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**BIOGRAPHICAL SKETCH Giovanni Tosi**

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NAME	POSITION TITLE
Giovanni Tosi	Associate Professor, department of LIFE Sciences

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Liceo Scientifico TASSONI	Maturità Scientifica Degree	1991-1996	Scientific and Humanistic Sciences
University of Modena and Reggio Emilia, Faculty of Pharmacy		1996-2002	Pharmacy
University of Modena and Reggio Emilia		2002-2003	Drug Sciences
Department of Pharmaceutical Sciences, Specialization Upgrade in Drug Sciences.			
University of Modena and Reggio Emilia. PhD school in Drug Sciences.	PhD	2003-2006	Nanomedicine, Pharmaceutical Technology
Academic researcher/Assistant Professor	\	2006-today	Nanomedicine and Pharmaceutical Technology
Research associate at NEST, Istituto Nanoscienze-CNR, Piazza San Silvestro 12, 56127 Pisa (Italy)		2014-	Nanomedicine and Pharmaceutica Technology
Associate Professor in Pharmaceutical Technology, Department of Life Sciences, University of Modena and Reggio Emilia, Italy		2015-	Nanomedicine and Pharmaceutica Technolog

**A. Positions and Honors.**

Since November 2005, Dr. Giovanni Tosi is researcher in the scientific field of Pharmaceutical Technology at the University of Modena and Reggio Emilia (PI at the department of Pharmaceutical Sciences, which belongs to the faculty of Pharmacy). Since 2015, he is associate professor in the same field.

He was born in 1977 (March, 2<sup>nd</sup>) in Bologna, Italy, and got his degree in Pharmacy in 2002 with 110/110. He got his PhD in Pharmaceutical Sciences in 2005 at the University of Modena and Reggio Emilia, Italy. He is now Coordinator of "Applied Technology" curricula for the PhD school in Health Products, member of Instruments Commission of Dep.Pharm.Sci., Contact Person ILO of Dep.Pharm.Sci, Research products, Representative of the Dep.Pharm.Sci. in the Central Board of Animal House of University of Modena and Reggio Emilia. He is now also Research associate at NEST, Istituto Nanoscienze-CNR, Pisa (Italy).

His works on Nanoparticles for CNS delivery and targeting were honored with national prizes and awards (La Manna Prize for Student Thesis he drove), Jorge Heller Outstanding Paper Award, 2005) and Innovation price (AFI2005, AFI 2006). His work on Nanoparticles for CNS drug delivery has been recently awarded as one of the Hot Topic (150 selected research over 19.000 proposals) at the World Neuroscience Meeting (Society for Neuroscience) in Washington DC, November 2011 and World Neuroscience Meeting (Society for Neuroscience) in New Orleans,

November 2012.

He is author or co-author of more than 90 publications in international journals (of which 5 are reviews and 3 are book chapters) and gave over 200 presentations (invited speaker, oral presentations and posters) in international and national congresses.

He participated as collaborator in several Italian projects supported by the Italian Research Ministry (main 2005-2009, project on Nanoparticles for CNS drug delivery, 160kEuro funding) and HDF funding (project on Nanoparticles for Huntington Disease, 20k Euro). He is now collaborating with a broad network of scientists at the University of Uppsala (S), University of Ulm (D), University of Marsilles (Fr), University of Alabama (USA), University of Wien (A), University of Padova (IT), UniSTEM Milano (IT), Istituto Superiore della Sanità Rome (IT), IRCCS Burlo Garofolo, Trieste (IT) and many national and international industries (Gilead Sciences, Biomarin). He currently acts as referee for the top journals in nanotechnology and nanomedicine such as Journal of Controlled Release, Biomaterial, Nanomedicine and many other journals dealing with Nanotechnology, Drug Delivery and Nanomedicine.

He is Member of the Editorial Advisory Board of "Drug Delivery Letters", "Journal of Nanoneuroscience" and "ISRN Pharmaceutical". In 2009, he organized the Italian Chapter Controlled Release Society meeting in Modena (November, 3<sup>rd</sup>-5<sup>th</sup>) with national and international invited speakers, expert in the different fields of neuroscience and nanotechnology.

He is also member of the Committee for Research of University of Modena and Reggio Emilia.

He is scientific delegate for international cooperation and coordinator of UNIMORE Nanomedicine Platform since 2017.

### RESEARCH interest:

The research activity is based on the development of lipid and polymeric systems for the delivery and the targeting of drugs to diseased tissues or cells. In particular, drug delivery to the Central Nervous System, by using nanoparticulate vectors (Np). In particular, the research is focus on the planning, preparation, characterization and administration of Np after surface modifications.

By applying in vivo pharmacological tests, personally performed by dr. Tosi, several interesting results have been reached, confirming the high potential of these systems. In particular, the NPs, loaded with selected drugs or labeled with fluorescent dyes, were found to be able to cross the Blood-brain barrier, opening the study to the possibility of a non-invasive treatment of cerebral pathologies. At the same time, considering the guidelines of the European Community and FDA, a number of studies on the biodistribution of these vectors, by using fluorescent dye and HPLC/fluorimetric methodologies, have been performed.

Furthermore, over the last years, his interest was also deputed to the preparation and optimization of liposomal nanocarriers for the delivery of gene material (in particular oligonucleotides) in Keratinocytes (biological target: skin pathologies) and tumor targeting. After in vitro test, the research reached an increased transfection efficacy mediated by these novel vectors, confirmed by confocal microscopy and citofluorimetric analysis.

### B. Selected peer-reviewed publications (in chronological order).

- Belletti D, Grabrucker AM, Pederzoli F, Menrath I, Vandelli MA, **Tosi G**, Duskey TJ, Forni F, Ruozi B. Hybrid nanoparticles as a new technological approach to enhance the delivery of cholesterol into the brain. *Int J Pharm.* 2018 May 30;543(1-2):300-310.
- Pederzoli F, **Tosi G**, Genovese F, Belletti D, Vandelli MA, Ballestrazzi A, Forni F, Ruozi B.
- Qualitative and semiquantitative analysis of the protein coronas associated to different functionalized nanoparticles. *Nanomedicine (Lond).* 2018 Feb;13(4):407-422.
- Vilella A, Belletti D, Sauer AK, Hagemeyer S, Sarowar T, Masoni M, Stasiak N, Mulvihill JJE, Ruozi B, Forni F, Vandelli MA, **Tosi G**, Zoli M, Grabrucker AM. Reduced plaque size and inflammation in the APP23 mouse model for Alzheimer's disease after chronic application of polymeric nanoparticles for CNS targeted zinc delivery. *J Trace Elem Med Biol.* 2018 Sep;49:210-221.
- Duskey JT, Belletti D, Pederzoli F, Vandelli MA, Forni F, Ruozi B, **Tosi G**. Current Strategies for the Delivery of Therapeutic Proteins and Enzymes to Treat Brain Disorders. *Int Rev Neurobiol.* 2017;137:1-28.
- Belletti D, Riva G, Luppi M, **Tosi G**, Forni F, Vandelli MA, Ruozi B, Pederzoli F. Anticancer drug-loaded quantum dots engineered polymeric nanoparticles: Diagnosis/therapy combined approach. *Eur J Pharm Sci.* 2017 Sep 30;107:230-239.
- Ruozi B, Belletti D, Pederzoli F, Masoni M, Keller J, Ballestrazzi A, Vandelli MA, **Tosi G**, Grabrucker AM. Novel Curcumin loaded nanoparticles engineered for Blood-Brain Barrier crossing and able to disrupt Abeta

aggregates. *Int J Pharm.* 2017 Jun 30;526(1-2):413-424.

- Pederzoli F, **Tosi** G, Vandelli MA, Belletti D, Forni F, Ruozi B. Protein corona and nanoparticles: how can we investigate on? *Wiley Interdiscip Rev Nanomed Nanobiotechnol.* 2017 Nov;9(6).
- Ruozi B, Veratti P, Vandelli MA, Tombesi A, Tonelli M, Forni F, Pederzoli F, Belletti D, **Tosi** G. Apoferritin nanocage as streptomycin drug reservoir: Technological optimization of a new drug delivery system. *Int J Pharm.* 2017 Feb 25;518(1-2):281-288.
- Wen MM, El-Salamouni NS, El-Refai WM, Hazzah HA, Ali MM, **Tosi** G, Farid RM, Blanco-Prieto MJ, Billa N, Hanafy AS. Nanotechnology-based drug delivery systems for Alzheimer's disease management: Technical, industrial, and clinical challenges. *J Control Release.* 2017 Jan 10;245:95-107.
- Pederzoli F, **Tosi** G, Genovese F, Belletti D, Vandelli MA, Ballestrazzi A, Forni F, Ruozi B. Qualitative and semiquantitative analysis of the protein coronas associated to different functionalized nanoparticles. *Nanomedicine (Lond).* 2018 Feb;13(4):407-422.
- Vilella A, Belletti D, Sauer AK, Hagemeyer S, Sarowar T, Masoni M, Stasiak N, Mulvihill JJE, Ruozi B, Forni F, Vandelli MA, **Tosi** G, Zoli M, Grabrucker AM. Reduced plaque size and inflammation in the APP23 mouse model for Alzheimer's disease after chronic application of polymeric nanoparticles for CNS targeted zinc delivery. *J Trace Elem Med Biol.* 2017 Dec 27. 10.1016/j.jtemb.2017.12.006. [Epub ahead of print]
- Duskey JT, Belletti D, Pederzoli F, Vandelli MA, Forni F, Ruozi B, **Tosi** G. Current Strategies for the Delivery of Therapeutic Proteins and Enzymes to Treat Brain Disorders. *Int Rev Neurobiol.* 2017;137:1-28.
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- Ruozi B, Veratti P, Vandelli MA, Tombesi A, Tonelli M, Forni F, Pederzoli F, Belletti D, **Tosi** G. Apoferritin nanocage as streptomycin drug reservoir: Technological optimization of a new drug delivery system. *Int J Pharm.* 2017 Feb 25;518(1-2):281-288.
- **Tosi** G., Belletti D, Pederzoli F, Ruozi B. Apoferritin nanocage as drug reservoir: is it a reliable drug delivery system? *Expert Opin Drug Deliv.* 2016 Aug 26:1-3.
- Belletti D, Grabrucker AM, Pederzoli F, Menrath I, Cappello V, Vandelli MA, Forni F, **Tosi** G, Ruozi B. Exploiting the versatility of Cholesterol in nanoparticles formulation, *Int J Pharm.* 2016 Sep 10;511(1):331-40.
- **Tosi**, G., Musumeci, T., Ruozi, B., Carbone, C., Belletti, D., Pignatello, R., Vandelli, M.A., Puglisi, G. The "fate" of polymeric and lipid nanoparticles for brain delivery and targeting: Strategies and mechanism of blood-brain barrier crossing and trafficking into the central nervous system, (2016) *Journal of Drug Delivery Science and Technology*, 32, pp. 66-76.
- Salvalaio M, Rigon L, Belletti D, D'Avanzo F, Pederzoli F, Ruozi B, Marin O, Vandelli MA, Forni F, Scarpa M, Tomanin R, **Tosi** G Targeted Polymeric Nanoparticles for Brain Delivery of High Molecular Weight Molecules in Lysosomal Storage Disorders. *PLoS One.* 2016 May 26;11(5):e0156452.
- Belletti, D., **Tosi**, G., Forni, F., Lagreca, I., Barozzi, P., Pederzoli, F., Vandelli, M.A., Riva, G., Luppi, M., Ruozi, B., PEGylated siRNA lipoplexes for silencing of BLIMP-1 in Primary Effusion Lymphoma: In vitro evidences of antitumoral activity, (2016) *European Journal of Pharmaceutics and Biopharmaceutics*, 99, pp. 7-17.
- Valenza, M., Chen, J.Y., Di Paolo, E., Ruozi, B., Belletti, D., Ferrari Bardile, C., Leoni, V., Caccia, C., Brillì, E., Di Donato, S., Boido, M.M., Vercelli, A., Vandelli, M.A., Forni, F., Cepeda, C., Levine, M.S., **Tosi**, G., Cattaneo, E., Cholesterol-loaded nanoparticles ameliorate synaptic and cognitive function in Huntington's disease mice, (2015) *EMBO Molecular Medicine*, 7 (12), pp. 1547-1564.
- Pederzoli, F., Ruozi, B., Pracucci, E., Signore, G., Zapparoli, M., Forni, F., Vandelli, M.A., Ratto, G., **Tosi**, G. Nanoimaging: Photophysical and pharmaceutical characterization of poly-lactide-co-glycolide nanoparticles engineered with quantum dots, (2015) *Nanotechnology*, 27 (1), art. no. 015704, .
- **Tosi**, G., Vandelli, M.A., Forni, F., Ruozi, B. Nanomedicine and neurodegenerative disorders: So close yet so far (2015) *Expert Opinion on Drug Delivery*, 12 (7), pp. 1041-1044.
- Ruozi, B., Belletti, D., Sharma, H.S., Sharma, A., Muresanu, D.F., Mössler, H., Forni, F., Vandelli, M.A., **Tosi**, G. PLGA Nanoparticles Loaded Cerebrolysin: Studies on Their Preparation and Investigation of the Effect of Storage and Serum Stability with Reference to Traumatic Brain Injury, (2015) *Molecular Neurobiology*, 52

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- Vilella, A., Ruozi, B., Belletti, D., Pederzoli, F., Galliani, M., Semeghini, V., Forni, F., Zoli, M., Vandelli, M.A., **Tosi, G.**, Endocytosis of nanomedicines: The case of glycopeptide engineered PLGA nanoparticles, (2015) *Pharmaceutics*, 7 (2), pp. 74-89.
- Belletti, D., **Tosi, G.**, Riva, G., Lagreca, I., Galliana, M., Luppi, M., Vandelli, M.A., Forni, F., Ruozi, B. Nutlin-3 loaded nanocarriers: Preparation, characterization and in vitro antineoplastic effect against primary effusion lymphoma, (2015) *International Journal of Pharmaceutics*, 490 (1-2), art. no. 14899, pp. 85-93.
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- Monsalve, Y., **Tosi, G.**, Ruozi, B., Belletti, D., Vilella, A., Zoli, M., Vandelli, M.A., Forni, F., López, B.L., Sierra, L., PEG-g-chitosan nanoparticles functionalized with the monoclonal antibody OX26 for brain drug targeting, (2015) *Nanomedicine*, 10 (11), pp. 1735-1750.
- Chhabra, R., Ruozi, B., Vilella, A., Belletti, D., Mangus, K., Pfaender, S., Sarowar, T., Boeckers, T.M., Zoli, M., Forni, F., Vandelli, M.A., **Tosi, G.**, Grabrucker, A.M., Application of polymeric nanoparticles for CNS targeted zinc delivery in vivo, (2015) *CNS and Neurological Disorders - Drug Targets*, 14 (8), pp. 1041-1053.
- Riva, G., Lagreca, I., Mattiolo, A., Belletti, D., Lignitto, L., Barozzi, P., Ruozi, B., Vallerini, D., Quadrelli, C., Corradini, G., Forghieri, F., Marasca, R., Narni, F., Tosi, G., Forni, F., Vandelli, M.A., Amadori, A., Chieco-Bianchi, L., Potenza, L., Calabrò, M.L., Luppi, M., Antineoplastic effects of liposomal short interfering RNA treatment targeting BLIMP1/PRDM1 in primary effusion lymphoma, (2015) *Haematologica*, 100 (11), pp. e467-e470.
- **Tosi, G.**, Vilella, A., Chhabra, R., Schmeisser, M.J., Boeckers, T.M., Ruozi, B., Vandelli, M.A., Forni, F., Zoli, M., Grabrucker, A.M. Insight on the fate of CNS-targeted nanoparticles. Part II: Intercellular neuronal cell-to-cell transport, (2014) *Journal of Controlled Release*, 177 (1), pp. 96-107.
- Vilella, A., **Tosi, G.**, Grabrucker, A.M., Ruozi, B., Belletti, D., Vandelli, M.A., Boeckers, T.M., Forni, F., Zoli, M. Insight on the fate of CNS-targeted nanoparticles. Part I: Rab5-dependent cell-specific uptake and distribution, (2014) *Journal of Controlled Release*, 174 (1), pp. 195-201.
- Ruozi, B., Belletti, D., Pederzoli, F., Veratti, P., Forni, F., Vandelli, M.A., **Tosi, G.** Nanotechnology and Alzheimer's disease: What has been done and what to do' (2014) *Current Medicinal Chemistry*, 21 (36), pp. 4169-4185.
- **Tosi, G.**, Ruozi, B., Vandelli, M.A. Brain targeting with polymeric nanoparticles: Which administration route should we take? (2013) *Nanomedicine*, 8 (9), pp. 1361-1363.
- **Tosi, G.**, Ruozi, B., Belletti, D., Vilella, A., Zoli, M., Vandelli, M.A., Forni, F., Brain-targeted polymeric nanoparticles: In vivo evidence of different routes of administration in rodents, (2013) *Nanomedicine*, 8 (9), pp. 1373-1383. Cited 10 times.
- **Tosi, G.**, Bortot, B., Ruozi, B., Dolcetta, D., Vandelli, M.A., Forni, F., Severini, G.M. Potential use of polymeric nanoparticles for drug delivery across the blood-brain barrier (2013) *Current Medicinal Chemistry*, 20 (17), pp. 2212-2225.
- **Tosi, G.**, Ruozi, B., Badiali, L., Bondioli, L., Belletti, D., Forni, F., Vandelli, M.A. Immunonanosystems to CNS pathologies: State of the art, (2012) *Nanotechnology in Health Care*, pp. 107-168.
- **Tosi, G.**, Ruozi, B., Belletti, D. Nanomedicine: the future for advancing medicine and neuroscience (2012) *Nanomedicine*, 7 (8), pp. 1113-1116.
- Ruozi, B., Belletti, D., Bondioli, L., De Vita, A., Forni, F., Vandelli, M.A., **Tosi, G.** Neurotrophic Factors and Neurodegenerative Diseases. A Delivery Issue. (2012) *International Review of Neurobiology*, 102, pp. 207-247.
- **Tosi, G.**, Badiali, L., Ruozi, B., Vergoni, A.V., Bondioli, L., Ferrari, A., Rivasi, F., Forni, F., Vandelli, M.A. Can leptin-derived sequence-modified nanoparticles be suitable tools for brain delivery? (2012) *Nanomedicine*, 7 (3), pp. 365-382
- Bondioli, L., Ruozi, B., Belletti, D., Forni, F., Vandelli, M.A., **Tosi, G.** Sialic acid as a potential approach for the protection and targeting of nanocarriers (2011) *Expert Opinion on Drug Delivery*, 8 (7), pp. 921-937.
- **Tosi, G.**, Fano, R.A., Bondioli, L., Badiali, L., Benassi, R., Rivasi, F., Ruozi, B., Forni, F., Vandelli, M.A. Investigation on mechanisms of glycopeptide nanoparticles for drug delivery across the blood-brain barrier, (2011) *Nanomedicine*, 6 (3), pp. 423-436.
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- Ruozi, B., Riva, G., Belletti, D., **Tosi, G.**, Barozzi, P., Luppi, M., Forni, F., Vandelli, M.A. Immunoliposomal systems targeting primary effusion lymphoma: In vitro study , (2010) *Nanomedicine*, 5 (7), pp. 1051-1064

- **Tosi, G.**, Vergoni, A.V., Ruozi, B., Bondioli, L., Badiali, L., Rivasi, F., Costantino, L., Forni, F., Vandelli, M.A. Sialic acid and glycopeptides conjugated PLGA nanoparticles for central nervous system targeting: In vivo pharmacological evidence and biodistribution (2010) *Journal of Controlled Release*, 145 (1), pp. 49-57.
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- Costantino, L., **Tosi, G.**, Ruozi, B., Bondioli, L., Vandelli, M.A., Forni, F. Colloidal systems for CNS drug delivery, (2009) *Progress in Brain Research*, 180 (C), pp. 35-69.
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### C. Research Support.

#### National Grants:

2013- CARIPARO Grant, Paediatric research 2012-2014: Paediatric neurodegenerative disorders: preclinical evaluation of a nanoparticle-mediated brain therapy and identification of biomarkers of pathogenesis and treatment efficacy, total budget 270.000 Euro. Role: unit coordinator.

2015- FAR UNIMORE grant: Single Particle Tracking: nanomedicine and quantum dots, 33.000 Euro, Role: Coordinator

2016- FARUNIMORE dipartimentale: Nanomedicina applicata a patologie multiorgano: direzionamento di enzimi al cervello, PI Tosi

2017-Telethon grant: Targeting neurons with cholesterol. How can it change the future of Huntington Disease patients, 179.000 Euro, PI Prof. E. Cattaneo, role of UNIMORE: partner

2017 Cariparo Grant Paediatric research: Pediatric neurodegenerative disorders: optimizing nanoparticle-mediated strategy for brain treatment, budget: 249.000 Euro, role of UNIMORE: partner,

#### International Grant:

2011- DAAD Vigoni: Valutazione di carrier nanoparticellari modificati per il superamento della Barriera Emato-Encefalica per il direzionamento cellulo-specifico di farmaci al Sistema Nervoso Centrale, role: co-P.I.

2011-ELA Research Foundation: Leading nanomedicine into the therapy for Leukodystrophies: nanoparticles overcoming the blood-brain barrier to treat the mouse model of Krabbe Disease; role: unit partecipant.

2012-Hereditary disease foundation: Effects of Cholesterol Delivery Using Nanoparticles in the R6/2 Mouse Model of Huntington's Disease, Role: Principal Investigator

2016-ELA Research Foundation: Development of a novel, nanovector-mediated enzyme replacement therapy for Globoid Cell Leukodystrophy (GLD), Role: Unit Coordinator

2018-IMI EU Grants: Investigating Mechanisms and Models Predictive of Accessibility of Therapeutics (IM2PACT) Into the Brain, total budget 18 Mln Euro, Role: Partner