

Prof. Giovanna Riccardi, Full Professor in Microbiology, born May 2<sup>nd</sup>, 1952, Golferenzo, Pavia.

#### Education, Professional Position, academic roles

1976 - Master Degree *cum laude* in Biology (University of Pavia).

1984-1998 - Researcher at the Department of Genetics and Microbiology, University of Pavia.

1999-2002 - Associate Professor of Microbiology at the Department of Experimental, Environmental and Applied Biology, University of Genoa.

From October 2002 - Full Professor of Microbiology, at the Department of Genetics and Microbiology, University of Pavia.

From January 2010 to December 2012 - President of the SIMGBM (Italian Society of General Microbiology and Microbial Biotechnologies).

From January 2016 to July 2018 - Member of the University Board of Pavia.

2016-18 - Member of the Academic Commission for the ASN 05/I2 Microbiology Italian National License.

From August 2011 - Member of the European Academy of Microbiology.

#### Research interests and Grants

##### 1) RESISTANCE MECHANISMS AND TARGET IDENTIFICATION OF NEW DRUGS FOR *Mycobacterium tuberculosis*

*Mycobacterium tuberculosis* strains that are resistant to an increasing number of antitubercular drugs (MDR-TB, XDR-TB, and TDR-TB) are becoming a threat to public health worldwide. Consequently, there is an urgent need of new TB drugs. More precisely, our laboratory is aimed to find the target and the mechanism of action of new molecules. Within the EC-VI framework cluster "New Medicines for Tuberculosis" we have identified the target of a new drug, belonging to the class of benzothiazinones, whose antitubercular activity has been well demonstrated *in vitro*, *ex vivo*, and in a mouse model of TB. The drug is now in clinical-trials. The achieved results have been published in SCIENCE and the article has been cited as one of the "key papers" published in 2009 (see: Nature Medicines 15: 1349).

##### 2) IDENTIFICATION OF NEW DRUGS AND NEW TARGETS FOR *Burkholderia cenocepacia*

*Burkholderia cenocepacia* is a Gram-negative bacterium that infects the airways of patients with cystic fibrosis (CF). Eradication of this infection is complicated by the intrinsic resistance of this microorganism to different antibiotics. In this way, the development of novel antibiotics remains a major issue for the treatment of infectious lung disease, such as that in CF. Within this topic, we are currently studying new molecules effective against *B. cenocepacia*. We recently found that a benzothiadiazol compound (10126109) is very active and we identified a mechanism of resistance, which relies on the extrusion of the new drug by RND-9 transporter. The compound is active against clinical isolates and other members of the Bcc, as well as against other Gram-negative and -positive bacteria. We recently identified the mechanism of action, which relies on the inhibition of the activity of FtsZ cell division.

Several grants from different sources: WHO; CNR-Bilateral Project; CNR-RAISA; MURST 40%; MURST-PRIN-1998, 2001, 2003, 2008; 2017; EC-V, VI and -VII frameworks; Istituto Superiore di Sanità, Fondazione Fibrosi Cistica 2004, 2006, 2009, 2012, 2015. Cystic Fibrosis Foundation-USA 2017. Regarding the EC grants, she was always part of the steering committee.

#### Bibliometrics

Author of 115 peer-reviewed articles, 5 chapter books, two International Patent Applications (PCT/EP2008/001088; PCT/EP2008/009231) and several national and international communications.

H-index Google Scholar: 44, Citations: 6721). <https://scholar.google.it/citations?hl=it&user=N7NgMwQAAAAJ>

#### A few prominent publications

1. Buroni S, Makarov V, Scoffone VC, Trespidi G, Riccardi G, Chiarelli LR. (2020) The cell division protein FtsZ as a cellular target to hit cystic fibrosis pathogens. *Eur J Med Chem.* 190:112132. IF: 5.572
2. Chiarelli LR, Salina eg, Mori G, Azhikina T, Riabova O, Lepioshkin A, Grigorov A, Forbak M, Madacki J, Orena BS, Manfredi M, Gosetti F, Buzzi A, Degiacomi G, Sammartino JC, Marengo E, Korduláková J, Riccardi G, Mikušová K, Makarov V, Pasca MR. (2020) New Insights Into the Mechanism of Action of the Thienopyrimidine Antitubercular Prodrug TP053. *ACS Infect Dis* 6:313-323. IF: 4.96
3. Mori G, Orena BS, Chiarelli LR, Degiacomi G, Riabova O, Sammartino JC, Makarov V, Riccardi G, Pasca MR. (2020) Rv0579 Is Involved in the Resistance to the TP053 Antitubercular Prodrug. *Front Microbiol* 11:292. IF: 4.235
4. SCOFFONE VC, BARBIERI G, BURONI S, SCARSELLI M, PIZZA MG, RAPPUOLI R, RICCARDI G. (2020) Vaccines to Overcome Antibiotic Resistance: The Challenge of *Burkholderia cenocepacia*. *TRENDS IN MICROBIOL.* IF: 13.546
5. Costabile G, Provenzano R, Azzalin A, Scoffone VC, Chiarelli LR, Rondelli V, Grillo I, Zinn T, Lepioshkin A, Savina S, Miro A, Quaglia F, Makarov V, Coenye T, Brocca P, Riccardi G, Buroni S, Ungaro F. (2020) PEGylated mucus-penetrating nanocrystals for lung delivery of a new FtsZ inhibitor against *Burkholderia cenocepacia* infection. *Nanomedicine.* IF: 6.500
6. Chiarelli LR, Mori G, Orena BS, Esposito M, Lane T, de Jesus Lopes Ribeiro AL, Degiacomi G, Zemanová J, Szádocka S, Huszár S, Palčeková Z, Manfredi M, Gosetti F, Lelièvre J, Ballell L, Kazakova E, Makarov V, Marengo E, Mikusova K, Cole ST, Riccardi G, Ekins S, Pasca MR. (2018) A multitarget approach to drug discovery inhibiting *Mycobacterium tuberculosis* PyrG and PanK. *Sci Rep.* IF: 4.011
7. Hogan AM, Scoffone VC, Makarov V, Gislason AS, Tesfu H, Stietz MS, Brassinga AKC, Domaratzki M, Li X, Azzalin A, Biggiogera M, Riabova O, Monakhova N, Chiarelli LR, Riccardi G, Buroni S, Cardona ST. (2018) Competitive fitness of essential gene knockdowns reveals a broad-spectrum antibacterial inhibitor of the cell division protein FtsZ. *Antimicrob Agents Chemother.* IF: 4.715
8. Esposito M, Szadocka S, Degiacomi G, Orena BS, Mori G, Piano V, Boldrin F, Zemanová J, Huszár S, Barros D, Ekins S, Lelièvre J, Manganelli R, Mattevi A, Pasca MR, Riccardi G, Ballell L, Mikušová K, Chiarelli LR. A (2017). A Phenotypic Based Target Screening Approach Delivers New Antitubercular CTP Synthetase Inhibitors. *ACS Infect Dis.* IF: 4.96
9. ISRAYILOVA A, BURONI S, FORNERIS F, SCOFFONE VC, SHIXALIYEV NQ, RICCARDI G, CHIARELLI LR. (2016) Biochemical Characterization of Glutamate Racemase-A New Candidate Drug Target against *Burkholderia cenocepacia* Infections. *PLoS One.* 11:e0167350. IF: 4.011
10. Albesa-Jové D, Comino N, Tersa M, Mohorko E, Urresti S, Dainese E, Chiarelli Lr, Pasca Mr, Manganelli R, Makarov V, Riccardi G, Svergun Di, Glockshuber R, Guerin Me (2015). The redox state regulates the conformation of Rv2466c to activate the antitubercular prodrug TP053. *JOURNAL OF BIOLOGICAL CHEMISTRY.* IF: 4.239
11. Buroni S, Matthijs N, Spadaro F, Van Acker H, Scoffone VC, Pasca M, Riccardi G, Coenye T (2014). Differential role of RND efflux pumps in antimicrobial drug resistance of sessile and planktonic *Burkholderia cenocepacia* cells. *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY*, vol. 58, p. 7424-7429, ISSN: 0066-4804, doi: 10.1128/AAC.03800-14
12. HARTKOORN R, RYABOVA O, CHIARELLI L, RICCARDI G, MAKAROV V, COLE ST. (2014). The mechanism of action of 5-nitrothiophenes against *Mycobacterium tuberculosis*. *ANTIMICROBIAL AGENTS AND CHEMOTHERAPY.* IF: 4.715
13. Trefzer C, Skovierová H, Buroni S, Bobovská A, Nenci S, Molteni E, Pojer F, Pasca M, Makarov V, Cole ST, Riccardi G, Mikušová K, Johnsson K (2012). Benzothiazinones Are Suicide Inhibitors of Mycobacterial Decaprenylphosphoryl-B-d-ribofuranose 2'-Oxidase DprE1. *JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.* IF: 14.612
14. Neres J, Pojer F, Molteni E, Chiarelli LR, Dhar N, Boy-Röttger S, Buroni S, Fullam E, Degiacomi G, Lucarelli AP, Read RJ, Zanoni G, Edmondson DE, De Rossi E, Pasca MR, McKinney JD, Dyson PJ, Riccardi G, Mattevi A, Cole ST, Binda C. (2012). Structural Basis for Benzothiazinone-Mediated Killing of *Mycobacterium tuberculosis*. *SCIENCE TRANSLATIONAL MEDICINE.* IF: 16.304
15. Cole ST, Riccardi G. (2011). New tuberculosis drugs on the horizon. *CURRENT OPINION IN MICROBIOLOGY.* IF: 6.610
16. MAKAROV V, MANINA G, MIKUSOVA K, MÖLLMANN U, RYABOVA O, SAINT-JOANIS B, DHAR N, PASCA M, BURONI S, LUCARELLI A, MILANO A, DE ROSSI E, BELANOVA M, BOBOVSKA A, DIANISKOVA P, KORDULAKOVA J, SALA C, FULLAM E, SCHNEIDER P, MCKINNEY JD, BRODIN P, CHRISTOPHE T, WADDELL S, BUTCHER P, ALBRETHSEN J, ROSENKRANDS I, BROSCHE R, NANDI V, BHARATH S, GAONKAR S, SHANDIL RK, BALASUBRAMANIAN V, BALGANESH T, TYAGI S, GROSSET J, RICCARDI G, COLE ST. (2009). Benzothiazinones Kill *Mycobacterium tuberculosis* by Blocking Arabinan Synthesis. *SCIENCE.* IF: 31.364
17. Christophe T, Jackson M, Jeon HK, Fenistein D, Contreras-Dominguez M, Kim J, Genovesio A, Carralot JP, Ewann F, Kim EH, Lee SY, Kang S, Seo MJ, Park EJ, Skovierová H, Pham H, Riccardi G, Nam JY, Marsollier L, Kempf M, Joly-Guillou ML, Oh T, Shin WK, No Z, Nehrbass U, Brosch R, Cole ST, Brodin P. (2009). High content screening identifies decaprenyl-phosphoribose 2' epimerase as a target for intracellular antimycobacterial inhibitors. *PLOS PATHOGENS.* IF: 8.412

