

## CURRICULUM VITAE

Name: Grazia Raffaella Tundo

Work address: via Montpellier, 1, 00100, University of Rome Tor Vergata, Italy

Phone number: +390677208722; +393209736540

E-mail: grazia.raffaella.tundo@uniroma2.it

### Education and Actual Position

**2006**-University of Tor Vergata: Degree in Medical Biotechnology with final mark 110/110 cum Laude.

**2008**: Passed the government exam and licensed as a profession biologist.

**2011**: University of Tor Vergata: Ph.D. in Biochemistry and Molecular Biology

**2010-2016**: Fellowship at the laboratory of Biochemistry at the University of Rome Tor Vergata.

**2017**: National Scientific Habilitation for full professorship (scientific-disciplinary sector: E1-BIO/10)

**2018**: Degree in Medicine and Surgery at the University of Tor Vergata, Rome, with mark 110/110 cum Laude.

**2019**: Certified in the profession of Surgeon

**2018:2020**: Untenured Professor of Chemistry and Introductory Biochemistry (BIO-10); Degree in Medicine and Surgery at Unicamillus International University

**2018-2021**: Research position at University of Rome Tor Vergata

**2019-2022**: Rsearcher at IRCCS-Fondazione GB Bietti, Rome, Italy

**Actual**: RTD-B at University of Rome Tor Vergata

### Academic Teaching

**2007-Actual:** Teaching Assistant - Chemistry (Italian and English courses) for the Medicine and Surgery Course at the Tor Vergata University of Rome, Italy.

**2013-2016:** Teaching Assistant - Chemistry for the Medicine and Surgery Course at the “Madre Teresa del Buon Consiglio” University of Tirana, Albania.

**2010-2018:** Teaching Assistant - Molecular Biology for the Medical Biotechnology Course at the University of Tor Vergata, Rome, Italy.

**2018-2020: Teaching position-** Chemistry (English course) for the Medicine and Surgery Course at the Unicamillus University of Rome, Italy

**Actual:** Teaching position- Chemistry (Italian and English courses) for the Medicine and Surgery Course at the Tor Vergata University of Rome, Italy.

### **Current Research Topics**

Characterization of dy-regulation of UPS in glaucoma and ocular diseases, in collaboration with Doctor Francesco Oddone, IRCSS Fondazione Bietti, Rome, Italy, Prof. Assfalg, University of Verona.

Characterization of Insulin-degrading-enzyme-proteasome interaction, in collaboration with Prof. Purrello, University of Catania, Prof. Bolognesi, Università di Milano, Van Endert, Institut Necker Des Malades, Paris, France and prof. Deprez-Poulain, University of Lille, France, Prof

Characterization of IDE role in the Heat-shock –response, in collaboration with Prof.Orlandi, University of Rome Tor Vergata and prof. Van Endert, Institut Necker Des Malades.

Characterization of autophagy and UPS dys-regulation in Rett Syndrome, in collaboration with Prof. Curatolo, University of Rome Tor Vergata, Prof. Defelice, University of Siena, Italy and Prof. Valacchi, University of Ferrara, Italy.

Characterization of dys-regulation of proteasome activity in Huntigton Disease in collaboration with prof. Reits, Institut für Biochemie/CCM, Charité´-Universita`tsmedizin Berlin, Germany

Characterization of dy-regulation of UPS in Multiple Sclerosis in collaboration with prof. Ale,Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, Russian Federation.

## Full List of publications

**H-Index:** 18 (*Scopus*, 08-04-2022)

Ciaccio C\*, **Tundo GR\***, Grasso G, Spoto G, Marasco D, Ruvo M, Gioia M, Rizzarelli E, Coletta M. Somatostatin: a novel substrate and a modulator of insulin-degrading enzyme activity. *J Mol Biol.* 2009 385:1556-67. \*These authors have equally contributed to the study.

Ascenzi P, Bolli A, di Masi A, **Tundo GR**, Fanali G, Coletta M, Fasano M. Isoniazid and rifampicin inhibit allosterically heme binding to albumin and peroxynitrite isomerization by heme-albumin. *J Biol Inorg Chem.* 2011 16:97-108. 2016.

Grasso G, Pietropaolo A, Spoto G, Pappalardo G, **Tundo GR**, Ciaccio C, Coletta M, Rizzarelli E. Copper(I) and copper(II) inhibit A $\beta$  peptides proteolysis by insulin-degrading enzyme differently: implications for metallostasis alteration in Alzheimer's disease. *Chemistry.* 2011 17:2752-62.

Ascenzi P, Cao Y, **Tundo GR**, Coletta M, Fanali G, Fasano M. Ibuprofen and warfarin modulate allosterically ferrous human serum heme-albumin nitrosylation. *Biochem Biophys Res Commun.* 2011 411: 185-9.

Cao Y, Nicoletti FP, De Sanctis G, Bocedi A, Ciaccio C, Gullotta F, Fanali G, **Tundo GR**, di Masi A, Fasano M, Smulevich G, Ascenzi P, Coletta M. Evidence for pH-dependent multiple conformers in iron(II) heme-human serum albumin: spectroscopic and kinetic investigation of carbon monoxide binding. *J Biol Inorg Chem.* 2012 (1):133-47.

Sbardella D., Fasciglione GF, Gioia M, Ciaccio C, **Tundo GR**, Marini S, Coletta M. Human matrix metalloproteinases: An ubiquitous class of enzymes involved in several pathological processes. *Molecular Aspects of Medicine.* 2012,33 119-208.

**Tundo GR**, Ciaccio C, Sbardella D, Boraso M, Viviani B, Coletta M, Marini S. Somatostatin modulates insulin-degrading-enzyme metabolism: implications for the regulation of microglia activity in AD. *PLoS One.* 2012 7.

Grasso G, Salomone F, **Tundo GR**, Pappalardo G, Ciaccio C, Spoto G, Pietropaolo A, Coletta M, Rizzarelli E. Metal ions affect insulin-degrading enzyme activity. *J Inorg Biochem.* 2012 117:351-8.

**Tundo GR**, Sbardella D, Ciaccio C, Bianculli A, Orlandi A, Desimio MG, Arcuri G, Coletta M, Marini S. Insulin-degrading enzyme (IDE): a novel heat shock-like protein. *J Biol Chem.* 2013 26:1821-31.

Ciaccio C, Pesce A, **Tundo GR**, Tilleman L, Bertolacci L, Dewilde S, Moens L, Ascenzi P, Bolognesi M, Nardini M, Coletta M. Functional and structural roles of the N-terminal extension in *Methanosarcina acetivorans* protoglobin. *Biochim Biophys Acta.* 2013 1834:1813-23.

Bocedi A, De Sanctis G, Ciaccio C, **Tundo GR**, Di Masi A, Fanali G, Nicoletti FP, Fasano M, Smulevich G, Ascenzi P, Coletta M. Reciprocal allosteric modulation of carbon monoxide and warfarin binding to ferrous human serum heme-albumin. *PLoS One.* 2013 8-31.

*Tutto quanto dichiarato in questo documento corrisponde a verità, ai sensi degli articoli 46 e 47 del D.P.R. 445 del 2000.*

Ascenzi P, **Tundo GR**, Fanali G, Coletta M, Fasano M. Warfarin modulates the nitrite reductase activity of ferrous human serum heme-albumin. *J Biol Inorg Chem*. 2013 18:939-46.

Ascenzi P, di Masi A, **Tundo GR**, Pesce A, Visca P, Coletta M. Nitrosylation mechanisms of *Mycobacterium tuberculosis* and *Campylobacter jejuni* truncated hemoglobins N, O, and P. *PLoS One*. 2014 9:e102811.

Sbardella D, **Tundo GR**, Fasciglione GF, Gioia M, Bisicchia S, Gasbarra E, Ippolito E, Tarantino U, Coletta M, Marini S. Role of metalloproteinases in tendon pathophysiology. *Mini Rev Med Chem*. 2014 14:978-87.

Ciaccio C, Ocaña-Calahorra F, Droghetti E, **Tundo GR**, Sanz-Luque E, Polticelli F, Visca P, Smulevich G, Ascenzi P, Coletta M. Functional and Spectroscopic Characterization of *Chlamydomonas reinhardtii* Truncated Hemoglobins. *PLoS One*. 2015, 10(5).

**Tundo GR**, Sbardella D, De Pascali SA, Ciaccio C, Coletta M, Fanizzi FP, Marini S. Novel Platinum(II) compounds modulate insulin-degrading enzyme activity and induce cell death in neuroblastoma cells. *J Biol Inorg Chem*. 2015 20:101-8.

Sbardella D, **Tundo GR**, Sciandra F, Bozzi M, Gioia M, Ciaccio C, Tarantino U, Brancaccio A, Coletta M, Marini S. Proteasome Activity Is Affected by Fluctuations in Insulin-Degrading Enzyme Distribution.. *PLoS One*. 2015, 10(7).

**Tundo GR**, Sbardella D, Ciaccio C, De pascali S, Campanella V, Cozza P, Tarantino U, Coletta M, Fanizzi FP, Marini S. Effect of cisplatin on proteasome activity. *J Inorg Biochem*. 2015, 153:253-8. 2016

Donatucci B., Sbardella D., **Tundo GR**, Casasco M., Di Daniele N., Rogliani P., Marini S. Antioxidant supplement and sports *Medicina dello Sport* 2015, 68, 359-366.

Santoro AM, Cunsolo A, D'Urso A, Sbardella D, **Tundo GR**, Ciaccio C, Coletta M, Diana D, Fattorusso, R, Persico M, Di Dato A, Fattorusso C, Milardi D, Purrello R. Cationic porphyrins are tunable gatekeepers of the 20S proteasome *Chemical Science* 2016, 7, 1286-1297.

**Tundo GR**, Di Muzio E, Ciaccio C, Sbardella D, Di Pierro D, Polticelli F, Coletta M, Marini S. Multiple allosteric sites are involved in the modulation of insulin-degrading-enzyme activity by somatostatin. *FEBS J*. 2016, 283, 3755-3770.

Ciaccio C, Di Pierro D, Sbardella D, **Tundo GR**, Curatolo P, Galasso C, Santarone ME, Casasco M, Cozza P, Cortelazzo A, Rossi M, De Felice C, Hayek J, Coletta M, Marini S. Oxygen exchange and energy metabolism in erythrocytes of Rett syndrome and their relationships with respiratory alterations. *Mol Cell Biochem*. 2017, 426, 205-213.

Grasso G; Santoro AM, Lanza V , Sbardella D, **Tundo GR**, Ciaccio C, Marini S, Coletta M, Milardi D. The double faced role of copper in A beta homeostasis: A survey on the interrelationship between metal dyshomeostasis, UPS functioning and autophagy in neurodegeneration. *Coordination chemistry reviews*. 2017, 347: 1-22.

Gioia M, Tomao L, Sbardella D, Ciaccio C, **Tundo GR**, Di Masi A, Fasciglione GF, Marini S, Cozza P, Ascenzi P, Coletta M. Enzyme catalysis: the case of the prostate-specific antigen. *Rendiconti Lincei-scienze fisiche e naturali*. 2017, 28: 229-237.

**Tundo GR**, Sbardella D, Ciaccio C, Grasso G, Gioia M, Coletta A, Polticelli F, Di Pierro D, Milardi D, Van Endert P, Marini S, Coletta M. Multiple functions of insulin-degrading enzyme: a metabolic crosslight? *Crit Rev Biochem Mol Biol*. 2017, 52:554-582. 2016.

Sbardella D\*, **Tundo GR\***, Campagnolo L, Valacchi G, Orlandi A, Curatolo P, Borsellino G, D'Esposito M, Ciaccio C, Di Cesare S, Di Pierro D, Galasso C, Santarone ME, Hayek J, Coletta M, Marini S. Retention of Mitochondria in Mature Human Red Blood Cells as the Result of Autophagy Impairment in Rett Syndrome. *Sci Rep*. 2017. 26:12297. \*These authors have equally contributed to the study.

Dato AD, Cunsolo A, Persico M, Santoro AM, D'Urso A, Milardi D, Purrello R, Stefanelli M, Paolesse R, **Tundo GR**, Sbardella D, Fattorusso C, Coletta M. Electrostatic Map Of Proteasome  $\alpha$ -Rings Encodes The Design of Allosteric Porphyrin-Based Inhibitors Able To Affect 20S Conformation By Cooperative Binding. *Sci Rep*. 2017. 7: 17098.

Sbardella D\*, **Tundo GR\***, Coletta A, Marcoux J, Koufogeorgou EI, Ciaccio C, Santoro AM, Milardi D, Grasso G, Cozza P, Bousquet-Dubouch MP, Marini S, Coletta M. The Insulin Degrading Enzyme is an Allosteric Modulator of the 20S Proteasome and a Potential Competitor of the 19S. *Cell Molecular Life Sciences* 2018. 18:3441-3456. \*These authors have equally contributed to the study.

Ascenzi P, **Tundo GR**, Coletta M. The nitrite reductase activity of ferrous human hemoglobin:haptoglobin 1-1 and 2-2 complexes. *J. Inorg. Biochem*. 2018. 187:116-122.

**Tundo GR**, Sbardella D, Coletta M. Insights into Proteasome Conformation Dynamics and Intersubunit Communication. *Trends Biochem Sci*. 2018. 43:852-853.

**Tundo GR**, Sbardella D, Lacal PM, Graziani G, Marini S. On the Horizon: Targeting Next-Generation Immune Checkpoints for Cancer Treatment. *Chemotherapy*. 2019;64(2):62-80.

Milardi D, Santoro AM, Lanza V, Bellia F, Sbardella D, **Tundo GR**, Cannizzo A, Grasso G, Arizzi M, Nicoletti VG, Alcaro S, Costa G, Pietropaolo A, Malgieri G, D'Abrosca G, Fattorusso R, García-Viñuales S, Ahmed IMM, Coletta M. Pyrazolones activate proteasome by gating mechanisms and protect neuronal cells from A $\beta$  amyloid toxicity. *ChemMedChem*. 2019 15(3):302-316.

Bellia F, Lanza V, García-Viñuales S, Ahmed IMM, Pietropaolo A, Iacobucci C, Malgieri G, D'Abrosca G, Fattorusso R, Nicoletti VG, Sbardella D, **Tundo GR**, Coletta M, Pirone L, Pedone E, Calcagno D, Grasso G, Milardi D. Ubiquitin binds the amyloid  $\beta$  peptide and interferes with its clearance pathways. *Chem Sci*. 2019 Jan 10;10(9):2732-2742.

Santoro AM, Lanza V, Bellia F, Sbardella D, **Tundo GR**, Cannizzo A, Grasso G, Arizzi M, Nicoletti VG, Alcaro S, Costa G, Pietropaolo A, Malgieri G, D'Abrosca G, Fattorusso R, García-Viñuales S, Ahmed IMM, Coletta M, Milardi D. Pyrazolones Activate the Proteasome by Gating Mechanisms and Protect Neuronal Cells from  $\beta$ -Amyloid Toxicity. *ChemMedChem*. 2020 Feb 5;15(3):302-316.

Di Pierro D, Ciaccio C, Sbardella D, **Tundo GR**, Bernardini R, Curatolo P, Galasso C, Pironi V, Coletta M, Marini S. Effects of oral administration of common antioxidant supplements on the energy metabolism of red blood cells. Attenuation of oxidative stress-induced changes in Rett syndrome erythrocytes by CoQ10. *Mol Cell Biochem*. 2020 Jan;463(1-2):101-113.

**Tundo GR**, Sbardella D, Santoro AM, Coletta A, Oddone F, Grasso G, Milardi D, Lacal PM, Marini S, Purrello R, Graziani G, Coletta M. The proteasome as a druggable target with multiple therapeutic potentialities: Cutting and non-cutting edges. *Pharmacol Ther*. 2020.

Ascenzi P, De Simone G, **Tundo GR**, Platas-Iglesias C, Coletta M. Ferric nitrosylated myoglobin catalyzes peroxynitrite scavenging. *J Biol Inorg Chem*. 2020 May;25(3):361-370.

Ascenzi P, De Simone G, **Tundo GR**, Coletta M. Kinetics of cyanide and carbon monoxide dissociation from ferrous human haptoglobin:hemoglobin(II) complexes. *J Biol Inorg Chem*. 2020 May;25(3):351-360.

Sbardella D, Coletta A, **Tundo GR**, Ahmed IMM, Bellia F, Oddone F, Manni G, Coletta M. Structural and functional evidence for citicoline binding and modulation of 20S proteasome activity: Novel insights into its pro-proteostatic effect. *Biochem Pharmacol*. 2020.

Sbardella D, **Tundo GR**, Cunsolo V, Grasso G, Cascella R, Caputo V, Santoro AM, Milardi D, Pecorelli A, Ciaccio C, Di Pierro D, Leoncini S, Campagnolo L, Pironi V, Oddone F, Manni P, Foti S, Giardina E, De Felice C, Hayek J, Curatolo P, Galasso C, Valacchi G, Coletta M, Graziani G, Marini S. Defective proteasome biogenesis into skin fibroblasts isolated from Rett syndrome subjects with MeCP2 non-sense mutations. *Biochim Biophys Acta Mol Basis Dis*. 2020.

Gioia G, Ciaccio C, Calligari P, De Simone G, Sbardella D, **Tundo GR**, Fasciglione GF, Di Masi A, Di Pierro D, Bocedi A, Ascenzi P, Coletta M. Role of proteolytic enzymes in the COVID-19 infection and promising therapeutic approaches. *Biochem Pharmacol*. 2020. 182:114225.

Santoro AM, D'Urso A, Cunsolo A, Milardi D, Purrello R, Sbardella D, **Tundo GR**, Donatella D, Fattorusso R, Di Dato A, Paladino A, Persico M, Coletta M, Fattorusso C. Cooperative Binding of the Cationic Porphyrin Tris-T4 Enhances Catalytic Activity of 20S Proteasome Unveiling a Complex Distribution of Functional States *Int J Mol Sci*. 2020. 21(19):7190.

G.R. **Tundo**, D. Sbardella, A.M. Santoro, A. Coletta, F. Oddone, G. Grasso, D. Milardi, P.M. Lacal, S. Marini, R. Purrello, G. Graziani, M. Coletta. The proteasome as a druggable target with multiple therapeutic potentialities: Cutting and non-cutting edges *Pharmacol Ther.* 2020 Sep; 213: 107579.

Diego Sbardella, Grazia Raffaella **Tundo**, Massimo Coletta, Gianluca Manni, Francesco Oddone. Dexamethasone Downregulates Autophagy through Accelerated Turn-Over of the Ulk-1 Complex in a Trabecular Meshwork Cells Strain: Insights on Steroid-Induced Glaucoma Pathogenesis. *Int J Mol Sci.* 2021 Jun; 22(11): 5891.

García-Viñuales, Sara, Sciacca, Michele F.M, Lanza, Valeria; Santoro, Anna Maria<sup>a</sup>; Grasso, Giulia; **Tundo, Grazia R.**; Sbardella, Diego; Coletta, Massimiliano; Grasso, Giuseppe; La Rosa, Carmelo; Milardi, Danilo The interplay between lipid and A $\beta$  amyloid homeostasis in Alzheimer's Disease: risk factors and therapeutic opportunities *Chemistry and Physics of Lipids* 2021. 23: 105072.

Benvenuto, M., Ciuffa, S., Focaccetti, C., **Tundo, G.R.**, ..Coletta, M., Bei, R. Proteasome inhibition by bortezomib parallels a reduction in head and neck cancer cells growth, and an increase in tumor-infiltrating immune cells *Scientific Reports*, 2021, 11(1), 19051.

**Tundo, Grazia R.**; Sbardella, Diego; Oddone, Francesco; Kudriaeva, Anna A.Lacal, Pedro M; Belogurov, Alexey A; Graziani, Grazia; Marini, Stefano At the cutting edge against cancer: A perspective on immunoproteasome and immune checkpoints modulation as a potential therapeutic intervention. *Cancers* 202113:4852.

**Tundo, G.R.**, Sbardella, D., Oddone, F., ...Parravano, M., Coletta, M. Insulin-Degrading Enzyme Is a Non Proteasomal Target of Carfilzomib and Affects the 20S Proteasome Inhibition by the Drug. *Biomolecules*, 2022, 12(2), 315.

## **Patents**

**2017:** Methods for the Quick Diagnosis of Rett Syndrome. Patent number: 102016000117469

## **Achievements:**

Received “Raeli” Award for best academic achievement (2007).