MARIE SKŁODOWSKA-CURIE POSTDOCTORAL FELLOWSHIPS 2025

EXPRESSION OF INTEREST FOR HOSTING MARIE CURIE FELLOWS

HOST INSTITUTION

UCIBIO, NOVA FCT

RESEARCH GROUP AND URL

Molecular Microbiology of Bacterial Pathogens
https://ucibio.pt/research-groups/lab/molmicro-bacterial-pathogens

SUPERVISOR (NAME AND E-MAIL)

Rita Sobral (rgs@fct.unl.pt)

SHORT CV OF THE SUPERVISOR

CURRICULUM VITÆ - Rita Gonçalves Sobral de Almeida
Place and date of birth: Lisbon, Portugal - 10/28/1975.
Researcher ID: http://www.researcherid.com/rid/H-4710-2011
ORCID: http://orcid.org/0000-0003-4533-7531
H-index: scopus **–** 20; Scholars – 23.

Associate Professor at the Department of Life Sciences and head of the Lab of Molecular Microbiology of Bacterial Pathogens at FCT NOVA (Portugal). With a background in microbiology and infectious diseases, received the doctoral degree in Molecular Biology in 2006. Did part of the doctoral studies at the Rockefeller University, under the supervision of A. Tomasz and was twice awarded the ESCMID young researcher grant. Her past and current research is on the elucidation of the molecular mechanisms of resistance to antibiotics in MRSA strains, focussing on cell wall physiology, biofilm formation and host interaction. Coordinator of the "MSc in Medical Microbiology" and responsible of the courses "Molecular and Cellular Biology", "Applied Microbiology", "Biofilms in chronic infections".

Academic Degrees
2006. Ph.D. in Biology. ITQB NOVA, Portugal.
1998. Degree in Applied Chemistry– Biotechnology, FCT NOVA.
Present and previous positions

- Associate Professor at the Department of Life Sciences, FCT NOVA, since 2024.
- Assistant Professor at the Department of Life Sciences, FCT NOVA, from 2016 to 2024.
- Principal Investigator, Head of Lab. of Molecular Microbiology of Bacterial Pathogens, UCIBIO, FCT NOVA.

2010-2015. Assistant Researcher at CREM, Centro de Recursos Microbiológicos, FCT NOVA.
2006-2010. Post-doc. ITQB NOVA and Rockefeller University, NY.
2001-2006. Ph.D. student. ITQB NOVA and Rockefeller University, NY.

Funding
- "StaphAID. The dynamics of staphylococci in the pathogenesis of atopic dermatitis (AD): towards the identification of therapeutic targets". LISBOA2030-FEDER-00726600. Projeto nº 16115.
- "StaphOUT. Fighting *S. aureus* - Peptidoglycan amidation as a new target". FCT-MCTES. PTDC/BIA-MIC/31645/2017.
- "Microfluidics Liquid Crystal Based Bifunctional Bacterial Infection Sensor". FCT-MCTES. PTDC/FIS-NAN/0117/2014.

▪ “Amidation of peptidoglycan of Gram-positive bacteria: an unexplored potential target for antibiotics”. FCT-MCTES. PTDC/BIA-MIC/3195/2012.
▪ “Metabolic circuits in inflicted bacterial cell death”. FCT-MCTES. PTDC/BIA-MIC/101375/2008.
▪ **Participation in 8 research projects as team member**

Prizes and awards

▪ “A new target inside an old molecule: glutamate amidation of peptidoglycan”. ESCMID Young Researcher 2015.
▪ “Association of extracellular DNA to *S. aureus* surface”. ESCMID Young Researcher Award 2011.

Supervision - 3 post-doctoral fellows
- 7 PhD Theses concluded and 4 ongoing.
- 22 MSc Theses concluded and 1 ongoing.

41 Publications in Peer-reviewed Journals (Citations: scopus-1638; scholars-2278; 147 co-authors)
9 Conference Proceeding Publications, 9 Invited oral communications, 40 selected oral communications and 90 poster presentations in conferences and meetings.
2 National Patents

5 SELECTED PUBLICATIONS

- S.C. Ersoy, R.A. Proctor, W.E. Rose, W. Abdelhady, S. Fan, S.L. Madrigal, A.M. Elsayed, H.F. Chambers, R.G. Sobral, A.S. Bayer. **2024.** Sensitizing methicillin-resistant *Staphylococcus aureus* (MRSA) to cefuroxime: the synergic effect of bicarbonate and the wall teichoic acid inhibitor ticlopidine. **Antimicrob Agents Chemother**. 6;68(3):e0162723. doi: 10.1128/aac.01627-23.Epub 2024 Feb 13.
- Ersoy S.C., B. Gonçalves, G. Cavaco, A. C. Manna, R.G. Sobral, C.C. Nast, R. A. Proctor, H.F. Chambers, A. Cheung, A.S. Bayer. **2022**. Influence of Sodium Bicarbonate on Wall Teichoic Acid Synthesis and β-Lactam Sensitization in NaHCO3-Responsive and Nonresponsive Methicillin-Resistant *Staphylococcus aureus*. **Microbiology Spectrum**. e03422-22.
- Portela R.P., N.A. Faria, M. Mwangi, M. Miragaia, H. de Lencastre, A. Tomasz, R.G. Sobral. **2022**. Analysis of a Cell Wall Mutant Highlights Rho-Dependent Genome Amplification Events in *Staphylococcus aureus*. **Microbiology Spectrum**. 10(5). e02483-21.
- Gonçalves B., R. Portela, R. Lobo, T.A. Figueiredo, I.R. Grilo, A.M. Ludovice, H. de Lencastre, J.S. Dias, R.G. Sobral. **2019**. The role of MurT C-terminal domain in the amidation of *Staphylococcus aureus* peptidoglycan. **Antimicrobial Agents Chemotherapy**. 63(10). pii: e00957-19. https://doi.org/10.1128/AAC.00957-19. (IF-5 years: 5.938; Q1. 5 citations)
- Harrison E.M., X. Ba, F. Coll, B. Blane, O. Restif, H. Carvell, C. U. Koser, D. Jamrozy, S. Reuter, A. Lovering, N. Gleadall, K.L. Bellis, A. Uhlemann, F.D. Lowy, R.C. Massey, I.R. Grilo, R. Sobral, J. Larsen, A.R. Larsen, C.V. Lundberg, J. Parkhill, G.K. Paterson, M.T.G. Holden, S.J. Peacock, M.A. Holmes. **2019.** Genomic identification of cryptic susceptibility to penicillins and β-lactamase inhibitors in methicillin-resistant *Staphylococcus aureus*. **Nature microbiology**. 4, 1680–1691. https://doi.org/10.1038/s41564-019-0471-0.

PROJECT TITLE AND SHORT DESCRIPTION

“Study of a novel host-internalization mechanism of *Staphylococcus aureus*”

Staphylococcus aureus is one of the most feared human pathogens, namely methicillin resistant *S. aureus* (MRSA) strains, due to their extraordinary capacity to acquire antibiotic resistance mechanisms and to their high number of virulence factors.
Our team has been studying two small genes, *skfA* and *skfB*, exclusive of *Staphylococcus* and that encode two peptides that have no function attributed yet. We recently showed that the *skf* genes are highly over-expressed in the presence of human macrophages and that the SkfA/B peptides can interact with biological membranes. Furthermore, the overexpression of SkfA/B peptides increases the internalization of *S. aureus* into human macrophages. Our observations strongly suggest that *skfA* and *skfB* genes are deeply involved in interaction with the host, most probably through membrane destabilization.

Our aim is to contribute to the elucidation of the molecular mechanisms and role of the SkfAB system in the success of *S. aureus* as a pathogen.

Workplan

Identification of host-like conditions that trigger the production of the Skf peptides

S. aureus will be grown in the presence of human macrophages, of other bacterial species (to mimic the microbiota), oxygen reactive species, cytokines and at different pHs and saline concentrations, (representative of different host tissues). Anti-SkfA and anti-SkfB polyclonal antibodies will be used to detect the Skf peptides by western blotting.

Cellular localization of Skf peptides

To determine if the SkfA and SkfB peptides are excreted into the external environment, or associate to the cytoplasmic membrane, whole cell extracts from the *skf* overexpression mutant will be produced and fractionated. Anti-SkfA and anti-SkfB polyclonal antibodies will be used to detect the presence of the Skf peptides in each fraction, by western blotting.

Definition of the interactome of SkfA/B peptides

To determine the set of *S. aureus* proteins with which the SkfA and SkfB peptides interact, the intracellular proteins of the *skf* overexpression mutant will be crosslinked with a membrane-permeable crosslinker reagent. The cells will be lysed and the total cell extract will be incubated with the anti-SkfA and anti-SkfB polyclonal antibodies, followed by immunoprecipitation. The pull-down fractions will be analysed and the interaction partners identified by Mass Spectrometry.

SCIENTIFIC AREA WHERE THE PROJECT FITS BEST*

Life Sciences (LIF)