

PROF. MARIA LETIZIA BARRECA
(CV updated on 27/10/2021)

CURRENT ACADEMIC POSITION

Associate Professor in Medicinal Chemistry

Address: In Silico Drug Discovery Laboratory (I2D Lab), Department of Pharmaceutical Sciences, University of Perugia, Via Fabretti 48, 06123, Perugia, Italy

Phone: +39-075-5855157

Fax: +39-075-5855115

E-mail: maria.barreca@unipg.it

Website: <https://www.unipg.it/personale/maria.barreca;>

<https://d2medchem.wixsite.com/unipg;>

<https://www.sibyllabiotech.it/>

In possession of national qualification (round 2016) for the competition sector 03/D1 - CHIMICA E TECNOLOGIE FARMACEUTICHE, TOSSICOLOGICHE E NUTRACEUTICO-ALIMENTARI. Eligibility as Full Professor obtained on 04 April 2018

EDUCATION

1996: Title of PhD in Pharmaceutical Sciences (IX Cycle) at the University of Messina.

1996: Qualified to practice as a Pharmacist.

1992: MSc cum laude in Pharmaceutical Chemistry and Technology (CTF) at the University of Messina

PROFESSIONAL EXPERIENCES

01/12/2016-present Associate Professor (SSD CHIM-08), Department of Pharmaceutical Sciences, University of Perugia

1/11/2007-30/11/2016: Assistant Professor (SSD CHIM-08), Faculty of Pharmacy and then from 2014 Department of Pharmaceutical Sciences, University of Perugia

7/4-31/ 10/2007: Visiting scientist at the Laboratory of Chemometry and Chemoinformatics, Department of Chemistry, University of Perugia

30/3/2000-28/8/2001: Fellowship for research activities (30/03 / 2000-14 / 05/2000) within the "International exchange program for short-term mobility (CNR Short - Term Mobility)" carried out at the Department of Biology and Biochemistry, University of Houston, Texas, USA. (At the end of the fellowship, Prof. Barreca extended her stay at the University of Houston as a visiting scientist until August 2001)

4/3/1999-31/10/2007: Assistant Professor (SSD CHIM-08), Pharmaco-Chemical Department, Faculty of Pharmacy, University of Messina

1997-98: Post-doc in Pharmaceutical Sciences at the Pharmaco-Chemical Department of the University of Messina

1993: "Fondazione Bonino-Pulejo" Scholarship at the research laboratories of the Pharmaco-Chemical Department - Faculty of Pharmacy of the University of Bari. Later, part of the activities of the research doctorate were carried out in the same laboratories.

OTHER ACADEMIC POSITIONS

2019-present: Delegate for the "Third Mission" sector of the Department of Pharmaceutical Sciences, University of Perugia (DSF-UNIPG)
2013-present: Head of AQ (Quality Assurance) of the Degree Course in Pharmaceutical Biotechnology (DSF-UNIPG)
2016-present: Member of the Steering Committee of the Degree Course in Pharmaceutical Biotechnologies (DSF-UNIPG).
2019-present: Member of the Didactic Commission of the DSF-UNIPG.
2017-present: Member of the Commission for the distribution of funds for the functioning of the didactic laboratories of the DSF-UNIPG
2004-2005: Secretary of the Master Course in CTF, University of Messina.

SCIENTIFIC RESEARCH ACTIVITIES

03/1999 - 10/2007: research activities at the Pharmaco-Chemical Department of the University of Messina, where Prof. Barreca has started a laboratory in the field of computational chemistry applied to drug discovery.

10/2007-present: research activities at the Department of Pharmaceutical Sciences of the University of Perugia, where she was responsible for creating and directing the In silico Drug Discovery laboratory (I2D Lab).

Prof. Barreca has significant expertise in the field of medicinal chemistry and drug discovery. In particular, the research activities mainly concern the application/development of advanced methodologies of molecular modeling, computational chemistry, chemoinformatics and library design in order to: 1) study the structure-function relationships of macromolecules of biological interest; 2) identify and optimize new bioactive compounds through rational ligand- and target-based design, characterization of structure-activity relationships as well as virtual screening; 3) understand the factors determining the binding of a ligand to the biological target, 5) predict the physico-chemical properties and pharmacokinetics of compounds of pharmaceutical interest, and more recently 6) develop predictive models of machine learning.

She is/was member of several national and international multidisciplinary research projects and has linked successful collaborations with international groups.

BIBLIOMETRIC INDICATORS RELATED TO PUBLICATIONS AND CITATIONS

Up to October, 26th 2021

Total number of papers: 96

Author h-index: 34 (Scopus Database); 37 (Google Scholar)

Total Citations: 3288 (Scopus Database)

NATIONAL AND INTERNATIONAL AWARDS AND RECOGNITIONS FOR RESEARCH ACTIVITIES

9/01/2018-present: Prof. Barreca is included in the list of Top Italian Scientists (TIS) of the VIA-Academy (Area: chemistry-medicine; Macroarea: Chemistry)

07/12/2016: 1st Prize at "BioSolveIT's scientific challenge winter 2015" (duration of the 3-step challenge: December 2015-December 2016), organized by BioSolveIT GmbH (Germany). Awarded project: "Identification of pharmacological chaperones for cellular prion protein "

21/1/2015: ChemMedChem's praise for the full paper "Pharmacophore-based discovery of small-molecule inhibitors of protein-protein interactions between HIV-1 integrase and cellular cofactor LEDGF / p75" to be among the top 10 most cited articles published in 2009.

14/9/2008: 'Italian Chemical Society-Farindustria' Award for the best young researcher in Pharmaceutical research

5/10/2007: "James Kaminsky Award" for the best oral presentation at the "10th EU Catalyst User Group Meeting 2007 and Advanced Seminars in Catalyst", Messina. Award-winning presentation: Pharmacophore modeling approaches to the discovery of novel HIV-1 integrase inhibitors

5/4/2002: First prize for the best poster at the MGMS Annual International Meeting 2002-Biomolecular Interactions, Bristol (UK). Award-winning poster: Computational approaches in discovering novel anti-AIDS agents

2021-present: mentor (by invitation) of PhDs /Postdocs within the "EFMC-YSN Mentoring Program - 2021".

2019 – present: member of the *ACS Medicinal Chemistry Letters* Editorial Advisory Board (EAB)

2017-present: consultant for the international law firm "Herbert Smith Freehills LLP" (<https://www.herbertsmithfreehills.com/>) on topics related to medicinal chemistry and drug discovery (this consultation is confidential)

SCIENTIFIC RESPONSIBILITY/ PARTICIPATION IN NATIONAL AND INTERNATIONAL RESEARCH PROJECTS

Principal Investigator/Co-Investigator

1. **2021-2022:** Dr. Andrea Astolfi (applicant), formerly a postdoc in the I2D Lab, is one of the winners of the "Post-doctoral fellowship 2021" of the Umberto Veronesi Foundation. Prof. Barreca is officially the principal investigator of the submitted project: "Tuning the Precision Oncology on the PI3K / AKT / mTOR pathway". 01-04-2021-present (principal investigator)
2. **2018-2019:** University funds for basic research "A multidisciplinary approach to the discovery of p38 α MAPK inhibitors" 24-07-2018 a 24-06-2019 (principal investigator)
3. **2016-2017:** Pilot Grant 2016, National Multiple Sclerosis Society, New York (USA): "Targeting cellular prion protein in multiple sclerosis". 01-09-2016 al 30-08-2017 (co-investigator)

Scientific Head of UNIPG Unit

4. **2013-2016:** Young Investigator Award (Ricerca Finalizzata 2010, GR-2010-2312769) from Italian Ministry of Health: Designing molecular chaperones for proteins: a new strategy for drug discovery in neurodegenerative diseases. 12-06-2013 al 11-06-2016
5. **2011-2013:** Italian Program for AIDS research 2009-2010: Discovery of innovative Tat-mimic compounds to be used in HIV-1 eradication strategies. 06-04-2011 al 30-06-2013.
6. **2008-2012:** FP7-HEALTH-2007 - EU Project THINC (Targeting HIV integration co-factors, targeting cellular proteins during nuclear import or integration of HIV). 01-03-2008 al 29-02-2012.

Member of research unit

7. **2021-present:** EU-OPENSREEN-DRIVE Chemoproteomics and Mass Spectrometry Imaging (MSI) Call 2021 - Identification of the Pharmacological Target of Compounds Modulating the Activity of the Cellular Prion Protein (CHEMPRION). 1/10/2021-present
8. **2021-2024:** Grant Telethon 2020: "Development of drugs capable of promoting cellular degradation of the prion protein". 1/10/2021-30/09/2024
9. **2020-2023.** FISM 2019 - Research Project - Single Centre 2019: "Targeting cellular prion protein in multiple sclerosis" 1/03/2020-28/02/2023
10. **2018-2022:** AIRC Investigator Grant - IG 2017: Tackling Interleukin 4 Induced 1, IL4i1, as a novel target enzyme for tumor immunotherapy. 1-01-2018 a 31-12-2022
11. **2017-2018:** Pilot Project Cystic Fibrosis Research Foundation 2017: "Identification of new efflux pumps inhibitors able to contrast nontuberculous mycobacterial infections in cystic fibrosis patients" (FFC#17/2017). 01-09-2017 a 31-08-2018
12. **2017-2018:** Fondazione Cassa di Risparmio di Perugia: "Reduction of neurotoxicity induced by the prion protein with molecules with a heterocyclic structure: implications in Alzheimer's disease. 01-06-2017 al 31-05-2018

13. **2016-2017**: University Funds for basic research 2015: "Development of PA / PB1 interaction inhibitors of influenza polymerase as new antiviral agents" 12-05-2016 to 12-05-2017
14. **2013-2016**: PRIN ("Relevant projects of National Interest") 2010-11: Blocking HIV-1 replication through an approach aimed at different molecular targets. 01-02-2013 to 01-02-2016
15. **2012-2014**: "Discovery of influenza A virus non-structural protein 1 (NS1) inhibitors" funded by the Ministry of Health. 01-06-2012 to 31-05-2014
16. **2011-2013**: "Discovery of Tat-mimicking compounds to fight HIV latency" funded by the Bill & Melinda Gates Foundation. from 01-09-2011 to 01-03-2013
17. **2010-2012**: PRIN-2008: Inhibitors of HIV transcriptional regulation. 22-03-2010 to 22-09-2012
18. **20010-2011**: "How to fight the flu pandemic: identification of new effective drugs" funded by the Ministry of Health. 02/02/2010 to 01-08-2012
19. **2009-2011**: Fondazione Roma 2009: Intracellular protein-protein interactions regulating viral replication as targets for novel antiviral strategies. 01-06-2009 to 31-05-2011
20. **2006**: University Research Program-2005: Design, synthesis and SAR of neuroprotective agents. Duration: 12 months 01-01-2006 to 31-12-2006
21. **2006**: University Research Program-2005: Design, synthesis and SAR of new HIV-1 reverse transcriptase and integrase inhibitors. 01-01-2006 to 31-12-2006
22. **2004-2007**: FP6-HEALTH-2003 - EU project TRIoH (Targeting Replication and Integration of HIV). 01-01-2004 to 30-06-2007
23. **2004-2006**: PRIN-2004: Molecular modeling, design and synthesis of potential anti-AIDS agents. 30-11-2004 to 29-11-2006
24. **2005-2006**: University Research Program-2004: Design, synthesis and biological evaluation of new inhibitors of HIV-1 reverse transcriptase (RT) and integrase (IN). 01-01-2005 to 31-12-2006
25. **2004**: University Research Program-2003: AMPA receptor antagonists: Rational design, synthesis and SAR. 01-01-2004 to 31-12-2004
26. **2004**: University Research Program-2003: Design, synthesis and biological evaluation of new HIV-1 reverse transcriptase and integrase inhibitors. from 01-01-2004 to 31-12-2004
27. **2002-2004**: PRIN-2002: Molecular modeling, design and synthesis of potential anti-AIDS agents. 16-12-2002 to 15-12-2004
28. **2003**: University Research Program-2002: Synthesis and Molecular Modeling of AMPA-antagonists. 01-01-2003 to 31-12-2003
29. **2003**: University Research Program-2002: Design, synthesis and biological evaluation of new inhibitors of reverse transcriptase and HIV-1 integrase. 01-01-2003 to 31-12-2003
30. **2000-2002**: PRIN-2000: Molecular modeling, design and synthesis of potential anti-AIDS agents. 20-12-2000 to 19-12-2002

ACADEMIC ENTREPRENEURSHIP AND PATENTS

05/10/2017-present. Co-founder and member of the Scientific Board of the innovative Start-up Sibylla Biotech SRL (SB), (<https://www.sibyllabiotech.it/>), currently spin off of the University of Perugia, the University of Trento and the National Institute of Nuclear Physics. Sibylla Biotech enters the pharmaceutical research market at a preclinical level, having developed an innovative approach for the discovery of potential drugs (PPI-FIT - Pharmacological Protein inactivation by Targeting Folding Intermediates).

Sibylla Biotech currently has 9 employees and has recently achieved the following milestones:

- in November 2019, SB collected a 2.4M euro seed round, subscribed by the Vertis Venture 3 Technology Transfer fund.
- in May 2021, SB announced a research collaboration with Takeda Pharmaceutical Company Limited to identify innovative small molecules capable of modulating the activity of selected drug targets.
- in June 2021, SB was one of the eight finalists for Nature's prestigious "The Spinoff Prize 2021" (<https://www.nature.com/articles/d41586-021-01668-7>)
- in October 2021, SB has been selected as a finalist of the SDG accelerator for female founders.

1. **2014-present.** International patent WO/2014/025785, "Prion protein ligands as therapeutic agents for neurodegenerative disorders". Autori: Biasini, E., Harris, D.A., Beeler, A., Fluharty, B.R., Barreca M.L., Iraci, N. Ingham, O. Co-owners: UNIPG: 30%, Boston University: 70%
2. **27/03/2020:** Patent application ITA N 10202000006517, "Small molecules inducing the degradation of the cellular prion protein". Autori: E. Biasini, ML Barreca, P. Faccioli. Co-owners: Università degli Studi di Perugia: 30%, Fondazione Telethon: 20%, Università degli Studi di Trento: 20%, INFN: 30%
3. **29/05/2020:** Patent application ITA N. 102020000012814, "Repurposing of 102020000012814 for diseases requiring the lowering of ACE2 expression". Autori: Astolfi A, Boldrin L, Massignan T, Terruzzi L, Pieri L. Owner: Sibylla Biotech
4. **8/06/2020:** Patent application ITA N. 102020000013564, "Repurposing of Artefenomel for diseases requiring the lowering of ACE2 expression". Autori: Astolfi, Boldrin, Massignan, Terruzzi, Pieri. Owner: Sibylla Biotech
5. **18/12/2020:** Patent application ITA N. 102020000031403, "Composti attivi su K-Ras". Autori: Astolfi, Boldrin, Massignan, Terruzzi, Pieri. Owner: Sibylla Biotech
6. **21/05/2021:** Patent application ITA N 102021000013244, "Modulators of PrP and uses thereof". Autori: Barreca ML, Biasini E, Fallarino F, Manfroni G. Co-owners: Università degli Studi di Perugia - 75%, Università degli Studi di Trento - 12,5%, Fondazione Telethon - 12,5%

ACTIVITIES AS REVIEWER

Journal of Medicinal Chemistry, Journal of Chemical Information and Modelling, European Journal of Medicinal Chemistry, ACS Medicinal Chemistry Letters, Bioorganic & Medicinal Chemistry, Bioorganic & Medicinal Chemistry Letters, Journal of Computer-Aided Molecular Design, Drug Discovery Today, Expert Opinion on Drug Discovery, Computational Biology and Chemistry: Advances and Applications, Theoretical Chemistry Accounts, Tetrahedron, Epilepsia, Acta Pharmacologica Sinica, Molecules, Future Medicinal Chemistry, Scientific Reports, Antiviral Research, Journal of Molecular Graphics and Modelling, ChemMedChem, Current Medicinal Chemistry

In the past, Research Grant Reviewer for the Research Foundation Flanders and Scientific Reviewer for LinkSCEEM/Cy-Tera.

PUBLICATIONS

* Corresponding/co-corresponding author

- (1) Spagnolli, G.; Massignan, T.; Astolfi, A.; Biggi, S.; Rigoli, M.; Brunelli, P.; Libergoli, M.; Ianeselli, A.; Orioli, S.; Boldrini, A.; Terruzzi, L.; Bonaldo, V.; Maietta, G.; Lorenzo, N. L.; Fernandez, L. C.; Codeseira, Y. B.; Tosatto, L.; Linsenmeier, L.; Vignoli, B.; Petris, G.; Gasparotto, D.; Pennuto, M.; Guella, G.; Canossa, M.; Altmepfen, H. C.; Lolli, G.; Biressi, S.; Pastor, M. M.; Requena, J. R.; Mancini, I.; **Barreca, M. L.***; Faccioli, P.; Biasini, E. Pharmacological Inactivation of the Prion Protein by Targeting a Folding Intermediate. *Commun. Biol.* **2021**, 4 (1). <https://doi.org/10.1038/s42003-020-01585-x>.
- (2) Pismataro, M. C.; Felicetti, T.; Bertagnin, C.; Nizi, M. G.; Bonomini, A.; **Barreca, M. L.**; Cecchetti, V.; Jochmans, D.; De Jonghe, S.; Neyts, J.; Tabarrini, O.; Massari, S. 1,2,4-Triazolo[1,5-a]Pyrimidines: Efficient One-Step Synthesis and Functionalization as Influenza Polymerase PA-PB1 Interaction Disruptors. *Eur. J. Med. Chem.* **2021**, 221. <https://doi.org/10.1016/j.ejmech.2021.113494>.
- (3) Felicetti, T.; Burali, M. S.; Gwee, C. P.; Ki Chan, K. W.; Alonso, S.; Massari, S.; Sabatini, S.; Tabarrini, O.; **Barreca, M. L.**; Cecchetti, V.; Vasudevan, S. G.; Manfroni, G. Sustainable, Three-Component, One-Pot Procedure to Obtain Active Anti-Flavivirus Agents. *Eur. J. Med. Chem.* **2021**, 210. <https://doi.org/10.1016/j.ejmech.2020.112992>.
- (4) Cedrarò, N.; Cannalire, R.; Astolfi, A.; Mangiaterra, G.; Felicetti, T.; Vaiasicca, S.; Cernicchi, G.; Massari, S.; Manfroni, G.; Tabarrini, O.; Cecchetti, V.; **Barreca, M. L.**; Biavasco, F.; Sabatini, S. From Quinoline to

- Quinazoline-Based *S. Aureus* NorA Efflux Pump Inhibitors by Coupling a Focused Scaffold Hopping Approach and a Pharmacophore Search. *ChemMedChem* **2021**. <https://doi.org/10.1002/cmdc.202100282>.
- (5) Manfroni, G.; Ragonese, F.; Monarca, L.; Astolfi, A.; Mancinelli, L.; Iannitti, R. G.; Bastioli, F.; **Barreca, M. L.**; Cecchetti, V.; Fioretti, B. New Insights on KCa3.1 Channel Modulation. *Curr. Pharm. Des.* **2020**, *26* (18), 2096–2101. <https://doi.org/10.2174/1381612826666200316152645>.
 - (6) Felicetti, T.; Mangiaterra, G.; Cannalire, R.; Cedraro, N.; Pietrella, D.; Astolfi, A.; Massari, S.; Tabarrini, O.; Manfroni, G.; **Barreca, M. L.**; Cecchetti, V.; Biavasco, F.; Sabatini, S. C-2 Phenyl Replacements to Obtain Potent Quinoline-Based *Staphylococcus Aureus* NorA Inhibitors. *J. Enzyme Inhib. Med. Chem.* **2020**, *35* (1), 584–597. <https://doi.org/10.1080/14756366.2020.1719083>.
 - (7) Biggi, S.; Pancher, M.; Stincardini, C.; Luotti, S.; Massignan, T.; Dalle Vedove, A.; Astolfi, A.; Gatto, P.; Lolli, G.; **Barreca, M. L.**; Bonetto, V.; Adami, V.; Biasini, E. Identification of Compounds Inhibiting Prion Replication and Toxicity by Removing PrPC from the Cell Surface. *J. Neurochem.* **2020**, *152* (1), 136–150. <https://doi.org/10.1111/jnc.14805>.
 - (8) Nizi, M. G.; Desantis, J.; Nakatani, Y.; Massari, S.; Mazzarella, M. A.; Shetye, G.; Sabatini, S.; **Barreca, M. L.**; Manfroni, G.; Felicetti, T.; Rushton-Green, R.; Hards, K.; Latacz, G.; Satała, G.; Bojarski, A. J.; Cecchetti, V.; Kolář, M. H.; Handzlik, J.; Cook, G. M.; Franzblau, S. G.; Tabarrini, O. Antitubercular Polyhalogenated Phenothiazines and Phenoselenazine with Reduced Binding to CNS Receptors. *Eur. J. Med. Chem.* **2020**, *201*. <https://doi.org/10.1016/j.ejmech.2020.112420>.
 - (9) Cannalire, R.; Ki Chan, K. W.; Burali, M. S.; Gwee, C. P.; Wang, S.; Astolfi, A.; Massari, S.; Sabatini, S.; Tabarrini, O.; Mastrangelo, E.; **Barreca, M. L.**; Cecchetti, V.; Vasudevan, S. G.; Manfroni, G. Pyridobenzothiazolones Exert Potent Anti-Dengue Activity by Hampering Multiple Functions of NS5 Polymerase. *ACS Med. Chem. Lett.* **2020**, *11* (5), 773–782. <https://doi.org/10.1021/acsmchemlett.9b00619>.
 - (10) Cannalire, R.; Mangiaterra, G.; Felicetti, T.; Astolfi, A.; Cedraro, N.; Massari, S.; Manfroni, G.; Tabarrini, O.; Vaiasicca, S.; **Barreca, M. L.**; Cecchetti, V.; Biavasco, F.; Sabatini, S. Structural Modifications of the Quinolin-4-Yloxy Core to Obtain New *Staphylococcus Aureus* NorA Inhibitors. *Int. J. Mol. Sci.* **2020**, *21* (19), 1–18. <https://doi.org/10.3390/ijms21197037>.
 - (11) Astolfi, A.; Spagnolli, G.; Biasini, E.; **Barreca, M. L.*** The Compelling Demand for an Effective PrPC-Directed Therapy against Prion Diseases. *ACS Med. Chem. Lett.* **2020**, *11* (11), 2063–2067. <https://doi.org/10.1021/acsmchemlett.0c00528>.
 - (12) Bartolini, D.; Bührmann, M.; **Barreca, M. L.**; Manfroni, G.; Cecchetti, V.; Rauh, D.; Galli, F. Co-Crystal Structure Determination and Cellular Evaluation of 1,4-Dihydropyrazolo[4,3-c] [1,2] Benzothiazine 5,5-Dioxide P38 α MAPK Inhibitors. *Biochem. Biophys. Res. Commun.* **2019**, *511* (3), 579–586. <https://doi.org/10.1016/j.bbrc.2019.02.063>.
 - (13) Cannalire, R.; Tarantino, D.; Piorkowski, G.; Carletti, T.; Massari, S.; Felicetti, T.; **Barreca, M. L.**; Sabatini, S.; Tabarrini, O.; Marcello, A.; Milani, M.; Cecchetti, V.; Mastrangelo, E.; Manfroni, G.; Querat, G. Broad Spectrum Anti-Flavivirus Pyridobenzothiazolones Leading to Less Infective Virions. *Antiviral Res.* **2019**, *167*, 6–12. <https://doi.org/10.1016/j.antiviral.2019.03.004>.
 - (14) Felicetti, T.; Machado, D.; Cannalire, R.; Astolfi, A.; Massari, S.; Tabarrini, O.; Manfroni, G.; **Barreca, M. L.**; Cecchetti, V.; Viveiros, M.; Sabatini, S. Modifications on C6 and C7 Positions of 3-Phenylquinolone Efflux Pump Inhibitors Led to Potent and Safe Antimycobacterial Treatment Adjuvants. *ACS Infect. Dis.* **2019**, *5* (6), 982–1000. <https://doi.org/10.1021/acsinfectdis.9b00041>.
 - (15) Palazzotti, D.; Bissaro, M.; Bolcato, G.; Astolfi, A.; Felicetti, T.; Sabatini, S.; Sturlese, M.; Cecchetti, V.; **Barreca, M. L.***; Moro, S. Deciphering the Molecular Recognition Mechanism of Multidrug Resistance *Staphylococcus Aureus* Nora Efflux Pump Using a Supervised Molecular Dynamics Approach. *Int. J. Mol. Sci.* **2019**, *20* (16). <https://doi.org/10.3390/ijms20164041>.
 - (16) Astolfi, A.; Kudolo, M.; Brea, J.; Manni, G.; Manfroni, G.; Palazzotti, D.; Sabatini, S.; Cecchetti, F.; Felicetti, T.; Cannalire, R.; Massari, S.; Tabarrini, O.; Loza, M. I.; Fallarino, F.; Cecchetti, V.; Laufer, S. A.; **Barreca, M. L.*** Discovery of Potent P38 α MAPK Inhibitors through a Funnel like Workflow Combining in Silico Screening and in Vitro Validation. *Eur. J. Med. Chem.* **2019**, *182*. <https://doi.org/10.1016/j.ejmech.2019.111624>.
 - (17) Acchioni, C.; Remoli, A. L.; Marsili, G.; Acchioni, M.; Nardolillo, I.; Orsatti, R.; Farcomeni, S.; Palermo, E.;

- Perrotti, E.; **Barreca, M. L.**; Sabatini, S.; Sandini, S.; Parolin, C.; Lin, R.; Borsetti, A.; Hiscott, J.; Sgarbanti, M. Alternate NF-KB-Independent Signaling Reactivation of Latent HIV-1 Provirus. *J. Virol.* **2019**, 93 (18). <https://doi.org/10.1128/jvi.00495-19>.
- (18) Cannalire, R.; Tarantino, D.; Astolfi, A.; **Barreca, M. L.**; Sabatini, S.; Massari, S.; Tabarrini, O.; Milani, M.; Querat, G.; Mastrangelo, E.; Manfroni, G.; Cecchetti, V. Functionalized 2,1-Benzothiazine 2,2-Dioxides as New Inhibitors of Dengue NS5 RNA-Dependent RNA Polymerase. *Eur. J. Med. Chem.* **2018**, 143, 1667–1676. <https://doi.org/10.1016/j.ejmech.2017.10.064>.
- (19) Felicetti, T.; Cannalire, R.; Pietrella, D.; Latacz, G.; Lubelska, A.; Manfroni, G.; **Barreca, M. L.**; Massari, S.; Tabarrini, O.; Kieć-Kononowicz, K.; Schindler, B. D.; Kaatz, G. W.; Cecchetti, V.; Sabatini, S. 2-Phenylquinoline *S. Aureus* NorA Efflux Pump Inhibitors: Evaluation of the Importance of Methoxy Group Introduction. *J. Med. Chem.* **2018**, 61 (17), 7827–7848. <https://doi.org/10.1021/acs.jmedchem.8b00791>.
- (20) Felicetti, T.; Cannalire, R.; Nizi, M. G.; Tabarrini, O.; Massari, S.; **Barreca, M. L.**; Manfroni, G.; Schindler, B. D.; Cecchetti, V.; Kaatz, G. W.; Sabatini, S. Studies on 2-Phenylquinoline *Staphylococcus Aureus* NorA Efflux Pump Inhibitors: New Insights on the C-6 Position. *Eur. J. Med. Chem.* **2018**, 155, 428–433. <https://doi.org/10.1016/j.ejmech.2018.06.013>.
- (21) **Barreca, M. L.***; Iraci, N.; Biggi, S.; Cecchetti, V.; Biasini, E. Pharmacological Agents Targeting the Cellular Prion Protein. *Pathogens* **2018**, 7 (1). <https://doi.org/10.3390/pathogens7010027>.
- (22) Astolfi, A.; Manfroni, G.; Cecchetti, V.; **Barreca, M. L.*** A Comprehensive Structural Overview of P38 α Mitogen-Activated Protein Kinase in Complex with ATP-Site and Non-ATP-Site Binders. *ChemMedChem* **2018**, 13 (1), 7–14. <https://doi.org/10.1002/cmdc.201700636>.
- (23) Madia, V. N.; Benedetti, R.; **Barreca, M. L.**; Ngo, L.; Pescatori, L.; Messori, A.; Pupo, G.; Saccoliti, F.; Valente, S.; Mai, A.; Scipione, L.; Zheng, Y. G.; Tintori, C.; Botta, M.; Cecchetti, V.; Altucci, L.; Di Santo, R.; Costi, R. Structure–Activity Relationships on Cinnamoyl Derivatives as Inhibitors of P300 Histone Acetyltransferase. *ChemMedChem* **2017**, 12 (16), 1359–1368. <https://doi.org/10.1002/cmdc.201700040>.
- (24) Felicetti, T.; Cannalire, R.; Burali, M. S.; Massari, S.; Manfroni, G.; **Barreca, M. L.**; Tabarrini, O.; Schindler, B. D.; Sabatini, S.; Kaatz, G. W.; Cecchetti, V. Searching for Novel Inhibitors of the *S. Aureus* NorA Efflux Pump: Synthesis and Biological Evaluation of the 3-Phenyl-1,4-Benzothiazine Analogues. *ChemMedChem* **2017**, 12 (16), 1293–1302. <https://doi.org/10.1002/cmdc.201700286>.
- (25) Desantis, J.; Nannetti, G.; Massari, S.; **Barreca, M. L.**; Manfroni, G.; Cecchetti, V.; Palù, G.; Goracci, L.; Loregian, A.; Tabarrini, O. Exploring the Cycloheptathiophene-3-Carboxamide Scaffold to Disrupt the Interactions of the Influenza Polymerase Subunits and Obtain Potent Anti-Influenza Activity. *Eur. J. Med. Chem.* **2017**, 138, 128–139. <https://doi.org/10.1016/j.ejmech.2017.06.015>.
- (26) Cannalire, R.; Machado, D.; Felicetti, T.; Santos Costa, S.; Massari, S.; Manfroni, G.; **Barreca, M. L.**; Tabarrini, O.; Couto, I.; Viveiros, M.; Sabatini, S.; Cecchetti, V. Natural Isoflavone Biochanin A as a Template for the Design of New and Potent 3-Phenylquinolone Efflux Inhibitors against *Mycobacterium Avium*. *Eur. J. Med. Chem.* **2017**, 140, 321–330. <https://doi.org/10.1016/j.ejmech.2017.09.014>.
- (27) Astolfi, A.; Felicetti, T.; Iraci, N.; Manfroni, G.; Massari, S.; Pietrella, D.; Tabarrini, O.; Kaatz, G. W.; **Barreca, M. L.***; Sabatini, S.; Cecchetti, V. Pharmacophore-Based Repositioning of Approved Drugs as Novel *Staphylococcus Aureus* NorA Efflux Pump Inhibitors. *J. Med. Chem.* **2017**, 60 (4), 1598–1604. <https://doi.org/10.1021/acs.jmedchem.6b01439>.
- (28) Massignan, T.; Sangiovanni, V.; Biggi, S.; Stincardini, C.; Elezgarai, S. R.; Maietta, G.; Andreev, I. A.; Ratmanova, N. K.; Belov, D. S.; Lukyanenko, E. R.; Belov, G. M.; **Barreca, M. L.**; Altieri, A.; Kurkin, A. V.; Biasini, E. A Small-Molecule Inhibitor of Prion Replication and Mutant Prion Protein Toxicity. *ChemMedChem* **2017**, 12 (16), 1286–1292. <https://doi.org/10.1002/cmdc.201700302>.
- (29) **Barreca, M. L.*** Maria Letizia Barreca on Hepatitis C Virus Treatment and Control. *Future Med. Chem.* **2016**, 8 (1), 7–9. <https://doi.org/10.4155/fmc.15.170>.
- (30) Cannalire, R.; **Barreca, M. L.**; Manfroni, G.; Cecchetti, V. A Journey around the Medicinal Chemistry of Hepatitis C Virus Inhibitors Targeting NS4B: From Target to Preclinical Drug Candidates. *J. Med. Chem.* **2016**, 59 (1), 16–41. <https://doi.org/10.1021/acs.jmedchem.5b00825>.
- (31) Kaushik-Basu, N.; Ratmanova, N. K.; Manvar, D.; Belov, D. S.; Cevik, O.; Basu, A.; Yerukhimovich, M. M.; Lukyanenko, E. R.; Andreev, I. A.; Belov, G. M.; Manfroni, G.; Cecchetti, V.; Frick, D. N.; Kurkin, A. V.; Altieri, A.; **Barreca, M. L.*** Bicyclic Octahydrocyclohepta[b]Pyrrol-4(1H)One Derivatives as Novel

- Selective Anti-Hepatitis C Virus Agents. *Eur. J. Med. Chem.* **2016**, *122*, 319–325. <https://doi.org/10.1016/j.ejmech.2016.06.041>.
- (32) Tarantino, D.; Cannalire, R.; Mastrangelo, E.; Croci, R.; Querat, G.; **Barreca, M. L.**; Bolognesi, M.; Manfroni, G.; Cecchetti, V.; Milani, M. Targeting Flavivirus RNA Dependent RNA Polymerase through a Pyridobenzothiazole Inhibitor. *Antiviral Res.* **2016**, *134*, 226–235. <https://doi.org/10.1016/j.antiviral.2016.09.007>.
- (33) Iraci, N.; Stincardini, C.; **Barreca, M. L.**; Biasini, E. Decoding the Function of the N-Terminal Tail of the Cellular Prion Protein to Inspire Novel Therapeutic Avenues for Neurodegenerative Diseases. *Virus Res.* **2015**, *207*, 62–68. <https://doi.org/10.1016/j.virusres.2014.10.015>.
- (34) Sabatini, S.; Manfroni, G.; **Barreca, M. L.***; Bauer, S. M.; Gargaro, M.; Cannalire, R.; Astolfi, A.; Brea, J.; Vacca, C.; Pirro, M.; Massari, S.; Tabarrini, O.; Loza, M. I.; Fallarino, F.; Laufer, S. A.; Cecchetti, V. The Pyrazolobenzothiazine Core as a New Chemotype of P38 Alpha Mitogen-Activated Protein Kinase Inhibitors. *Chem. Biol. Drug Des.* **2015**, *86* (4), 531–545. <https://doi.org/10.1111/cbdd.12516>.
- (35) Astolfi, A.; Iraci, N.; Manfroni, G.; **Barreca, M. L.***; Cecchetti, V. A Comprehensive Structural Overview of P38 α MAPK in Complex with Type I Inhibitors. *ChemMedChem* **2015**, *10* (6), 957–969. <https://doi.org/10.1002/cmdc.201500030>.
- (36) Franci, G.; Manfroni, G.; Cannalire, R.; Felicetti, T.; Tabarrini, O.; Salvato, A.; **Barreca, M. L.**; Altucci, L.; Cecchetti, V. Tumour Cell Population Growth Inhibition and Cell Death Induction of Functionalized 6-Aminoquinolone Derivatives. *Cell Prolif.* **2015**, *48* (6), 705–717. <https://doi.org/10.1111/cpr.12224>.
- (37) Astolfi, A.; Iraci, N.; Sabatini, S.; **Barreca, M. L.**; Cecchetti, V. P38 α MAPK and Type I Inhibitors: Binding Site Analysis and Use of Target Ensembles in Virtual Screening. *Molecules* **2015**, *20* (9), 15842–15861. <https://doi.org/10.3390/molecules200915842>.
- (38) Andreev, I. A.; Manvar, D.; **Barreca, M. L.***; Belov, D. S.; Basu, A.; Sweeney, N. L.; Ratmanova, N. K.; Lukyanenko, E. R.; Manfroni, G.; Cecchetti, V.; Frick, D. N.; Altieri, A.; Kaushik-Basu, N.; Kurkin, A. V. Discovery of the 2-Phenyl-4,5,6,7-Tetrahydro-1 H -Indole as a Novel Anti-Hepatitis C Virus Targeting Scaffold. *Eur. J. Med. Chem.* **2015**, *96*, 250–258. <https://doi.org/10.1016/j.ejmech.2015.04.022>.
- (39) **Barreca, M. L.***; Iraci, N.; Manfroni, G.; Gaetani, R.; Guercini, C.; Sabatini, S.; Tabarrini, O.; Cecchetti, V. Accounting for Target Flexibility and Water Molecules by Docking to Ensembles of Target Structures: The HCV NS5B Palm Site i Inhibitors Case Study. *J. Chem. Inf. Model.* **2014**, *54* (2), 481–497. <https://doi.org/10.1021/ci400367m>.
- (40) Manfroni, G.; Cannalire, R.; **Barreca, M. L.***; Kaushik-Basu, N.; Leyssen, P.; Winqvist, J.; Iraci, N.; Manvar, D.; Paeshuyse, J.; Guhamazumder, R.; Basu, A.; Sabatini, S.; Tabarrini, O.; Danielson, U. H.; Neyts, J.; Cecchetti, V. The Versatile Nature of the 6-Aminoquinolone Scaffold: Identification of Submicromolar Hepatitis C Virus NS5B Inhibitors. *J. Med. Chem.* **2014**, *57* (5), 1952–1963. <https://doi.org/10.1021/jm401362f>.
- (41) Manfroni, G.; Manvar, D.; **Barreca, M. L.***; Kaushik-Basu, N.; Leyssen, P.; Paeshuyse, J.; Cannalire, R.; Iraci, N.; Basu, A.; Chudaev, M.; Zamperini, C.; Dreassi, E.; Sabatini, S.; Tabarrini, O.; Neyts, J.; Cecchetti, V. New Pyrazolobenzothiazine Derivatives as Hepatitis C Virus NS5B Polymerase Palm Site i Inhibitors. *J. Med. Chem.* **2014**, *57* (8), 3247–3262. <https://doi.org/10.1021/jm401688h>.
- (42) Sancineto, L.; Iraci, N.; **Barreca, M. L.**; Massari, S.; Manfroni, G.; Corazza, G.; Cecchetti, V.; Marcello, A.; Daelemans, D.; Pannecouque, C.; Tabarrini, O. Exploiting the Anti-HIV 6-Desfluoroquinolones to Design Multiple Ligands. *Bioorganic Med. Chem.* **2014**, *22* (17), 4658–4666. <https://doi.org/10.1016/j.bmc.2014.07.018>.
- (43) Sancineto, L.; Iraci, N.; Massari, S.; Attanasio, V.; Corazza, G.; **Barreca, M. L.**; Sabatini, S.; Manfroni, G.; Avanzi, N. R.; Cecchetti, V.; Pannecouque, C.; Marcello, A.; Tabarrini, O. Computer-Aided Design, Synthesis and Validation of 2-Phenylquinazolinone Fragments as CDK9 Inhibitors with Anti-HIV-1 Tat-Mediated Transcription Activity. *ChemMedChem* **2013**, *8* (12), 1941–1953. <https://doi.org/10.1002/cmdc.201300287>.
- (44) Martelli, A.; Manfroni, G.; Sabbatini, P.; **Barreca, M. L.**; Testai, L.; Novelli, M.; Sabatini, S.; Massari, S.; Tabarrini, O.; Masiello, P.; Calderone, V.; Cecchetti, V. 1,4-Benzothiazine ATP-Sensitive Potassium Channel Openers: Modifications at the C-2 and C-6 Positions. *J. Med. Chem.* **2013**, *56* (11), 4718–4728. <https://doi.org/10.1021/jm400435a>.
- (45) Sabatini, S.; Gosetto, F.; Iraci, N.; **Barreca, M. L.**; Massari, S.; Sancineto, L.; Manfroni, G.; Tabarrini, O.;

- Dimovska, M.; Kaatz, G. W.; Cecchetti, V. Re-Evolution of the 2-Phenylquinolines: Ligand-Based Design, Synthesis, and Biological Evaluation of a Potent New Class of Staphylococcus Aureus NorA Efflux Pump Inhibitors to Combat Antimicrobial Resistance. *J. Med. Chem.* **2013**, *56* (12), 4975–4989. <https://doi.org/10.1021/jm400262a>.
- (46) **Barreca, M. L.***; Manfroni, G.; Leyssen, P.; Winqvist, J.; Kaushik-Basu, N.; Paeshuyse, J.; Krishnan, R.; Iraci, N.; Sabatini, S.; Tabarrini, O.; Basu, A.; Danielson, U. H.; Neyts, J.; Cecchetti, V. Structure-Based Discovery of Pyrazolobenzothiazine Derivatives as Inhibitors of Hepatitis C Virus Replication. *J. Med. Chem.* **2013**, *56* (6), 2270–2282. <https://doi.org/10.1021/jm301643a>.
- (47) Manfroni, G.; Meschini, F.; **Barreca, M. L.***; Leyssen, P.; Samuele, A.; Iraci, N.; Sabatini, S.; Massari, S.; Maga, G.; Neyts, J.; Cecchetti, V. Pyridobenzothiazole Derivatives as New Chemotype Targeting the HCV NS5B Polymerase. *Bioorganic Med. Chem.* **2012**, *20* (2), 866–876. <https://doi.org/10.1016/j.bmc.2011.11.061>.
- (48) Shytaj, I. L.; Norelli, S.; Chirullo, B.; Della Corte, A.; Collins, M.; Yalley-Ogunro, J.; Greenhouse, J.; Iraci, N.; Acosta, E. P.; **Barreca, M. L.**; Lewis, M. G.; Savarino, A. A Highly Intensified ART Regimen Induces Long-Term Viral Suppression and Restriction of the Viral Reservoir in a Simian AIDS Model. *PLoS Pathog.* **2012**, *8* (6). <https://doi.org/10.1371/journal.ppat.1002774>.
- (49) **Barreca, M. L.***; Iraci, N.; Manfroni, G.; Cecchetti, V. Allosteric Inhibition of the Hepatitis C Virus NS5B Polymerase: In Silico Strategies for Drug Discovery and Development. *Future Med. Chem.* **2011**, *3* (8), 1027–1055. <https://doi.org/10.4155/fmc.11.53>.
- (50) Bajorath, J.; **Barreca, M. L.**; Bender, A.; Bryce, R.; Hutter, M.; Laggner, C.; Laughton, C.; Martin, Y.; Mitchell, J.; Padova, A.; Renner, S.; Selzer, P. M.; Sherman, W.; Sippl, W.; Taft, C.; Tuccinardi, T.; Vistoli, G.; Willett, P. Ask the Experts: Focus on Computational Chemistry. *Future Med. Chem.* **2011**, *3* (8), 909–921. <https://doi.org/10.4155/fmc.11.57>.
- (51) Massari, S.; Daelemans, D.; **Barreca, M. L.**; Knezevich, A.; Sabatini, S.; Cecchetti, V.; Marcello, A.; Pannecouque, C.; Tabarrini, O. A 1,8-Naphthyridone Derivative Targets the HIV-1 Tat-Mediated Transcription and Potently Inhibits the HIV-1 Replication. *J. Med. Chem.* **2010**, *53* (2), 641–648. <https://doi.org/10.1021/jm901211d>.
- (52) Ferro, S.; De Luca, L.; **Barreca, M. L.**; Grazia, S. De; Christ, F.; Debyser, Z.; Chimirri, A. New Chloro,Fluorobenzylindole Derivatives as Integrase Strand-Transfer Inhibitors (INSTIs) and Their Mode of Action. *Bioorganic Med. Chem.* **2010**, *18* (15), 5510–5518. <https://doi.org/10.1016/j.bmc.2010.06.063>.
- (53) De Luca, L.; Ferro, S.; Gitto, R.; **Barreca, M. L.**; Agnello, S.; Christ, F.; Debyser, Z.; Chimirri, A. Small Molecules Targeting the Interaction between HIV-1 Integrase and LEDGF/P75 Cofactor. *Bioorganic Med. Chem.* **2010**, *18* (21), 7515–7521. <https://doi.org/10.1016/j.bmc.2010.08.051>.
- (54) Lewis, M. G.; Norelli, S.; Collins, M.; **Barreca, M. L.**; Iraci, N.; Chirullo, B.; Yalley-Ogunro, J.; Greenhouse, J.; Titti, F.; Garaci, E.; Savarino, A. Response of a Simian Immunodeficiency Virus (SIVmac251) to Raltegravir: A Basis for a New Treatment for Simian AIDS and an Animal Model for Studying Lentiviral Persistence during Antiretroviral Therapy. *Retrovirology* **2010**, *7*. <https://doi.org/10.1186/1742-4690-7-21>.
- (55) Ferro, S.; De Grazia, S.; De Luca, L.; **Barreca, M. L.**; Debyser, Z.; Chimirri, A. Structural Modification of Diketo Acid Portion in 1H-Benzylindole Derivatives HIV-1 Integrase Inhibitors. *Heterocycles* **2009**, *78* (4), 947–959. <https://doi.org/10.3987/COM-08-11573>.
- (56) Ferro, S.; De Luca, L.; **Barreca, M. L.**; Iraci, N.; De Grazia, S.; Christ, F.; Witvrouw, M.; Debyser, Z.; Chimirri, A. Docking Studies on a New Human Immunodeficiency Virus Integrase-Mg-DNA Complex: Phenyl Ring Exploration and Synthesis of 1H-Benzylindole Derivatives through Fluorine Substitutions. *J. Med. Chem.* **2009**, *52* (2), 569–573. <https://doi.org/10.1021/jm8009266>.
- (57) De Luca, L.; **Barreca, M. L.***; Ferro, S.; Christ, F.; Iraci, N.; Gitto, R.; Monforte, A. M.; Debyser, Z.; Chimirri, A. Pharmacophore-Based Discovery of Small-Molecule Inhibitors of Protein-Protein Interactions between HIV-1 Integrase and Cellular Cofactor LEDGF/P75. *ChemMedChem* **2009**, *4* (8), 1311–1316. <https://doi.org/10.1002/cmdc.200900070>.
- (58) **Barreca, M. L.***; Iraci, N.; De Luca, L.; Chimirri, A. Induced-Fit Docking Approach Provides Insight into the Binding Mode and Mechanism of Action of HIV-1 Integrase Inhibitors. *ChemMedChem* **2009**, *4* (9), 1446–1456. <https://doi.org/10.1002/cmdc.200900166>.
- (59) Ferro, S.; Agnello, S.; **Barreca, M. L.**; De Luca, L.; Christ, F.; Gitto, R. Synthesis of New Pyridazine

- Derivatives as Potential Anti-HIV-1 Agents. *J. Heterocycl. Chem.* **2009**, 46 (6), 1420–1424. <https://doi.org/10.1002/jhet.230>.
- (60) De Luca, L.; **Barreca, M. L.**; Ferro, S.; Iraci, N.; Michiels, M.; Christ, F.; Debyser, Z.; Witvrouw, M.; Chimirri, A. A Refined Pharmacophore Model for HIV-1 Integrase Inhibitors: Optimization of Potency in the 1H-Benzylindole Series. *Bioorganic Med. Chem. Lett.* **2008**, 18 (9), 2891–2895. <https://doi.org/10.1016/j.bmcl.2008.03.089>.
- (61) Hombrouck, A.; Van Remoortel, B.; Michiels, M.; Noppe, W.; Christ, F.; Eneroth, A.; Sahlberg, B. L.; Benkestock, K.; Vrang, L.; Johansson, N. G.; **Barreca, M. L.**; De Luca, L.; Ferro, S.; Chimirri, A.; Debyser, Z.; Witvrouw, M. Preclinical Evaluation of 1H-Benzylindole Derivatives as Novel Human Immunodeficiency Virus Integrase Strand Transfer Inhibitors. *Antimicrob. Agents Chemother.* **2008**, 52 (8), 2861–2869. <https://doi.org/10.1128/AAC.00210-08>.
- (62) Monforte, A. M.; Rao, A.; Logoteta, P.; Ferro, S.; De Luca, L.; **Barreca, M. L.**; Iraci, N.; Maga, G.; De Clercq, E.; Pannecouque, C.; Chimirri, A. Novel N1-Substituted 1,3-Dihydro-2H-Benzimidazol-2-Ones as Potent Non-Nucleoside Reverse Transcriptase Inhibitors. *Bioorganic Med. Chem.* **2008**, 16 (15), 7429–7435. <https://doi.org/10.1016/j.bmc.2008.06.012>.
- (63) Billamboz, M.; Bailly, F.; **Barreca, M. L.**; De Luca, L.; Mouscadet, J. F.; Calmels, C.; Andréola, M. L.; Witvrouw, M.; Christ, F.; Debyser, Z.; Cotelle, P. Design, Synthesis, and Biological Evaluation of a Series of 2-Hydroxyisoquinoline-1,3(2H,4H)-Diones as Dual Inhibitors of Human Immunodeficiency Virus Type 1 Integrase and the Reverse Transcriptase RNase H Domain. *J. Med. Chem.* **2008**, 51 (24), 7717–7730. <https://doi.org/10.1021/jm8007085>.
- (64) Norelli, S.; Daker, S.; D'Ostilio, D.; Mele, F.; Mancini, F.; Taglia, F.; Ruggieri, A.; Ciccozzi, M.; Cauda, R.; Ciervo, A.; **Barreca, M. L.**; Pistello, M.; Bendinelli, M.; Savarino, A. Response of Feline Immunodeficiency Virus (FIV) to Tipranavir May Provide New Clues for Development of Broad-Based Inhibitors of Retroviral Proteases Acting on Drug-Resistant HIV-1. *Curr. HIV Res.* **2008**, 6 (4), 306–317. <https://doi.org/10.2174/157016208785132527>.
- (65) **Barreca, M. L.***; De Luca, L.; Iraci, N.; Rao, A.; Ferro, S.; Maga, G.; Chimirri, A. Structure-Based Pharmacophore Identification of New Chemical Scaffolds as Non-Nucleoside Reverse Transcriptase Inhibitors. *J. Chem. Inf. Model.* **2007**, 47 (2), 557–562. <https://doi.org/10.1021/ci600320q>.
- (66) Ferro, S.; **Barreca, M. L.***; De Luca, L.; Rao, A.; Monforte, A. M.; Debyser, Z.; Witvrouw, M.; Chimirri, A. New 4-[(1-Benzyl-1H-Indol-3-Yl)Carbonyl]-3-Hydroxyfuran-2(5H)-Ones, β -Diketo Acid Analogs as HIV-1 Integrase Inhibitors. *Arch. Pharm. (Weinheim)*. **2007**, 340 (6), 292–298. <https://doi.org/10.1002/ardp.200700066>.
- (67) Gitto, R.; Ficarra, R.; Stancanelli, R.; Guardo, M.; De Luca, L.; **Barreca, M. L.**; Pagano, B.; Rotondo, A.; Bruno, G.; Russo, E.; De Sarro, G.; Chimirri, A. Synthesis, Resolution, Stereochemistry, and Molecular Modeling of (R)- and (S)-2-Acetyl-1-(4'-Chlorophenyl)-6,7-Dimethoxy-1,2,3,4-Tetrahydroisoquinoline AMPAR Antagonists. *Bioorganic Med. Chem.* **2007**, 15 (16), 5417–5423. <https://doi.org/10.1016/j.bmc.2007.05.059>.
- (68) Savarino, A.; Pistello, M.; D'Ostilio, D.; Zabogli, E.; Taglia, F.; Mancini, F.; Ferro, S.; Matteucci, D.; De Luca, L.; **Barreca, M. L.**; Ciervo, A.; Chimirri, A.; Ciccozzi, M.; Bendinelli, M. Human Immunodeficiency Virus Integrase Inhibitors Efficiently Suppress Feline Immunodeficiency Virus Replication in Vitro and Provide a Rationale to Redesign Antiretroviral Treatment for Feline AIDS. *Retrovirology* **2007**, 4. <https://doi.org/10.1186/1742-4690-4-79>.
- (69) **Barreca, M. L.***; Ortuso, F.; Iraci, N.; De Luca, L.; Alcaro, S.; Chimirri, A. Tn5 Transposase as a Useful Platform to Simulate HIV-1 Integrase Inhibitor Binding Mode. *Biochem. Biophys. Res. Commun.* **2007**, 363 (3), 554–560. <https://doi.org/10.1016/j.bbrc.2007.08.199>.
- (70) **Barreca, M. L.***; Rao, A.; Luca, L. De; Iraci, N.; Monforte, A. M.; Maga, G.; Clercq, E. De; Pannecouque, C.; Balzarini, J.; Chimirri, A. Discovery of Novel Benzimidazolones as Potent Non-Nucleoside Reverse Transcriptase Inhibitors Active against Wild-Type and Mutant HIV-1 Strains. *Bioorganic Med. Chem. Lett.* **2007**, 17 (7), 1956–1960. <https://doi.org/10.1016/j.bmcl.2007.01.025>.
- (71) **Barreca, M. L.**; De Luca, L.; Ferro, S.; Rao, A.; Monforte, A. M.; Chimirri, A. Computational and Synthetic Approaches for the Discovery of HIV-1 Integrase Inhibitors. *Arkivoc* **2006**, 2006 (7), 224–244. <https://doi.org/10.3998/ark.5550190.0007.717>.
- (72) **Barreca, M. L.***; De Luca, L.; Iraci, N.; Chimirri, A. Binding Mode Prediction of Strand Transfer HIV-1

- Integrase Inhibitors Using Tn5 Transposase as a Plausible Surrogate Model for HIV-1 Integrase. *J. Med. Chem.* **2006**, 49 (13), 3994–3997. <https://doi.org/10.1021/jm060323r>.
- (73) De Luca, L.; Gitto, R.; **Barreca, M. L.**; Caruso, R.; Quartarone, S.; Citraro, R.; De Sarro, G.; Chimirri, A. 3D Pharmacophore Models for 1,2,3,4-Tetrahydroisoquinoline Derivatives Acting as Anticonvulsant Agents. *Arch. Pharm. (Weinheim)*. **2006**, 339 (7), 388–400. <https://doi.org/10.1002/ardp.200600022>.
- (74) Sarro, G.; Gitto, R.; Russo, E.; Ibbadu, G.; **Barreca, M. L.**; Luca, L.; Chimirri, A. AMPA Receptor Antagonists as Potential Anticonvulsant Drugs. *Curr. Top. Med. Chem.* **2005**, 5 (1), 31–42. <https://doi.org/10.2174/1568026053386999>.
- (75) Ottanà, R.; MacCari, R.; **Barreca, M. L.**; Bruno, G.; Rotondo, A.; Rossi, A.; Chiricosta, G.; Di Paola, R.; Sautebin, L.; Cuzzocrea, S.; Vigorita, M. G. 5-Arylidene-2-Imino-4-Thiazolidinones: Design and Synthesis of Novel Anti-Inflammatory Agents. *Bioorganic Med. Chem.* **2005**, 13 (13), 4243–4252. <https://doi.org/10.1016/j.bmc.2005.04.058>.
- (76) De Luca, L.; Vistoli, G.; Pedretti, A.; **Barreca, M. L.**; Chimirri, A. Molecular Dynamics Studies of the Full-Length Integrase-DNA Complex. *Biochem. Biophys. Res. Commun.* **2005**, 336 (4), 1010–1016. <https://doi.org/10.1016/j.bbrc.2005.08.211>.
- (77) **Barreca, M. L.***; Ferro, S.; Rao, A.; De Luca, L.; Zappalà, M.; Monforte, A. M.; Debyser, Z.; Witvrouw, M.; Chimirri, A. Pharmacophore-Based Design of HIV-1 Integrase Strand-Transfer Inhibitors. *J. Med. Chem.* **2005**, 48 (22), 7084–7088. <https://doi.org/10.1021/jm050549e>.
- (78) **Barreca, M. L.***; Rao, A.; De Luca, L.; Zappalà, M.; Monforte, A. M.; Maga, G.; Pannecouque, C.; Balzarini, J.; De Clercq, E.; Chimirri, A.; Monforte, P. Computational Strategies in Discovering Novel Non-Nucleoside Inhibitors of HIV-1 RT. *J. Med. Chem.* **2005**, 48 (9), 3433–3437. <https://doi.org/10.1021/jm049279a>.
- (79) Gitto, R.; Caruso, R.; Orlando, V.; Quartarone, S.; **Barreca, M. L.**; Ferreri, G.; Russo, E.; De Sarro, G.; Chimirri, A. Synthesis and Anticonvulsant Properties of Tetrahydroisoquinoline Derivatives. *Farmaco* **2004**, 59 (1), 7–12. <https://doi.org/10.1016/j.farmac.2003.10.003>.
- (80) Chimirri, A.; De Sarro, G.; Quartarone, S.; **Barreca, M. L.**; Caruso, R.; De Luca, L.; Gitto, R. Search for Noncompetitive 2-Amino-3-(3-Hydroxy-5-Methyl-4-Isoxazolyl) Propionic Acid Receptor (AMPA) Antagonists: Synthesis, Pharmacological Properties, and Computational Studies. *Pure Appl. Chem.* **2004**, 76 (5), 931–939. <https://doi.org/10.1351/pac200476050931>.
- (81) Gitto, R.; **Barreca, M. L.**; Francica, E.; Caruso, R.; De Luca, L.; Russo, E.; De Sarro, G.; Chimirri, A. Synthesis and Anticonvulsant Properties of 1,2,3,4-Tetrahydroisoquinolin-1-Ones. *Arkivoc* **2004**, 2004 (5), 170–180. <https://doi.org/10.3998/ark.5550190.0005.516>.
- (82) Macchiarulo, A.; De Luca, L.; Costantino, G.; **Barreca, M. L.**; Gitto, R.; Pellicciari, R.; Chimirri, A. QSAR Study of Anticonvulsant Negative Allosteric Modulators of the AMPA Receptor. *J. Med. Chem.* **2004**, 47 (7), 1860–1863. <https://doi.org/10.1021/jm0310838>.
- (83) **Barreca, M. L.***; Rao, A.; De Luca, L.; Zappalà, M.; Gurnari, C.; Monforte, P.; De Clercq, E.; Van Maele, B.; Debyser, Z.; Witvrouw, M.; Briggs, J. M.; Chimirri, A. Efficient 3D Database Screening for Novel HIV-1 Inhibitors. *J. Chem. Inf. Comput. Sci.* **2004**, 44 (4), 1450–1455. <https://doi.org/10.1021/ci034296e>.
- (84) Gitto, R.; **Barreca, M. L.**; De Luca, L.; Chimirri, A. New Trends in the Development of AMPA Receptor Antagonists. *Expert Opin. Ther. Pat.* **2004**, 14 (8), 1199–1213. <https://doi.org/10.1517/13543776.14.8.1199>.
- (85) De Luca, L.; Macchiarulo, A.; Costantino, G.; **Barreca, M. L.**; Gitto, R.; Chimirri, A.; Pellicciari, R. Binding Modes of Noncompetitive AMPA Antagonists: A Computational Approach. *Farmaco* **2003**, 58 (2), 107–113. [https://doi.org/10.1016/S0014-827X\(02\)00027-7](https://doi.org/10.1016/S0014-827X(02)00027-7).
- (86) Gitto, R.; **Barreca, M. L.**; De Luca, L.; De Sarro, G.; Ferreri, G.; Quartarone, S.; Russo, E.; Constanti, A.; Chimirri, A. Discovery of a Novel and Highly Potent Noncompetitive AMPA Receptor Antagonist. *J. Med. Chem.* **2003**, 46 (1), 197–200. <https://doi.org/10.1021/jm0210008>.
- (87) **Barreca, M. L.**; Lee, K. W.; Chimirri, A.; Briggs, J. M. Molecular Dynamics Studies of the Wild-Type and Double Mutant HIV-1 Integrase Complexed with the 5CITEP Inhibitor: Mechanism for Inhibition and Drug Resistance. *Biophys. J.* **2003**, 84 (3), 1450–1463. [https://doi.org/10.1016/S0006-3495\(03\)74958-3](https://doi.org/10.1016/S0006-3495(03)74958-3).
- (88) **Barreca, M. L.***; Gitto, R.; Quartarone, S.; De Luca, L.; De Sarro, G.; Chimirri, A. Pharmacophore Modeling as an Efficient Tool in the Discovery of Novel Noncompetitive AMPA Receptor Antagonists. *J. Chem. Inf. Comput. Sci.* **2003**, 43 (2), 651–655. <https://doi.org/10.1021/ci025625q>.

- (89) **Barreca, M. L.**; Chimirri, A.; De Clercq, E.; De Luca, L.; Monforte, A. M.; Monforte, P.; Rao, A.; Zappalà, M. Anti-HIV Agents: Design and Discovery of New Potent RT Inhibitors. *Farmaco* **2003**, 58 (3), 259–263. [https://doi.org/10.1016/S0014-827X\(03\)00024-7](https://doi.org/10.1016/S0014-827X(03)00024-7).
- (90) De Luca, L.; Pedretti, A.; Vistoli, G.; **Barreca, M. L.**; Villa, L.; Monforte, P.; Chimirri, A. Analysis of the Full-Length Integrase-DNA Complex by a Modified Approach for DNA Docking. *Biochem. Biophys. Res. Commun.* **2003**, 310 (4), 1083–1088. <https://doi.org/10.1016/j.bbrc.2003.09.120>.
- (91) Carrieri, A.; Carotti, A.; **Barreca, M. L.**; Altomare, C. Binding Models of Reversible Inhibitors to Type-B Monoamine Oxidase. *J. Comput. Aided. Mol. Des.* **2002**, 16 (11), 769–778. <https://doi.org/10.1023/A:1023815426730>.
- (92) **Barreca, M. L.**; Balzarini, J.; Chimirri, A.; De Clercq, E.; De Luca, L.; Höltje, H. D.; Höltje, M.; Monforte, A. M.; Monforte, P.; Pannecouque, C.; Rao, A.; Zappalà, M. Design, Synthesis, Structure - Activity Relationships, and Molecular Modeling Studies of 2,3-Diaryl-1,3-Thiazolidin-4-Ones as Potent Anti-HIV Agents. *J. Med. Chem.* **2002**, 45 (24), 5410–5413. <https://doi.org/10.1021/jm020977+>.
- (93) **Barreca, M. L.**; Chimirri, A.; De Luca, L.; Monforte, A. M.; Monforte, P.; Rao, A.; Zappalà, M.; Balzarini, J.; De Clercq, E.; Pannecouque, C.; Witvrouw, M. Discovery of 2,3-Diaryl-1,3-Thiazolidin-4-Ones as Potent Anti-HIV-1 Agents. *Bioorganic Med. Chem. Lett.* **2001**, 11 (13), 1793–1796. [https://doi.org/10.1016/S0960-894X\(01\)00304-3](https://doi.org/10.1016/S0960-894X(01)00304-3).
- (94) **Barreca, M. L.**; Carotti, A.; Carrieri, A.; Chimirri, A.; Monforte, A. M.; Pellegrini Calace, M.; Rao, A. Comparative Molecular Field Analysis (CoMFA) and Docking Studies of Non- Nucleoside HIV-1 RT Inhibitors (NNIs). *Bioorganic Med. Chem.* **1999**, 7 (11), 2283–2292. [https://doi.org/10.1016/S0968-0896\(99\)00181-9](https://doi.org/10.1016/S0968-0896(99)00181-9).
- (95) Altomare, C.; Cellamare, S.; Carotti, A.; **Barreca, M. L.**; Chimirri, A.; Monforte, A. M.; Gasparrini, F.; Villani, C.; Cirilli, M.; Mazza, F. Substituent Effects on the Enantioselective Retention of Anti-HIV 5-Aryl- Δ^2 -1,2,4-Oxadiazolines on R,R-DACH-DNB Chiral Stationary Phase. *Chirality* **1996**, 8 (8), 556–566. [https://doi.org/10.1002/\(sici\)1520-636x\(1996\)8:8<556::aid-chir4>3.0.co;2-7](https://doi.org/10.1002/(sici)1520-636x(1996)8:8<556::aid-chir4>3.0.co;2-7).
- (96) Carrieri, A.; Altomare, C.; **Barreca, M. L.**; Contento, A.; Carotti, A.; Hansch, C. Papain Catalyzed Hydrolysis of Aryl Esters: A Comparison of the Hansch, Docking and CoMFA Methods. *Farmaco* **1994**, 49 (9), 573–585.