Prof. Antonio Macchiarulo

Research Activity

The research activity of Prof. Antonio Macchiarulo during the last five years (2009-2013) is documented by the publication of 40 scientific articles in international peer-reviewed journal as well as by many communications at national and international congresses. The research activity has been mainly carried out at the former “Dipartimento di Chimica e Tecnologia del Farmaco” (now “Dipartimento di Scienze Farmaceutiche”) of the University of Perugia.

The total number of citations of Prof. Antonio Macchiarulo until 31/12/2013 is 1674 (1535, excluding self-citations), with the h-index = 21 (according to ISI Web of Knowldge, Web of Science).

The research activity of Prof. Macchiarulo follows integrates computational chemistry and biology with experimental scientific areas including medicinal chemistry, biology and pharmacology. It is aimed at addressing the following goals: (i) design of biologically active compounds with drug-like properties; (ii) aid the interpretation of results from cell biology and pharmacology, developing molecular understanding of mechanism of action of compounds, also on the basis of polypharmacology; (iii) depict structure-activity relationships of active compounds at biological targets; (iv) characterize conformational and dynamic properties of small molecules and biological targets.

Research Funding.

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Publications

1. *Macchiarulo A*, Camaioni E, Nuti R, Pellicciari R. **Highlights at the gate of tryptophan catabolism: a review on the mechanisms of activation and regulation of indoleamine 2,3-dioxygenase (IDO), a novel target in cancer disease.** *Amino Acids*. 2009 Jul; 37(2):219-29.
2. Natalini B, Sardella R, Camaioni E, *Macchiarulo A*, Gioiello A, Carbone G, Pellicciari R. **Derived chromatographic indices as effective tools to study the self-aggregation process of bile acids.** *J. Pharm. Biomed. Anal*. 2009 Nov 1; 50(4):613-21.
3. Filosa R, Carmela Fulco M, Marinozzi M, Giacchè N, *Macchiarulo A*, Peduto A, Massa A, de Caprariis P, Thomsen C, Christoffersen CT, Pellicciari R. **Design, synthesis and biological evaluation of novel bicyclo[1.1.1]pentane-based omega-acidic amino acids as glutamate receptors ligands.** *Bioorg. Med. Chem*. 2009, 17(1):242-50.
4. *Macchiarulo A,* Nuti R, Eren G, Pellicciari R. **Charting the Chemical Space of Target Sites: Insights into the Binding Modes of Amine and Amidine Groups***. J. Chem. Inf. Model.* 2009, Apr;49(4):900-12.
5. Natalini B, Sardella R, Carbone G., *Macchiarulo A*, Pellicciari R. **The effect of the copper(II) salt anion in the Chiral Ligand-Exchange Chromatography of amino acids.** *Analytica Chimica Acta.* 2009, 638(2), 225-233.
6. *Macchiarulo A*., Pelliciari R. **MDM2/MDMX Inhibitor Peptide - WO2008106507**. *Expert Opinion on Therapeutic Patents*, 2009, 19(5), 721-726.
7. Carotti A., *Macchiarulo A.*, Giacchè N., Pellicciari R. **Targeting the Conformational Transitions of MDM2 and MDMX: Insights into Key Residues Affecting p53 Recognition**. *Proteins*. 2009, Apr 28; 77(3):524-535.
8. Formentini L, *Macchiarulo A*, Cipriani G, Camaioni E, Rapizzi E, Pellicciari R, Moroni F, Chiarugi A. **Poly(ADP-ribose) catabolism triggers AMP-dependent mitochondrial energy failure**. *J. Biol. Chem*. 2009, 284(26), 17668-76.
9. Fringuelli R, Giacchè N, Milanese L, Cenci E, Macchiarulo A, Vecchiarelli A, Costantino G, Schiaffella F. **Bulky 1,4-benzoxazine derivatives with antifungal activity**. *Bioorg. Med. Chem.* 2009, 17(11), 3838-46.
10. Thomas C, Gioiello A, Noriega L, Strehle A, Oury J, Rizzo G, Macchiarulo A, Yamamoto H, Mataki C, Pruzanski M, Pellicciari R, Auwerx J, Schoonjans K. **TGR5-mediated bile acid sensing controls glucose homeostasis.** *Cell Metab.* 2009, 10(3):167-77.

11. Bellocchi D, Macchiarulo A,* Carotti A, Pellicciari R. **Quantum Mechanics/Molecular Mechanics (QM/MM) Modeling of the Irreversible Transamination of L-Kynurenine to Kynurenic Acid: The Round Dance of Kynurenine Aminotransferase II.** *Biochim Biophys Acta.* 2009, 1794(12), 1802-12.
12. Moretti S, De Falco V, Tamburrino A, Barbi F, Tavano M, Avenia N, Santeusanio F, Santoro M, Macchiarulo A,* Puxeddu E.* **Insights into the molecular function of the inactivating mutations of B-Raf involving the DFG motif.** *Biochim Biophys Acta.* 2009, 1793(11):1634-45.
13. Macchiarulo A.,* Thornton J.M., Nobeli I.* **Mapping Human Metabolic Pathways in the Small Molecule Chemical Space.** *J. Chem. Inf. Model.* 2009, 49(10):2272-89.
14. Pellicciari R., Gioiello A., Macchiarulo A., Thomas C., Rosatelli E., Natalini B., Sardella R., Pruzanski M., Roda A., Pastorini E., Schoonjans K., Auwerx J. **Discovery of 6α-Ethyl-23(S)-methylcholic Acid (S-EMCA, INT-777) as a Potent and Selective Agonist for the TGR5 Receptor, a Novel Target for Diabesity.** *J Med Chem*. 2009, 52(24):7958-61.
15. Mancini F, Di Conza G, Monti O, Macchiarulo A, Pellicciari R, Pontecorvi A, Moretti F. **Puzzling over MDM4-p53 network**. *Int J Biochem Cell Biol.* 2010. 2010 Jul;42(7):1080-3.
16. Natalini B, Sardella R, Giacchè N, Palmiotto S, Camaioni E, Marinozzi M, Macchiarulo A, Pellicciari R. **Chiral ligand-exchange separation and resolution of extremely rigid glutamate analogs: 1-aminospiro[2.2]pentyl-1,4-dicarboxylic acids.** *Anal Bioanal Chem.* 2010 Jul;397(5):1997-2011.
17. Zhou T, Zhang Y, Macchiarulo A, Yang Z, Cellanetti M, Coto E, Xu P, Pellicciari R, Wang L. **Novel polymorphisms of nuclear receptor SHP associated with functional and structural changes.** *J Biol Chem.* 2010 Aug 6;285(32):24871-81.
18. Dezi C, Carotti A, Magnani M, Baroni M, Padova A, Cruciani G, Macchiarulo A,* Pellicciari R. **Molecular Interaction Fields and 3D-QSAR Studies of p53-MDM2 Inhibitors Suggest Additional Features of Ligand-Target Interaction.** *J Chem Inf Model.* 2010 Aug 23;50(8):1451-65.
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21. Macchiarulo A,* Giacchè N, Mancini F, Puxeddu E, Moretti F, Pellicciari R. **Alternative strategies for targeting mouse double minute 2 activity with small molecules: novel patents on the horizon?** *Expert Opin Ther Pat.* 2011 Mar;21(3):287-94.

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23. Antimo Gioiello, Paola Sabbatini, Emiliano Rosatelli, Antonio Macchiarulo, Roberto Pellicciari. **Divergent and stereoselective synthesis of dafachronic acids.** *Tetrahedron*. 2011, 67 (10), 1924-1929.

24. Antonio Macchiarulo,* Nicola Giacchè, Andrea Carotti, Fabiola Moretti and Roberto Pellicciari. **Expanding the horizon of chemotherapeutic targets: From MDM2 to MDMX (MDM4).** *Med. Chem. Commun*., 2011, 2, 455-465.

25. Roberto Pellicciari, Emidio Camaioni, Adam M. Gilbert, Antonio Macchiarulo, Jack A. Bikker, Falgun Shah, Joel Bard, Gabriele Costantino, Antimo Gioiello, Graeme M. Robertson, Paola Sabbatini, Francesco Venturoni, Paride Liscio, Andrea Carotti, Daniele Bellocchi, Andrea Cozzi, Andrew Wood, Cathleen Gonzales, Margaret M. Zaleska, John W. Ellingboe and Flavio Moroni. **Discovery and characterization of novel potent PARP-1 inhibitors endowed with neuroprotective properties: From TIQ-A to HYDAMTIQ**. *Med. Chem. Commun.*, 2011, 2, 559-565.

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31. Roberto Pellicciari, Antimo Gioiello, Paola Sabbatini, Francesco Venturoni, Roberto Nuti, Carolina Colliva, Giovanni Rizzo, Luciano Adorini, Mark Pruzanski, Aldo Roda, and Antonio Macchiarulo. **Avicholic Acid: A Lead Compound from Birds on the Route to Potent TGR5 Modulators.** *ACS Med. Chem. Lett.*, 2012, *3* (4), pp 273–277

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33. Chiara Custodi, Roberto Nuti, Tudor I. Oprea, Antonio Macchiarulo.* **Fitting the Complexity of GPCRs Modulation into Simple Hypotheses of Ligand Design.** *J Mol Graph Model.* 2012, 38, 70-81. doi: 10.1016/j.jmgm.2012.07.002.

34. Antimo Gioello, Emiliano Rosatelli, Roberto Nuti, Antonio Macchiarulo, Roberto Pellicciari. **Patented TGR5 Modulators: a Review (2006 – present).** *Expert Opin Ther Pat.* 2012, 22(12), 1399-414.

35. Antonio Macchiarulo,* Andrea Carotti, Marco Cellanetti, Roccaldo Sardella, Antimo Gioiello. **Navigations of Chemical Space to Further the Understanding of Polypharmacology in Human Nuclear Receptors.** *Med. Chem. Commun*., 2013, 4(1), 216-227.

36. Antolin AA, Carotti A, Nuti R, Hakkaya A, Camaioni E, Mestres J, Pellicciari R, Macchiarulo A.* **Exploring the effect of PARP-1 flexibility in docking studies.** *J Mol Graph Model.* 2013, 45, 192-201.

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40. Antonio Macchiarulo,* Charles Thomas, Thijs W.H. Pols, Roberto Nuti, Cristina Ferrari, Nicola Giacchè, Francesca De Franco, Antimo Gioiello, Mark Pruzanski, Johan Auwerx, Kristina Schoonjans, Roberto Pellicciari. **Probing the Binding Site of Bile Acids in TGR5.** *ACS Med. Chem. Lett.*, 2013, 4 (12), pp 1158-1162.

Invited Lectures at National and International Congresses.

1. **Antonio Macchiarulo.** *Protein-Protein Interactions as Druggable Targets.* Dipartimento di Scienze Biochimiche "A. Rossi-Fanelli", " Università degli Studi di Roma La Sapienza (Italy). Febbraio 2009.
2. **Antonio Macchiarulo. Moderatore Tavola Rotonda:** *Nuove Prospettive Terapeutiche nella Neurodegenerazione.* Nuove Prospettive in Chimica Farmaceutica, III° Meeting-Workshop. 13-14 Febbraio 2009, Il Ciocco, Castelvecchio Pascoli (LU) (Italy).
3. **Antonio Macchiarulo.** *The Human Metabolome in the Chemical Space.* Gillespie Centre, Clare College, Cambridge (UK). Giugno 2009.
4. **Antonio Macchiarulo.** *Voyages into the Chemical Space of Human Metabolome and Beyond*. VII European Workshop in Drug Design, 24-30 May 2009, Certosa di Pontignano, Siena (Italy).
5. **Antonio Macchiarulo**, Marco Cellanetti, Roberto Pellicciari. *Combining Homology Modeling, Docking and Molecular Dynamic Simulations to Study the Binding Mode and Mechanism of Action of Ligands to the Small Heterodimer Partner (SHP)*. XXIII Congresso Nazionale della Società Chimica Italiana. 05-10 July 2009. Sorrento (Italy).
6. **Antonio Macchiarulo**, Laura Amori, Daniele Bellocchi, Emidio Camaioni, Andrea Carotti, Alberto Chiarugi, Gabriele Costantino, Maura Marinozzi, Roberto Nuti, Francesco Venturoni, Robert Schwarcz, Flavio Moroni and Roberto Pellicciari. *Exploring Ligand Recognition in the Kynurenine Pathway to Advance the Medicinal Chemistry of Kynurenines*. 12° Meeting of the International Society for Tryptophan Research (ISTRY). 9-11 July 2009, Florence (Italy).
7. **Antonio Macchiarulo.** *Tackling the Challenges of small Molecule for Protein-Protein Interaction – the Case of p53/MDM2 Inhibitors.* Vienna Summer School on Drug Design. 13-18 September 2009. Vienna (Austria).

8. **Antonio Macchiarulo**, Chiara Custodi, Roberto Nuti, Tudor Oprea, Roberto Pellicciari. *Recovering Design Strategies of GPCRs Modulators from Explorations of the Chemical Space*. 18th EuroQSAR Symposium. 19-24 September 2010. Rhodes (Greece)
9. **Antonio Macchiarulo**. *Alternative Strategies to Target p53/MDM2-MDMX Interactions.* Institute of Cell Biology and Neurobiology – CNR, Rome (Italy). Maggio 2011.
10. **Antonio Macchiarulo,** Marco Cellanetti, Andrea Carotti, Roberto Pellicciari. *Furthering the Understand of Polypharmacology in Nuclear Receptor Superfamily.* XXIV Congresso Nazionale della Società Chimica Italiana. 11-16 September 2011. Lecce (Italy).
11. **Antonio Macchiarulo.** *Sailing the Chemical Space for Polypharmacology.* Vienna Summer School on Drug Design. 11-16 September 2011. Vienna (Austria).
12. **Antonio Macchiarulo.** *Approaches to Investigate the Polypharmacology of Nuclea Receptors.* Centro di ricerche Servier, Parigi (France). Aprile 2012.
13. **Antonio Macchiarulo.** *From Target Specificity to Targeted Polypharmacology. Special Interest Symposium: ADP-ribosylation in Signalling Events. The EMBO Meeting 2012*. 22-25 September 2012. Nice (France).
14. **Antonio Macchiarulo.** *Targeting DAF-12 for Novel Therapeutic Opportunities in Parasitic Nematode Diseases.* Centro di ricerche IRBM – Pomezia (Italy). Aprile 2013.
15. **Antonio Macchiarulo.** *Innovative Approaches to Target Discovery and Validation in Drug Discovery.* Università di Genova, ISSUGE, Ottobre 2013.

Teaching Activity

The teaching activity of Prof. Macchiarulo during the last five years (2009-2013) has been carried out in the degree of "Chimica e Tecnologia Farmaceutiche (C.T.F.)" and "Biotecnologie Farmaceutiche", at the Faculty of Pharmacy of the University of Perugia. A summary of teaching lectures given by Prof. Antonio Macchiarulo is provided below.

A.A. 2009-2010:

Chimica Farmaceutica III (6 CFU), degree in "C.T.F". at the Faculty of Pharmacy of the University of Perugia.

Elementi di Chimica Genomica (3 CFU), degree in "Biotecnologie Farmaceutiche" at the Faculty of Pharmacy of the University of Perugia.

*Biologia dei Sistemi e Scoperta di Nuovi Farmac*i (*3 CFU*), degree in “Biotecnologie Farmaceutiche” at the Faculty of Pharmacy of the University of Perugia.

A.A. 2010-2011:

Chimica Farmaceutica III (6 CFU), degree in “C.T.F”. at the Faculty of Pharmacy of the University of Perugia.

A.A. 2011-2012:

Chimica Farmaceutica III (6 CFU), degree in “C.T.F”. at the Faculty of Pharmacy of the University of Perugia.

Chimica Farmaceutica Avanzata (6 CFU), degree in “Biotecnologie Farmaceutiche” at the Faculty of Pharmacy of the University of Perugia.

A.A. 2012-2013:

Chimica Farmaceutica III (6 CFU), degree in “C.T.F”. at the Faculty of Pharmacy of the University of Perugia.

Chimica Farmaceutica Avanzata (6 CFU), degree in “Biotecnologie Farmaceutiche” at the Faculty of Pharmacy of the University of Perugia.