

CURRICULUM VITÆ

Name: Maria Alexandra de Oliveira Silva Braga Pedreira de Brito

ORCID: <https://orcid.org/0000-0002-8493-4649>

SCOPUS: <https://www.scopus.com/authid/detail.uri?authorId=7103088772>

Academic Degrees

- 1984 Degree in Pharmaceutical Sciences, Option C (Chemico-Biological Analysis), Faculty of Pharmacy (FF), University of Lisbon (UL)
 - 1992 Degree in Pharmaceutical Sciences, Option A (Community and Hospital Pharmacy), FFUL
 - 2001 PhD in Pharmacy, UL
 - 2012 Habilitation (Tenure) Degree in Pharmacy, UL
-

Previous and present positions

- 1984-85 Monitor, FFUL
 - 1985-94 Training Assistant, FFUL
 - 1991-01 Assistant, FFUL
 - 2001-12 Assistant Professor, FFUL
 - 2012- Associate Professor, FFUL
 - 2023- Full Professor, FFUL
-

Teaching Activity

FFUL

Chair

- 2012- Integrated Master in Pharmaceutical Sciences: Human Anatomy
- 2010- Master in Biopharmaceutical Sciences: Development and Organization of the Nervous System
- 2010- Master in Biopharmaceutical Sciences: Brain Barriers in Drug Development
- 2010- Master in Biopharmaceutical Sciences: Neuropathology and Neuropharmacology

Staff

- 1991- Integrated Master in Pharmaceutical Sciences: Histology and Embriology
- 2003- Integrated Master in Pharmaceutical Sciences: Neurobiology
- 2020-23 PhD in Pharmacy: Advances in Neuropharmaceutics

Faculty of Sciences, UL

Chair

- 2010-21 Integrated Master in Biomedical and Biophysical Engineering: Human Anatomy
 - 2021- Bachelor in Biomedical and Biophysical Engineering: Human Anatomy
-

Scientific Activity

Insertion

Head of the Neurovascular Lab – Blood-brain barrier in neuropathology, at the Research Institute for Medicines (<http://www.imed.ul.pt/>), FFUL.

Main área of interest

Nervous system pathologies such as brain metastases and glioblastoma, aiming the discovery of biomarkers, as well as the identification and modulation of therapeutic targets. Role of the blood-brain barrier in disease pathogenesis, as a source of biomarkers, as a target for modulation and as an obstacle to overcome. Evaluation of safety and efficacy of drug candidates.

Research Projects (selected)

Principal Investigator

1. “Study of the blood-brain barrier disruption by neurotoxins and modulation by therapeutic agents in a human model: effects of bilirubin and endotoxin on brain microvascular endothelial cell monolayer integrity and protective role of bile acids” (PTDC/SAU-FCF/68819/2006), 2007-2011.
2. “Brain metastasization of breast cancer: from phenotype to pathways and signaling”. Portugal–Hungary Collaborative projects. FCT and NKFIH - Proc. 441.00 HUNGRIA 2017-18. Principal investigator of the Portuguese team.
3. “Detect, prevent, eradicate: a multi-step strategy to abrogate brain metastasization of breast cancer” (FCT-PTDC/MED-ONC/29402/2017, 2018-2022).
4. “Pipeline for discovery of CDK4/6 inhibitors for metastatic breast cancer treatment” (Pfizer Medical Grant, 2022-2024).

Publications

Papers in Scientific journals with referees (selected, out of 89)

Bibliometric indicators (Web of Science, June 28, 2024): sum of times cited: 3732; H index: 39.

*, Corresponding author

1. Bernas MJ, Cardoso FL, Daley SK, Weinand M E, Campos AR, Gonçalves Ferreira AJ, Hoying JB, Witte MH, Brites D, Persidsky Y, Ramirez SH, **Brito MA***. Establishment of primary cultures of human brain microvascular endothelial cells to provide an in vitro cellular model of the blood-brain barrier. *Nat Protoc* 2010; 5: 1265-1272.
2. Cardoso FL, Sousa D, Brites D, **Brito MA***. Looking at the blood-brain barrier: molecular anatomy and possible investigation approaches. *Brain Res Rev* 2010; 64: 328-363.
3. Palmela I, Cardoso FL, Bernas M, Correia L, Vaz AR, Silva RFM, Fernandes A, Kim KS, Brites D, **Brito MA***. Elevated levels of bilirubin and long-term exposure impair human brain microvascular endothelial cell integrity. *Curr Neurovasc Res* 2011; 8: 153-169.
4. Mariano C, Silva SL, Pereira P, Fernandes A, Brites D, **Brito MA***. Evidence of tricellulin expression by immune cells, particularly microglia. *Biochem Biophys Res Commun* 2011; 409: 799-802.
5. Mariano C, Sasaki H, Brites D, **Brito MA***. A look at tricellulin and its role in tight junction formation and maintenance. *Eur J Cell Biol* 2011; 90: 787-796.
6. Cardoso FL, Kittel Á, Veszelka S, Palmela I, Tóth A, Brites D, Deli MA, **Brito MA***. Exposure to lipopolysaccharide and/or unconjugated bilirubin impair the integrity and function of brain microvascular endothelial cells. *PLoS ONE* 2012; 7: e35919.
7. Sá-Pereira I, Brites D, **Brito MA***. Neurovascular unit: a focus on pericytes. *Mol Neurobiol* 2012; 45: 327-347.
8. Palmela I, Sasaki H, Cardoso FL, Moutinho K, Kim KS, Brites D, **Brito MA***. Time-dependent dual effects of high levels of unconjugated bilirubin on the human blood-brain barrier lining. *Front Cell Neurosci* 2012; 6: 22.
9. Mariano C, Palmela I, Pereira P, Fernandes A, Falcão AS, Cardoso FL, Vaz AR, Campos AR, Gonçalves-Ferreira A, Kim KS, Brites D, **Brito MA***. Tricellulin expression in brain endothelial and neural cells. *Cell Tissue Res* 2013; 351: 397-407.
10. **Brito MA***, Palmela I, Cardoso FL, Sá-Pereira I, Brites D. Blood-brain barrier and bilirubin: clinical aspects and experimental data. *Arch Med Res*. 2014; 45:660-676.
11. Palmela I, Correia L, Silva RFM, Sasaki H, Kim KS, Brites D, **Brito MA***. Hydrophilic bile acids protect human blood-brain barrier endothelial cells from disruption by unconjugated bilirubin: an in vitro study. *Front Neurosci* 2015; 9: 80.
12. Coelho-Santos V, Leitão RA, Cardoso FL, Palmela I, Rito M, Barbosa M, **Brito MA**, Fontes-Ribeiro CA, Silva AP. The TNF- α /NF- κ B signaling pathway has a key role in methamphetamine-induced blood-brain barrier dysfunction. *J Cereb Blood Flow Metab*. 2015; 35: 1260-1271.
13. Janota CS, Brites D, Lemere CA, **Brito MA***. Glio-vascular changes during ageing in wild-type and Alzheimer's disease-like APP/PS1 mice. *Brain Res* 2015; 1620: 153-168.
14. Janota CS, Lemere CA, **Brito MA***. Dissecting the contribution of vascular alterations and aging to Alzheimer's Disease. *Mol Neurobiol* 2016; 53: 3793-3811.
15. Tenreiro MM, Ferreira R, Bernardino L, **Brito MA***. Cellular response of the blood-brain barrier to injury: potential biomarkers and therapeutic targets for brain regeneration. *Neurobiol Dis* 2016;91:262-73.
16. Magalhães A, Matias I, Palmela I, **Brito MA**, Dias S. LDL-Cholesterol increases the transcytosis of molecules through endothelial monolayers. *PLoS One* 2016;11:e0163988.

17. Pogačnik L, Pirc K, Palmela I, Skrt M, Kim KS, Brites D, **Brito MA**, Ulrich NP, Silva RFM. Potential for brain accessibility and analysis of stability of selected flavonoids in relation to neuroprotection in vitro. *Brain Res.* 2016;1651:17-26.
18. Marques F, Sousa JC, **Brito MA**, Pahnke J, Santos C, Correia-Neves M, Palha JA. The choroid plexus in health and in disease: dialogues into and out of the brain. *Neurobiol Dis* 2017; 107: 32-40.
19. Figueira I, Garcia G, Pimpão RC, Terrasso AP, Costa I, Almeida AF, Tavares L, Pais TF, Pinto P, Ventura MR, Filipe A, McDougall GJ, Stewart D, Kim KS, Palmela I, Brites D, **Brito MA**, Brito C, Santos CN. Polyphenols journey through blood-brain barrier towards neuronal protection. *Sci Rep* 2017; 7: 11456.
20. Figueira I, Tavares L, Jardim C, Costa I, Terrasso AP, Mes J, Gardner R, Becker JD, McDougall G, Stewart D, Filipe A, Kim KS, Brites D, Brito C, **Brito MA**, Santos CN. Blood-brain barrier transport and neuroprotective potential of blackberry-digested polyphenols: an in vitro study. *Eur J Nutr* 2019; 58: 113-130.
21. Angelino D, Carregosa D, Domenech-Coca C, Savi M, Figueira I, Brindani N, Jang S, Lakshman S, Molokin A, Urban Jr JF, Davis CD, **Brito MA**, Kim KS, Brighenti F, Curti C, Bladé C, del Bas JM, Stilli D, Solano-Aguilar GI, Nunes dos Santos C, Del Rio D, Mena P. 5-(Hydroxyphenyl)- γ -Valerolactone-Sulfate, a Key Microbial Metabolite of Flavan-3-ols, is Able to Reach the Brain: Evidence from Different In Silico, In Vitro and In Vivo Experimental Models. *Nutrients* 2019; 11: 2678.
22. Figueira I, Galego S, Custódio-Santos T, Vicente R, Molnár K, Haskó J, Malhó R, Videira M, Wilhelm I, Krizbai I, **Brito MA***. Picturing breast cancer brain metastasis development to unravel molecular players and cellular crosstalk. *Cancers* 2021; 13: 910.
23. Godinho-Pereira J, Garcia AR, Figueira I, Malhó R, **Brito MA***. Behind brain metastases formation: cellular and molecular alterations and blood-brain barrier disruption. *Int J Mol Sci* 2021; 22: 7057.
24. Franco C, Kausar S, Silva MFB, Guedes RC, Falcão AO, **Brito MA***. Multi-targeting approach in glioblastoma using computer-assisted drug discovery tools to overcome the blood-brain barrier and target EGFR/PI3Kp110 β signaling. *Cancers* 2022; 14: 3506.
25. Godinho-Pereira J, Lopes MD, Garcia AR, Botelho HM, Malhó R, Figueira I, **Brito MA***. A drug screening reveals minocycline hydrochloride as a therapeutic option to prevent breast cancer cells extravasation across the blood-brain barrier. *Biomedicines* 2022; 10: 1988.
26. Sánchez-Martínez JD, Garcia AR, Alvarez-Rivera G, Valdés A, **Brito MA***, Cifuentes A*. In vitro study of the blood-brain barrier transport of natural compounds recovered from agrifood by-products and microalgae. *Int J Mol Sci* 2022; 24: 533.
27. Ávila-Gálvez MA, Marques D, Figueira I, Cankar K, Bosch D, Brito MA, Nunes dos Santos C. Costunolide and parthenolide: novel blood-brain barrier permeable sesquiterpene lactones to improve barrier tightness. *Biomed Pharmacother* 2023; 167: 115413.
28. Gallardo-Fernández M, Garcia AR, Hornedo-Ortega R, Troncoso AM, Garcia-Parrilla MC, **Brito MA***. In vitro study of the blood-brain barrier transport of bioactives from Mediterranean foods. *Food Funct* 2024; 15: 3420-3432.
29. Carecho R, Marques D, Carregosa D, Masuero D, Garcia-Aloy Mar, Tramer F, Passamonti S, Vrhovsek U, Ventura R, **Brito MA**, Nunes dos Santos C, Figueira I. Circulating (poly)phenol metabolites in the brain: unveiling in vitro and in vivo blood-brain barrier transport. *Food Funct* 2024; 15: 7812–7827.
30. Garcia AR, Figueira I, Godinho-Pereira J, Botelho HM, Vaz AR, Malhó R, **Brito MA***. Unveiling the intricate dynamics of the interplay between triple-negative breast cancer cells and blood-brain barrier endothelium. *Acta Neuropathologica Communications* 2025 (In press).

Book chapters (selected, out of 15)

1. Palmela I, Brites D, **Brito MA**. Blood-brain barrier in health and disease. In: *The Blood-Brain Barrier: New Research*. Montenegro PA, Juárez SM (Eds). Nova Science Publishers, Inc. N.Y., 2012, pp 201-218. [ISBN: 978-1-62100-766-1 (hardcover); ISBN: 978-1-62100-812-5 (e-book)].
2. **Brito MA**. Endothelial cytoarchitecture and heterogeneity in the brain. In: *Advances in brain vascular research*. Ferreira R, Cristóvão AC and Bernardino L Eds. Cambridge Scholars Publishing 2020, pp 1-27. [ISBN (10): 1-5275-5067-2; ISBN (13): 978-1-5275-5067-4].
3. Garcia AR, **Brito MA**. Breast cancer cells extravasation across blood-brain barrier: from basic to translational research. In: *Interdisciplinary Cancer Research*, pp. 1-34. Ed. Rezaei N. Springer, Cham, 2023 [ISSN: 2731-4561; ISSN: 2731-457X].

Prizes (selected out of 11)

1. Portuguese Anatomical Society - Research Prize in Morphological Sciences. Best published paper (senior and corresponding author), 2016.
2. Portuguese Anatomical Society. Best oral communication (presenting author), 2017.
3. Immunotools Award 2018. Research project (principal investigator), 2018.
4. Fundação AstraZeneca Innovative Competition of the iMed Conference® 11.0. Best research project (principal investigator), 2019.
5. European Federation of Experimental Morphology. Best oral communication (senior author), 2023.

Organization of international scientific meetings

1. Symposium “Barrier Systems in Health and Disease”, Faculty of Pharmacy, University of Lisbon, May 31, 2011.
2. XII Congress of the European Association of Clinical Anatomy (EACA) jointly with the Congress of the British Association of Clinical Anatomy (BACA) and the Portuguese Anatomical Society (SAP), with the participation of the Spanish Anatomical Society (SAE) and the Brazilian Society of Anatomy (SBA), Faculty of Medicine, University of Lisbon, 2013.
3. Innovative approaches in targeted therapies: brain, infection and cancer. Institute of Molecular Medicine, Faculty of Medicine, University of Lisbon, December 13-14, 2018.
4. Models of the blood-brain barrier: scientific tools to target the brain. Online, March 18-20, 2021.
5. Scientific tools in biological assays: principles of cell cultures and genetics. Online, March 17-19, 2022.

Supervision experience

2 Post-Doc; 8 PhD thesis; 24 master thesis; 9 research fellows.

Jury member

PhD Thesis: 8 as vogal, 17 as main arguent and 28 as jury president.

Master Thesis: 14 as vogal, 4 as arguent and 27 as jury president.

Peer reviewer of scientific journals

Acta Neuropathologica; African Journal of Pharmacy and Pharmacology; Archives of Anatomy; Biochimica et Biophysica Acta; Biomedicine and Pharmacotherapy; Cancer Mangement and Research; Current Pharmaceutical Design; Free Radicals Biology and Medicine; Food and Chemical Toxicology; International Journal of Molecular Sciences; Journal of Biological Chemistry; Journal of Cellular Physiology; Journal of Neuroscience Research; Liver International; Medical Science Monitor; Neonatology; NeuroSci; Neurotoxicology; Nutrients; OncoTargets and Therapy; Pharmacological Reports; PloS ONE.

Scientific adviser for grants and projects

External evaluator, panel member or panel coordinator for PhD/Pos-doctoral grants, and projects, for: Auckland Medical Research Foundation, NewZealand; Belgian Foundation against Cancer, Belgium; European Commission; Faculty of Medicine, University of Lisbon, Portugal; Medical Research Council, United kingdom; National Science Center, Poland; National Cancer Institute, France; Portuguese Foundation for Science and Technology (FCT), Portugal; Research Foundation Flanders, Belgium; Science Fund of the Republic of Serbia, Serbia.

Mangement Activities (selected)

- | | |
|---------|---|
| 2018-21 | Member of the Scientific Council of the FFUL (Secretary) |
| 2021- | Member of the Scientific Council of the FFUL (Vice-President) |
| 2021- | Member of the Scientific Council of the Master in Biopharmaceutical Sciences Course, FFUL |
| 2021- | Coordinator of the Doctorate in Pharmacy, FFUL |
| 2014-21 | Member of the Board of the Portuguese Anatomical Society / Portuguese Anatomical Association (Treasurer) |
| 2021- | Member of the Board of the Portuguese Anatomical Society / Portuguese Anatomical Association (Fiscal Council Vogal) |
| 2021- | Member of the Board of the European Federation of Experimental Morphology (Delegate) |
| 2024- | Member of the Board of the European Federaton of Experimentaal Morphology (Secretary) |

Scientific Societies

Member of the Fluid and Barriers of the CNS Society.

Ten selected publications

*, Corresponding author

1. Bernas MJ, Cardoso FL, Daley SK, Weinand M E, Campos AR, Gonçalves Ferreira AJ, Hoying JB, Witte MH, Brites D, Persidsky Y, Ramirez SH, **Brito MA***. Establishment of primary cultures of human brain microvascular endothelial cells to provide an in vitro cellular model of the blood-brain barrier. *Nat Protoc* 2010; 5: 1265-1272.
2. Cardoso FL, Sousa D, Brites D, **Brito MA***. Looking at the blood-brain barrier: molecular anatomy and possible investigation approaches. *Brain Res Rev* 2010; 64: 328-363.
3. Palmela I, Sasaki H, Cardoso FL, Moutinho K, Kim KS, Brites D, **Brito MA***. Time-dependent dual effects of high levels of unconjugated bilirubin on the human blood-brain barrier lining. *Front Cell Neurosci* 2012; 6: 22.
4. Janota CS, Brites D, Lemere CA, **Brito MA***. Glio-vascular changes during ageing in wild-type and Alzheimer's disease-like APP/PS1 mice. *Brain Res* 2015; 1620: 153-168.
5. Marques F, Sousa JC, **Brito MA**, Pahnke J, Santos C, Correia-Neves M, Palha JA. The choroid plexus in health and in disease: dialogues into and out of the brain. *Neurobiol Dis* 2017; 107: 32-40.
6. Figueira I, Tavares L, Jardim C, Costa I, Terrasso AP, Mes J, Gardner R, Becker JD, McDougall G, Stewart D, Filipe A, Kim KS, Brites D, Brito C, **Brito MA**, Santos CN. Blood-brain barrier transport and neuroprotective potential of blackberry-digested polyphenols: an in vitro study. *Eur J Nutr* 2019; 58: 113-130.
7. Godinho-Pereira J, Garcia AR, Figueira I, Malhó R, **Brito MA***. Behind brain metastases formation: cellular and molecular alterations and blood-brain barrier disruption. *Int J Mol Sci* 2021; 22: 7057.
8. Franco C, Kausar S, Silva MFB, Guedes RC, Falcão AO, **Brito MA***. Multi-targeting approach in glioblastoma using computer-assisted drug discovery tools to overcome the blood-brain barrier and target EGFR/PI3Kp110 β signaling. *Cancers* 2022; 14: 3506.
9. Gallardo-Fernández M, Garcia AR, Hornedo-Ortega R, Troncoso AM, Garcia-Parrilla MC, **Brito MA***. In vitro study of the blood-brain barrier transport of bioactives from Mediterranean foods. *Food Funct* 2024; 15: 3420-3432.
10. Garcia AR, Figueira I, Godinho-Pereira J, Botelho HM, Vaz AR, Malhó R, **Brito MA***. Unveiling the intricate dynamics of the interplay between triple-negative breast cancer cells and blood-brain barrier endothelium. *Acta Neuropathologica Communications* 2025 (In press).