

Curriculum Vitae, Mauro Freccero

Current Position: P.I. of an Organic Synthesis Laboratory
Full Professor in Organic Chemistry
President of "Centro Grandi Strumenti" (CGS, Pavia University)

Professional career

4-2016 ; present. Professor at Pavia University.
1-10-2019; 30-9-2021 Vice-Chancellor for Research at the University of Pavia, Italy.
10-2013; 2-2019. Head of the Ph.D. School in Chemical and Pharmaceutical Sciences at Pavia University
10-2008; 2-2017. Adjunct Professor at Vita-Salute San Raffaele University
10-2002; 3-2016. Associate Professor at Pavia University.
9-1996; 9-2002. Assistant Professor at Pavia University.
1-1996; 9-1996. Post-doctorate at the Dept. of Organic Chemistry, Pavia University
8-1994; 12-1995. Post-doctorate at the Dept. of Chemistry, Dublin City University (DCU), Dublin (Ireland).
Beginning of 1994. R&D Chemist, at ACS Dobfar S.p.A., fine chemicals, MI (Italy).
3-1993; 10-1993. Visiting Scientist, Dep. of Chemistry & Biochemistry, University of Maryland USA.
1990-1993. Ph.D in Chemistry, at the Dept. of Chemistry, Pavia University.
1990. Degree in Chemistry (110/110 cum laude) at the University of Pavia.



Publications and citation statistics. 135 publications, 128 in peer review int. journals, 4 book chapters, 2 international patents.
[H-index 43, citations 4923, [google-scholar-citations](#); H-index 39, citations 4213 (Scopus)].

Research interests: organic synthesis and binding properties of selective ligands, targeting G-quadruplex (G4) in human telomeres and oncogene promoters for theranostic applications (i.e.: targeted anticancer therapy, and fluorescence emission diagnostic). Currently, MF is developing selective ligands targeting G4 in the HIV-1 genome as conceptually new antiviral drugs, also developing effective transient and activatable reactants [quinone metide and reactive oxygen species (ROS)] targeting DNA secondary structures.

Mentoring: 39 undergraduate students, 13 PhD students, and 10 postdoctorates.

Most important financed projects:

2022-2025 PNRR, PE13, One Health Basic and Translational Research Actions addressing Unmet Needs on Emerging Infectious Diseases. Coordinator of the Organic Synthesis Uni at UniPV: (247 K€).

2009-2015. Project: FIRB-IDEA RBID082ATK_003: "New drug for anticancer targeted therapy" Unit coordinator: (480 K€).

2011-2013. Project: PRIN 2009MFRKZ8. "Selective Molecular Devices Targeting "G-Quadruplexes" P.I. (250.6 K€).

2013-2016. Project: AIRC IG2013-14708: "Photoactive molecules targeting telomeric G-quadruplex as multimodal agents in anticancer therapy" P.I. (265 K€).

2014-2020. Project within the 7th FRAMEWORK PROGRAMME, HIV LTR G-4 (Consolidator Grant, no: 615879): "G-quadruplexes in the HIV-1 genome: novel targets for the development of selective antiviral drugs". Second beneficiary of a "Two-beneficiary contract". (PV Funding: 659.6 K€).

Recent and most Important References: *Nucleic Acids Res.* 2020, 48, 4627 [10.1093/nar/gkaa186](#). *J. Am. Chem. Soc.* 2018, 140, 14528 [10.1021/jacs.8b05337](#). *Nucleic Acids Res.*, 2018, 46, e115 [10.1093/nar/gky607](#). *Angew. Chem. Int. Ed.* 2017, 56, 7520 [10.1002/anie.201702096](#). *J. Med. Chem.* 2015, 58, 9639 [10.1021/acs.jmedchem.5b01283](#).

Publications (IF: 2021)

- 135) "Studying the Dynamics of a Complex G-Quadruplex System: Insights into the Comparison of MD and NMR Data" Castelli, M., Doria, F., Freccero, M., Colombo, G., Moroni, E. *J. Chem. Theory Comput.*, **2022**, 18(7), 4515-4528. IF:6.578.
- 134) "Photoactivatable V-Shaped Bifunctional Quinone Methide Precursors as a New Class of Selective G-quadruplex Alkylating Agents" Lena, A.; Benassi, A.; Stasi, M.; Saint-Pierre, C.; Freccero, M.; Gasparutto, D.; Bombard, S.; Doria, F.; Verga, D. *Chem. Eur. J.* **2022**, 28(35), e202200734. IF:5.020.
- 133) "G-Quadruplex DNA as a Target in Pathogenic Bacteria: Efficacy of an Extended Naphthalene Diimide Ligand and Its Mode of Action". Cebrián, R., Belmonte-Reche, E., Pirota, V., ...Freccero, M., Doria, F., Kuipers, O.P. *J. Med. Chem.*, **2022**, 65(6), 4752-4766. IF: 8.039.
- 132) "The Quest for the Right Trade-Off for an Efficient Photoclick Monitoring Reaction. Benassi, A., Pirota, V., Doria, F., Freccero, M." *ChemPhotoChem*, **2022**, 6(3), e202100204. IF:3.679.
- 131) "Thiosugar naphthalene diimide conjugates: G-quadruplex ligands with antiparasitic and anticancer activity" Belmonte-Reche E., Benassi A., Peñalver P., Cucchiarini A., Guédin A., Mergny J.L., Rosu F., Gabelica V., Freccero M., Doria F., Morales J.C. *Eur. J. Med. Chem.*, **2022**, 232, 114183. IF: 8.039.
- 130) "Selective Recognition of a Single HIV-1 G-Quadruplex by Ultrafast Small-Molecule Screening". Scalabrin, M., Nadai, M., Tassinari, M., ...Freccero, M., Richter, S.N." *Anal. Chem.*, **2021**, 93, 15243-15252. IF:8.008.
- 129) "Synthesis, crystal structure and antibacterial studies of 2,4,6-trimethoxybenzaldehyde based dihydropyrimidine derivatives". Huseynzada, A.E., Jelsch, C., Akhundzada, H.N., ...Ganbarov, K., Najafov, B. *J. Mol. Struct.*, **2021**, 1241, 130678. IF: 3.841.
- 128) "New perspectives in cancer drug development: computational advances with an eye to design". Castelli, M., Serapian, S.A., Marchetti, F., ...Freccero, M., Colombo, G. *RSC Med. Chem.*, **2021**, 12, 1491-1502. IF: 3.470.
- 127) "Selective binding and redox-activity on parallel G-quadruplexes by pegylated naphthalene diimide-copper complexes". Pirota, V., Lunghi, E., Benassi, A., ...Freccero, M., Doria, F. *Molecules*, **2021**, 26, 5025. IF: 4.927.
- 126) "Synthesis, crystal structure and antibacterial studies of 2,4,6-trimethoxybenzaldehyde based dihydropyrimidine derivatives". A.E. Huseynzada, C. Jelsch, H.N. Akhundzada, S. Soudani, C. Ben Nasr, F. Doria, U.A. Hasanova, M. Freccero, Z. Gakhramanova, K. Ganbarov, B. Najafov. *J. Mol. Struct.*, **2021**, 1241, 130678. IF: 3.841.
- 125) "The Binding Pocket at the Interface of Multimeric Telomere G-quadruplexes: Myth or Reality?" F. Manoli, F. Doria, G. Colombo, B. Zambelli, M. Freccero,* I. Manet.* *Chem. Eur. J.* **2021**, 27, 11707-11720. IF:5.020.
- 124) "Synthesis, crystal structure and antibacterial studies of dihydropyrimidines and their regioselectively oxidized products". Huseynzada, A.E., Jelch, C., Akhundzada, H.V.N., ...Khankishiyeva, R.F., Freccero, M. *RSC Advances*, **2021**, 11, 6312-6329. IF: 4.036
- 123) "On the binding of naphthalene diimides to a human telomeric G-quadruplex multimer model" Pirota, V., Platella, C., Musumeci, D., Benassi, A., Amato J., Pagano B., Colombo G., Freccero M., Doria, F., Montesarchio, D. *Int. J. Biol. Macromol.*, **2021**, 166, 1320-1334. IF: 8.025
- 122) On the interaction of an anticancer trisubstituted naphthalene diimide with G-quadruplexes of different topologies: A structural insight. Platella, C., Trajkovski, M., Doria, F., Freccero, M., Plavec, J., Montesarchio, D. *Nucleic Acids Res.*, **2020**, 48, 12380-12393. IF: 19.160.

- 121) Synthesis, crystal structure and antibacterial properties of 6-methyl-2-oxo-4-(quinolin-2-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate Huseynzada, A.E., Jelsch, C., Akhundzada, H.N., ...Hasanova, U.A., Freccero, M. *J. Mol. Struc.*, 2020, 1219, 128581. IF: 3.841.
- 120) Selective targeting of mutually exclusive DNA G-quadruplexes: HIV-1 LTR as paradigmatic model. Tassinari, M., Zuffo, M., Nadai, M., ...Freccero, M., Richter, S.N. *Nucleic Acids Res.*, 2020, 48, 4627-4642. IF: 19.160.
- 119) Trifunctionalized naphthalene diimides and dimeric analogues as g-quadruplex-targeting anticancer agents selected by affinity chromatography. Platella, C., Pirota, V., Musumeci, D., ...Freccero, M. Montesarchio, D., Doria, F. *Int. J. Mol. Sci.*, 2020, 2, 1964. IF:6.208
- 118) Design of disruptors of the Hsp90-Cdc37 interface D'Annessa, I., Hurwitz, N., Pirota, V., ... Freccero M., Mollapour M., Zaffaroni N., Wolfson, H., Colombo, G. *Molecules*, 2020, 25, 25. IF: 4.927.
- 117) Towards building blocks for supramolecular architectures based on azacryptates Miljkovic, A., La Cognata, S., Bergamaschi, G., Freccero, M., Poggi, A., Amendola, V. *Molecules*, 2020, 25, 1733. IF: 4.927.
- 116) The Oncogenic Signaling Pathways in BRAF-Mutant Melanoma Cells are Modulated by Naphthalene Diimide-Like G-Quadruplex Ligands Recagni, M., Tassinari, M., Doria, F., Freccero, M. Folini, M., Richter, S.N. *Cells*, 2019, 8, 1274. IF: 7.666.
- 115) "Dyads of G-Quadruplex Ligands Triggering DNA Damage Response and Tumour Cell Growth Inhibition at Subnanomolar Concentration" Doria, F., Salvati, E., Pompili, L., Pirota V., D'Angelo C., Manoli F., Nadai M., Richter S. N., Biroccio A., Manet, I., Freccero, M.* *Chem. Eur. J.*, 2019, 25,11085-11097. IF:5.020.
- 114) "Carbohydrate-naphthalene diimide conjugates as potential antiparasitic drugs: Synthesis, evaluation and structure-activity studies" Zuffo, M.; Stucchi, A.; Campos-Salinas, J.; Cabello-Donayre, M.; Martinez-Garcia, M.; Belmonte-Reche, E.; Perez-Victoria, J. M.; Mergny, J. L.; Freccero, M.; Morales, J. C.; Doria, F. *Eur. J. Med. Chem.* 2019, 163, 54-66. IF: 7.088.
- 113) "Synthesis and photocytotoxic activity of [1,2,3]triazolo[4,5-h][1,6]naphthyridines and [1,3]oxazolo[5,4-h][1,6]naphthyridines" Frasson, Ilaria; Spano, Virginia; Di Martino, Simona; Nadai, Matteo; Doria, Filippo; Parrino, Barbara; Carbone, Anna; Cascioferro, Stella Maria; Diana, Patrizia; Cirrincione, Girolamo; Freccero, Mauro; Barraja, Paola; Richter, Sara N.; Montalbano, Alessandra. *Eur. J. Med. Chem.* 2019, 162, 176-193. IF: 7.088.
- 112) "A Catalytic and Selective Scissoring Molecular Tool for Quadruplex Nucleic Acids" Nadai, M.; Doria, F.; Scalabrin, M.; Pirota, V.; Grande, V.; Bergamaschi, G.; Amendola, V.; Winnerdy, F. R.; Phan, A. T.; Richter, S. N.; Freccero, M. *J. Am. Chem. Soc.* 2018, 140, 14528-14532. IF: 16.383.
- 111) "More is not always better: Finding the right trade-off between affinity and selectivity of a G-quadruplex ligand Zuffo, M., Guédin, A., Leriche, E.-D., ...Mergny, J.-L., Freccero, M." *Nucleic Acids Res.*, 2018, 46, e115. IF: 19.160.
- 110) "Oxadiazole/pyridine-based ligands: a structural tuning for enhancing G-quadruplex binding" Doria, F.; Pirota, V.; Petenzi, M.; Teulade-fichou, M.-P.; Verga, D.; Freccero, M. *Molecules* 2018, 23, 2162/1-2162/18. IF: 4.927.
- 109) "A fragment-based approach for the development of G-quadruplex ligands: role of the amidoxime moiety" Tassinari, M.; Lena, A.; Butovskaya, E.; Pirota, V.; Nadai, M.; Freccero, M.; Doria, F.; Richter, S. N. *Molecules* 2018, 23, 1874/1-1874/18. IF: 4.927.
- 108) "Naphthalene diimide-derivatives G-quadruplex ligands induce cell proliferation inhibition, mild telomeric dysfunction and cell cycle perturbation in U251MG glioma cells" Muoio, D.; Berardinelli, F.; Leone, S.; Coluzzi,

E.; Di Masi, A.; Doria, F.; Freccero, M.; Sgura, A.; Folini, M.; Antocchia, A. *FEBS J.* **2018**, *285*, 3769-3785. IF: 5.622.

107) "Down-Regulation of the Androgen Receptor by G-Quadruplex Ligands Sensitizes Castration-Resistant Prostate Cancer Cells to Enzalutamide." Tassinari, M.; Cimino-Reale, G.; Nadai, M.; Doria, F.; Butovskaya, E.; Recagni, M.; Freccero, M.; Zaffaroni, N.; Richter, S. N.; Folini, M. *J. Med. Chem.* **2018**, *61*, 8625-8638.

106) "Controlled Pore Glass-based oligonucleotide affinity support: towards High Throughput Screening methods for the identification of conformation-selective G-quadruplex ligands". Chiara Platella; Platella, C.; Musumeci, D.; Arciello, A.; Doria, F.; Freccero, M.; Randazzo, A.; Amato, J.; Pagano, B.; Montesarchio, D. *Anal. Chim. Acta* **2018**, *1030*, 133-141.

105) "G-quadruplex identification in the genome of protozoan parasites points to naphthalene diimide ligands as new antiparasitic agents" Belmonte-Reche, E.; Martinez-Garcia, M.; Guedin, A.; Zuffo, M.; Arevalo-Ruiz, M.; Doria, F.; Campos-Salinas, J.; Maynadier, M.; Lopez-Rubio, J.-J.; Freccero, M.; Mergny, J.-L.; Perez-Victoria, J. M.; Morales, J. C. *J. Med. Chem.* **2018**, *61*, 1231-1240.

104) "An Aggregating Amphiphilic Squaraine: A Light-up Probe That Discriminates Parallel G-Quadruplexes" Grande, V.; Doria, F.; Freccero, M.;* Würthner, F.* *Angew. Chem. Int. Ed.* **2017**, *56*, 7520-7524.

103) Pyrrolo[3',2':6,7]cyclohepta[1,2-b]pyridines with potent photo-antiproliferative activity. Spano, V.; Giallombardo, D.; Cilibrasi, V.; Parrino, B.; Carbone, A.; Montalbano, A.; Frasson, I.; Salvador, A.; Richter, S. N.; Doria, F.; Freccero, M.; Cascioferro, S.; Diana, P.; Cirrincione, G.; Barraja, P. *Eur. J. Med. Chem.* **2017**, *128*, 300-318.

102) "Tuneable coumarin-NDI dyads as G-quadruplex specific light-up probes" Zuffo, M.; Ladame, S.; Doria, F.; Freccero, M.* *Sensors and Actuators, B: Chemical* **2017**, *245*, 780-788.

101) "A red-NIR fluorescent dye detecting nuclear DNA G-quadruplexes: in vitro analysis and cell imaging". Doria, F.; Nadai, M.; Zuffo, M.; Perrone, R.; Freccero, M.;* Richter, S. N. *Chem. Comm.* **2017**, *53*, 2268-2271.

100) "Synthesis, Binding Properties, and Differences in Cell Uptake of G-Quadruplex Ligands Based on Carbohydrate Naphthalene Diimide Conjugates". Arevalo-Ruiz, M.; Doria, F.; Belmonte-Reche, E.; De Rache, A.; Campos-Salinas, J.; Lucas, R.; Falomir, E.; Carda, M.; Perez-Victoria, J. M.; Mergny, J.-L.; Freccero, M.;* Morales, J. C.* *Chem. Eur. J.* **2017**, *23*, 2157-2164.

99) "G-quadruplex fluorescence sensing by core-extended naphthalene diimides" Zuffo M.; Doria F.; Botti S.; Bergamaschi G.; Freccero M.* *Biochim. Biophys. Acta. General Subjects* **2017**, *1861(5_Part_B)*, 1303-1311.

98) "Conjugation, Substituent, and Solvent Effects on the Photogeneration of Quinone Methides" Doria, F.; Lena, A.; Bargiggia, R.; Freccero, M.* *J. Org. Chem.* **2016**, *81*, 3665-3673.

97) "Extended Naphthalene Diimides with Donor/Acceptor Hydrogen-Bonding Properties Targeting G-Quadruplex Nucleic Acids" Doria, F.; Nadai, M.; Costa, G.; Sattin, G.; Gallati, C.; Bergamaschi, G.; Moraca, F.; Alcaro, S.; Freccero, M.*; Richter, S. N.* *Eur. J. Org. Chem.* **2016**, *28*, 4824-4833.

96) "Synthesis and antiproliferative mechanism of action of pyrrolo[3',2':6,7]cyclohepta[1,2-d]pyrimidin-2-amines as singlet oxygen photosensitizers". Spano, Virginia; Frasson, Ilaria; Giallombardo, Daniele; Doria, Filippo; Parrino, Barbara; Carbone, Anna; Montalbano, Alessandra; Nadai, Matteo; Diana, Patrizia; Cirrincione, Girolamo; Freccero, Mauro; Richter, Sara N.; Barraja, Paola. *Eur. J. Med. Chem.* **2016**, *123*, 447-461.

95) "Targeting of RET oncogene by naphthalene diimide-mediated gene promoter G-quadruplex stabilization exerts anti-tumor activity in oncogene-addicted human medullary thyroid cancer. Lopergolo A, Perrone R,

- Tortoreto M, Doria F, Beretta GL, Zuco V, Freccero M, Borrello MG, Lanzi C, Richter SN, Zaffaroni N, Folini M. *Oncotarget* 2016, 7, 49649-49663.
- 94) "A bimodal fluorescent and photocytotoxic naphthalene diimide for theranostic applications". Salvati, Erica; Doria, Filippo; Manoli, Francesco; D'Angelo, Carmen; Biroccio, Annamaria; Freccero, Mauro*; Manet, Ilse. *Org. Biomol. Chem.* 2016, 14, 7238-7249.
- 93) "Synthesis, Binding and Antiviral Properties of Potent Core-extended Naphthalene Diimides Targeting the HIV-1 Long Terminal Repeat Promoter G-quadruplexes". Perrone, R.; Doria, F.; Butovskaya, E.; Frasson, I.; Botti, S.; Scalabrin, M.; Lago, L.; Grande, V.; Nadai, M.; Freccero, M.; * Richter S. N.; * *J. Med. Chem.* 2015, 58, 9639-9652.
- 92) "Red/NIR G-Quadruplex Sensing, Harvesting Blue Light by a Coumarin-Naphthalene Diimide Dyad" Zuffo, M.; Doria, F.; Spalluto, V.; Ladame S.; Freccero, M.* *Chem. Eur. J.* 2015, 21, 17596-17600.
- 91) "A naphthalene diimide dyad for fluorescence switch-on detection of G-quadruplexes". Doria, F.; Oppi, A.; Manoli, F.; Botti, S.; Kandoth, N.; Grande, V.; Manet, I.; Freccero, M.* *Chem. Comm.* 2015, 51, 9105-9108.
- 90) "A Photoreactive G-Quadruplex Ligand Triggered by Green Light". Nadai, M.; Doria, F.; Germani, L.; Richter, S. N.; Freccero, M.* *Chem. Eur. J.* 2015, 21, 2330-2334.
- 89) "Naphthalene diimides as red fluorescent pH sensors for functional cell imaging". Doria, F.; Folini, M.; Grande, V.; Cimino-Reale, G.; Zaffaroni, N.; Freccero, M.* *Org. Biomol. Chem.* 2015, 13, 570-576.
- 88) "Assessment of gene promoter G-quadruplex binding and modulation by a naphthalene diimide derivative in tumor cells". Nadai, M.; Cimino-Reale, G.; Sattin, G.; Doria, F.; Butovskaya, E.; Zaffaroni, N.; Freccero, M.; Palumbo, M.; Richter, S. N.; Folini, M. *Int. J. Oncol.* 2015, 46, 369-380.
- 87) "Naphthalene diimides as selective naked-eye chemosensor for copper(II) in aqueous solution". Doria, F.; Amendola, V.; Grande, V.; Bergamaschi, G.; Freccero, M.* *Sensor Actuat. B-Chemical* 2015, 212, 137-144.
- 86) "Aryl ethynyl anthraquinones: a useful platform for targeting telomeric G-quadruplex structures". Percivalle, C.; Sissi, C.; Greco, M. L.; Musetti, C.; Mariani, A.; Artese, A.; Costa, G.; Perrone, M. L.; Alcaro, S.; Freccero, M.* *Org. Biomol. Chem.* 2014, 12, 3744-3754.
- 85) "Mechanochemical synthesis of bumetanide-4-aminobenzoic acid molecular cocrystals: A facile and green approach to drug optimization" Bruni, G.; Maietta, M.; Berbenni, V.; Mustarelli, P.; Ferrara, C.; Freccero, M.; Grande, V.; Maggi, L.; Milanese, C.; Girella, A. *J. Phys Chem B* 2014, 118, 9180-9190.
- 84) "Quinone Methides as DNA Alkylating Agents: An Overview on Efficient Activation Protocols for Enhanced Target Selectivity" Percivalle, C.; Doria, F.; Freccero, M.* *Curr. Org. Chem.* 2014, 18, 19-43.
- 83) "An Experimental and Theoretical Investigation of Loperamide Hydrochloride-Glutaric Acid Cocrystals" Bruni, G.; Maietta, M.; Maggi, L.; Mustarelli, P.; Ferrara, C.; Berbenni, V.; Freccero, M.; Scotti, F.; Milanese, C.; Girella, A. *J. Phys Chem B* 2013, 117, 8113-8121.
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