Curriculum Vitae

Personal Information:

Name and Surname: **Giuseppe Manfroni (PhD)**
Address: **Via del Liceo, 1; 06123 Perugia (Italy)**
Phone: **+39-075-5855126/46, +39-338-9484395**
E-mail: **giuseppe.manfroni@unipg.it**
Nationality: **Italian**
Birth date: **23/10/1975**
Actual position: **Assistant Professor (CHIM/08) Università degli Studi di Perugia**
ERC sectors: **PE5_23, LS7_3**

Scientific parameters:
a)Source ISI WEB OF KNOWLEDGE (November 2014)
Total papers: **28**
Total citations: **288**
h-index: **11**
b) Fonte GOOGLE SCHOLAR (November 2014)
Total papers and contributions: **27**
Total citations: **367**
h-index: **11**
First author in 6 papers and corresponding author in 5 papers

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Educational:

2006: PhD in Chemistry and Drug Technology at the University of Perugia. PhD Thesis title: Design and Synthesis of Non-peptidic Molecules for the Control of Hepatitis: Acridones as Anti-HCV Agents**.** Supervisor: Prof. Arnaldo Fravolini

2001: **5 years Degree with full marks (110/110) in Chimica e Tecnologia Farmaceutiche A.A. 1999-2000**
Thesis title: "Sintesi di Derivati Chinolonici ad Attività anti-HIV" Supervisor: Prof. Arnaldo Fravolini

Work experience:

2008-till now: Assistant Professor at Department of Pharmaceutical Sciences (Università di Perugia). Lecturer of Analisi dei Medicinali III at the CDlM in Pharmacy (Università di Perugia).

2005-2007: Post-doc position at the Dipartimento di Chimica e Tecnologia del Farmaco (Università di Perugia)

2006-2007: six months research experience at the Laboratorio di Chemiometria (Università di Perugia, Italy) headed by Prof. Gabriele Cruciani. Research project: Discovery of novel anti-HCV NS5B polymerase inhibitors by using the program GLUE.

January 2005: research experience as PhD student at the Rega Institute for Medical Research (Katholieke Universiteit of Leuven, Belgium), headed by Prof. Erik De Clercq. Supervisor: Prof. Johan Neyts.

Awards and honors:

AY 2005-2006: Winner for the selection as lecturer of Pharmaceutical Biotechnology for the Course of Pharmaceutical Biotechnology. DR1427 24/06/2005

August 2001: Winner of the Alfio Martani prize for the best thesis on the synthesis of heterocyclic compounds. Prize assigned by Department of Pharmaceutical Chemistry and Technology (Università di Perugia).

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Research activities and skills:

Giuseppe Manfroni is involved on the design, synthesis and discovery of new chemical entities with defined biological activity. In particular, his research is focused on the identification and optimization of new hit/lead compounds. The main skills are: (i) rational design of new compounds also through the use of basic computational methods, (ii) planning and optimization of synthetic routes, including the use of the microwave synthesis and parallel synthesis, for the preparation of new chemical entities, (iii) chemical characterization of the synthesized compounds by instrumental techniques such as NMR, IR, UV, HRMS and purification of the compounds through chromatographic separation methods, (iv) selection of new "drugable targets" for innovative antiviral therapies. Giuseppe Manfroni has particular experience on the synthesis of heterocyclic bioactive compounds such as: quinolones, acridones, benzothiazines, pyrazolobenzothiazines, dibenzothiazines.

Main research topics:

1. Design, synthesis and chemical characterization of compounds active against HIV, HCV, virus Dengue (DENV) and West Nile virus (WNV).

2. Design, synthesis, and chemical characterization of modulators of potassium channels for the treatment of hypertension.

3. Design, synthesis, and chemical characterization of anti-prion agents.

4. Design, synthesis, and chemical characterization of p38alpha MAPK inhibitors for the treatment of inflammatory and autoimmune diseases.

Scientific Collaborations:

Prof. Johan Neyts: Rega Institute For Medical Research, Katolieke Universiteit Leuven

Prof. Neerja Kaushik-Basu: New Jersey Medical School- Rutgers University, USA
Prof. Helena Danielson: Uppsala University, Sweden
Prof. Stefan Laufer: University of Tuebingen, Germany
Dr. Emiliano Biasini: Istituto Mario Negri, Milan, Italy
Prof. Martino Bolognesi: Università degli Studi di Milano, Italy
Dr. Mario Milani e Dr. Eloise Mastrangelo: CNR Milano, Italy

Founded Projects:

PRIN 2004: member (PhD student)
PRIN 2008: member (Assistant Professor)
PRIN 2010: member (Assistant Professor)
Fondazione cassa di risparmio Perugia: member
Fondazione Banco di Roma: member

Referee For The Following Indexed Journals:
Antiviral Research (IF= 3.685)
Bioorganic Medicinal Chemistry Letters (IF= 2.338)
European Journal of Medicinal Chemistry (IF= 3.499)
Journal of Medicinal Chemistry (IF= 5.61)

Actual Academic Educational Activities (Academic Year 2013-2014):

Lecturer of the integrated course of Pharmaceutical Analysis III (6 credits), Pharmacy course.
Supplementary teaching activities for undergraduate students: Pharmaceutical Analysis III (course of Pharmacy), Medicinal Chemistry II (course of Pharmacy), Pharmaceutical Biotechnology (course of Pharmaceutical Biotechnology).
Support activities for students and assessment: thesis supervisor for both non-reserch and experimental thesis; member of the examining boards for Pharmaceutical Analysis III (Pharmacy course), Pharmaceutical Analysis (CTF course), Pharmaceutical Biotechnology, Laboratory Structural Modeling (course of Pharmaceutical Biotechnology) and Medicinal Chemistry II (course of Pharmacy).

Pubblications:

1. Sardella, R.; Carotti, A.; **Manfroni, G.**; Tedesco, D.; Martelli, A.; Bertucci, C; Cecchetti, V.; Natalini, B. Enantioresolution, stereochemical characterization and biological activity of a chiral large-conductance calcium-activated potassium channel opener. *J. Chromatog. A.* **2014**, *1363*, 162-168.
2. 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. *Bioog. Med. Chem.* **2014**, *22*, 4658-4666.
3. Donalisio, M.; Massari, S.; Argenziano, M.; **Manfroni, G.**; Cagno, V.; Civra, A.; Sabatini, S.; Cecchetti, V.; Loregian, A.; Cavalli, R.; Lembo, D.; Tabarrini, O. Ethyl 1,8-

Naphthyridone-3-carboxylates Downregulate Human Papillomavirus-16 E6 and E7 Oncogene Expression. *J. Med. Chem.* **2014**, 57, 5649-5663.

4. **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.; Cecchett,i V. New Pyrazolobenzothiazine Derivatives as Hepatitis C Virus NS5B Polymerase Palm Site I Inhibitors. *J. Med. Chem.* **2014**, *57*, 3247-3262.
5. 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, 481-497.
6. **Manfroni, G.;*** Cannalire, R.; Barreca, M.L.; Kaushik-Basu, N.; Leyssen, P.; Winquist, 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, 1952-1963.
7. Massari, S.; Nannetti, G.; Goracci, L., Sancineto, L., Muratore, G., Sabatini, S., **Manfroni G**., Mercorelli, B., Cecchetti, V.; Facchini, M., Palù, G.; Cruciani, G.; Loregian, A.; Tabarrini, O. Structural investigation of cycloheptathiophene-3-carboxamide derivatives targeting influenza virus polymerase assembly. *J. Med. Chem.* **2013**, *56*, 10118-10131.
8. 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*, 1941-1953.
9. Blasi, P.; Schoubben, A.; Traina, G.; **Manfroni, G**.; Barberini, L.; Alberti, P.F.; Cirotto, C.; Ricci, M. Lipid nanoparticles for brain targeting III. Long-term stability and in vivo toxicity. *Int. J. Pharm.* **2013**, 454, 316-323.
10. 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*, 4975–4989.
11. Martelli, A.; **Manfroni, G.;*** Sabbatini, P.; Barreca, M. L.; Testai L., Novell,i 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*, 4718–4728.
12. Barreca M.L., **Manfroni, G.;*** Leyssen, P.; Winquist, 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*, 2270-2282.
13. Sabatini, S.; Gosetto, F.; Serritella, S.; **Manfroni, G.**; Tabarrini, O.; Iraci, N.; Brincat, J.P.; Carosati, E.; Villarini, M.; Kaatz, G.W.; Cecchetti, V. Pyrazolo[4,3-c][1,2]benzothiazines 5,5-Dioxide: A Promising New Class of Staphylococcus aureus NorA Efflux Pump Inhibitors. *J. Med. Chem*. **2012**, 55, 3568-3572.
14. **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. Bioorg. Med. Chem. **2012**, *20*, 866-876.

15. Sabatini, S.; Gosetto, F.; **Manfroni, G.**; Tabarrini, O.; Kaatz, G. W.; Patel, D.; Cecchetti, V. Evolution from a natural flavones nucleus to obtain 2-(4-propoxyphenyl)quinoline derivatives as potent inhibitors of the S. aureus NorA efflux pump. *J. Med. Chem.* **2011**, *54*, 5722–5736.
16. Brincat, J.P.; Carosati, E.; Sabatini, S.; **Manfroni, G**.; Fravolini, A.; Raygada, J.L.; Patel, D.; Kaatz, G.W.; Cruciani, G. Discovery of novel inhibitors of the NorA multidrug transporter of Staphylococcus aureus. *J. Med. Chem.* **2011**, *54*, 354-365.
17. **Manfroni, G.;*** Meschini, F.; Costantino, F.; Tabarrini, O.; Cecchetti, V. N-Benzoyl-N-methylsulfonylanthranilates: unexpected cyclization reaction to 4-alkoxy-2,1-benzothiazines. *Arkivoc* **2011**, (ix), 165-176.
18. Tabarrini, O.; Massari, S.; Sancineto, L.; Daelemans, D.; Sabatini, S.; **Manfroni, G.**; Cecchetti, V.; Pannecouque, C. Structural investigation of the naphthyridone scaffold: identification of a 1,6-naphthyridone derivative with potent and selective anti-HIV activity. *ChemMedChem* **2011**, *6*, 1249–1257.
19. 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*, 1027–1055.
20. Tabarrini, O.; Massari, S.; Daelemans, D.; Meschini, F.; **Manfroni, G.;** Bottega, L.; Gatto, B.; Palumbo, M.; Pannecouque, C.; Cecchetti, V. Studies of anti-HIV transcription inhibitor quinolones: identification of potent *N*1-vinyl derivatives. *ChemMedChem* **2010**, *5*, 1880-92.
21. Massari, S.; Daelemans, D.; **Manfroni, G**.; Sabatini, S.; Tabarrini, O.; Pannecouque, C.; Cecchetti, V. Studies on anti-HIV quinolones: new insights on the C-6 position. *Bioorg. Med. Chem.* **2009**, *17*, 667-674.
22. **Manfroni, G.**; Gatto, B.; Tabarrini, O.; Sabatini, S.; Cecchetti, V.; Giaretta, G.; Parolin, C.; Del Vecchio, C.; Calistri, A.; Palumbo, M.; Fravolini, A. Synthesis and biological evaluation of 2-phenylquinolones targeted at Tat/TAR recognition. *Bioorg. Med. Chem. Letters* **2009**, *19*, 714-717.
23. Spogli, R.; Sabatini, S.; **Manfroni, G**.; Tabarrini, O.; Cecchetti, V. Synthesis of 2-(Arylamino)ethanethiols via Lewis acid catalyzed aminolysis of 2,2-dimethylthiirane as precursors of the 1,4-benzothiazine Nucleus. *Synthesis* **2009**, *9*, 1513-1519.
24. **Manfroni, G.**; Paeshuyse, J.; Massari, S.; Zanoli, S.; Gatto, B.; Maga, G:, Tabarrini, O.; Cecchetti, V.; Fravolini, A.; Neyts J. Inhibition of subgenomic hepatitis C virus RNA replication by acridone derivatives: identification of an NS3 helicase inhibitor. *J. Med. Chem.* **2009**, *52*, 3354-3365.
25. Calderone, V.; Spogli, R.; Martelli, A.; **Manfroni, G**.; Testai, L.; Sabatini, S.; Tabarrini, O.; Cecchetti, V. Novel 1,4-benzothiazine derivatives as large conductance Ca2+-activated potassium channel openers. *J. Med. Chem.* **2008**, *51*, 5085-5092.
26. Tabarrini, O.; Massari, S.; Daelemans, D.; Stevens, M.; **Manfroni, G**.; Sabatini, S.; Balzarini, J.; Cecchetti, V.; Pannecouque, C.; Fravolini, A. Structure-activity relationship study on anti-HIV 6-desfluoroquinolones. *J. Med. Chem.* **2008**, *51*, 5454-5458.
27. Tabarrini, O.; **Manfroni, G**.; Fravolini, A.; Cecchetti, V.; Sabatini, S.; De Clercq, E.; Rozenski, J.; Canard, B.; Dutartre, H.; Paeshuyse, J.; Neyts, J. Synthesis and Anti-BVDV Activity of Acridones As New Potential Antiviral Agents. *J. Med. Chem.* **2006**, *49*, 2621-2627.
28. Tabarrini, O.; Stevens, M.; Cecchetti, V.; Sabatini. S.; Dell'Uomo, M.; **Manfroni, G**.; Palumbo, M.; Pannecouque, C.; De Clercq, E.; Fravolini, A. Structure Modifications of 6-Aminoquinolones with Potent Anti-HIV activity. *J. Med. Chem.* **2004**, *47*, 5567-5578.

*= corresponding author

Conference Proceedings 2010-2013

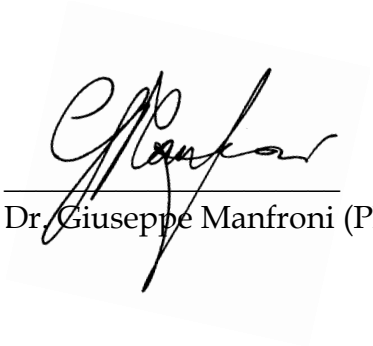
a. **Manfroni, G.;** Barreca, M.L.; Gosetto, F.; Leyssen, P.; Maga, G.; Neyts, J.; Tabarrini, O.; Cecchetti, V. Discovery of new HCV NS5B Polymerase Inhibistors: efforts and outcomes. *XX National Meeting on Medicinal Chemistry*. 12-16 September **2010**, Abano Terme (PD) (Italy), P 80.
b. Massari S.; Sancineto L.; **Manfroni, G**.; Daelemans, D.; Pannecouque, C.; Tabarrini, O.; Cecchetti, V. From the potent anti-HIV transcription inhibitor HM13N to an enlarged series of naphthyridone analogues. *XX National Meeting on Medicinal Chemistry*. 12-16 September **2010**, Abano Terme (PD) (Italy), P 86.
c. Capone, C. Sabatini, S.; Gosetto, F.; **Manfroni, G.**; Cecchetti, V. Sintesi di nuovi inibitori della pompa di efflusso NorA dello *S. aureus*: dalle 3-fenil-1,4benzotiazine alle 2-fenilchinosaline. *10° SAYCS*. 18-20 Ottobre **2010**, Pesaro (Italy), P 11.
d. Gosetto, F.; **Manfroni, G.**; Barreca, M.L.; Tabarrini, O.; Cecchetti, V. Disegno, sintesi e valutazione biologica di derivati *N*-sulfonilantranilici come agenti anti-HCV. *10° SAYCS*. 18-20 Ottobre **2010**, Pesaro (Italy), P 24.
e. Massari, S.; Iraci, N.; Sancineto, L.; Barreca, M.L.; **Manfroni, G.**; Cecchetti, V.; Tabarrini, O. Disegno di inibitori di P-TEFb come nuovi agenti anti-HIV attraverso approcci computazionali. XXX TUMA, Perugia, Italy, June 30-July 1, **2011**, P-9.
f. Cannalire, O.; Barreca, M.L.; **Manfroni, G.**; Iraci, N.; Cecchetti, V. 6-Amino-3-carboxyquinolone benzyl esters as HCV NS5B inhibitors. 11° SAYCS, Pesaro, 17-19 Ottobre **2011**, P-3.
g. Sabatini S., Gosetto F., Tabarrini O., **Manfroni G.**, Cecchetti V. Derivati 2-fenil-4-idrossichinolonici come potenti inibitori della pompa d'efflusso NorA dello *S. aureus***:** XXX Convegno Interregionale SCI TUMA- Perugina (Italy), 30 Giugno - 1 Luglio **2011**. O 14
h. **Manfroni, G.**; Barreca, M.L.; Iraci, N.; Cannalire, R.; Tabarrini, O.; Cecchetti, V. New chemotypes to fight HCV infection: discovery of selective inhibitors of HCV replication with pyrazolobenzothiazine scaffold. In: -. Book of Abstract. July 17-20, **2012**. Palermo – Italy.
i. Sabatini, S.; Gosetto, F.; **Manfroni, G**., Tabarrini, O., Carosati, E.; Cecchetti, V. A New Promising Class of pyrazolobenzothiazine inhibitors of *S. aureus* NorA Efflux Pump. P-88. 21st National Meeting on Medicinal Chemistry. July 17-20, **2012**, Palermo – Italy.
j. Tabarrini, O.; Sancineto, L., Iraci, N., Massari, S., Attanasio, V.; Sabatini, S., **Manfroni, G**.; Marcello, A., Cecchetti, V. Targeting the HIV Tat-mediated transcription machinery, P-TEFb complex inhibitors. P31, 21st National Meeting in Medicinal Chemistry. July, 17-20 **2012**, Palermo, Italy.
k. Tabarrini, O.; Sancineto, L.; Iraci, N.; Massari, S.; Attanasio, V.; **Manfroni, G.**; Marcello, A.; Cecchetti, V. P-TEFb inhibitors as new potential anti-HIV agents: hit-to-lead optimization. P032, 22nd International Symposium on Medicinal Chemistry, September 2 - 6, **2012**, Berlin, Germany.
l. Cannalire, R., **Manfroni, G.**; Barreca, M. L.; Massari, S.; Cecchetti, V. 6-Aminoquinolones targeting polymerase HCV NS5B Polymerase. P3.1, NCPF6, 15-17 Aprile **2012**, Riccione, Italy.
m. Iraci, N.; Sancineto, L.; Barreca, M.L.; Massari, S.; Sabatini, S.; **Manfroni, G.**; Cecchetti, V.; Tabarrini, O. Computer-Aided Identification of Fragments as CDK9 Inhibitors with

Anti-HIV-1 Tat-Mediated Transcription Activity., VII meeting-workshop Nuove Prospettive in Chimica Farmaceutica (NPCF7), 29-31 Maggio **2013**, Savigliano (CN), Italy, P6.1.

n. Sabatini, S.; Barreca, M.L.; **Manfroni, G.**; Tabarrini, O.; Kaatz, G. W.; Cecchetti, V. Structural investigations of the 2-phenyl-4-hydroxyquinoline class of *S. aureus* NorA EPIs., XXII National Meeting on Medicinal Chemistry. September 10-13, **2013**, Roma – Italy, P.ID.14.

o. Massari, S.; Donaliso, M.; Ansideri, F.; Sancineto, L.; Sabatini, S.; **Manfroni, G**.; Barreca, M.L.; Cecchetti, V.; Lembo, D.; Tabarrini, O. Small molecole targeting HPV E6 and E7 oncoproteins expression. XXII National Meeting on Medicinal Chemistry. September 10-13, **2013**, Roma – Italy, P.OE.38.

Perugia, il 18/11/2014



Dr. Giuseppe Manfroni (PhD)