VALOTI MASSIMO

CURRICULUM VITAE

Massimo Valoti, born 19th March 1956, Bergamo, Italy

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Experience and Knowledge:

Important academic appointments

1982	Degree in Chemistry , Università di Firenze
1984-1987	PhD in Pharmaceutical Sciences - Università di Siena
1988-2001	Assistant Professor at the Faculty of Pharmacy, University of Siena
1993	Co-organizer and teacher in the " Training Course in Biochemical Pharmacology" sponsored by the European Community (COMETT programme) held at the University of Siena
1993-1995	Lecturer in Applied Pharmacology, University of Siena
1995-	Lecturer in Toxicology, Faculty of Pharmacy, University of Siena.
1995-2010	Member of PhD School in "Dottorato di Ricerca in Fisiologia, Farmacologia e Tossicologia Molecolare" University of Siena, Firenze, Torino
1997	Teacher in the "Biochemical Pharmacological Techniques: Theoretical & Experimental Aspects" sponsored by ERASMUS and TEMPUS grants, organized by University of East London
1998	External examiner of PhD thesis at Universitat Autònoma de Barcelona, Spain
1999	Teacher at the course "Recent advance in Neurobiology" sponsored by SOCRATES grants, organized by Università di Siena
2000 e 2008	External examiner of PhD thesis at Trinity College, Dublin, Ireland
2002	Associate Professor in Pharmacology and Toxicology
2005-	External examiner of PhD thesis for University of Florence, Pisa, Bologna, Padova, Perugia
2013-	Member of PhD Course in Life Sciences, University of Siena
2017-	Coordinator of PhD program in Life Sciences

Research Experience

1985	Visiting Scientist, Department of Biochemistry, Trinity College, Dublin, Ireland
1987	Visiting Scientist, Biophysical Laboratory of Environmental Health Department, Triangle Park, NC,USA
1991	Visiting Scientist, Department of Pharmacology, University of Cambridge, UK
1993- 2008	Visiting Scientist Department of Biochemistry and Molecular Biology- Universitat Autònoma de Barcelona, Spain.

Peer reviewing, memberships and honours:

Member of International Advisory Committee of the meeting "*Microsomal Drug Oxidation, MDO 2006*" Budapest 3-7 September, 2006. Organizer of meetings on "*Cytochrome P450: Pharmacological, Toxicological and Environmental Aspects*" Siena, September 2005 and 2009.
Principal Investigator in the EU project: *Designing Therapeutic Protein-Protein Inhibitors for Brain Cancer Treatments* (DEPPICT, LSCH-CT-2007-037834) under FP6. Member of the COST action number: CM1103 "*Title: Structure-based drug design for diagnosis and treatment of*

neurological diseases: dissecting and modulating complex function in the monoaminergic systems of the brain".

Principal investigator in the MIUR projects : "*Occupational and environmental exposure to low levels of benzene and other volatile organic chemicals (VOCs): toxicological interactions, biological monitoring and risk assessment*" (2006 and 2003). Principal Investigator in *Training In Neurodegeneration, Therapeutics Intervention and Neurorepair-TINTIN*, under FP7 (People – ITN – Marie Curie Actions)

External Reviewer for grant projects for MIUR (Prin, Firb, Sir), Dutch Technology Foundation STW e National Science Centre, Poland, EFSA.

Referee for: Toxicology in Vitro, Toxicology Letters, Current Drug Metabolism, Journal of Chromatography, Journal of Food Composition and Analysis, Food and Chemical Toxicology, Chemical and Drug Toxicology, Toxicological Sciences. Member of the Editorial Board of Frontiers in Pharmacology and Pharmacologyonline.

Member of Società Italiana di Farmacologia (SIF), Società Italiana Tossicologia (SITOX) e International Society of the Studies on Xenobiotics (ISSX).

Research Activities:

The expertise of Dr. Valoti is focused on molecular mechanisms of xenobiotic toxicity as well as the metabolic biomarkers of exposure to natural and synthetic chemicals (drugs, food contaminants, industrial products and nanomaterials) He studies also on the biodisposition of drugs and xenobiotics, addressing the role of their cytochrome P450-dependent metabolism, and the effects of their interaction with transporter(s) in hepatic and extrahepatic tissues. He is also involved in studying the effects of novel inhibitors of P-glycoprotein and other transporters as reverting agents of MDR in cancer cells. Furthermore he is a Lecture in the area of pharmacology and toxicology.

He coordinates a research group composed by post doctoral- and PhD-students, technical university staff and students of the School of Pharmacy of the University of Siena.

He presented his research results in different International Symposium and Congresses.

He published about 126 full papers in international peer-reviewed journals (http://www.scopus.com).

Publications (2010-2019)

1. Reale A, Brogi S, Chelini A, Paolino M, Di Capua A, Giuliani G, Cappelli A, Giorgi G, Chemi G, Grillo A, **Valoti M**, Sautebin L, Rossi A, Pace S, La Motta C, Di Cesare Mannelli L, Lucarini E, Ghelardini C, Anzini M. Synthesis, biological evaluation and molecular modeling of novel selective COX-2 inhibitors: sulfide, sulfoxide, and sulfone derivatives of 1,5-diarylpyrrol-3-substituted scaffold. Bioorg Med Chem. **2019** ;27:115045.
2. Grillo A, Chemi G, Brogi S, Brindisi M, Relitti N, Fezza F, Fazio D, Castelletti L, Perdona E, Wong A, Lamponi S, Pecorelli A, Benedusi M, Fantacci M, **Valoti M**, Valacchi G, Micheli F, Novellino E, Campiani G, Butini S, Maccarrone M, Gemma S. Development of novel multipotent compounds modulating endocannabinoid and dopaminergic systems. Eur J Med Chem. **2019**;183:111674.
3. Fallacara AL, Zamperini C, Podolski-Renić A, Dinić J, Stanković T, Stepanović M, Mancini A, Rango E, Iovenitti G, Molinari A, Bugli F, Sanguinetti M, Torelli R, Martini M, Maccari L, **Valoti M**, Dreassi E, Botta M, Pešić M, Schenone S. A New Strategy for Glioblastoma Treatment: In Vitro and In Vivo Preclinical Characterization of Si306, a Pyrazolo[3,4-d]Pyrimidine Dual Src/P-Glycoprotein Inhibitor. Cancers **2019**;11. pii: E848.
4. Tzankova V, Aluani D, Yordanov Y, **Valoti M**, Frosini M, Spassova I, Kovacheva D, Tzankov B. In vitro toxicity evaluation of lomefloxacin-loaded MCM-41 mesoporous silica nanoparticles. Drug Chem Toxicol. **2019**:1-12.
5. Fernandez-Abascal J, Ripullone M, Valeri A, Leone C, *Valoti M*. β-Naphtoflavone and Ethanol Induce Cytochrome P450 and Protect towards MPP^+ Toxicity in Human Neuroblastoma SH-SY5Y Cells. Int J Mol Sci. **2018**;19. pii: E3369.
6. Fusi F, Sgaragli G, **Valoti M**. Gold nanoparticles potentiate Ca(V) channel currents in rat tail artery myocytes. Toxicol In Vitro. **2018**;47:89-93

7. Pietrobono S, Santini R, Gagliardi S, Dapporto F, Colecchia D, Chiariello M, Leone C, **Valoti M**, Manetti F, Petricci E, Taddei M, Stecca B. Targeted inhibition of Hedgehog-GLI signaling by novel acylguanidine derivatives inhibits melanoma cell growth by inducing replication stress and mitotic catastrophe. Cell Death Dis. **2018**;9:142.
8. Gazzano E, Rolando B, Chegaev K, Salaroglio IC, Kopecka J, Pedrini I, Saponara S, Sorge M, Buondonno I, Stella B, Marengo A, **Valoti M**, Brancaccio M, Fruttero R, Gasco A, Arpicco S, Riganti C. Folate-targeted liposomal nitrooxy-doxorubicin: An effective tool against P-glycoprotein-positive and folate receptor-positive tumors. J Control Release. **2018**; 270:37-52.
9. Vignaroli G, Iovenitti G, Zamperini C, Coniglio F, Calandro P, Molinari A, Fallacara AL, Sartucci A, Calgani A, Colecchia D, Mancini A, Festuccia C, Dreassi E, **Valoti M**, Musumeci F, Chiariello M, Angelucci A, Botta M, Schenone S. Prodrugs of Pyrazolo[3,4-d]pyrimidines: From Library Synthesis to Evaluation as Potential Anticancer Agents in an Orthotopic Glioblastoma Model. J Med Chem. **2017**;60:6305-6320.
10. De Deurwaerdère P, Binda C, Corne R, Leone C, Valeri A, **Valoti M**, Ramsay RR, Fall Y, Marco-Contelles J. Comparative analysis of the neurochemical profile and MAO inhibition properties of N-(furan-2-ylmethyl)-N-methylprop-2-yn-1-amine. ACS *Chem Neurosci*. 2016,. Ramsay RR, Majekova M, Medina M, **Valoti M**. Key Targets for Multi-Target Ligands Designed to Combat Neurodegeneration. *Front Neurosci*. **2016**;10:375. doi: 10.3389/fnins.2016.00375.
11. Vignaroli G, Calandro P, Zamperini C, Coniglio F, Iovenitti G, Tavanti M, Colecchia D, Dreassi E, **Valoti M**, Schenone S, Chiariello M, Botta M. Improvement of pyrazolo[3,4-d]pyrimidines pharmacokinetic properties: nanosystem approaches for drug delivery. *Sci Rep*. **2016**;6:21509. doi: 10.1038/srep21509.
12. Kadioglu O, Saeed ME, **Valoti M**, Frosini M, Sgaragli G, Efferth T. Interactions of human P-glycoprotein transport substrates and inhibitors at the drug binding domain: Functional and molecular docking analyses. Biochem Pharmacol. **2016**;104:42-51.
13. Zamperini C, Dreassi E, Vignaroli G, Radi M, Dragoni S, Schenone S, Musumeci F, **Valoti M**, Antiochia R, Botta M. CYP-dependent metabolism of antitumor pyrazolo[3,4-d]pyrimidine derivatives is characterized by an oxidative dechlorination reaction. Drug Metab Pharmacokinet. **2014**;29:433-40.
14. Mugnaini C, Pedani V, Casu A, Lobina C, Casti A, Maccioni P, Porcu A, Giunta D, Lamponi S, Solinas M, Dragoni S, **Valoti M** , Colombo G, Castelli MP, Gessa GL, Corelli F. Synthesis and Pharmacological Characterization of 2-(Acylamino)thiophene Derivatives as Metabolically Stable, Orally Effective, Positive Allosteric Modulators of the GABAB Receptor. J Med Chem. **2013** 9;56:3620-35.
15. Bechi N, Sorda G, Spagnoletti A, Bhattacharjee J, Vieira Ferro EA, de Freitas Barbosa B, Frosini M, **Valoti M** , Sgaragli G, Paulesu L, Ietta F. Toxicity assessment on trophoblast cells for some environment polluting chemicals and 17β-estradiol. Toxicol In Vitro. **2013**;27:995-1000.
16. Valeri A, Capasso R, **Valoti M** , Pessina F. Effects of St John's wort and its active constituents, hypericin and hyperforin, on isolated rat urinary bladder. J Pharm Pharmacol. **2012**;64 :1770-6
17. Gemma S, Camodeca C, Brindisi M, Brogi S, Kukreja G, Kunjir S, Gabellieri E, Lucantoni L, Habluetzel A, Taramelli D, Basilico N, Gualdani R, Tadini-Buoninsegni F, Bartolommei G, Moncelli MR, Martin RE, Summers RL, Lamponi S, Savini L, Fiorini I, **Valoti M** , Novellino E, Campiani G, Butini S. Mimicking the intramolecular hydrogen bond: synthesis, biological evaluation, and molecular modeling of benzoxazines and quinazolines as potential antimalarial agents. J Med Chem. **2012**;55:10387-404.
18. Frosini M, Larini A, Ricci L, Lucas L, Gorelli B, Sgaragli G, Tanganelli P, **Valoti M** . Effects of autologous, cross-linked erythrocytes on isolated hypoperfused rabbit heart dynamics. Pharmacology. **2012**;90:274-80.
19. Contartese A, **Valoti M** , Corelli F, Pasquini S, Mugnaini C, Pessina F, Aldinucci C, Sgaragli G, Frosini M. A novel CB2 agonist, COR167, potently protects rat brain cortical slices against OGD and reperfusion injury. Pharmacol Res. **2012**;66:555-63.

20. Valeri A, Fiorenzani P, Rossi R, Aloisi AM, **Valoti M** , Pessina F. The soy phytoestrogens genistein and daidzein as neuroprotective agents against anoxia-glucopenia and reperfusion damage in rat urinary bladder. Pharmacol Res. **2012** ;66:309-16.

21. Dragoni S, Franco G, Regoli M, Bracciali M, Morandi V, Sgaragli G, Bertelli E, **Valoti M** . Gold nanoparticles uptake and cytotoxicity assessed on rat liver precision-cut slices. Toxicol Sci. **2012**;128:186-97

22. Mugnaini C, Nocerino S, Pedani V, Pasquini S, Tafi A, De Chiaro M, Bellucci L, **Valoti M** , Guida F, Luongo L, Dragoni S, Ligresti A, Rosenberg A, Bolognini D, Cascio MG, Pertwee RG, Moaddel R, Maione S, Di Marzo V, Corelli F. Investigations on the 4-quinolone-3-carboxylic acid motif part 5: modulation of the physicochemical profile of a set of potent and selective cannabinoid-2 receptor ligands through a bioisosteric approach. ChemMedChem. **2012**;7:920-34.

23. Neri A, Frosini M, **Valoti M** , Cacace MG, Teodori E, Sgaragli G. N,N-bis(cyclohexanol)amine aryl esters inhibit P-glycoprotein as transport substrates. Biochem Pharmacol. **2011**;82 :1822-31.

24. Ricci L, **Valoti M** , Sgaragli G, Frosini M. Taurine-like GABA aminotransferase inhibitors prevent rabbit brain slices against oxygen-glucose deprivation-induced damage. Amino Acids. **2012**;42:2139-47.

25. Possidente M, Dragoni S, Franco G, Gori M, Bertelli E, Teodori E, Frosini M, **Valoti M** . Rat intestinal precision-cut slices as an in vitro model to study xenobiotic interaction with transporters. Eur J Pharm Biopharm. **2011** ;79:343-8

26. Radi M, Dreassi E, Brullo C, Crespan E, Tintori C, Bernardo V, **Valoti M** , Zamperini C, Daigl H, Musumeci F, Carraro F, Naldini A, Filippi I, Maga G, Schenone S, Botta M. Design, synthesis, biological activity, and ADME properties of pyrazolo[3,4-d]pyrimidines active in hypoxic human leukemia cells: a lead optimization study. J Med Chem. **2011**;54:2610-26

27. Bellik L, Dragoni S, Pessina F, Sanz E, Unzeta M, **Valoti M**. Antioxidant properties of PF9601N, a novel MAO-B inhibitor: assessment of its ability to interact with reactive nitrogen species. *Acta Biochim Pol*. **2010**;57:235-9.

28. Anzini M, Chelini A, Mancini A, Cappelli A, Frosini M, Ricci L, **Valoti M**, Magistretti J, Castelli L, Giordani A, Makovec F, Vomero S. Synthesis and biological evaluation of amidine, guanidine, and thiourea derivatives of 2-amino(6-trifluoromethoxy)benzothiazole as neuroprotective agents potentially useful in brain diseases. *J Med Chem*. **2010;**53:734-44.