

CURRICULUM VITAE OF MARIA ROSALIA PASCA

ACADEMIC POSITION

- 1st March 2021-Present: Full Professor in Microbiology (BIO/19), Department of Biology and Biotechnology “Lazzaro Spallanzani”, University of Pavia, Italy.
- 1st March 2015-February 2021: Associate Professor in Microbiology (BIO/19), Department of Biology and Biotechnology “Lazzaro Spallanzani”, University of Pavia, Italy.
- October 2006-February 2015: Researcher in Microbiology (BIO/19), Department of Biology and Biotechnology “Lazzaro Spallanzani”, University of Pavia, Italy.

EDUCATION

- 04/02/2002: PhD in Genetics and Molecular Evolution (XIII cycle), University of Bari, Italy.
- 21/03/1997: Degree in Natural Sciences (Mark: 110/110), University of Bari, Italy.

RESEARCH FELLOWSHIPS

- 04/2002-09/2006: Post-Doc researcher in the Laboratory of Molecular Microbiology, Department of Biology and Biotechnology “Lazzaro Spallanzani”, University of Pavia, Italy (supervisor: Prof. G. Riccardi).
- 1998-2002: PhD student in the Laboratory of Genetics of Microorganisms, University of Bari, Italy (supervisor: Prof. M.S. Ciampi).
- 01-12/2000: One-year internship in the Laboratory of Molecular Genetics of CNRS de Gif-sur-Yvette, Paris, France (supervisor: Dr. L. Bossi).
- 1999, 2001: Internships in the Laboratory of Molecular Genetics, University of Ancona, Italy (supervisor: Prof. A. La Teana).
- 12/1998-01/1999: Internship in the Laboratory of Molecular Genetics, University of Camerino (MC), Italy (supervisor: Prof. C. Gualerzi).

GRANTS

- Partner in the project “Deciphering host-pathogen interactions to eradicate intracellular mycobacteria pathogens: key drivers to design new precision nanomedicine tools” funded by PRIN 2020 (100.144,84 €; 2022-2024).
- Head of UNIPV Unit in the Project “ERA4TB funded by EC (IMI 2 - Horizon 2020; € 592.000, 1°/01/20-31/12/25).
- Principal Investigator in 3 projects (New weapons against *Mycobacterium abscessus* and other nontuberculous mycobacteria) funded by Fondazione Italiana Ricerca Fibrosi Cistica (FFC#18/2021: € 70.000; FFC#14/2020: € 57.000; FFC#19/2018: € 58.000).
- She was participant in 3 Projects funded by EC (V, VI, and VII FP) on TB topic.

MAIN FIELDS OF RESEARCH

European Regimen Accelerator For Tuberculosis (ERA4TB)

The aim of this Project is to develop at least 2 new combination regimens ready for Phase II clinical evaluation. We are characterizing the mechanism of action of 4 compounds, 3 of them have already been in Phase I clinical trial.

Collaborations: Cole ST (Pasteur Institute, Paris, France); Ramon-Garcia S (University of Saragoza, Spain); Manganello R (Department of Molecular Medicine, University of Padova, Italy).

Searching for new anti-TB drugs (MM4TB, NM4TB; present)

Tuberculosis (TB) is one of the leading cause of mortality due to a bacterial pathogen, *Mycobacterium tuberculosis* (*Mtb*). *Mtb* drug resistant strains are a threat to public health worldwide. So, there is an urgent need for new anti-TB drugs. We identified the target of benzothiazinones which are in phase II human clinical trials. The study of the mechanism of action/resistance of new anti-TB is in progress. Furthermore, we are studying new druggable cellular targets.

Collaborations: Makarov V (Russian Academy of Science, Moscow, Russia); Mikusova K (Comenius University, Bratislava, Slovakia); Baltas M (CNRS, Tolosa, Francia); Lherbet C (Università Paul Sabatier-

Toulouse III, Tolosa, France); Manetti F (Dipartimento di Biotecnologie, Chimica e Farmacia, University of Siena, Italy).

New weapons against *Mycobacterium abscessus* (FFC#19/2018; FFC#14/2020; FFC#18/2021)

The incidence of *Mycobacterium abscessus* (*Mab*) is dramatically increasing especially among CF patients worldwide. New active drugs are urgently needed.

Out of more than 700 compounds tested, only one is highly effective against *Mab in vitro* and *in vivo*. The study of its mechanism of action is in progress.

We also found that mefloquine, a repurposing antimalarial, is active against *Mab*, inhibiting mycolic acid metabolism.

Collaborations: Makarov V (Russian Academy of Science, Moscow, Russia); Ramon-Garcia S (University of Saragoza, Spain); Cirillo D (San Raffaele Hospital, Milan, Italy).

Design of new nanomedicines against intracellular mycobacteria (PRIN 2020)

This project will provide a new approach to study host-pathogens interactions with the aim of designing target to definitely eradicate *Mab* and *Mtb*, and to eliminate drug resistance. It is focussed on the study of nanomedicines against *Mab* and *Mtb* by using a multidisciplinary approach.

Collaborations: Rizzello L (Department of Pharmaceutical Sciences, University of Milan, Italy); Manganelli R (Department of Molecular Medicine, University of Padova, Italy).

EDITORIAL CONTRIBUTION

- Component of the Editorial Board of “International Journal of Molecular Sciences” (IF=6.132).
- Editor for the Special Issue of “International Journal of Molecular Sciences”: “New Drugs and Novel Strategies against Nontuberculous Mycobacteria”.
- Editor for the Special Issue of “International Journal of Molecular Sciences”: “New Drugs and Novel Cellular Targets against Tuberculosis”.
- Topic Editor for the Research topic of “Frontiers in Microbiology”: “New Approaches Against Drug-Resistant *M. tuberculosis*”.
- Topic Editor for the Research topic of “Frontiers in Microbiology”: “Rising Stars in Antimicrobials, Resistance and Chemotherapy: 2022”.

PERSONAL BIBLIOGRAPHY

She is author of 70 peer-reviewed papers (8 as 1st author, 18 as last author, 19 as corresponding author), 4 chapters for books, 2 international patent applications (one patent was sold to Sentinel Diagnostics, <http://www.sentinel.it/it/>) and several international and national communications to congresses.

Bibliometric indicators (at 25th August 2022):

TOTAL IF = 413.531 (Average IF= 5.9);

TOTAL H INDEX = SCOPUS: 32; WOS: 31; GOOGLE SCHOLAR: 36;

TOTAL CITATIONS: SCOPUS: 3460; WOS: 3269; GOOGLE SCHOLAR: 4590.

Peer-reviewed publications (IF=2020 5 years Impact factor da JCR)

1. **Pasca MR***, Gugliera P, Arcesi F, Bellinzoni M, De Rossi E, Riccardi G. Rv2686c-Rv2687c-Rv2688c, an ABC fluoroquinolone efflux pump in *Mycobacterium tuberculosis*. Antimicrob Agents Chemother. 2004. 48:3175-8 (IF=5.346).
2. Federici F, Vitali B, Gotti R, **Pasca MR**, Gobbi S, Peck AB, Brigidi P. Characterization and heterologous expression of the oxalyl coenzyme A decarboxylase gene from *Bifidobacterium lactis*. Appl Environ Microbiol. 2004. 70:5066-73 (IF= 5.26).
3. Bellinzoni M, Buroni S, **Pasca MR**, Gugliera P, Arcesi F, De Rossi E, Riccardi G. Glutamine amidotransferase activity of NAD⁺ synthetase from *Mycobacterium tuberculosis* depends on an amino-terminal nitrilase domain. Res Microbiol. 2005. 156:173-7 (IF=4.061).
4. **Pasca MR***, Gugliera P, De Rossi E, Zara F, Riccardi G. *mmpL7* gene of *Mycobacterium tuberculosis* is responsible for isoniazid efflux in *Mycobacterium smegmatis*. Antimicrob Agents Chemother. 2005. 49:4775-7 (IF=5.346).

5. Guglierame P*, **Pasca MR***, De Rossi E, Buroni S, Arrigo P, Manina G, Riccardi G. Efflux pump genes of the resistance-nodulation-division family in *Burkholderia cenocepacia* genome. *BMC Microbiol.* 2006. 6:66 (IF=4.283).
6. Buroni S, Manina G, Guglierame P, **Pasca MR**, Riccardi G, De Rossi E. LfrR is a repressor that regulates expression of the efflux pump LfrA in *Mycobacterium smegmatis*. *Antimicrob Agents Chemother.* 2006. 50:4044-52 (IF=5.346).
7. Maciag A, Dainese E, Rodriguez GM, Milano A, Provvedi R, **Pasca MR**, Smith I, Palù G, Riccardi G, Manganelli R. Global analysis of the *Mycobacterium tuberculosis* Zur (FurB) regulon. *J Bacteriol.* 2007. 189:730-40 (IF=3.534).
8. Riccardi G, Milano A, **Pasca MR**, Nies DH. Genomic analysis of zinc homeostasis in *Mycobacterium tuberculosis*. *FEMS Microbiol Lett.* 2008. 287:1-7 (IF=2.856).
9. Milano A*, **Pasca MR***, Provvedi R, Lucarelli AP, Manina G, Ribeiro AL, Manganelli R, Riccardi G. Azole resistance in *Mycobacterium tuberculosis* is mediated by the MmpS5-MmpL5 efflux system. *Tuberculosis (Edinb).* 2009. 89:84-90 (IF=2.966).
10. Makarov V, Manina G, Mikusova K, Möllmann U, Ryabova O, Saint-Joanis B, Dhar N, **Pasca MR**, Buroni S, Lucarelli AP, 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, Brosch R, Nandi V, Bharath S, Gaonkar S, Shandil RK, Balasubramanian V, Balganesht T, Tyagi S, Grosset J, Riccardi G, Cole ST. Benzothiazinones kill *Mycobacterium tuberculosis* by blocking arabinan synthesis. *Science.* 2009. 324:801-4 (IF=51.433).
11. Riccardi G, **Pasca MR**, Buroni S. *Mycobacterium tuberculosis*: drug resistance and future perspectives. *Future Microbiol.* 2009. 4:597-614 (IF=3.837).
12. Dalla Valle C, **Pasca MR**, De Vitis D, Marzani FC, Emmi V, Marone P. Control of MRSA infection and colonisation in an intensive care unit by GeneOhm MRSA assay and culture methods. *BMC Infect Dis.* 2009. 9:137 (IF=3.401).
13. Buroni S, **Pasca MR**, Flannagan RS, Bazzini S, Milano A, Bertani I, Venturi V, Valvano MA, Riccardi G. Assessment of three Resistance-Nodulation-Cell Division drug efflux transporters of *Burkholderia cenocepacia* in intrinsic antibiotic resistance. *BMC Microbiol.* 2009. 9:200 (IF=4.283).
14. **Pasca MR***§, Degiacomi G, Ribeiro AL, Zara F, De Mori P, Heym B, Mirrione M, Berra R, Pagani L, Pucillo L, Troupioti P, Makarov V, Cole ST, Riccardi G. Clinical isolates of *Mycobacterium tuberculosis* in four European hospitals are uniformly susceptible to benzothiazinones. *Antimicrob Agents Chemother.* 2010. 54:1616-8 (IF=5.346).
15. Perrin E, Fondi M, Papaleo MC, Maida I, Buroni S, **Pasca MR**, Riccardi G, Fani R. Exploring the HME and HAE1 efflux systems in the genus *Burkholderia*. *BMC Evol Biol.* 2010. 10:164 (IF=3.732).
16. Manina G*, Bellinzoni M*, **Pasca MR***, Neres J, Milano A, Ribeiro AL, Buroni S, Skovierová H, Dianišková P, Mikušová K, Marák J, Makarov V, Giganti D, Haouz A, Lucarelli AP, Degiacomi G, Piazza A, Chiarelli LR, De Rossi E, Salina E, Cole ST, Alzari PM, Riccardi G. Biological and structural characterization of the *Mycobacterium smegmatis* nitroreductase NfnB, and its role in benzothiazinone resistance. *Mol Microbiol.* 2010. 77:1172-85 (IF=3.996).
17. Manina G, **Pasca MR**, Buroni S, De Rossi E, Riccardi G. Decaprenylphosphoryl- β -D-ribose 2'-epimerase from *Mycobacterium tuberculosis* is a magic drug target. *Curr Med Chem.* 2010. 17:3099-108 (IF=4.676).
18. Lucarelli AP, Buroni S, **Pasca MR**, Rizzi M, Cavagnino A, Valentini G, Riccardi G, Chiarelli LR. *Mycobacterium tuberculosis* phosphoribosylpyrophosphate synthetase: biochemical features of a crucial enzyme for mycobacterial cell wall biosynthesis. *PLoS One.* 2010. 5:e15494 (IF=3.788).
19. Bazzini S, Udine C, Sass A, **Pasca MR**, Longo F, Emiliani G, Fondi M, Perrin E, Decorosi F, Viti C, Giovannetti L, Leoni L, Fani R, Riccardi G, Mahenthiralingam E, Buroni S. Deciphering the role of RND efflux transporters in *Burkholderia cenocepacia*. *PLoS One.* 2011. 6:e18902 (IF=3.788).
20. **Pasca MR***§, Dalla Valle C, De Jesus Lopes Ribeiro AL, Buroni S, Papaleo MC, Bazzini S, Udine C, Incandela ML, Daffara S, Fani R, Riccardi G, Marone P. Evaluation of fluoroquinolone resistance mechanisms in *Pseudomonas aeruginosa* multidrug resistance clinical isolates. *Microb Drug Resist.* 2012. 18:23-32 (IF=3.275).

21. Menendez C, Gau S, Lherbet C, Rodriguez F, Inard C, **Pasca MR**, Baltas M. Synthesis and biological activities of triazole derivatives as inhibitors of InhA and antituberculosis agents. *Eur J Med Chem.* 2011. 46:5524-31 (IF=6.099).
22. La Rosa V, Poce G, Canseco JO, Buroni S, **Pasca MR**, Biava M, Raju RM, Porretta GC, Alfonso S, Battilocchio C, Javid B, Sorrentino F, Ioerger TR, Sacchetti JC, Manetti F, Botta M, De Logu A, Rubin EJ, De Rossi E. MmpL3 is the cellular target of the antitubercular pyrrole derivative BM212. *Antimicrob Agents Chemother.* 2012. 56:324-31 (IF=5.346).
23. Ribeiro AL, Degiacomi G, Ewann F, Buroni S, Incandela ML, Chiarelli LR, Mori G, Kim J, Contreras-Dominguez M, Park YS, Han SJ, Brodin P, Valentini G, Rizzi M, Riccardi G, **Pasca MR**[§]. Analogous mechanisms of resistance to benzothiazinones and dinitrobenzamides in *Mycobacterium smegmatis*. *PLoS One.* 2011. 6:e2667 (IF=3.788).
24. Trefzer C, Škovierová H, Buroni S, Bobovská A, Nenci S, Molteni E, Pojer F, **Pasca MR**, Makarov V, Cole ST, Riccardi G, Mikušová K, Johnsson K. Benzothiazinones are suicide inhibitors of mycobacterial decaprenylphosphoryl- β -D-ribofuranose 2'-oxidase DprE1. *J Am Chem Soc.* 2012. 134:912-5 (IF=15.801).
25. Menendez C, Chollet A, Rodriguez F, Inard C, **Pasca MR**, Lherbet C, Baltas M. Chemical synthesis and biological evaluation of triazole derivatives as inhibitors of InhA and antituberculosis agents. *Eur J Med Chem.* 2012. 52:275-83 (IF=6.099).
26. Neres J, Pojer F, Molteni E, Chiarelli LR, Dhar N, Boy-Röttger S, Buroni S, Fullam E, Degiacomi G, Lucarelli AP, Read RJ, Zaroni G, Edmondson DE, De Rossi E, **Pasca MR**, McKinney JD, Dyson PJ, Riccardi G, Mattevi A, Cole ST, Binda C. Structural basis for benzothiazinone-mediated killing of *Mycobacterium tuberculosis*. *Sci Transl Med.* 2012. 4:150ra121 (IF=21.120).
27. Udine C, Brackman G, Bazzini S, Buroni S, Van Acker H, **Pasca MR**, Riccardi G, Coenye T. Phenotypic and genotypic characterisation of *Burkholderia cenocepacia* J2315 mutants affected in homoserine lactone and diffusible signal factor-based quorum sensing systems suggests interplay between both types of systems. *PLoS One.* 2013. 8:e55112 (IF=3.788).
28. Poce G, Bates RH, Alfonso S, Cocozza M, Porretta GC, Ballell L, Rullas J, Ortega F, De Logu A, Agus E, La Rosa V, **Pasca MR**, De Rossi E, Wae B, Franzblau SG, Manetti F, Botta M, Biava M. Improved BM212 MmpL3 inhibitor analogue shows efficacy in acute murine model of tuberculosis infection. *PLoS One.* 2013. 8:e56980 (IF=3.788).
29. Perrin E, Fondi M, Papaleo MC, Maida I, Emiliani G, Buroni S, **Pasca MR**, Riccardi G, Fani R. A census of RND superfamily proteins in the *Burkholderia* genus. *Future Microbiol.* 2013. 8:923-37 (IF=3.837).
30. Menendez C, Rodriguez F, Ribeiro AL, Zara F, Frongia C, Lobjois V, Saffon N, **Pasca MR**, Lherbet C, Baltas M. Synthesis and evaluation of α -ketotriazoles and α,β -diketotriazoles as inhibitors of *Mycobacterium tuberculosis*. *Eur J Med Chem.* 2013. 69:167-73 (IF=6.099).
31. Incandela ML, Perrin E, Fondi M, de Jesus Lopes Ribeiro AL, Mori G, Moiana A, Gramegna M, Fani R, Riccardi G, **Pasca MR**[§]. DprE1, a new taxonomic marker in mycobacteria. *FEMS Microbiol Lett.* 2013. 348:66-73 (IF=2.856).
32. Riccardi G, **Pasca MR**, Chiarelli LR, Manina G, Mattevi A, Binda C. The DprE1 enzyme, one of the most vulnerable targets of *Mycobacterium tuberculosis*. *Appl Microbiol Biotechnol.* 2013. 97:8841-8 (IF=4.697).
33. Matviiuk T, Rodriguez F, Saffon N, Mallet-Ladeira S, Gorichko M, de Jesus Lopes Ribeiro AL, **Pasca MR**, Lherbet C, Voitenko Z, Baltas M. Design, chemical synthesis of 3-(9H-fluoren-9-yl)pyrrolidine-2,5-dione derivatives and biological activity against enoyl-ACP reductase (InhA) and *Mycobacterium tuberculosis*. *Eur J Med Chem.* 2013. 70:37-48 (IF=6.099).
34. Matviiuk T, Mori G, Lherbet C, Rodriguez F, **Pasca MR**, Gorichko M, Guidetti B, Voitenko Z, Baltas M. Synthesis of 3-heteryl substituted pyrrolidine-2,5-diones via catalytic Michael reaction and evaluation of their inhibitory activity against InhA and *Mycobacterium tuberculosis*. *Eur J Med Chem.* 2014. 71:46-52 (IF=6.099).
35. Naik M, Humnabadkar V, Tantry SJ, Panda M, Narayan A, Guptha S, Panduga V, Manjrekar P, Jena LK, Koushik K, Shanbhag G, Jatheendranath S, Manjunatha MR, Gorai G, Bathula C, Rudrapatna S, Achar V, Sharma S, Ambady A, Hegde N, Mahadevaswamy J, Kaur P, Sambandamurthy VK, Awasthy D, Narayan C, Ravishankar S, Madhavapeddi P, Reddy J, Prabhakar K, Saralaya R, Chatterji

- M, Whiteaker J, McLaughlin B, Chiarelli LR, Riccardi G, **Pasca MR**, Binda C, Neres J, Dhar N, Signorino-Gelo F, McKinney JD, Ramachandran V, Shandil R, Tommasi R, Iyer PS, Narayanan S, Hosagrahara V, Kavanagh S, Dinesh N, Ghorpade SR. 4-aminoquinolone piperidine amides: noncovalent inhibitors of DprE1 with long residence time and potent antimycobacterial activity. *J Med Chem*. 2014. 57:5419-34 (IF=7.319).
36. Albesa-Jové D*, Chiarelli LR*, Makarov V*, **Pasca MR***, Urresti S, Mori G, Salina E, Vocat A, Comino N, Mohorko E, Ryabova S, Pfeiffer B, Lopes Ribeiro AL, Rodrigo-Unzueta A, Tersa M, Zanoni G, Buroni S, Altmann KH, Hartkoorn RC, Glockshuber R, Cole ST, Riccardi G, Guerin ME. Rv2466c mediates the activation of TP053 to kill replicating and non-replicating *Mycobacterium tuberculosis*. *ACS Chem Biol*. 2014. 9:1567-75 (IF=5.159).
 37. Riccardi G, **Pasca MR**. Trends in discovery of new drugs for tuberculosis therapy. *J Antibiot (Tokyo)*. 2014. 67:655-9 (IF=2.772).
 38. Buroni S, Matthijs N, Spadaro F, Van Acker H, Scoffone VC, **Pasca MR**, Riccardi G, Coenye T. Differential role of RND efflux pumps in antimicrobial drug resistance of sessile and planktonic *Burkholderia cenocepacia* cells. *Antimicrob Agents Chemother*. 2014. 58:7424-9 (IF=5.346).
 39. Neres J, Hartkoorn R, Chiarelli L, Gadupudi R, **Pasca MR**, Mori G, Farina D, Savina S, Makarov V, Kolly G, Molteni E, Binda C, Dhar N, Ferrari S, Brodin P, Delorme V, Landry V, Ribeiro AL, Venturelli A, Saxena P, Pojer F, Carta A, Luciani R, Porta A, Zanoni G, de Rossi E, Costi MP, Riccardi G, Cole ST. 2-Carboxyquinoxalines kill *Mycobacterium tuberculosis* through non-covalent inhibition of DprE1. *ACS Chem Biol*. 2015.10:705-14. (IF=5.159).
 40. Perdigão G, Deraeve C, Mori G, **Pasca MR**, Pratviel G, Bernardes-Génisson V. 2015. Pyridine-3,4-dicarboximide as starting material for the total synthesis of the natural product eupolauramine and its isomer iso-eupolauramine endowed with anti-tubercular activities. *Tetrahedron*. 2015. 71:1555-1559 (IF=2.22).
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 47. Matviiuk T, Madacki J, Mori G, Orena BS, Menendez C, Kysil A, André-Barrès C, Rodriguez F, Korduláková J, Mallet-Ladeira S, Voitenko Z, **Pasca MR**, Lherbet C, Baltas M. Pyrrolidinone and pyrrolidine derivatives: Evaluation as inhibitors of InhA and *Mycobacterium tuberculosis*. *Eur J Med Chem*. 2016. 123:462-475 (IF=6.099).
 48. Chiarelli LR, Mori G, Esposito M, Orena BS, **Pasca MR**[§]. New and old hot drug targets in tuberculosis. *Curr Med Chem*. 2016. 23:3813-3846. ([§]Corresponding author) (IF= 4.676).
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51. Oliveira PFM, Guidetti B, Chamayou A, André-Barrès C, Madacki J, Korduláková J, Mori G, Orena BS, Chiarelli LR, **Pasca MR**[§], Lherbet C, Carayon C, Massou S, Baron M, Baltas M. Mechanochemical Synthesis and Biological Evaluation of Novel Isoniazid Derivatives with Potent Antitubercular Activity. *Molecules*. 2017. 22(9). pii: (IF= 4.587).
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53. Mori G, Rampelli S, Orena BS, Rengucci C, De Maio G, Barbieri G, Passardi A, Casadei Gardini A, Frassinetti GL, Gaiarsa S, Albertini AM, Ranzani GN, Calistri D, **Pasca MR**[§]. Shifts of Faecal Microbiota During Sporadic Colorectal Carcinogenesis. *Sci Rep*. 2018. 8(1):10329 (IF= 5.133).
54. Mori G, Orena BS, Franch C, Mitchenall LA, Godbole AA, Rodrigues L, Aguilar-Pérez C, Zemanová J, Huszár S, Forbak M, Lane TR, Sabbah M, Deboosere N, Frita R, Vandeputte A, Hoffmann E, Russo R, Connell N, Veilleux C, Jha RK, Kumar P, Freundlich JS, Brodin P, Aínsa JA, Nagaraja V, Maxwell A, Mikušová K, **Pasca MR**, Ekins S. The EU approved antimalarial pyronaridine shows antitubercular activity and synergy with rifampicin, targeting RNA polymerase. *Tuberculosis (Edinb)*. 2018. 112:98-109 (IF= 2.966).
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