

## CURRICULUM VITAE

July 2020

### Daniele Zacchetti

Born in Udine / Italia, 9 November 1964

Italian

Married, four children

Work address:

Dibit - Istituto Scientifico Ospedale San Raffaele

via Olgettina 58, 20132 Milano - Italia

tel. +39-2-2643.4817/5363

e-mail: zacchetti.daniele@hsr.it, danzac64@gmail.com

### EDUCATION:

- Maturita' Classica, Liceo Classico "G. Parini", Milano, Italy. July 1983

- Degree in Pharmaceutical Chemistry and Technology, 110/110 with honors, University of Milano, Italy. 12 July 1989.

- PhD in Cellular and Molecular Biology, University of Milano, Italy. 14 September 1993

### RESEARCH EXPERIENCE

March 1987 - July 1989

Undergraduate student, Cellular Pharmacology Laboratory (prof. Jacopo Meldolesi), Scientific Institute San Raffaele Hospital and Department of Pharmacology, School of Medicine, University of Milano, Italy.

August 1989 - November 1991

PhD student, Department of Pharmacology and Scientific Institute San Raffaele Hospital, University of Milano, Italy.

December 1991 - December 1994

Junior Researcher, Dibit - Scientific Institute San Raffaele Hospital, Italy.

(March 1992 - March 1993 Military leave)

January 1995 - September 1997

PostDoctoral fellow, Kai Simons Laboratory, Cell Biology Programme, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany [EMBO fellow, "Marie Curie" Fellow]

October 1997 - present

Researcher (since 2002 Senior Researcher and Principal Investigator), Dibit - Scientific Institute San Raffaele Hospital, Italy.

### TEACHING ACTIVITY

- Adjunct Professor in Pharmacology, San Raffaele University (a.y. from 1999-2000 to 2001-2002).

- Adjunct Professor in Biotechnology, San Raffaele University (a.y. from 2003-2004 to 2010-2011); Master's degree in biotechnology, coordinator of the integrated course in "Expression and purification of eukaryotic proteins".

- Adjunct Professor in Pharmacology, San Raffaele University (a.y. since 2010-2011); School of Medicine, coordinator of integrated courses of general pharmacology

### FINANCIAL SUPPORT (last 5 years)

Ivascomar project; Cluster Tecnologico Nazionale Scienze della Vita "Alisei" - MIUR

Budget of the project: 9 MEuro

Partenariat: Dompe', Sentinel, Primm, C4T, UniMiB, UniSR, FCSR

Roles: Coordinator of the proposal; Coordinator and responsible for the budget of the whole project towards MIUR;

Coordinator and responsible for the FCSR budget (total of ~1 MEuro, specifically allocated to DZ as PI: ~400,000 Euro)

Start and end date: 2013-07-01 – 2017-12-31

NeOn project; Call "Accordi" of Regione Lombardia

Budget of the project: 7 MEuro

Partenariat: Dompe', UniSR, UniMi, IN-CNR, PoliMi, NeuroZone, Proxentia, IEO, IIT

Roles: Co-Coordinator of the call application (together with the Grant Office of Dompe' Farmaceutici); Co-Coordinator and responsible (together with prof. Banfi) for UniSR funds

Start and end date: 2017-07-01 – 2020-12-31

### RESEARCH TOPICS

Mechanisms of protein translation in neurons: relevance in Alzheimer's disease and synaptopathies

Molecular mechanisms of glia activation in neuroinflammatory and neurodegenerative diseases

### MANAGEMENT ACTIVITIES

2016-present. Scientific and Operative Directorate. Responsible for the Service Center for Research ("Centro Servizi Tecnico-Operativi della Ricerca"). Focal point for research-related issues on instrumentations, informatics, building maintenance, logistics, safety.

2016-present. Institutional representative for San Raffaele in the Life Science Cluster of Lombardy (Research and Innovation)

2015-present. Person in charge for chemical safety in the San Raffaele Research Area

2004-present. Teacher (Chemical safety) in the Introductory Course for new fellows of the Research Area (about 5 editions/year)

1999-present. Creator and admin of the Intranet of the Research Area

2010-15. Board (vice-coordinator) of the PhD program in Neuroscience

PhD selection committee at UniSR (several times)

Reviewer for the grants issued by the Alzheimer's Association USA

Reviewer for several peer-reviewed international journals

Committee for the evaluation of the calls opened by a national foundation (2017)

## PUBLICATIONS

Scopus Author ID: 7003648910 Publications: 47 (Scopus-SciVal)

H-index: 23 (Scopus-SciVal); 26 (GoogleScholar)

Total citations: 1748 (Scopus-SciVal); 2233 (GoogleScholar)

- Bettgazzi B, Pelizzoni I, Salerno Scarzella F, Restelli LM, **Zacchetti** D, Maltecca F, Casari G, Grohovaz F, Codazzi F. Upregulation of Peroxiredoxin 3 Protects A $\beta$ 312-KO Cortical Neurons In Vitro from Oxidative Stress: A Paradigm for Neuronal Cell Survival under Neurodegenerative Conditions. *Oxid Med Cell Longev*. 2019 Oct 31;2019:4721950

- Ragni E, Perucca Orfei C, De Luca P, Lugano G, Viganò M, Colombini A, Valli F, **Zacchetti** D, Bollati V, de Girolamo L. Interaction with hyaluronan matrix and miRNA cargo as contributors for in vitro potential of mesenchymal stem cell-derived extracellular vesicles in a model of human osteoarthritic synoviocytes. *Stem Cell Res Ther*. 2019 Mar 29;10(1):109

- Bettgazzi B, Bellani S, Roncon P, Guarnieri FC, Bertero A, Codazzi F, Valtorta F, Simonato M, Grohovaz F, **Zacchetti** D. eIF4B phosphorylation at Ser504 links synaptic activity with protein translation in physiology and pathology. *Scientific Reports* (2017) 7, 10563

- Codazzi F, Pelizzoni I, **Zacchetti** D, Grohovaz F. Iron entry in neurons and astrocytes: a link with synaptic activity. *Front Mol Neurosci*. 2015 Jun 3;8:18.

- Lazzaro M, Bettgazzi B, Barbariga M, Codazzi F, **Zacchetti** D, Alessio M (2014) Ceruloplasmin potentiates nitric oxide synthase activity and cytokines secretion in activated microglia. *Journal of Neuroinflammation*, 11:164

- Sardi C, Zambusi L, Finardi A, Ruffini F, Tolun AA, Dickerson IM, Righi M, **Zacchetti** D, Grohovaz F, Provini L, Furlan R, and Morara S. (2014) Involvement of Calcitonin Gene-Related Peptide and Receptor Component Protein in experimental autoimmune encephalomyelitis. *J Neuroimmunol*. 2014 Jun 15;271(1-2):18-29.

- Cesani M, Cavalca E, Macco R, Leoncini G, Terreni MR, Lorioli L, Furlan R, Comi G, Doglioni C, **Zacchetti** D, Sessa M, Scherzer CR, Biffi A. (2014) Metallothioneins as dynamic markers for brain disease in lysosomal disorders. *Ann Neurol*. 2014 Jan;75(1):127-37

- Macco R, Pelizzoni I, Consonni A, Vitali I, Giacalone G, Martinelli Boneschi F, Codazzi F, Grohovaz F, and **Zacchetti** D (2013) Astrocytes acquire resistance to iron-dependent oxidative stress upon proinflammatory activation. *J. Neuroinflamm.*, 10:130

- Pelizzoni I, **Zacchetti** D, Campanella A, Grohovaz F, and Codazzi F (2013) Iron uptake in quiescent and inflammation-activated astrocytes: a potentially neuroprotective control of iron burden. *Biochim Biophys Acta - Molecular Basis of Disease* 1832:1326-33

- Pelizzoni I, **Zacchetti** D, Smith CP, Grohovaz F, and Codazzi F (2012) Expression of divalent metal transporter 1 in primary hippocampal neurons: reconsidering its role in non-transferrin-bound iron influx. *J. Neurochem.*, 120: 269-278

- Consonni A, Morara S, Codazzi F, Grohovaz F, and **Zacchetti** D (2011) Inhibition of Lipopolysaccharide-induced Microglia Activation by Calcitonin Gene Related Peptide and Adrenomedullin. *Mol Cell Neurosci*. 48, 151-160

- Bettgazzi B, Mihailovich M, Di Cesare A, Consonni A, Macco R, Pelizzoni I, Codazzi F, Grohovaz F, and **Zacchetti** D (2011)  $\beta$ -secretase Activity in Rat Astrocytes: Translational Block of BACE1 and Modulation of BACE2 Expression. *Eur J Neurosci*. 33, 236-243

- Pelizzoni I, Macco R, Morini M, **Zacchetti** D, Grohovaz F, and Codazzi F (2011) Iron handling in hippocampal neurons: activity-dependent iron entry and mitochondria-mediated neurotoxicity. *Aging Cell*. 10, 172-183

- D'Antoni S, Zambusi L, Codazzi F, **Zacchetti** D, Grohovaz F, Provini L, Catania MV, Morara S (2010) Calcitonin Gene-Related Peptide (CGRP) stimulates Purkinje cell dendrite growth in culture. *Neurochem Res*. 2010 Dec;35(12):2135-43.

- Pelizzoni I, Macco R, **Zacchetti** D, Grohovaz F, Codazzi F (2008) Iron and calcium in the central nervous system: a close relationship in health and sickness. *Biochem Soc Trans*. 2008 Dec;36(Pt 6):1309-12.

- Chiulli N, Codazzi F, Di Cesare A, Gravaghi C, **Zacchetti** D\*, Grohovaz F\* [\*corresponding authors] Sphingosylphosphocholine effects on cultured astrocytes reveal mechanisms potentially involved in neurotoxicity in Niemann-Pick type A disease. *Eur. J. Neurosci.*, 26:875-881 (2007)

- Mihailovich M, Thermann R, Grohovaz F, Hentze MW, **Zacchetti** D. Complex translational regulation of BACE1 involves upstream uAUGs and stimulatory elements within the 5' untranslated region. *Nucl. Acids Res*. 35:2975-2985. (2007)

- **Zacchetti** D, Chieragatti E, Bettgazzi B, Mihailovich M, Sousa VL, Grohovaz F, Meldolesi J. BACE1 expression and activity: relevance in Alzheimer's disease. *Neurodegenerative Dis*. 4:117-126 (2007)

- Di Cesare A, Del Piccolo P, **Zacchetti D\***, and Grohovaz F\* [\*corresponding authors] EP2 receptor stimulation promotes calcium responses in astrocytes via activation of the adenylyl cyclase pathway. *Cell. Mol. Life Scie.* 63: 2546-2553 (2006)
- Codazzi F, Di Cesare A, Chiulli N, Albanese A, Meyer T, **Zacchetti D**, and Grohovaz F. Synergistic control of Protein Kinase Cgamma activity by ionotropic and metabotropic glutamate receptor inputs in hippocampal neurons. *J. Neurosci.*, 26: 3404-3411 (2006)
- De Pietri Tonelli D., Mihailovich M., Di Cesare A., Codazzi F., Grohovaz F., and **Zacchetti D**. Translational regulation of BACE-1 expression in neuronal and non-neuronal cells. *Nucl. Acids Res.* 32: 1808-1817 (2004)
- De Pietri Tonelli D., Mihailovich M., Schnurbus R., Pesole G., Grohovaz F., and **Zacchetti D**. Translational control of Scamper expression via a cell-specific internal ribosome entry site. *Nucl. acids Res.* 31: 2508-2513 (2003)
- Eehalt R, Michel B, De Pietri Tonelli D, **Zacchetti D**, Simons K, and Keller P. Splice variants of the beta-site APP-cleaving enzyme BACE1 in human brain and pancreas. *Biochem. Biophys. Res. Comm.* 293: 30-37 (2002)
- Schnurbus R., De Pietri Tonelli D., Grohovaz F., and **Zacchetti D**. Re-evaluation of primary structure, topology and localisation of Scamper, a putative intracellular Ca<sup>2+</sup> channel activated by sphingosylphosphocholine. *Biochem. J.* 362: 183-189 (2002)
- Benting J., Lecat S., **Zacchetti D.**, and Simons K. Protein expression in Drosophila Schneider cells. *Anal. Biochem.* 278: 59-68 (2000)
- Cheong K.H., **Zacchetti D.**, Schneeberger E.E., and Simons K. VIP17/MAL, a lipid raft-associated protein, is involved in apical transport in MDCK cells. *Proc.Natl. Acad. Sci.USA.* 96: 6241-6248 (1999)
- Bertuzzi F., **Zacchetti D.**, Berra C., Soggi C., Pozza G., Pontiroli A.E., and Grohovaz F. Intercellular Ca<sup>2+</sup> waves sustain coordinate insulin secretion in pig islets of Langerhans. *FEBS Lett.* 379: 21-25 (1996)
- **Zacchetti D.**, Peranen J., Murata M., Fiedler K., and Simons K. VIP17/MAL, a proteolipid in apical transport vesicles. *FEBS Lett.* 377: 465-469 (1995)
- Lorenzon P.\*, **Zacchetti D.\*** [\*coauthorship], Codazzi F., Fumagalli G., Meldolesi J., and Grohovaz F. Ca<sup>2+</sup> waves in PC12 neurites: a bidirectional, receptor-oriented form of Ca<sup>2+</sup> signalling. *J. Cell Biol.* 129:797-804 (1995)
- Codazzi F., Menegon A., **Zacchetti D.**, Ciardo A., Grohovaz F., and Meldolesi J. HIV-1 gp120 glycoprotein induces [Ca<sup>2+</sup>]<sub>i</sub> responses not only in type-2 but also in type-1 astrocytes and oligodendrocytes of rat cerebellum. *Europ. J. Neurosci.* 7:1333-1341 (1995)
- D'Andrea P., Codazzi F., **Zacchetti D.**, Meldolesi J., and Grohovaz F. Oscillations of cytosolic calcium in rat chromaffin cells: dual modulation in frequency and amplitude. *Biochem. Biophys. Res. Comm.* 205: 1264-1269 (1994)
- D'Andrea P., **Zacchetti D.**, Meldolesi J., and Grohovaz F. Mechanism of [Ca<sup>2+</sup>]<sub>i</sub> oscillations in rat chromaffin cells: complex Ca<sup>2+</sup> dependent regulation of a ryanodine-insensitive oscillator. *J. Biol. Chem.* 268: 15213-15220 (1993)
- Grohovaz F., **Zacchetti D.**, Lorenzon P., Meldolesi J., and D'Andrea P. Receptor-mediated intracellular signalling: oscillations and waves of cytosolic calcium. *Biochem. Soc. Trans.* 21: 1129-1132 (1993)
- Clementi E., Racchetti G., **Zacchetti D.**, Panzeri M.C., and Meldolesi J. Differential expression of markers and activities in a group of PC12 nerve cell clones. *Europ. J. Neurosci.* 4: 944-953 (1992)
- Clementi E., Sheer H., **Zacchetti D.**, Fasolato C., Pozzan T., and Meldolesi J. Receptor-activated Ca<sup>2+</sup> influx: two independently regulated mechanisms of influx stimulation coexist in neurosecretory PC12 cells. *J. Biol. Chem.* 267: 2164-2172 (1992)
- Meldolesi J., Villa A., Podini P., Clementi E., **Zacchetti D.**, D'Andrea P., Lorenzon P., and Grohovaz F. Intracellular Ca<sup>2+</sup> stores in neurons. Identification and functional aspects. *J. Physiol. (Paris)* 86: 23-30 (1992)
- Fasolato C., Zottini M., Clementi E., **Zacchetti D.**, Meldolesi J., and Pozzan T. Intracellular Ca<sup>2+</sup> pools in PC12 cells: three intracellular pools are distinguished by their turnover and mechanisms of Ca<sup>2+</sup> accumulation, storage, and release. *J. Biol. Chem.* 266: 20159-20167 (1991)
- **Zacchetti D.**, Clementi E., Fasolato C., Lorenzon P., Zottini M., Grohovaz F., Fumagalli G., Pozzan T., and Meldolesi J. Intracellular Ca<sup>2+</sup> pools in PC12 cells: a unique, rapidly-exchanging pool is sensitive to both inositol 1,4,5-trisphosphate and caffeine-ryanodine. *J. Biol. Chem.* 266: 20152-20158 (1991)
- Grohovaz F., **Zacchetti D.**, Clementi E., Meldolesi J., and Fumagalli G. Ca<sup>2+</sup> imaging in PC12 cells: multiple response patterns to receptor activation reveal new aspects of transmembrane signalling. *J. Cell Biol.* 113: 1341-1350 (1991)
- Fumagalli G., **Zacchetti D.**, Lorenzon P., and Grohovaz F. Fluorimetric approaches to the study of calcium transients in living cells. *Cytotechnology* 5: 99-102 (1991)
- Meldolesi J., Clementi E., Fasolato C., **Zacchetti D.**, and Pozzan T. Ca<sup>2+</sup> influx following receptor activation. *Trends in Pharm. Sci.* 12: 289-292 (1991)
- Rosenthal L., **Zacchetti D.**, Madeddu L., and Meldolesi J. Mode of action of alpha-latrotoxin: role of divalent cations in Ca<sup>2+</sup>-dependent and Ca<sup>2+</sup>-independent effects mediated by the toxin. *Mol. Pharmacol.* 38: 917-923 (1990).