

GIOVANNI GOTTE – ASSOCIATE PROFESSOR - BIOCHEMISTRY, BIO/10

Date and Place of Birth: February 17th, 1968; Padova, Italy.

Citizenship: Italian

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C.V.

1994: Degree in Chemistry. Post-lauream studies of “Interactions between chinolones drugs and DNA: role of Fe ions”. Center of Biopolymers’ Studies, Dept. of Organic Chemistry, University of Padova.

1995: “Procter & Gamble” grant, studies on the activation of hydrogen peroxide by metals; Organic Chemistry Dept., University of Padova.

1995-1999: PhD in Biochemical Sciences: “Ribonuclease A oligomers: structural, catalytical and biological properties”: investigations on RNase A oligomers obtained with bifunctional crosslinking or by induced aggregation of the enzyme Inst. of Biological Chemistry, then, since 1998, Biological Chemistry Section, University of Verona.

2000-2001: Grant “RNase A oligomers: structural and functional determinations of the RNase A aggregates and their possible physiopathological role” (Biological Chemistry Section, University of Verona).

2001-2005: Post-doc grant for “Studies on protein aggregation processes. Implications for Amyloid Formation” Biological Chemistry Section, University of Verona.

March 1st 2006: Permanent Position, as a Research assistant in the same Biological Chemistry Section, that since January 1st 2006 belongs to the Dept. of Morphological and Biomedical Sciences, the University of Verona.

March 1st 2009: Confirmed position in the same Biological Chemistry Section, that since May 1st 2010 belongs to the Dept. of Life and Reproduction Sciences, Medicine Faculty, the University of Verona.

October 1st 2015: Associated Professor in Biochemistry (BIO-10), Biological Chemistry Section, Dept of Neurological, Biomedical and Movement Sciences, University of Verona.

March 2017: National Scientific Qualification as Full Professor in Biochemistry (BIO-10).

Member of the Italian Society of Biochemistry and Molecular Biology.

PUBLICATIONS (see later)

40 peer-reviewed publications.

Total I.F.: 141; average I.F. 3.62 (JCR 2016).

Scopus H-Index: 20; total citations reported in ‘Scopus’: 1175.

12 Publications as first author, 12 second, and 7 as Corresponding Author.

2014 chapter “Protein Oligomerization” chapter as corresponding author in the ‘e-Book’ “Oligomerization of Chemical and Biological Compounds”. InTech-Open, ISBN 978-953-51-1617-2; doi org/10.5772/57489.

RESEARCH TOPICS AND EXPERTISE

Structural and functional investigations on oligomers and multimers of proteins in general, and of some pancreatic-type ribonucleases in particular, obtained by means of chemical modifications and/or cross-linking, or through aggregation via three dimensional domain swapping (3D-DS).

In particular, several of these studies are focused on the aggregation mechanism that displayed to be similar or identical to the ones followed by proteins directly involved in neurodegenerative pathologies. Other studies are currently focused on the modification or magnification of the enzymatic and/or biological activity of the oligomers of various RNases, especially bovine seminal RNase and onconase in their native, or subjected to self-association forms. Now also RNase 4 angiogenin (RNase 5) are available in the labs together with human pancreatic RNase (RNase 1).

In the last years the investigations have been focused also on the dimerization-oligomerization-multimerization mechanisms of proteins different from RNases, in particular of human alanine:glyoxilate amino-transferase (hAGT) and STAT-3, and in collaboration with other italian or foreign research groups. In these years the prof. G. Gotte acquired expertise of various lab techniques, such as different chromatography purificative and analytical approaches, non-denaturing and SDS-PAGE electrophoresis, WB, spectroscopic analyses (UV-Vis, CD, fluorescence), DLS. Limited proteolysis, protein cross-linking, covalent derivatization and modification of protein adducts, heterologous production of WT and site-specific protein mutations.

Principal Research Collaborators in other Universities:

Prof. Delia Picone, 'Federico II' University, Naples, Italy

Prof. Antonello Merlino, 'Federico II' University, Naples, Italy

Prof. Stefano Moro, University of Padova, Italy

Prof. Vincenzo De Filippis, University of Padova, Italy

Prof. David Eisenberg, U.C.L.A., Los Angeles, U.S.A.

Dr. Douglas V. Laurents, Instituto de Quimica Fisica 'Rocasolano', Madrid, Spain.

MEETINGS: Invited Oral Communications:

- 'S.I.B.' Meeting, Catania, Italy, June 11-13, 1998.

Gotte, G. & Libonati, M. "Ribonucleasi A oligomerica: proprietà strutturali, catalitiche e biologiche". Congress Proceedings.

- 'N.A.N.G.' Meeting, Rosa Marina (BR), Italy, June 9-11, 2002.

Gotte, G., Matousek, J., Pouckova, P., Soucek, J., Slavik, T., Vottariello, F., & Libonati, M. "Biological Actions of RNase A oligomeric aggregates". Proceedings, p.17.

- "Istituto di Chimica Fisica 'Rocasolano', Madrid, Spain, Oct 7, 2004, Seminar. Gotte, G. "Structural versatility of Ribonuclease A: Two novel 3D domain swapped tetramers".

- '7th International Engelhardt Conference On Molecular Biology', Suzdal (Russia), Nov 28–Dec 2, 2004.

Gotte, G., & Libonati, M. "Two novel RNase A tetramers". Proceedings.

- Scientific Meeting 'Aggregazione di proteine', C.N.R., Rome, April 18, 2005. Gotte, G., & Libonati M. Oligomerizzazione della ribonucleasi A: proprietà strutturali dei multimeri.

- 7th International Meeting on Ribonucleases, Stará Lesná, Slovak Republic, June 16-20th, 2005. Gotte, G., Donadelli, M., Morbio, M., Vottariello, F., & Libonati, M. "Oligomerization by Three Dimensional Domain-Swapping of Three Ribonuclease A Mutants". Proceedings.

- Oral Selected Communication, "S.I.B. 2007", Riccione (RN) September 26-28, 2007 Gotte, G., Morbio, M.,

Vottariello, F., Donadelli, M., Costanzo, C. & Libonati, M. Antitumor activity of polyspermine-ribonuclease A and polyspermine-dimeric ribonuclease A", Atti, It. J. Biochem. 56, Special Issue: P14.03, p. 159.

In addition, 30 Posters presented in many National and International Meetings.

FUNDINGS

- Member of the Verona Operative Unit for the P.R.I.N. 2002 project, entitled 'Oligomeri di Ribonucleasi A da pancreas bovino: studi strutturali e funzionali'.
- Member of the Verona Operative Unit for the P.R.I.N. 2004 project, entitled 'Indagini sul meccanismo di formazione degli oligomeri della ribonucleasi A e sulle loro attività biologiche'.
- Italian Ministry of University and Scientific Research Fundings 'Ex 60%, now 'FUR', in the years 2006-2017.
- April 2010 funding as 'Incentivo alla ricerca per progetti valutati positivamente PRIN 2008' Verona University, Italy.
- Telethon Project 2010 (participant) "Development of new strategies for the treatment of Primary Hyperoxaluria Type I" – P.I.: Prof. Carla Voltattorni, University of Verona, 36 months (2011-2013).
- PRIN 2010-2011 (Participant) "Enzimi e coenzimi piridinici e flavinici in neuropatologie umane: approcci molecolari e cellulari per terapie innovative". National P.I. Andrea Mozzarelli. positively evaluated. (score 91/100).

ACADEMIC ACTIVITY

- Since 2007, member of the PhD Research School in Biosciences. Then, since 2013, PhD School in Biomolecular Medicine Research, University of Verona.
- Member of the Bachelor Commission for Biomedical Lab Techniques Bachelorate, since 2008-2009.
- Assistant supervisor for the bachelorate of five students and for three PhD students since 2007-2008.
- 2011- Responsible of one-year Research Grant, of the Banca Popolare di Verona, Fondo "CTBPOPGOTT", € 20000, Primary Hyperoxaluria Type I: identification of small molecules as "enzyme enhancement therapy".
- 18 July, 2014: Referee for "Senior Grants", Area 'Scienze del Farmaco' Dipartimento di Scienze del Farmaco, University of Padova.
- Since January 2015: member of the Academic Senatus of the University of Verona.

TEACHING

Since **2001-2002** to date: Teaching Chemistry and Biochemistry, BIO-10, in the Verona University, Poles of Verona, Trento, Rovereto, Ala, Vicenza.

Since 2001 to 2006 annual contracts.

Since 2006/2007 to 2014/2015 as a Permanent Researcher of the University of Verona.

Since 2015/2016 to date as Associate Professor in the same University.

In particular, the last ten years:

2008-09, 2009-10

- Contract for Chemistry (BIO/10) teaching; integrated teaching of 'Chemistry and Biochemistry', then 'Structural and Functional Sciences of the biomolecules' Bachelor in Techniques of Biomedical Laboratory, University of Verona, Verona and Rovereto (TN) Poles, Italy.

- Contract for Biochemistry (BIO/10) teaching; integrated teaching of 'Medicinal Chemistry and Biochemistry Propaedeutics', Bachelor in Dental Hygiene, University of Verona, Ala (TN), Italy.

2010-11, 2011-12, 2012-13; 2013-14; 2014-15.

Contract for Chemistry (BIO/10) teaching; integrated teaching of 'Structural and Functional Sciences of the biomolecules' Bachelor in Techniques of Biomedical Laboratory, University of Verona, Verona and Rovereto (TN) Poles, Italy.

2015-16, 2016-17; 2017-18

- Chemistry (BIO/10) teaching; integrated teaching of 'Structural and Functional Sciences of the biomolecules' Bachelor in Techniques of Biomedical Laboratory, University of Verona, Italy.

- Biochemistry (BIO/10), Integrated Course 'Physical and Biological Propedeutical Sciences' 1st year, bachelor in Physiotherapy, University of Verona, Verona, 20 h, Vicenza 20 h, Rovereto(TN), 20 h.

In Rovereto joined with Biochemistry for Bachelor in in Igiene Dental Hygiene and Psychiatric Rehabilitation Techniques..

- Biochemistry (BIO/10), Integrated Course in 'Biological and Biochemical Sciences' 1st year, Bachelor in 'Cardiocirculatory Physiopathology and Cardiovascular Perfusion Techniques', University of Verona, Polo di Verona, 20 h.

List of Publications (I.F. 2016)

1. Bertoldi M., **Gotte G.**, Sorrentino S. & Libonati M. Artificial Ribonuclease A oligomers degrade double-stranded RNA with efficiency that increases as a function of the size of the oligomer. *It J. Biochem.* (1996) **45**, pp. 186-187 ISSN: 0021-2938. **NO I.F.** (*Non indicizzato*)
2. **Gotte G.**, Testolin L., Costanzo C., Sorrentino S., Armato U. & Libonati M. Cross-linked trimers of bovine ribonuclease A: activity on double-stranded RNA and antitumor action. *FEBS Lett.* (1997) **415** (3), 308-312. **I.F. 3.623**
3. **Gotte G.** & Libonati M. Two different forms of aggregated dimers of Ribonuclease A. *Biochim. Biophys. Acta* (1998) **1386** (1), 106-112. **I.F. 2.773**
4. **Gotte G.**, Bertoldi M. & Libonati M. Structural versatility of bovine ribonuclease A: distinct conformers of trimeric and tetrameric aggregates of the enzyme. *Eur. J. Biochem.* (1999) **265** (2), 680-687. **I.F. 3.902**
5. Sorrentino S., Barone R., Bucci E., **Gotte G.**, Russo N., Libonati M. & D'Alessio G. The two dimeric forms of RNase A. *FEBS Lett.* (2000) **466** (1), 35-39. **I.F. 3.623**
6. Nenci A., **Gotte G.**, Maras B. & Libonati M. Different susceptibility of the two dimers of ribonuclease A to subtilisin. Implications for their structure. *Biochim. Biophys. Acta* (2001) **1545** (1-2), 255-262. **I.F. 2.773**
7. Liu Y., **Gotte G.**, Libonati M. & Eisenberg D. A domain-swapped RNase A dimer with implications for amyloid formation. *Nat. Struct. Biol.* (2001) **8** (3), 211-214. **I.F. 12.595**
8. Nenci A., **Gotte G.**, Bertoldi M. & Libonati M. Structural properties of trimers and tetramers of ribonuclease A. *Protein Sci.* (2001) **10** (10), 2017-2027. **I.F. 2.523**
9. Liu Y., **Gotte G.**, Libonati M. & Eisenberg D. Structures of the two 3D domain-swapped RNase A trimers. *Protein Sci.* (2002) **11** (2), 371-380. **I.F. 2.523**
10. **Gotte G.**, Amelio E., Russo S., Marlinghaus E., Musci G. & Suzuki H. Short-time non-enzymatic nitric oxide synthesis from L-arginine and hydrogen peroxide induced by shock waves treatment. *FEBS Lett.* (2002) **520** (1-3), 153-155. **I.F. 3.623**
11. **Gotte G.**, Vottariello F. & Libonati M. Thermal Aggregation of Ribonuclease A. A contribution to the understanding of the role of 3D domain swapping in protein aggregation. *J. Biol. Chem.* (2003) **278** (12), 10763-10769. **I.F. 4.125**
12. Matousek J., **Gotte G.**, Pouckova P., Soucek J., Slavik T., Vottariello F., & Libonati M. Antitumor Activity and Other Biological Actions of Oligomers of Ribonuclease A. *J. Biol. Chem.* (2003) **278** (26), 23817-23822. **I.F. 4.125**
13. **Gotte G.**, Libonati M. & Laurents D.V. Glycosylation and Specific Deamidation of Ribonuclease B Affect the Formation of Three-dimensional Domain-swapped Oligomers. *J. Biol. Chem.* (2003) **278** (47), 46241-46251. **I.F. 4.125**
14. Libonati M. & **Gotte G.** Oligomerization of bovine ribonuclease A. Structural and functional features of its multimers. *Biochem. J.* (2004) **380** (2), 311-327. **I.F. 3.797**
15. **Gotte G.** & Libonati M. Oligomerization of Ribonuclease A. Two novel three-dimensional domain-swapped tetramers. *J. Biol. Chem.* (2004) **279** (35), 36670-36679. **I.F. 4.125**
16. Naddeo M., Vitagliano L., Russo A., **Gotte G.**, D'Alessio G. & Sorrentino S. Interactions of the cytotoxic RNase A dimers with the cytosolic ribonuclease inhibitor. *FEBS Lett.* (2005) **579** (12), 2663-2668. **I.F. 3.623**
17. **Gotte G.**, Laurents D.V. & Libonati M. Three-dimensional domain-swapped oligomers of ribonuclease A: identification of a fifth tetramer, pentamers and hexamers, and detection of trace heptameric, octameric and nonameric species. *Biochim. Biophys. Acta (BBA) – Prot. & Proteom.* (2006) **1764** (1), 44-54. **I.F. 2.773**

18. Pouckova, P., Skvor, J., **Gotte G.**, Vottariello, F., Slavik, J.T., Matousek, J., Laurents, D.V., Libonati, M., & Soucek, J. Some biological actions of PEG-conjugated RNase A oligomers. *Neoplasma* (2006) **53** (1), 79-85. *I.F.* **1.871**
19. Lopez-Alonso J.P., Bruix M., Font J., Ribo M., Vilanova M., Rico M., **Gotte G.**, Libonati M., Gonzales C., & Laurents D.V. Formation, structure, and dissociation of the ribonuclease S three-dimensional domain-swapped dimer. *J. Biol. Chem.* (2006) **281** (14), 9400-9406. *I.F.* **4.125**
20. **Gotte G.**, Donadelli M., Laurents D.V., Vottariello F., Morbio M. & Libonati M. Increase of RNase a N-terminus polarity or C-terminus apolarity changes the two domains' propensity to swap and form the two dimeric conformers of the protein. *Biochemistry* (2006) **45** (36) 10795-10806. *I.F.* **2.938**
21. Pouckova P., Morbio M., Vottariello F., Laurents D.V., Matoušek J., Soucek J., **Gotte G.**, Donadelli M., Costanzo C. & Libonati M. Cytotoxicity of polyspermine-ribonuclease a and polyspermine-dimeric ribonuclease A. *Bioconjugate Chem.* (2007) **18** (6), 1946-1955. *I.F.* **4.818**
22. Matoušek J., Tomanek M., Vottariello F., Morbio M., **Gotte G.** & Libonati M. Degenerative action on mice and rats testes of polyspermine and its complexes with RNase A. *J. Appl. Biomed.* (2007) **5** (4), 195-207. *I.F.* **1.433**
23. Cozza G., Moro S. & **Gotte G.**[#] Elucidation of the ribonuclease A aggregation process mediated by 3D domain swapping: A computational approach reveals possible new multimeric structures. *Biopolymers* (2008) **89** (1), 26–39. *I.F.* **1.908**
24. **Gotte G.**[#] & Libonati M. Oligomerization of ribonuclease A under reducing conditions. *Biochim. Biophys. Acta (BBA) – Prot. & Proteom.* (2008) **1784** (4), 638-650. *I.F.* **2.773**
25. Libonati M., **Gotte G.** & Vottariello F. Novel Biological Actions Acquired by Ribonuclease A Through Oligomerization. *Curr. Pharm. Biotech.* (2008) **9** (1), 200-209. *I.F.* **2.459**
26. López-Alonso J.P., **Gotte G.** & Laurents D.V. Kinetic Analysis Provides Insight into the Mechanism of Ribonuclease A Oligomer Formation. *Arch. Biochem. Biophys.* (2009) **489** (1-2), 41-47. *I.F.* **3.165**
27. Lopez-Alonso J.P., Diez-Garcia F., Font J., Ribò M., Vilanova M., Scholtz J.M., Gonzalez C., Vottariello F., **Gotte G.**, Libonati M. & Laurents, D.V. Carbodiimide EDC Induces Cross-Links That Stabilize RNase A C-Dimer against Dissociation: EDC Adducts Can Affect Protein Net Charge, Conformation, and Activity. *Bioconjugate Chem.* (2009) **20** (8), 1459–1473. *I.F.* **4.818**
28. Vottariello F., Costanzo C., **Gotte G.** & Libonati M. “Zero-length” Dimers of Ribonuclease A: Further Characterization and No Evidence of Citotoxicity. *Bioconjugate Chem.* (2010) **21** (4), 635–645. *I.F.* **4.818**
29. Vottariello F., Giacomelli E., Pozzi N., Frasson, R., De Filippis, V., & **Gotte G.**[#] Ribonuclease A domain-swapped oligomerization is affected by a residue located out of the domains involved in the swapping-mechanism. *Biochimie* (2011) **93** (10), 1846-1857. *I.F.* **3.112**
30. **Gotte G.**[#], Mahmoud Helmy A., Ercole C., Spadaccini R., Laurents D.V., Donadelli M. & Picone D. Double Domain Swapping in Bovine Seminal RNase: Formation of Distinct N- and C-swapped Tetramers and Multimers with Increasing Biological Activities. *PLoS One* (2012) **7** (10) e46804. *I.F.* **2.806**
31. **Gotte G.**, Laurents D.V., Merlino A., Picone D. & Spadaccini R. Structural and functional relationships of natural and artificial dimeric bovine ribonucleases: New scaffolds for potential antitumor drugs. *FEBS Lett.* (2013) **587** (22), 3601-3608. *I.F.* **3.623**
32. Fiorini C., **Gotte G.**[#], Donnarumma F., Picone D. & Donadelli M.[#] Bovine seminal ribonuclease triggers Beclin1-mediated autophagic cell death in pancreatic cancer cells. *Biochim. Biophys. Acta – Mol. Cell. Res.* (2014) **1843** (5), 976-984. *I.F.* **4.521**
33. Fiorini C., Cordani M., **Gotte G.**, Picone D. & Donadelli M. Onconase promotes Beclin1-mediated autophagy and ROS/Akt/mTOR pathway prompting pancreatic cancer cell chemosensitivity. *Biochim. Biophys. Acta – Mol. Cell. Res.* (2015) **1853** (3), 549-560. *I.F.* **4.521**

34. Picone D., Donnarumma F., Ferraro G., Russo Krauss I., Fagagnini A., **Gotte G.** & Merlino A. Platinated oligomers of bovine pancreatic ribonuclease: structure and stability. *J. Inorg. Biochem.* (2015) **146**, 37-43. **I.F. 3.348**
35. Montioli R., Oppici E., Dindo M., Alessandro Roncador, **Gotte G.**, Cellini B. & Borri Voltattorni C. Misfolding caused by the pathogenic mutation G47R on the minor allele of alanine:glyoxilate aminotransferase and chaperoning activity of pyridoxine. *Biochim. Biophys. Acta (BBA) – Prot. & Proteom.* (2015) **1854**, 1280-1289. **I.F. 2.773**
36. Butturini E., **Gotte G.**, Dell’Orco D., Chiavegato G., Marino V., Canetti D., Cozzolino F., Monti M., Pucci P. & Mariotto S. Intermolecular disulfide bond influences unphosphorylated STAT3 dimerization and function. *Biochem. J.* (2016) **473**, 3205-3219. **I.F. 3.797**
- 37- Fagagnini A., Montioli R., Caloiu A., Ribó M., Laurents D.V. & **Gotte G.**[#] Extensive Deamidation Inhibits RNase A Oligomerization through 3D Domain Swapping. *Biochim. Biophys. Acta (BBA)– Prot & Proteom.* (2017) **1865** (1), 76-87. **I.F. 2.773**
- 38- Picone D., Donnarumma F., Ferraro G., **Gotte G.**, Fagagnini A., Butera G., Donadelli M., & Merlino A. A comparison study on RNase A oligomerization induced by cisplatin, carboplatin and oxaliplatin. *J. Inorg. Biochem.* (2017) **173**, 106-112. **I.F. 3.348**
- 39- Fagagnini A., Pica A., Fasoli S., Montioli R., Donadelli M., Cordani M., Butturini E., Acquasaliente L., Picone D, & **Gotte G.**[#] Onconase Dimerization Through 3D Domain Swapping: Structural Investigations and Increase In The Apoptotic Effect In Cancer Cells. *Biochem. J.* (2017) **474**, 3767-3781. **I.F. 3.797**
- 40- Zaffini R., **Gotte G.**, & Menegazzi M. Asthma and poly (ADP-ribose) polymerase inhibition: a new therapeutic approach. *Drug Des. Develop. Ther.* (2018) **12**, 281-293. **I.F. 2.822**
- Fagagnini A., Fasoli S., Montioli R., Raineri A., Caloiu A., Smania M., & **Gotte G.**[#] Different incubation methods affect the structural and functional features of RNase A and of its domain-swapped dimers. (Manuscript in preparation).
- **Gotte G.**[#], Fasoli S., Butturini E., Mahmoud Helmy A. & Fagagnini A. RNase A extensive aggregation tendency favored by its N-terminal-swapped oligomers. A step approaching fibrils? (Manuscript in preparation).

[#] Corresponding author(s)

Book Chapter (Corresponding Author)

Gotte G.[#] & Libonati M. (2014). Capitolo libro (E-Book): “Protein Oligomerization” **cap. 8**, pp 239-278, in *Oligomerization of Chemical and Biological Compounds*, InTech - OpenBook, Editor: C. Lesieur, ISBN: 978-953-51-1617-2, <http://www.intechopen.com/books/oligomerization-of-chemical-and-biological-compounds/protein-oligomerization>, doi.org/10.5772/57489.

Verona, July 31st 2018