

## **BIOGRAPHICAL SKETCH**

NAME: **Massimo Bertinaria**

POSITION TITLE: **Associate Professor in Medicinal Chemistry – Department of Drug Science and Technology- University of Turin- Italy**

## **EDUCATION/TRAINING**

Nov 1993 MD in Pharmaceutical Chemistry and Technologies- 110/110 summa cum Laudae - University of Turin (Italy).  
Oct 1994 MD in Pharmacy – 110/110 summa cum Laudae - University of Turin (Italy).  
July 1995- Apr 1996 Fellowship student at University of East Anglia- Norwich (UK)  
1996 – 1999 PhD in Medicinal Chemistry – University of Turin (Italy)

## **EMPLOYMENT HISTORY**

2015-today **Member of the scientific board**, Master degree in “Pharmaceutical Technologies and regulatory affairs” Department of Drug Science and Technology, University of Turin, Italy.  
2011- today **Associate Professor in Medicinal Chemistry**, Department of Drug Science and Technology, University of Turin, Italy.  
1999-2011 **Assistant Professor in Medicinal Chemistry**, Department of Drug Science and Technology, University of Turin, Italy.

## **OTHER APPOINTMENTS**

1999 **Laboratory demonstrator**, School of Pharmacy, University of Turin, Italy.  
1994 **Laboratory demonstrator**, School of Pharmacy, University of Turin, Italy.

## **AFFILIATIONS**

2000 - today Professor at the Department of Drug Science and Technology, University of Turin, Italy.  
2010 – today Professor and supervisor at the Doctoral School of Sciences and Innovative Technology, University of Turin, Italy.  
2006 - today Member of The American Chemical Society, Medicinal Chemistry Division.  
2001 - today Member of the Italian Chemical Society, Medicinal Chemistry Division.  
2002 - 2007 Elected member of the board of Italian Chemical Society (SCI), Piemonte-Valle d’Aosta section.

## **RESEARCH ACTIVITY**

After graduating, I specialized in synthetic chemistry at the School of Chemistry, University of East Anglia (UK) working in the field of heterocyclic synthesis under the supervision of Prof. A McKillop. Since 1999, I have been involved in medicinal chemistry research and I gained a long experience in drug design and synthesis. In years 2000-2012, my work was mainly dedicated to the synthesis of NO-donor drugs and to the design of NO-donor-based multitarget drugs, exploiting the role of nitric oxide hybrid drugs within different GPCRs and cellular systems.

Since 2013, I lead the SynBioMed research group at DSTF. SynBioMed research is focused on the design and synthesis of new chemical entities (NCEs) acting on inflammatory signaling; at present we are actively developing NLRP3-inflammasome inhibitors and dual TP receptor antagonists/COX-2 inhibitors. The design and synthesis of NCEs able to modulate DNA methylation and active demethylation is also implemented in our research group. We are currently actively developing these projects thanks to a network of national and international collaborations. I am author of over 40 peer-reviewed publications and two patents.

Our laboratories are fully equipped to perform drug synthesis and physicochemical characterization of new molecules, stability studies, and preliminary evaluations of new chemical entities either on isolated enzymes or in *ex vivo* and *in vivo* systems. ADME studies and pharmacokinetics are also performed in our labs.

### **PUBLICATIONS with bibliometric indicators**

Publications: 44 research articles, 2 review articles, 2 editorials; 2 patents; h-index 21 (Source Scopus), total citations 1021 ORCID: <https://orcid.org/0000-0002-2533-5830>

### **TEACHING ACTIVITY**

Since 2000, I have been regularly teaching different BSc-, MD- and PhD degree courses in the field of medicinal chemistry and supervising PhD students in Pharmaceutical and Biomolecular Sciences.

- Preparazioni estrattive dei principi attivi di origine vegetale
- Analisi dei Farmaci 1 (modulo 2)
- Chimica Farmaceutica e Tossicologica 2
- Metodologie di sviluppo di processo farmaceutico
- Drug design for PhD students (in English)

### **FUTURE PROGRAMMES**

In the next years, the activity of my research team will focus on the development of new chemical entities for the treatment of inflammatory diseases. In particular, we are developing new drugs to treat inflammation associated with neurodegenerative diseases and certain forms of cancer. We have recently discovered a novel class of compounds able to efficiently inhibit COX-mediated inflammation and to block thromboxane TP $\alpha$  receptor. We are now patenting this class of compounds in collaboration with the University of Milan (prof Rovati and prof Sala) and the Goethe University, Frankfurt am Main, Germany (prof. Steinhilber, prof Proshack). In the near future we intend to go on with the development of this promising class of compounds for different therapeutic applications. In collaboration with University of Pisa (prof. Fornai's group) we discovered a new class of NLRP3 inhibitors that will be object of a patent application. These objectives will be pursued thanks to the collaboration with scientists experts in the field of pharmacology, immunology, inflammation and cancer from national and international centers, among them Prof Genrico Rovati (University of Milan, Milano - Italy), Prof Dieter Steinhilber (Goethe University, Frankfurt am Main, Germany), Dr. Pablo Pelegrin (Instituto Murciano de Investigacion Biosanitaria, Hospital Universitario Virgen de la Arrixaca- Spain), Prof. Paola Patrignani (University of Chieti-Pescara, Italy), and Dr. Francesca Montarolo (Neuroscience Institute Cavalieri Ottolenghi, Orbassano – Italy).

## INSTITUTIONAL/SCHOLARLY ACTIVITY

- Guest Editor: Research Topic “Neurological, Metabolic and Inflammatory Disorders: A Common Root In Inflammasome” *Frontiers in Pharmacology* 2020.
- Guest Editor: Special Issue “Inflammasome Inhibitors” *Molecules* 2020.
- Member of the editorial board for the Journal “Molecules”, Medicinal Chemistry Section.
- Member of the editorial board for the Journal “Arkivoc”.

## RECENT PUBLICATIONS

Massimo Bertinaria, Simone Gastaldi and Elisabetta Marini. Development of selective NLRP3 inflammasome inhibitors. In “Inflammasome Biology. Fundamentals, Role in Disease States, and Therapeutic Opportunities.” Edited by Pablo Pelegrin. Chapter 36, pages 565-582. Academic Press. Copyright © 2023 Elsevier Inc. ISBN: 978-0-323-91802-2.

Marini E, Marino M, Gionfriddo G, Maione F, Pandini M, Oddo D, Giorgis M, Rolando B, Blua F, Gastaldi S, Marchiò S, Kovachka S, Spyraakis F, Gianquinto E, Di Nicolantonio F, Bertinaria M. Investigation into the Use of Encorafenib to Develop Potential PROTACs Directed against BRAF<sup>V600E</sup> Protein. *Molecules*. **2022** Dec 3; 27(23):8513.

Marini, E.; Giorgis, M.; Leporati, M.; Rolando, B.; Chegaev, K.; Lazzarato, L.; Bertinaria, M.; Vincenti, M.; Di Stilo, A. Multitarget Antioxidant NO-Donor Organic Nitrates: A Novel Approach to Overcome Nitrates Tolerance, an Ex Vivo Study. *Antioxidants* **2022**, *11*, 166.

Pellegrini C, Antonioli L, Lopez-Castejon G and Bertinaria M. (2021) Editorial: Neurological, Metabolic and Inflammatory Disorders: A Common Root in Inflammasome. *Front. Pharmacol.* 12:808400.

Bertinaria, M. Inflammasome Inhibitors. *Molecules* **2021**, *26*, 6912.

Gastaldi S, Boscaro V, Gianquinto E, Sandall CF, Giorgis M, Marini E, Blua F, Gallicchio M, Spyraakis F, MacDonald JA and Bertinaria M. Chemical modulation of the 1-(piperidin-4-yl)-1,3-dihydro-2H-benzo[d]imidazole-2-one scaffold as a novel NLRP3 inhibitor. *Molecules* **2021**, *26*(13), 3975.

Patent application. Domanda numero: 102021000011237. Data di presentazione: 03/05/2021 IT “COMPOSTI INIBITORI DELL’INFLAMMASOMA NLRP3 E LORO USO”. Inventori: Blandizzi Corrado, Pellegrini Carolina, Fornai Matteo, Antonioli Luca, Colucci Rocchina, Bertinaria Massimo, Marini Elisabetta, Boscaro Valentina, Gastaldi Simone, Cocco Mattia.

Gütschow M, Vanden Eynde JJ, Jampilek J, Kang C, Mangoni AA, Fossa P, Karaman R, Trabocchi A, Scott PJH, Reynisson J, Rapposelli S, Galdiero S, Winum J-Y, Brullo C, Prokai-Tatrai K, Sharma AK, Schapira M, Azuma Y-T, Cerchia L, Spetea M, Torri G, Collina S, Geronikaki A, García-Sosa A-T, Vasconcelos MH, Sousa ME, Kosalec I, Tuccinardi T, Duarte IF, Salvador JAR, Bertinaria M. Pellicchia M, Amato J, Rastelli G, Gomes PAC, Guedes RC, Sabatier J-M, Estévez-Braun A, Pagano B, Mangani S, Ragno R, Kokotos G, Brindisi M, González FV, Borges F, Miloso M, Rautio J, Muñoz-Torrero D. Breakthroughs in Medicinal Chemistry: New Targets and Mechanisms, New Drugs, New Hopes–7. (Editorial) *Molecules* **2020**, *25*, 2968

Penna C, Aragno M, Cento A. S, Femminò, s, Russo I, Dal Bello F, Chiazza F, Collotta D, Ferreira Alves G, Bertinaria M. Zicola E, Mercurio V, Medana C, Collino M, Pagliaro P. "Ticagrelor Conditioning Effects Are Not Additive to Cardioprotection Induced by Direct NLRP3 Inflammasome

Inhibition: role of RISK, NLRP3 and Redox cascades". *Ox. Med. Cell. Longev.* **2020** Art. ID 9219825.

Bertinaria, M., Gastaldi, S., Marini, E., Giorgis, M. Development of covalent NLRP3 inflammasome inhibitors: Chemistry and biological activity. *Arch. Biochem. Biophys.* **2019**, 670, 116-139.

Pellegrini C., Fornai M., Colucci R., Benvenuti L., D'Antongiovanni V., Natale G., Fulceri F., Giorgis M., Marini E., Gastaldi S., Bertinaria M., Blandizzi C. and Antonioli L. A Comparative Study on the Efficacy of NLRP3 Inflammasome Signaling Inhibitors in a Pre-clinical Model of Bowel Inflammation. *Front. Pharmacol.* **2018**, 9:1405.

Atlante, S., Visintin, A., Marini, E., Savoia, M., Dianzani, C., Giorgis, M., Sürün, D., Maione, F., Schnütgen, F., Farsetti, A., Zeiher, A.M., Bertinaria, M., Giraudo, E., Spallotta, F., Cencioni, C., Gaetano, C.  $\alpha$ -ketoglutarate dehydrogenase inhibition counteracts breast cancer-associated lung metastasis. *Cell Death Dis.* **2018**, 9:756

Spallotta, F., Cencioni, C., Atlante, Garella, D., Cocco, M., Mori, M., Mastrocola, R., Kuenne, C., Guenther, S., Nanni, S., Azzimato, V., Zukunft, S., Kornberger, A., Sürün, D., Schnütgen, F., von Melchner, H., Di Stilo, A., Aragno, M., Braspenning, M., van Crieckinge, W., De Blasio, M., Ritchie, R. H., Zaccagnini, G., Martelli, F., Farsetti, A., Fleming, I., Braun, T., Beiras-Fernandez, A., Botta, B., Collino, M., Bertinaria, M., Zeiher, A., M., Gaetano, C. Stable oxidative cytosine modifications accumulate in cardiac mesenchymal cells from Type2 diabetes patients: rescue by alpha-ketoglutarate and TET-TDG functional reactivation. *Circ. Res.* **2018**, 122, 31-46.

Cocco M, Pellegrini C, Martinez-Banaclocha H, Giorgis M, Marini E, Costale A, Miglio G, Fornai M, Antonioli L, Lopez-Castejon G, Tapia-Abellan A, Angosto D, Hafner-Bratkovic I, Regazzoni L, Blandizzi C, Pelegrin P, Bertinaria M. Development of an acrylate derivative targeting the NLRP3 inflammasome for the treatment of Inflammatory Bowel Disease. *J. Med. Chem.* **2017**, 60, 3656-3671.

Carnevali S, Buccellati C, Bolego C, Bertinaria M., Rovati G.E, Sala A. Non Steroidal Anti-Inflammatory Drugs: exploiting Bivalent COXIB/TP antagonists for the control of cardiovascular risk. *Curr. Med. Chem.* **2017**, 24(30):3218-3230.

## **FUNDED PROJECTS**

- H2020 BRAVE - Protecting the brain from COVID-19-mediated neurodegeneration through inflammasome inhibition - GA: 945539. *Granting agency:* European Commission (2021). Role: Team Member (Head of drug synthesis).
- Fighting Neuroinflammation in Parkinson's Disease: development of NLRP3 inhibitors". BERM S1618 EX-POST 19\_01 *Granting agency:* Compagnia di San Paolo/Unito (2018). Role: Project coordinator and Principal investigator.
- "Nuovi Farmaci per le malattie neurodegenerative" BERM CRT 18\_02. *Granting agency:* Fondazione CRT (2018). Role: Project coordinator and Principal investigator.