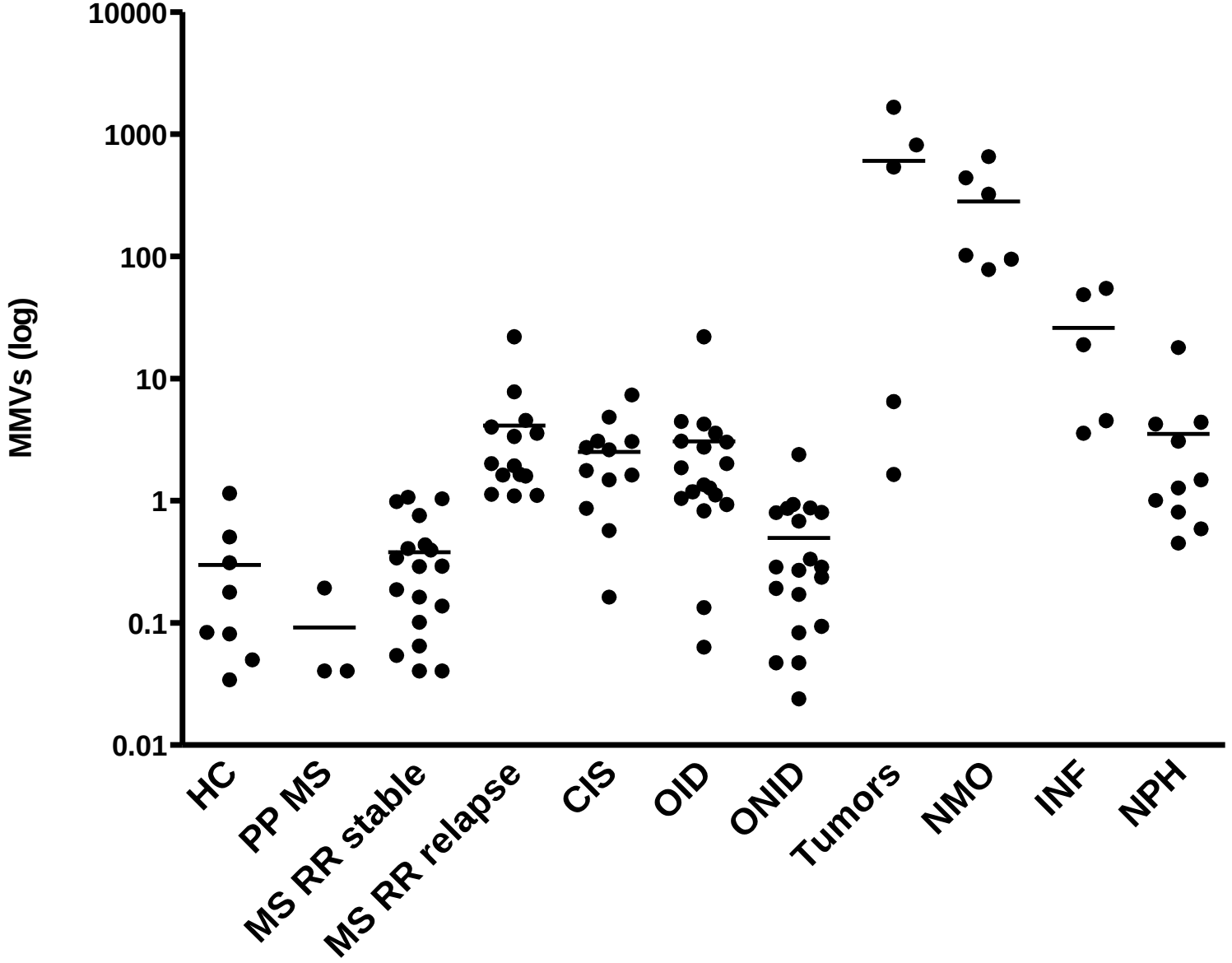

ectosomes
multivesicular bodies
exosomes
B. Borgiani


B.Borgiani

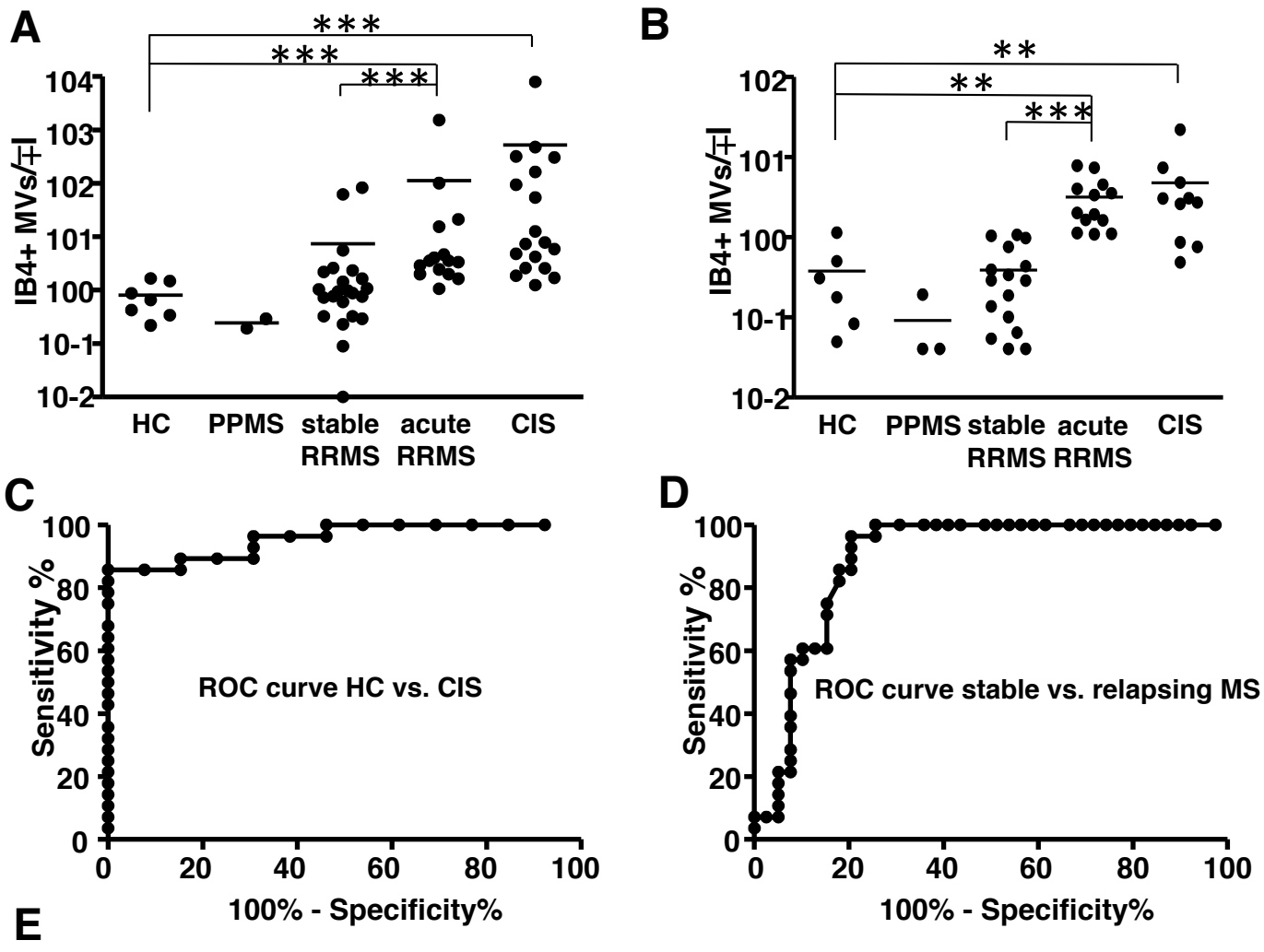
Neuroinflammation induces shed vesicles release by myeloid cells



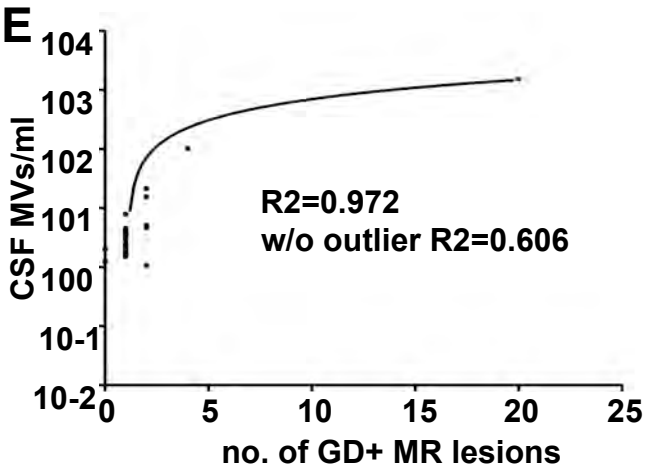
Myeloid shed vesicles are increased in the CSF of patients with neuroinflammation

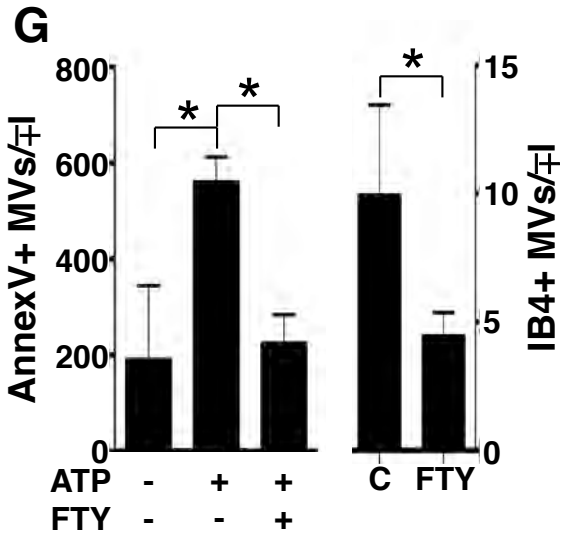


Myeloid shed vesicles are increased in the CSF of patients with neuroinflammation



Myeloid shed vesicles correlate with neuroinflammation and response to treatment with FTY720

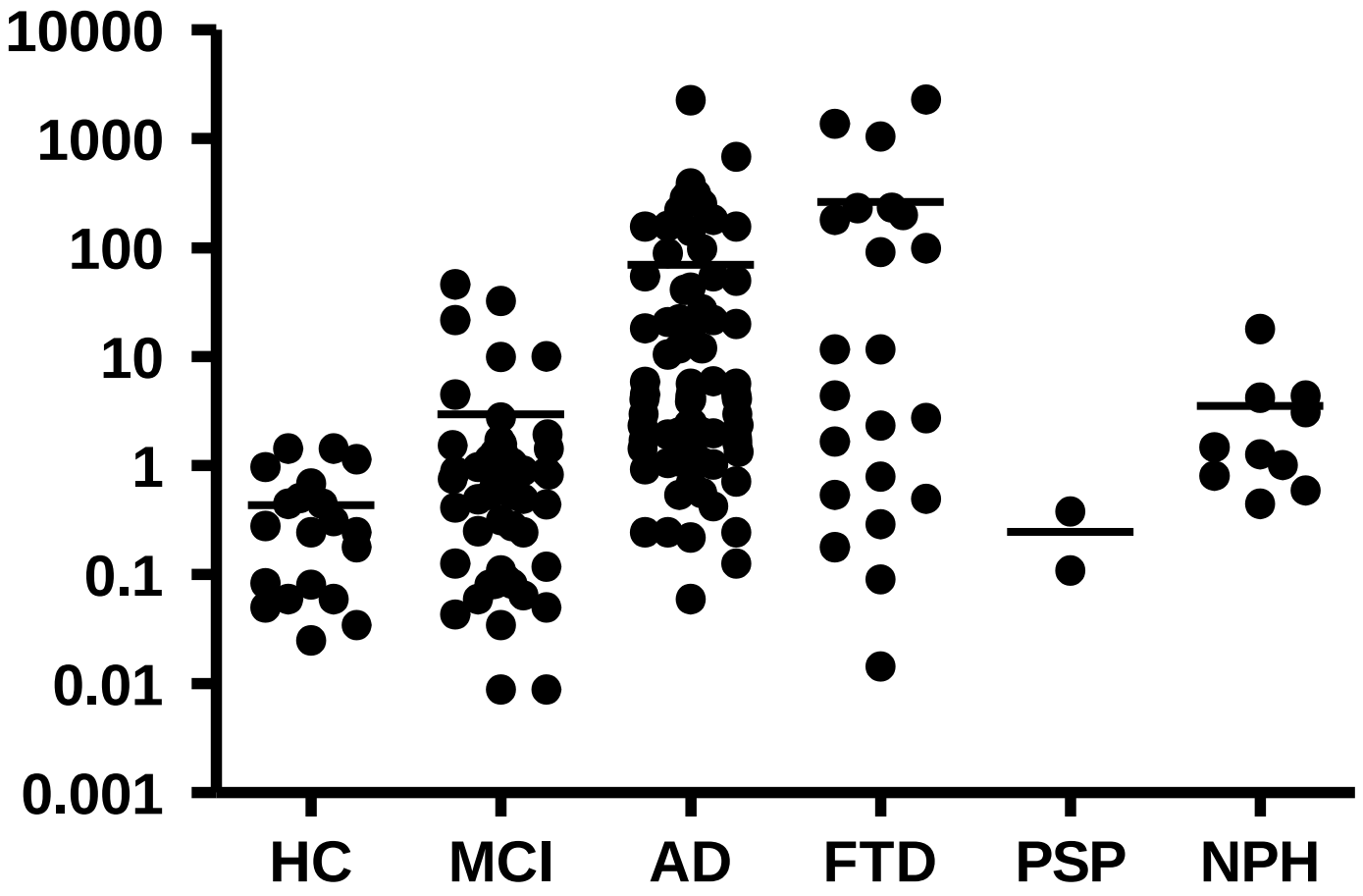




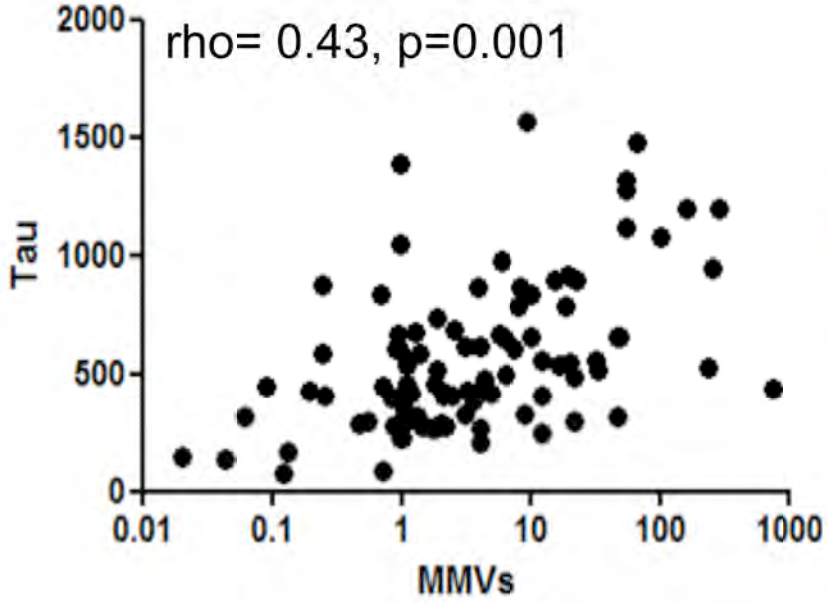
Myeloid Microvesicles in Cerebrospinal Fluid Are Associated with Myelin Damage and Neuronal Loss in Mild Cognitive Impairment and Alzheimer Disease

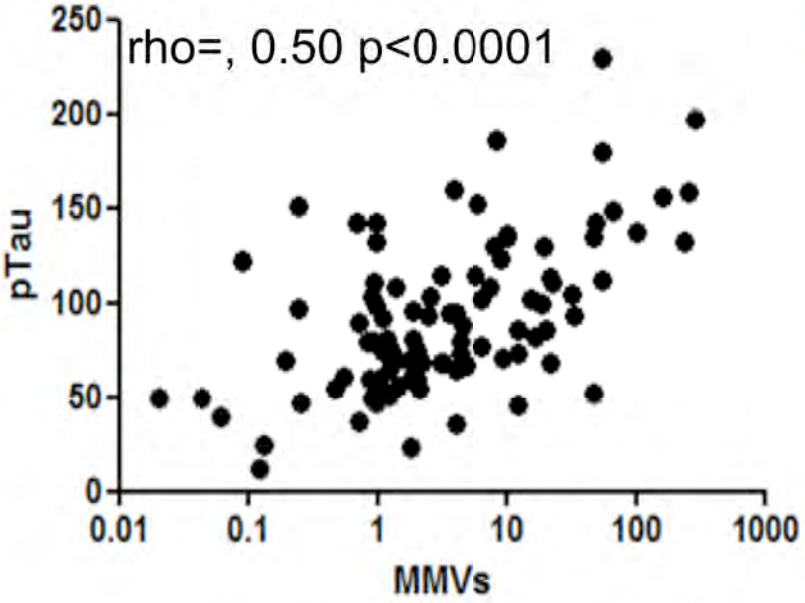
Federica Agosta, MD, PhD,[1] Dacia Dalla Libera, MD,[1] Edoardo Gioele Spinelli, MD,[1] Annamaria Finardi, BSci,[1] Elisa Canu, PhD,[1] Alessandra Bergami, MLT,[1] Luisella Bocchio Chiavetto, PhD,[2] Manuela Baronio, MD,[3] Giancarlo Comi, MD,[1,4] Gianvito Martino, MD,[1] Michela Matteoli, PhD,[5,6] Giuseppe Magnani, MD,[1] Claudia Verderio, PhD,[5,6] and Roberto Furlan, MD, PhD[1]

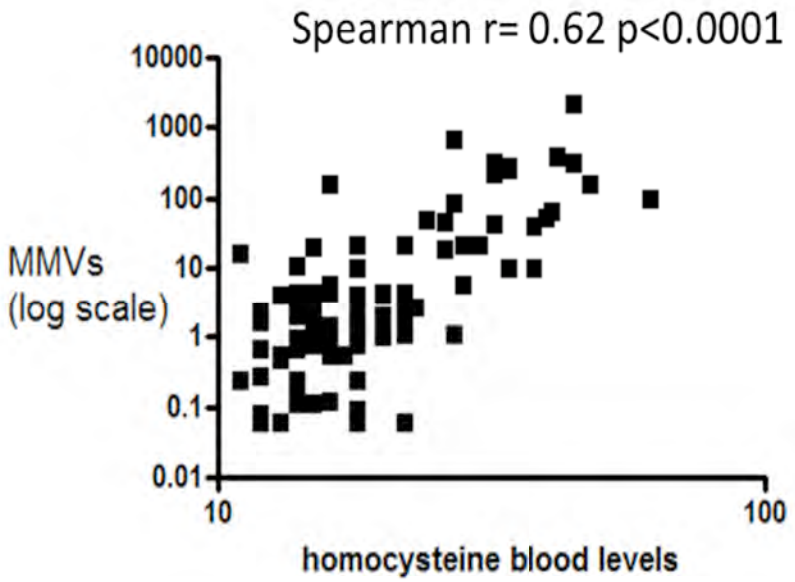
ANN NEUROL 2014;76:813–825

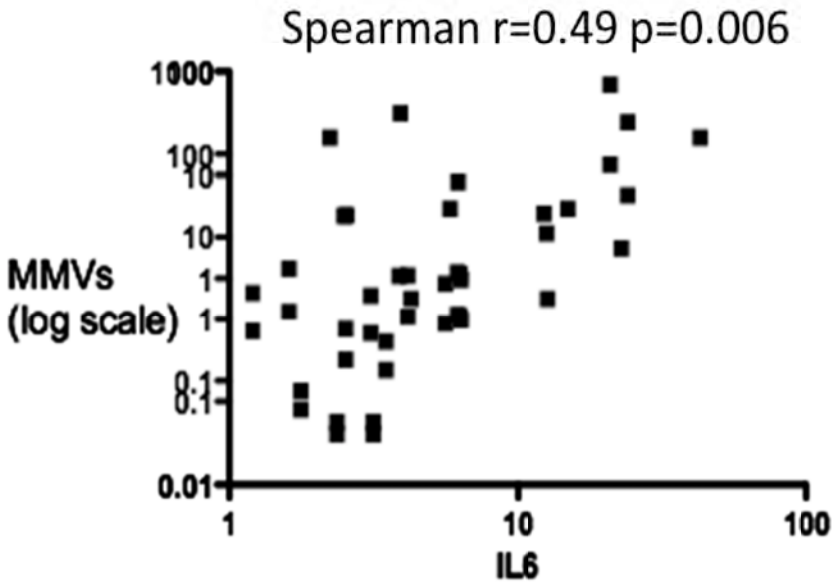


Dacia Dalla Libera
Giuseppe Magnani

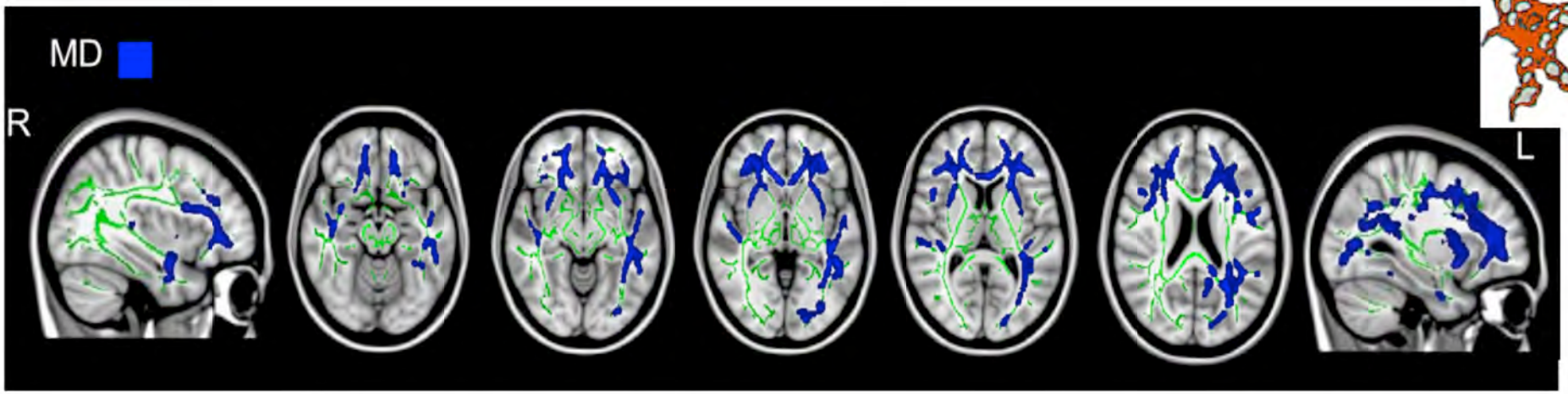

rho= 0.43, p=0.001
Tau
2000
1500
1000
500
0
0.01
0.1
1
10
100
1000
MMVs

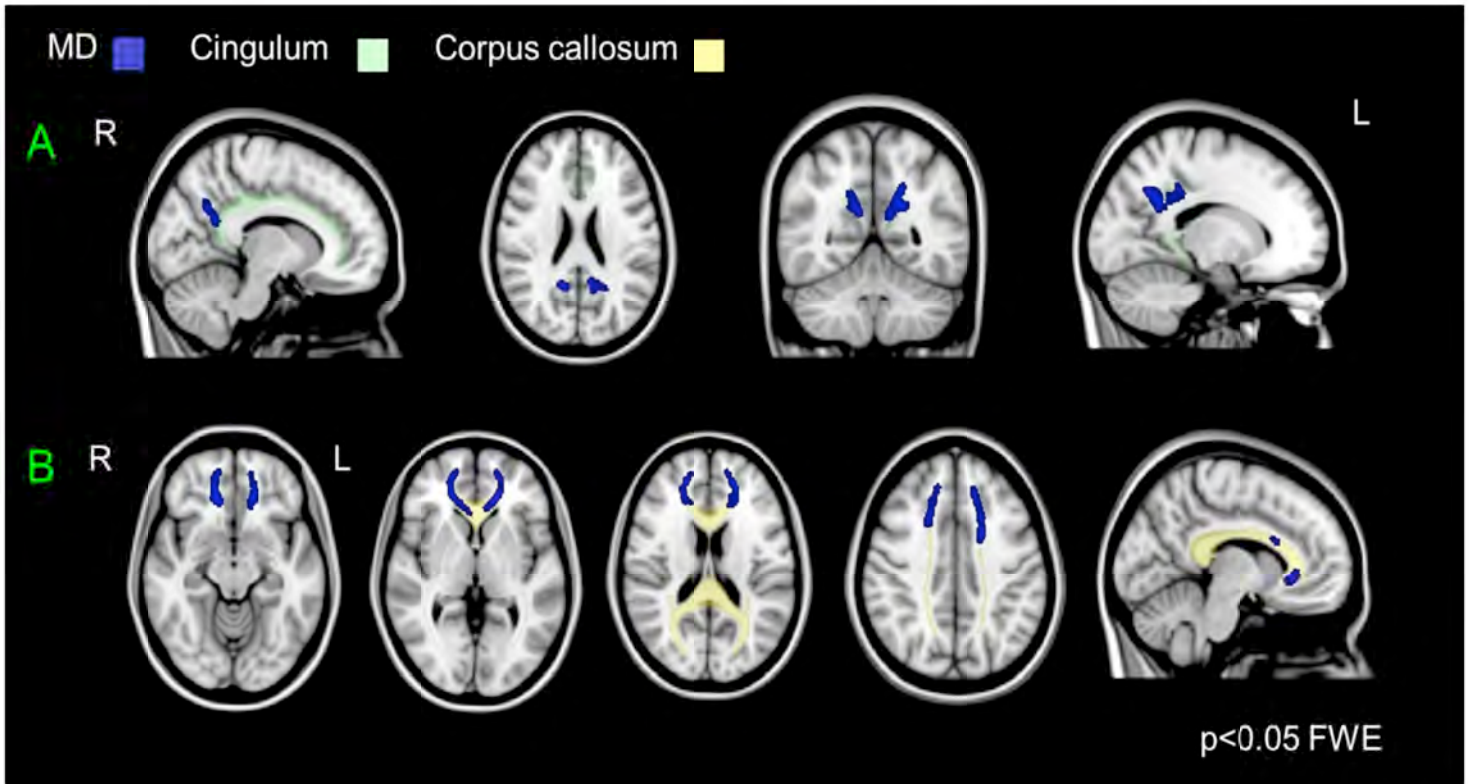

rho=, 0.50 p<0.0001
pTau
250
200
150
100
50
0
0.01
0.1
1
10
100
1000
MMVs


Spearman r= 0.62 p<0.0001
MMVs
(log scale)
10000
1000
100
10
1
0.1
0.01
10
100
homocysteine blood levels


Spearman r=0.49 p=0.006
MMVs
(log scale)
1000
100
10
1
0.1
0.01
1
10
100
IL6

WM MD, but not FA, is associated to MMVs in MCI





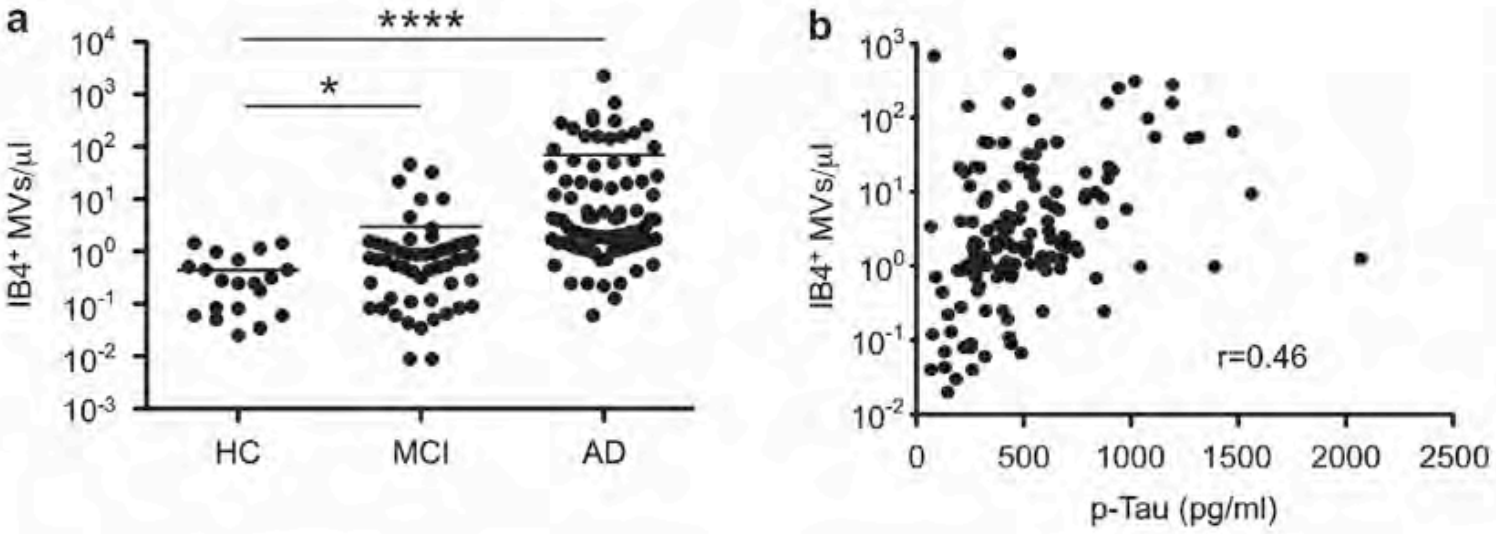
Federica Agosta
Edoardo Spinelli
Massimo Filippi

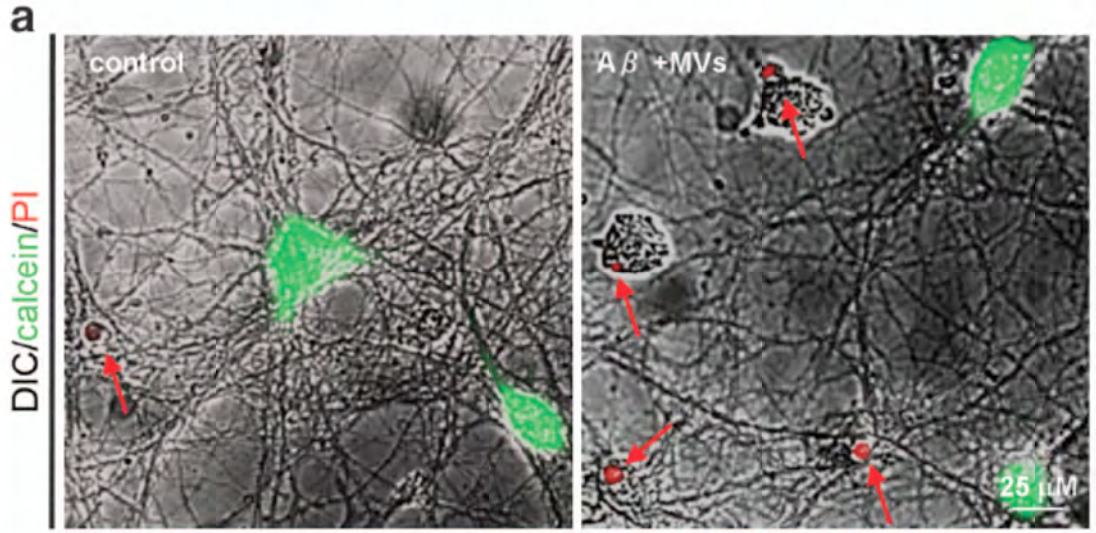
Cell Death and Differentiation (2013), 1–12

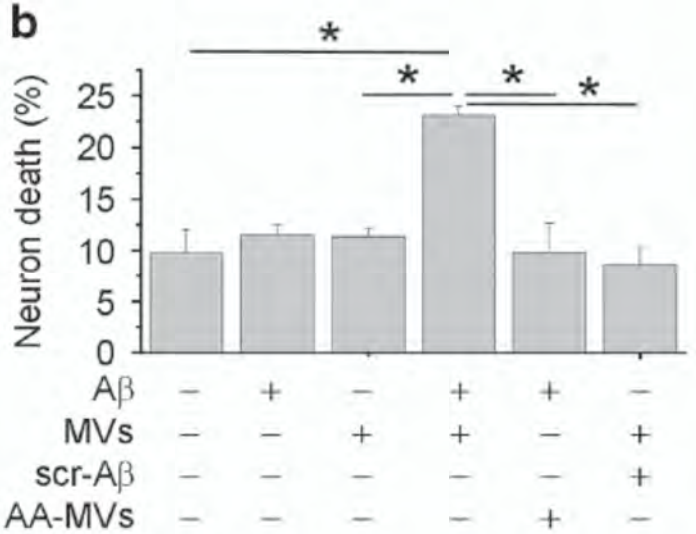
www.nature.com/cdd

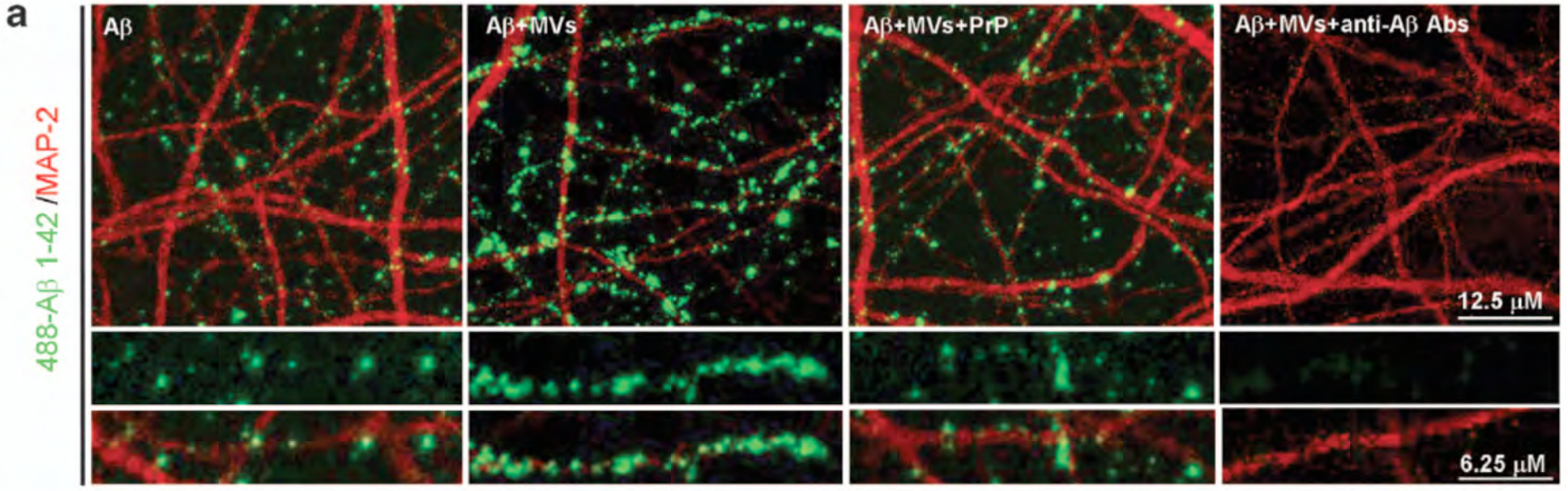
Microglia convert aggregated amyloid-β into neurotoxic forms through the shedding of microvesicles

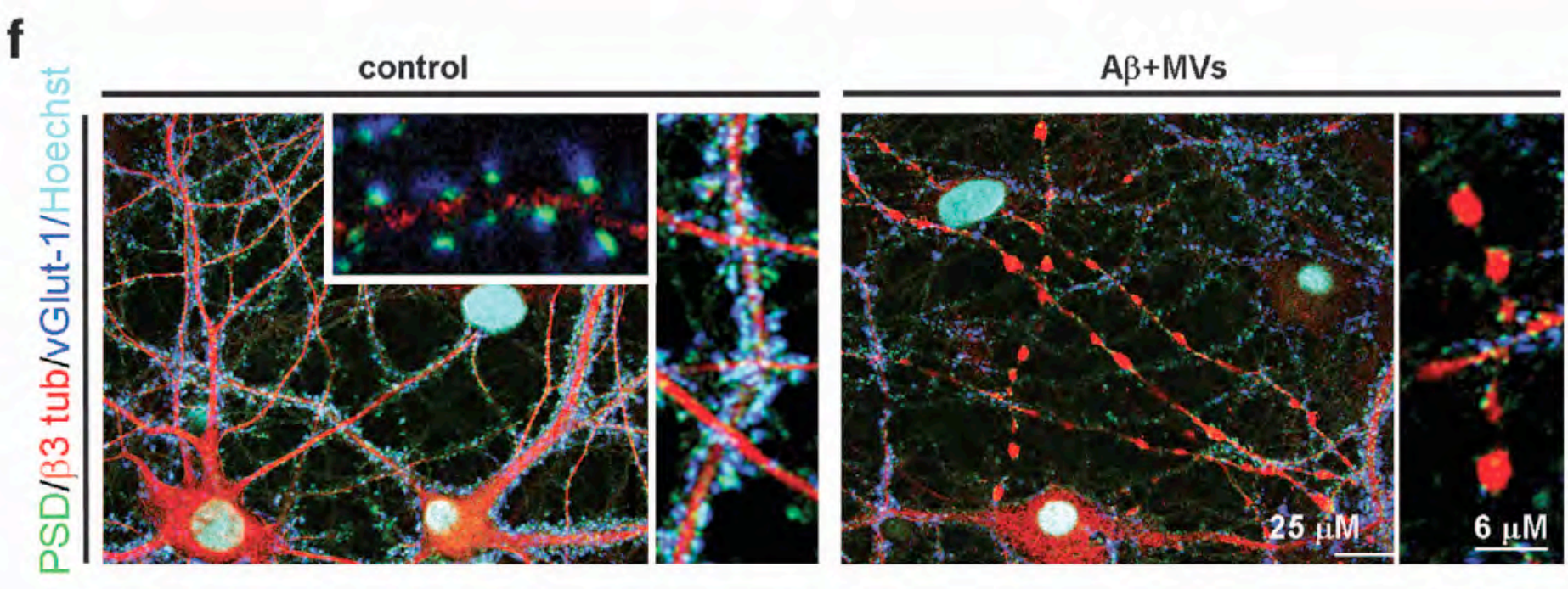
P Joshi[1,2], E Turola[1,2], A Ruiz[1], A Bergami[3], DD Libera[3], L Benussi[4], P Giussani[1], G Magnani[3], G Comi[3], G Legname[5], R Ghidoni[4], R Furlan[3], M Matteoli*[,1,6,7] and C Verderio*[,2,6,7]

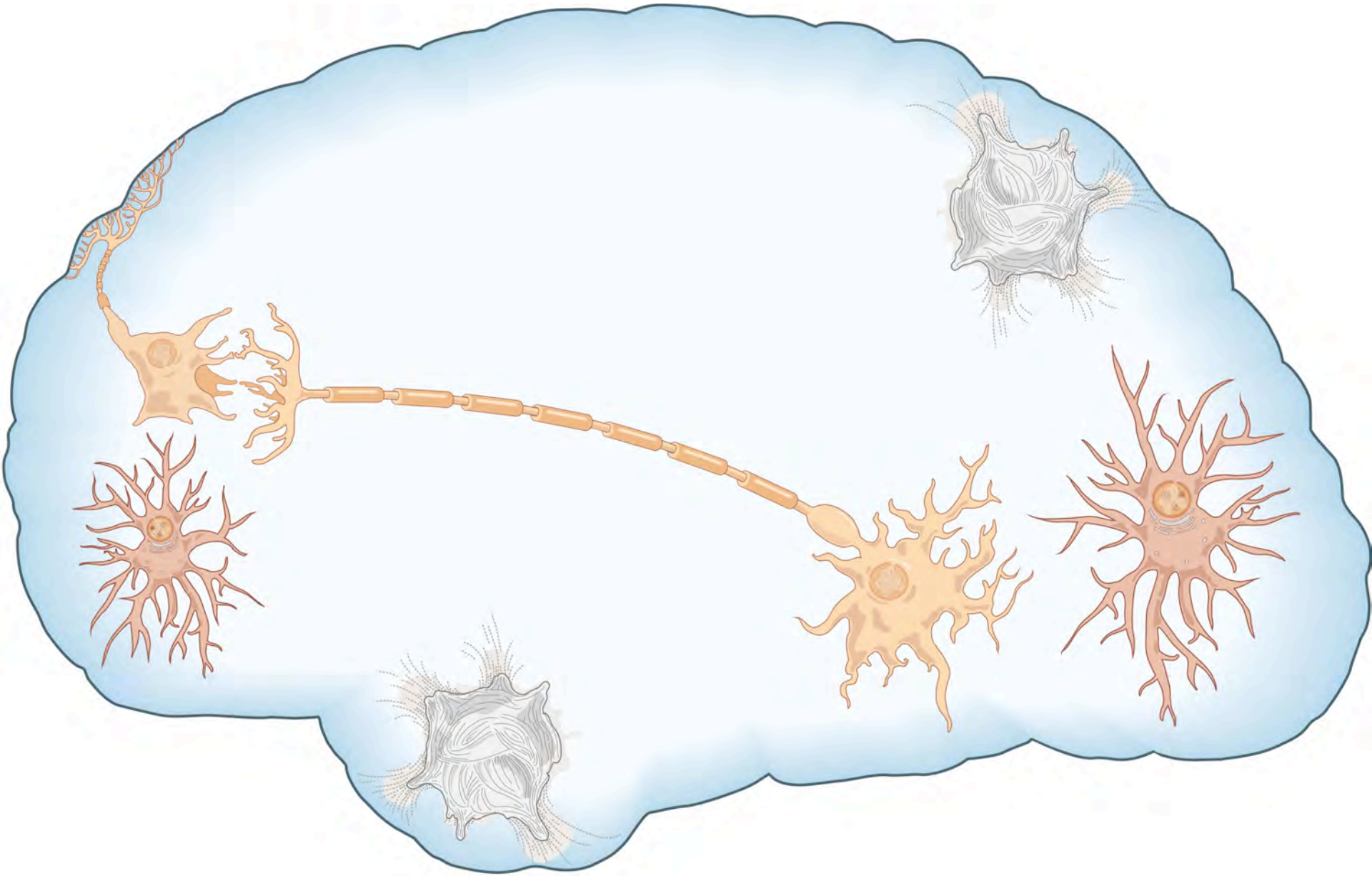


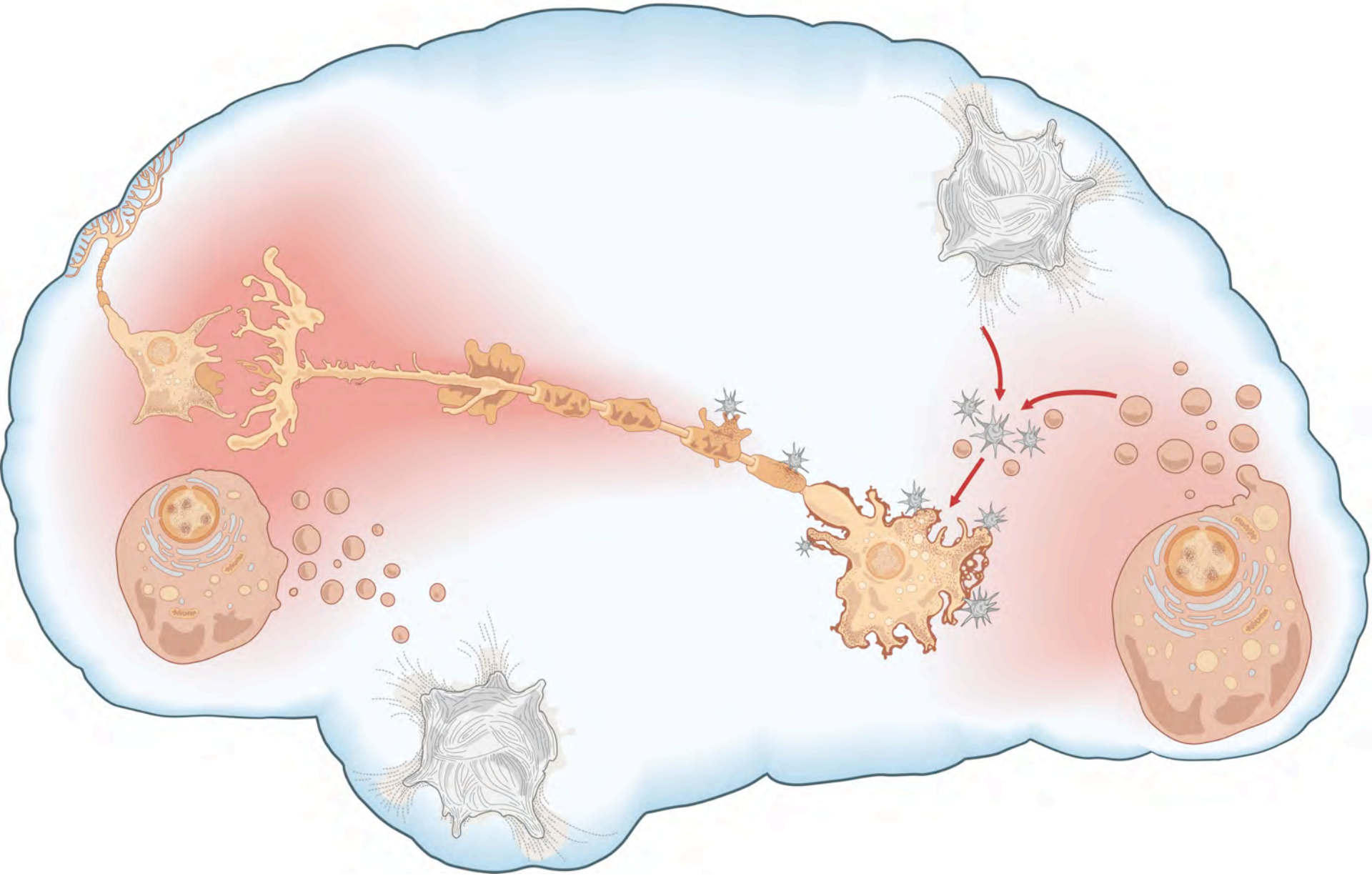

a
control
Aβ +MVs
25 μM
DIC/calcein/PI


b
Neuron death (%)
0
5
10
15
20
25
*
*
*
*
Aβ – + – + + –
MVs – – + + – +
scr-Aβ – – – – – +
AA-MVs – – – – + –


a
Aβ
Aβ+MVs
Aβ+MVs+PrP
Aβ+MVs+anti-Aβ Abs
12.5 μM
6.25 μM
488-Aβ 1-42 /MAP-2


f
control
Aβ+MVs
PSD/β3 tub/vGlut-1/Hoechst
25 μM
6 μM





Detection technology is an issue

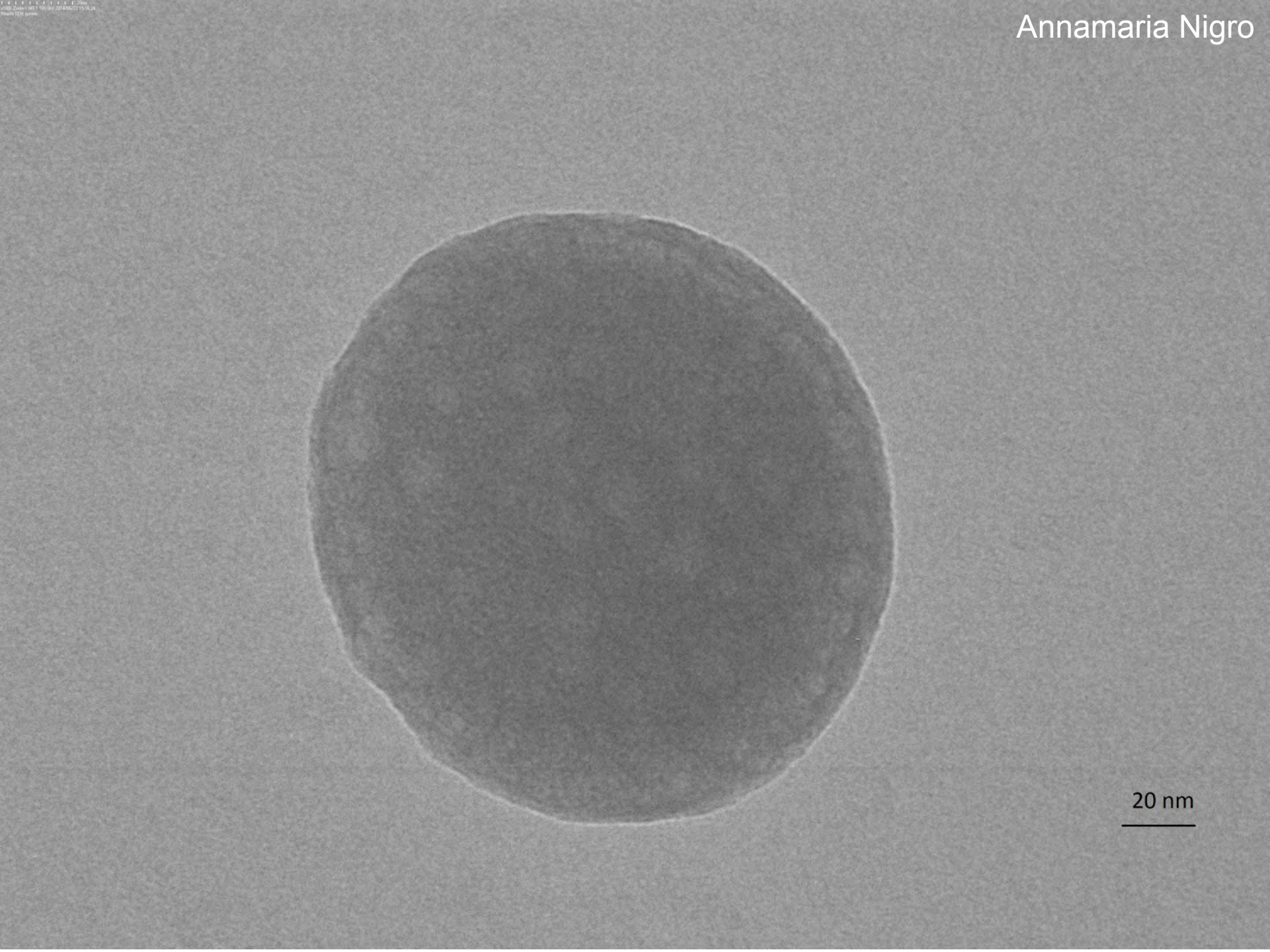
Journal of Thrombosis and Haemostasis, **12**: 1182–1192 DOI: 10.1111/jth.12602

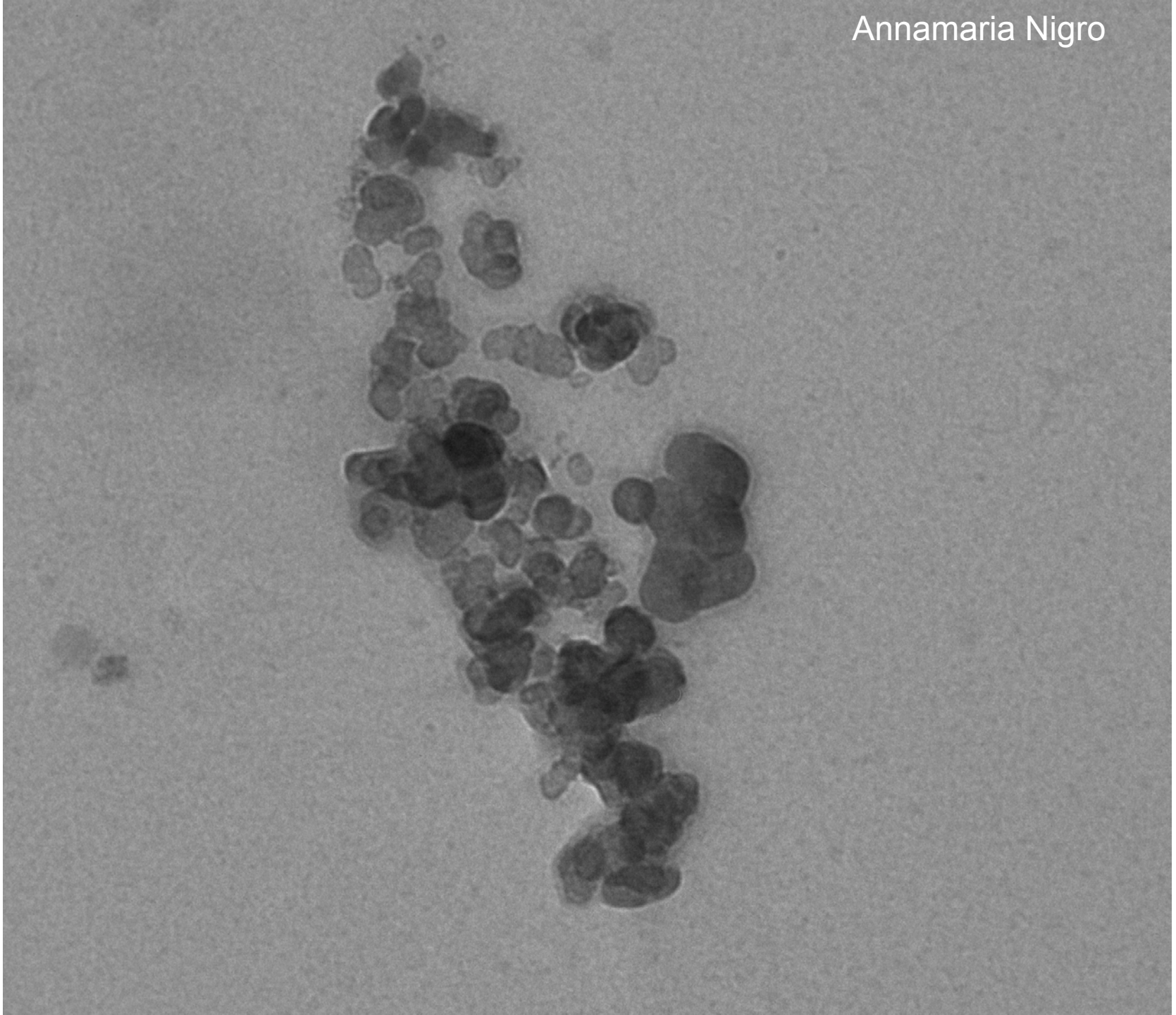
ORIGINAL ARTICLE

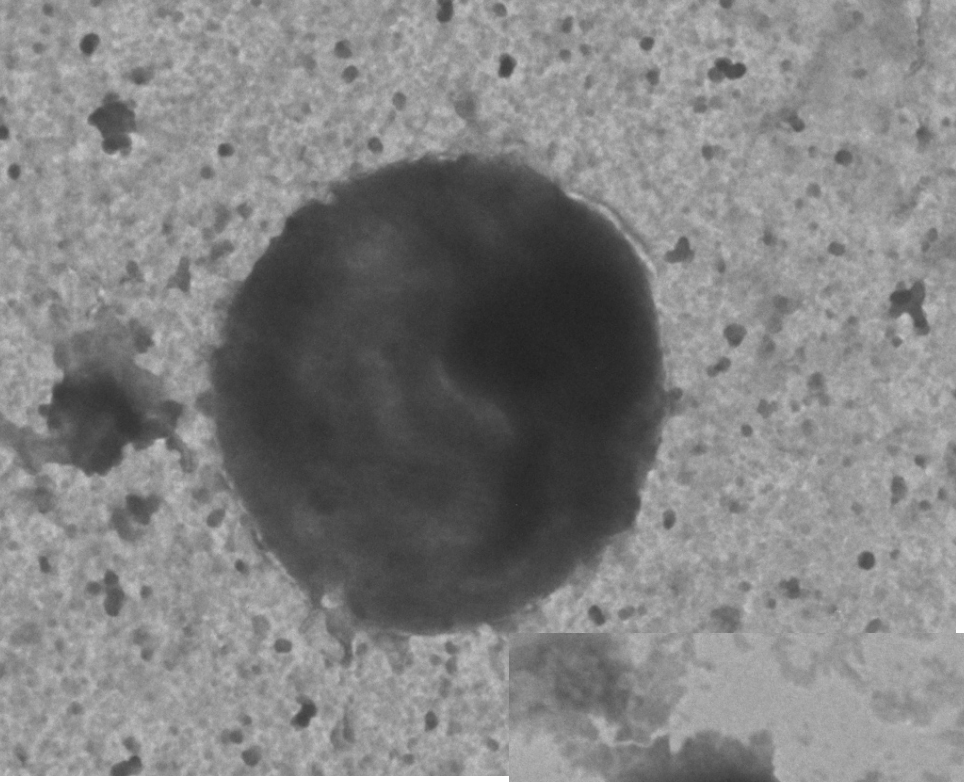
Particle size distribution of exosomes and microvesicles determined by transmission electron microscopy, flow cytometry, nanoparticle tracking analysis, and resistive pulse sensing

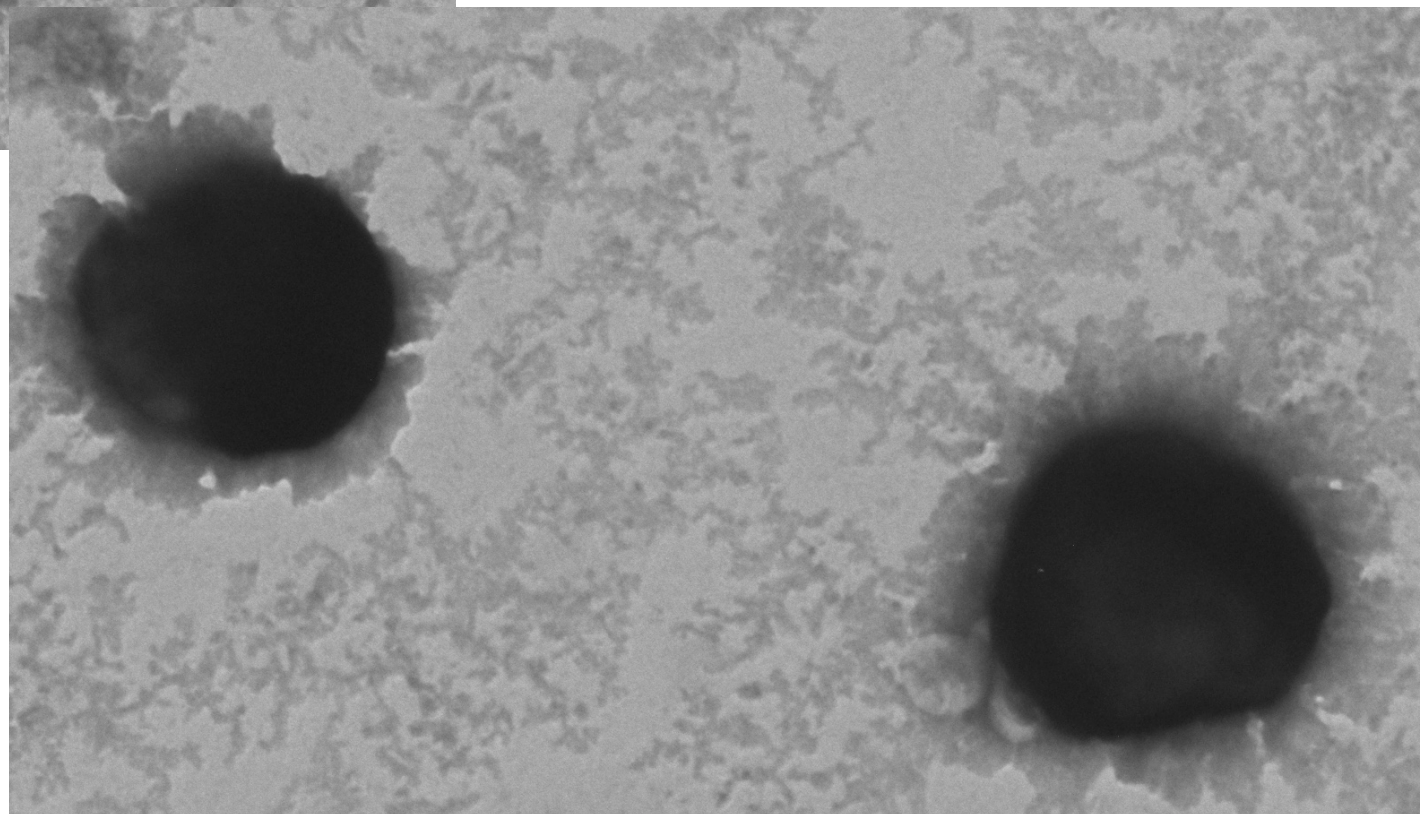
E. VAN DER POL,*† F. A. W. COUMANS,*† A. E. GROOTEMAAT,* C. GARDINER,‡ I. L. SARGENT,‡ P. HARRISON,§ A. STURK,* T. G. VAN LEEUWEN† and R. NIEUWLAND*

**Laboratory of Experimental Clinical Chemistry, Academic Medical Center, University of Amsterdam; †Biomedical Engineering and Physics, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands; ‡Nuffield Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Oxford; and §School of Immunity and Infection, University of Birmingham Medical School, Birmingham, UK*


Annamaria Nigro
20 nm


Annamaria Nigro






what about
their biology?

Epub ahead of print December 30, 2013 - doi:10.1189/jlb.0913485

JLB

Article

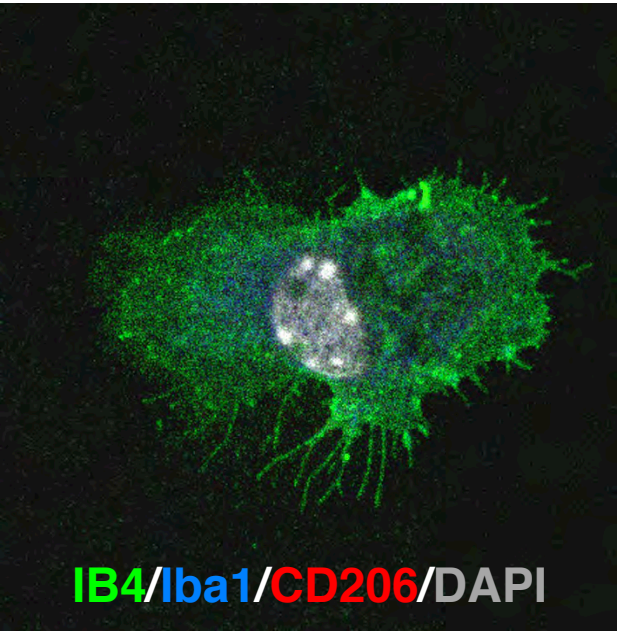
Activated macrophages release microvesicles containing polarized M1 or M2 mRNAs

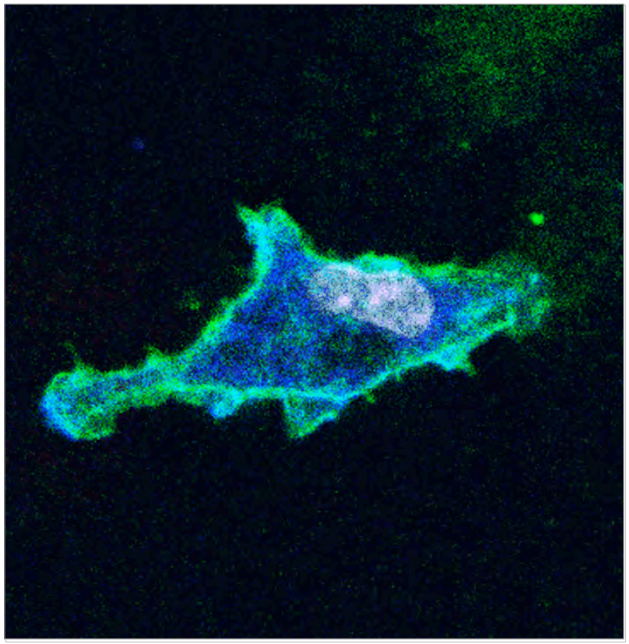
Livia Garzetti, Ramesh Menon,* Annamaria Finardi,* Alessandra Bergami,* Antonio Sica,† Gianvito Martino,* Giancarlo Comi,* Claudia Verderio,†,‡ Cinthia Farina,* and Roberto Furlan*,1*

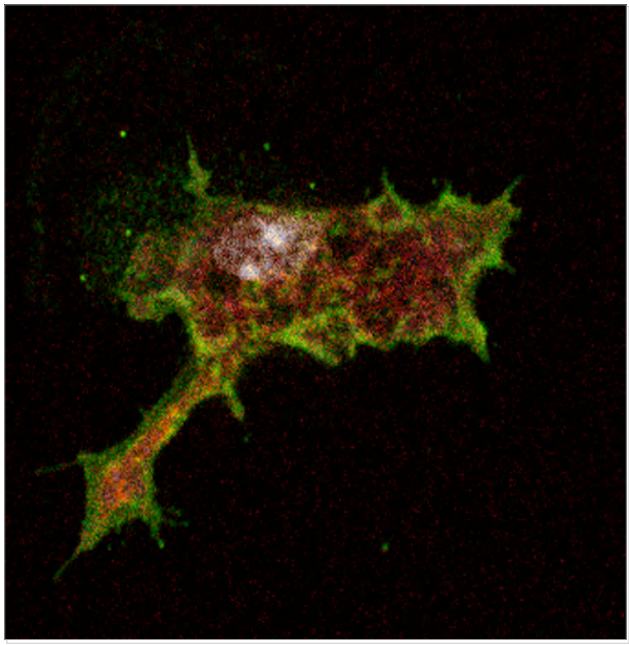
*Institute of Experimental Neurology, Division of Neuroscience, San Raffaele Scientific Institute, Milano, Italy; †Humanitas Clinical and Research Center, Rozzano, Italy; and ‡Consiglio Nazionale delle Ricerche, Institute of Neuroscience, Milano, Italy

RECEIVED SEPTEMBER 5, 2013; REVISED DECEMBER 11, 2013; ACCEPTED DECEMBER 13, 2013. DOI: 10.1189/jlb.0913485

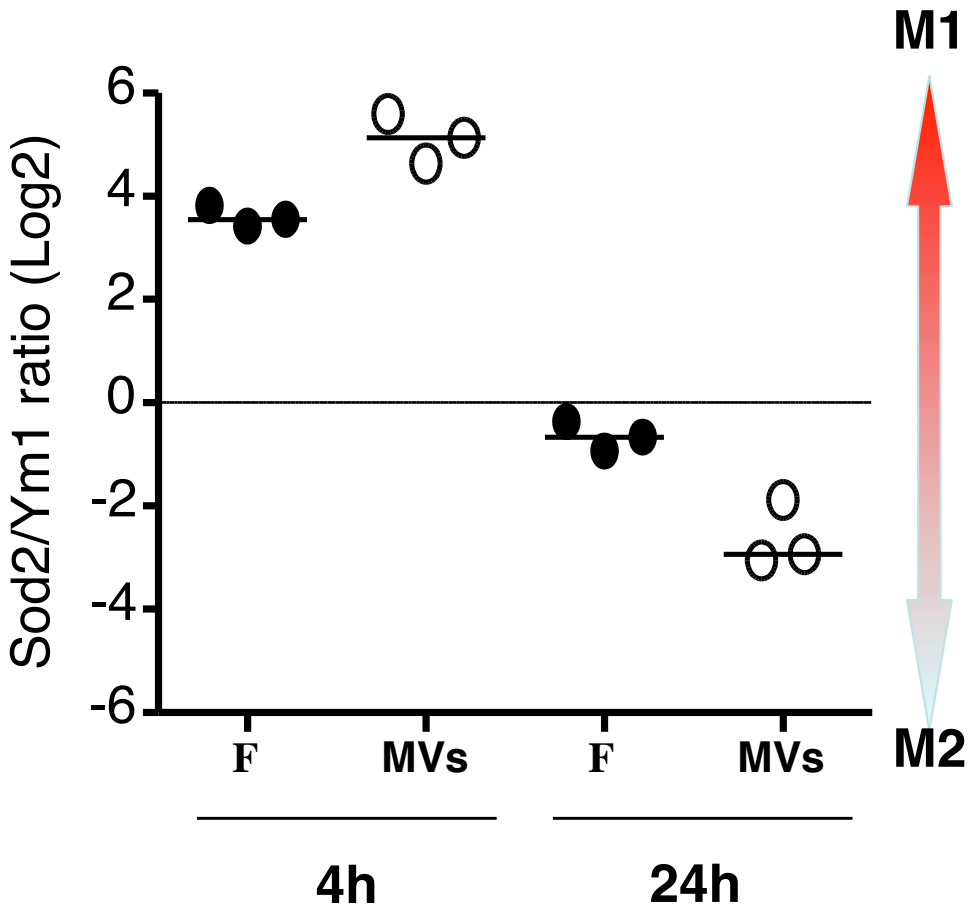
NS **M1** **M2**







Garzetti et al. J. Leuk. Biol. 2014



Garzetti et al. J. Leuk. Biol. 2014

Oligo-Neurons

Neurotransmitter-triggered transfer of exosomes mediates oligodendrocyte-neuron communication.
Frühbeis C, Fröhlich D, Kuo WP, Amphornrat J, Thilemann S, Saab AS, Kirchhoff F, Möbius W, Goebbels S, Nave KA, Schneider A, Simons M, Klugmann M, Trotter J, Krämer-Albers EM.
PLoS Biol. 2013 Jul;11(7):e1001604. doi: 10.1371/journal.pbio.1001604. Epub 2013 Jul 9.

Microglia-Neurons

Microvesicles released from microglia stimulate synaptic activity via enhanced sphingolipid metabolism.
Antonucci F, Turola E, Riganti L, Caleo M, Gabrielli M, Perrotta C, Novellino L, Clementi E, Giussani P, Viani P, Matteoli M, Verderio C.
EMBO J. 2012 Mar 7;31(5):1231-40. doi: 10.1038/emboj.2011.489. Epub 2012 Jan 13.

Astrocyte-Neurons

Immunogold detection of L-glutamate and D-serine in small synaptic-like microvesicles in adult hippocampal astrocytes.
Bergersen LH, Morland C, Ormel L, Rinholm JE, Larsson M, Wold JF, Røe AT, Stranna A, Santello M, Bouvier D, Ottersen OP, Volterra A, Gundersen V.
Cereb Cortex. 2012 Jul;22(7):1690-7. doi: 10.1093/cercor/bhr254. Epub 2011 Sep 12.

Tumors

Protein typing of circulating microvesicles allows real-time monitoring of glioblastoma therapy.
Shao H, Chung J, Balaj L, Charest A, Bigner DD, Carter BS, Hochberg FH, Breakefield XO, Weissleder R, Lee H.
Nat Med. 2012 Dec;18(12):1835-40. doi: 10.1038/nm.2994. Epub 2012 Nov 11.

Alzheimer

Exosome-associated tau is secreted in tauopathy models and is selectively phosphorylated in cerebrospinal fluid in early Alzheimer disease.
Saman S, Kim W, Raya M, Visnick Y, Miro S, Saman S, Jackson B, McKee AC, Alvarez VE, Lee NC, Hall GF.
J Biol Chem. 2012 Feb 3;287(6):3842-9. doi: 10.1074/jbc.M111.277061. Epub 2011 Nov 4.

Distinct cerebrospinal fluid amyloid-beta peptide signatures in cognitive decline associated with Alzheimer's disease and schizophrenia.
Albertini V, Benussi L, Paterlini A, Glionna M, Prestia A, Bocchio-Chiavetto L, Amicucci G, Galluzzi S, Adorni A, Geroldi C, Binetti G, Frisoni GB, Ghidoni R.
Electrophoresis. 2012 Dec;33(24):3738-44. doi: 10.1002/elps.201200307. Epub 2012 Nov 26.

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