Microbial Development Group
ITQB-UNL

Curriculum Vitae, October 2012

Adriano O. Henriques

Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

PRESENT SITUATION:

Associate Professor
New University of Lisbon
Institute for Chemical and Biological Technology (I.T.Q.B.)
Head, Biology Division
Head, Laboratory of Microbial Development
Avenida da República, Apartado 127
2781-901 Oeiras Codex, Portugal

Tel.: +351-1-446 9521
Fax: +351-1-441 1277

E-mail: aoh@itqb.unl.pt
Web site: *www.itqb.unl.pt/Research/Biology/Microbial_Development/*

DATE AND PLACE OF BIRTH: April 2nd, 1964, in Coimbra, Portugal.

ID NUMBER: 6562962.

CITIZENSHIP: Portuguese.

EDUCATION:

1993. Ph.D Degree, Cellular Biology. University of Coimbra, Coimbra, Portugal.
1986. "Licenciatura" (B.Sc.) in Biology. University of Coimbra, Coimbra, Portugal.

PROFESSIONAL EXPERIENCE:

2005-2008. Associate Professor, Institute for Chemical and Biological Technology (I.T.Q.B.), New University of Lisbon, Oeiras, Portugal.

2002 (December)-present. Adjunct Assistant Professor, The Rockefeller University, New York, N.Y., USA.

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e Biológica
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1999-2000 (November-February). Visiting scientist, Department of Microbiology, University of Marburg, and Max Planck Institüt für Terrestrische Mikrobiologie, Marburg, Germany, in the Laboratory of Dr. Uwe Völker. Research project: Genome-wide analysis of temporally-regulated and compartment-specific gene expression during development in *Bacillus subtilis* using DNA macroarrays.

1999-2005. Invited Assistant Professor. Head of the Microbial Development Laboratory. Institute for Chemical and Biological Technology (I.T.Q.B.), Oeiras, Portugal.

1998-1999. Postdoctoral fellow (*ad hoc*) in the Institute for Chemical and Biological Technology (I.T.Q.B.), Oeiras, Portugal.

1993-1997. Postdoctoral fellow in the Laboratory of Prof. Charles P. Moran Jr. Emory University School of Medicine, Department of Microbiology and Immunology, Atlanta, GA, USA.

1991-1993. Graduate Student, Institute for Chemical and Biological Technology (I.T.Q.B.), Oeiras, Portugal. Research project: Genetic analysis of the *Bacillus subtilis* developmental gene *spoVE*, under the supervision of Prof. Hermínia de Lencastre.

1990-1991. Visiting Scientist, Department of Microbiology and Immunology, Temple University, School of Medicine, Philadelphia, PA. Research project: Transcriptional regulation of the *Bacillus subtilis* developmental gene *spoVE*, under the supervision of Prof. Patrick J. Piggot.

1987-1989. Graduate Student, Gulbenkian Institute for Science. Research project: Genetic analysis of the *Bacillus subtilis* developmental gene *spoVE*, under the supervision of Prof. Hermínia de Lencastre.

External positions of responsibility:

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2005. Member of the Executive Commission for the Life Sciences Area, appointed by the Rector, for the restructuring of 2nd cycle courses in the Universidade Nova de Lisboa.

2002-2004. Member of the Steering Committee, European Science Foundation initiative on Integrated Approaches for Functional Genomics.

2002-present. Treasurer, Portuguese Society for Microbiology (SPM).

2002-present. Member of the European Union Research and Development Group on Biological and Chemical risk.

Internal positions of responsibility:

2011 - Member of the Scientific Committee, ITQB PhD course.

2009 (March)-present. Head, Biology Division, Institute for Chemical and Biological Technology (I.T.Q.B.), New University of Lisbon, Oeiras, Portugal.

2009 (March)-present. Member elected of the Institute Council, Institute for Chemical and Biological Technology (I.T.Q.B.), New University of Lisbon, Oeiras, Portugal.

2009 (March)-present. Member elected of the Pedagogic Council, Institute for Chemical and Biological Technology (I.T.Q.B.), New University of Lisbon, Oeiras, Portugal.

2009 (March)-present. Member elected of the Scientific Council, Institute for Chemical and Biological Technology (I.T.Q.B.), New University of Lisbon, Oeiras, Portugal.

2006-2009. Member (substitute) of the Scientific Advisory Committee (SAC) of the Instituto de Tecnologia Química e Biológica (ITQB).

2006- Member of the Search Committee for the new Director of the ITQB.

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2005 - Member of the Juri for a position of Technician (Técnico Superior, 2ª classe) at the ITQB. July15.

2005 - Member of the Juri for two positions of Research Assistant, at the ITQB-IGC-IBET Associate Laboratory. May 23.

2005. Organization and supervision of the Genetics and Molecular Biology (GMB) Teaching Laboratory at the ITQB.

2005 – present. Member of the Radiation Safety Committee of the ITQB.

2008 – present. Member of the Library Committee of the ITQB.

2003-2010 – Implemented and has been responsible for the following pieces of common equipment at the ITQB: Leica DMRA2 fluorescence deconvolution microscope; Storm 860, Laser Scanner; Light Cycler, Real Time PCR system; Biacore 2000, surface plasmon resonance analyzer; French Pressure Cell.

2003 - Member of the Juri for a position of Research Assistant in the discipline of Microbiology at the ITQB-IGC-IBET Associate laboratory. July 23.

2003-present. Member of the Scientific Advisory Committee (SAC) of the Instituto de Tecnologia Química e Biológica (ITQB).

2003 – **2006**. Member of the Coordinating Committee of the PhD Program at the Instituto de Tecnologia Química e Biológica (ITQB).

2003 – **present**. Member of the Radiation Safety Sub-committee of the Safety and Floor Coordinating Committee (SFCC) of the Instituto de Tecnologia Química e Biológica (ITQB).

2002 – **2006**. Organization and supervision of the Qiagen and Freezer Programs at the Instituto de Tecnologia Química e Biológica (ITQB).

1999-2002. Member of the Co-ordinating Committee of the Scientific Council of the Instituto de Tecnologia Química e Biológica (ITQB).

Teaching experience:

2011 – Organizer and lecturer, module on "Host Pathogen Interactions", Gulbenkian Program on Advanced Medical Training. Gulbenkian Institute of Science, Oeiras, December 5-9.

2011 – Invited lecturer. "Life as we know it?" IMaster Degree Course on Science Communication. *Faculdade de Ciências Sociais e Humanas*, *Universidade Nova de Lisboa*, November 14.

2011 – Co-organizer and lecturer, European Science Foundation (ESF) Networking Program "Functional Dynamics in Complex Chemical and Biological Systems"; Theme School on "Basic Experimental Techniques in Biological Dynamics". ITQB, Oeiras, September 5-9.

2011 - Lecturer on "Probiotics". Advanced Course on Chronic Inflammation and Immunomodulation (Gulbenkian Programme in Advanced Medical Training, InterUniversity Programme in Ageing, PhD Programme of the Medical School, New University of Lisbon). Course coordinator: Miguel Seabra. Lisbon, February 7-11.

2011-2012 – Lecturer on "Prokaryotic Cell Division", Graduate Program in Areas of Basic and Applied Biology (GABBA). Institute of Molecular and Cell Biology (IBMC), Porto. Course coordinator: Hélder Maiato. Porto, February 3rd.

2011 – Organizer and lecturer, module on "Host Pathogen Interactions", Gulbenkian Program on Advanced Medical Training. Gulbenkian Institute of Science, Oeiras, January 3-7.

2010 – Organizer and lecturer, module on "Host Pathogen Interactions", Gulbenkian Program on Advanced Medical Training. Gulbenkian Institute of Science, Oeiras, January 4-8.

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2010 – Lecturer on "Prokaryotic Cell Division", Graduate Program in Areas of Basic and Applied Biology (GABBA). Institute of Molecular and Cell Biology (IBMC). Course coordinator: Helder Maiato. Porto, February 3rd.

2003 – **2010**. Introductory course on **Bacterial Genetics** (BG) and Advanced course on **Microbial Development** (MD). 1st-4th Editions of the Master Course on Medical Microbiology, IHMT/FM/ITQN, UNL. Both the BG and MD courses include theoretical and practical modules.

2003 – 2010. Member of the Scientific and Coordinating Committee, Master Degree Course on Medical Microbiology, organized jointly by the Instituto de Tecnologia Química e Biológica (ITQB), the Instituto de Higiene e Medicina Tropical (IHMT), the Faculdade de Ciências Médicas (FCM), and the Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa (UNL). The course is now on its 4th edition.

2008 – present. Member of the organizing committee of the ITQB PhD Program in Chemical and Biological Sciences and Engineering. Co-coordinator of the course entitled Free Option in the present edition of the ITQB PhD Program.

2007-2008 - Experimental approaches to study protein-protein interactions. PhD Program in Computational Biology; module on *in* Protein Interaction networks. Course organizer: J. Pereira-Leal, Computational Genomics Laboratory, Gulbenkian Institute of Science, Oeiras, Portugal. March 23-27.

2005 – 2006. Member of a committee for the design and implementation of a second cycle (Master Degree) course, under the Bologna format, at the ITQB. The course, on Functional Biology, was submitted to and approved by the Direcção Geral do Ensino Superior.

2006 – Invited Professor. Gene expression and protein-protein interactions. ICRO-UNESCO, 7th Workshop on Molecular Biology and Disease. National Institute of Hygiene and Epidemiology, Hanoi, Vietnam. August, 16-30.

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2003 – Invited Professor, Portuguese Catholic University, School of Engineering. Undergraduate courses on Microbiology and on the Molecular Basis of Bacterial Pathogenesis. Degree in Health Engineering. January-April. Both courses included practicals.

2002 – Invited Professor, Portuguese Catholic University, School of Engineering. Undergraduate course on Microbiology. Degree in Health Engineering. January-April. The course included a practical component.

2001 – Invited Professor. Gulbenkian advanced course on Functional Genomics. Department of Biology, University of Aveiro, Aveiro, Portugal. September, 17-21.

2001 – Invited Professor. Course on Bioinformatics. Society of General Microbiology, 5th Workshop on Molecular Biology and Disease. Vietnam National University, Hanoi, Vietnam. August, 13-17.

2001 – Invited Professor. Master course in Advanced Biomolecular Methods, section on Methods in Functional Genomics. Departments of Chemistry and Biology, University of Aveiro, Aveiro, Portugal.

2001 – Orientation of a discussion group on the Human Genome Sequence. Ciência Viva initiative of the Portuguese Ministry of Science and Technology.

2000 – Invited Professor. Course on Molecular Biology (I). New University of Lisbon, School of Sciences and Technology, Lisbon, Portugal.

1999 – Lecturer, PhD. Course. Institute for Chemical and Biological Technology (I.T.Q.B.). New University of Lisbon, Lisbon, Portugal.

1998 - Invited Professor. Course on Genetic Engineering (II). New University of Lisbon, School of Sciences and Technology, Lisbon, Portugal.

1989 - Teaching assistant. Master in Biotechnology, Section on Prokaryotic Molecular Biology. Gulbenkian Institute of Science, Oeiras, Portugal.

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1988 - Teaching assistant. Course on “Molecular Biology of Prokaryotic Differentiation”. Advanced courses of the Gulbenkian Institute of Science. Supervision: Prof. P.J. Piggot, Prof. K.F. Chater, Prof. R. Losick, and Prof. H. de Lencastre.

1**987 -** Teaching assistant. Course on “Dopamine and Serotonine Receptors". Advanced courses, Center for Cell Biology, University of Coimbra, Coimbra, Portugal. Supervision: Prof. J. Leysen, Dr. P. Pauwels, and Prof. C. Oliveira.

1987 - Teaching assistant, course on " Na^+/H^+ and Na^+/Ca^{2+} Exchange in Lymphocytes and Nerve Cells". Advanced courses, Center for Cell Biology, University of Coimbra, Coimbra, Portugal. Supervision: Prof. S. Grinstein, and Prof. C.A.M. Carvalho.

1987 - Demonstrator, Cell Phisyology. University of Coimbra, School of Sciences and Technology, Department of Zoology. Coimbra, Portugal. Supervision: Prof. Dr. Arsélio Pato de Carvalho.

1986 - Demonstrator, Enzymology. University of Coimbra, School of Sciences and Technology, Department of Zoology. Coimbra, Portugal. Supervision: Prof. Dr. Euclides V. Pires.

Courses attended:

2002 - "BIAcore training course", BIAcore AB. Uppsala, Sweeden. May, 29-31.

1986 - "Protein Separation and Phosphorylation", Advanced Course, Center for Cellular Biology, University of Coimbra, Portugal. Supervision: Prof. A. Moir (University of Sheffield) and Prof. E. V. Pires (University of Coimbra).

1987 - "Na^+/H^+ and Na^+/Ca^{2+} Exchange in Lymphocytes and Nerve Cells", Advanced Course, Center for Cellular Biology, University of Coimbra, Portugal. Supervision: Prof. S. Grinstein and Prof. C.A.M. Carvalho (University of Coimbra).

1987 - "Dopamine and Serotonine Receptors", Advanced Course, Center for Cellular Biology, University of Coimbra, Portugal. Supervision: Prof. J. Leysen, Dr. P. Pauwels (University of Leyden) and Prof. C. Oliveira (University of Coimbra).

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1988 - "Molecular Biology of Prokaryotic Differentiation", Advanced Course of the Gulbenkian Institute of Science, Oeiras, Portugal. Supervision: Prof. P.J. Piggot (Temple University), Prof. K.F. Chater (John Innes Institute), Prof. R. Losick (Harvard University) and Prof. H. de Lencastre (University of Lisbon).

Other Professional Activities:

Ad hoc reviewer for Molecular Microbiology, the Journal of Bacteriology, Microbiology, *PNAS USA*, PLoSOne, PlosPathogens, Applied and Environmental Microbiology, Proteomics, BMC Evolutionary Biology, Journal of Proteome Research, the European Journal of Biochemistry, Biochimica Biophysica Acta, Biotechnology and Applied Biochemistry, Biotechnology and Bioengineereing, Journal of General and Molecular Microbiology, Biochimie, FEMS Letters, Vaccine, BMC Biotechnology, BMC Genomes, Research in Microbiology, Archives of Microbiology, Process Biochemistry, Food Science and Technology International, The Journal of Biotechnology, *IEEE* Electron Device Letters, The Journal of Medical Microbiology, The Journal of Microbiology, Current Microbiology, Current Biotechnology, Journal of Applied Microbiology and Biotechnology, and Extremophiles.

Ad hoc reviewer for the National Science Foundation (NSF, USA), MCB Divison (Cellular Systems).

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2012 - Member of the evaluation panel for the Portuguese Research Council, "Fundação para a Ciência e a Tecnologia" (FCT), PhD fellowships, Biological Sciences section.

Ad hoc reviewer for the Biotechnolgy and Biological Sciences Research Council (BBSRC, UK). Biochemistry and Cell Biology section.

Ad hoc reviewer for the Agence National de la Recherche, Centre National de la Recherche Scientifique (ARN, CNRS, France).

Ad hoc reviewer for the Israel Science Foundation (ISF, Israel).

Ad hoc reviewer for the European Office of Aerospace Research and Development (EOARD), Chemistry and Life Sciences Program; London, UK.

Ad hoc reviewer for the Fonds de la Recherche Scientifique (FNRS, Belgium).

Ad hoc reviewer for the Netherlands Organisation for Scientific Research (NWO), Chemical Sciences (ECHO Program: Chemistry in Relation to Biological and Medical Sciences).

Ad hoc reviewer for the Portuguese Research Council, Fundação para a Ciência e a Tecnologia (FCT.).

Ad hoc reviewer for the European Center for Disease Control and Prevention (ECDC).

Ad hoc reviewer for Agência de Inovação (ADI, Portugal).

2004 - Member of the Juri for the Pfeizer prize for young investigators, *Sociedade de Ciências Médicas de Lisboa*.

2006 – present. Consultant, DSM Nutritional Products AG, Wurmisweg 576, CH-4303 Kaiseraugust, Switzerland.

2006 – 2010. Member of the Evaluation Committee for the fellowship Program Prof. António Xavier (Fellowships for Scientific Excellency and Installation Grants for Young Scientists) of the Municipality of Oeiras. Oeiras, Portugal.

2011 - Member of the juri, High School Program on "Astrobiology and the Origin of Life. Promoted by *Ciência Viva*. Astronomic Observatory of the University of Lisbon, Lisbon, Portugal. May 2011.

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PROFESSIONAL SOCIETIES:

Portuguese Society for Biochemistry (1987-present).
Portuguese Society for Genetics (1987-present).
Portuguese Society for Microbiology (1987-present).
American Society for Microbiology (1990-present).
American Society for the Advancement of Science (1995-2000).
American Society for Biochemistry and Molecular Biology (2002-2000).
Society for General Microbiology (2002-2005).
Portuguese Society for Developmental Biology (2006-present).

AWARDS:

PhD Fellowship from the Gulbenkian Foundation, 1986.

Postdoctoral Fellowship from the J.N.I.C.T. ("Junta Nacional de Investigação Científica e Tecnológica"), 1993-1994.

Postdoctoral Fellowship from the J.N.I.C.T. ("Junta Nacional de Investigação Científica e Tecnológica") / Praxis XXI, 1995.

RESEARCH GRANTS:

Pending

Project Title: "The spore-colonic mucosa interface during infection by the human pathogen *Clostridium difficile*". Project reference: FCT-ANR/MHC-CED/0076/2012. Joint call FCT ("Fundação para a Ciência e a Tecnologia")/ANR ("Association National our la Recherche, France"). P.I.: Adriano O. Henriques. Start date: January 1st, 2013; duration: 3 years.

Project Title: "Single cell analyis of toxinogenesis and sporogenesis in the human pathogen *Clostridium difficile*". Project reference: PTDC/BIA-MIC/3304/2012, FCT. P.I.: Adriano O. Henriques. Start date: January 1st, 2013; duration: 3 years.

Project Title: "Powering Microbial Hemicellulolytic Capabilities". Project reference: PTDC/AGR-TEC/3767/2012. FCT ("Fundação para a Ciência e a Tecnologia"). P.I.: Isabel de Sá Nogueira (FCT-UNL). Start date: January 1st, 2013; duration: 3 years.

Project Title: "Imaging the structure and dynamics of molecules in living organisms". Project reference: RECI/BEX3BCM/0083/2012, FCT, equipment grant (super-resolution microscopy). P.I.: Nuno Moreno (IGC). Start date: January 1st, 2013; duration: 3 years.

Sub-contract/Research Agreement from *Astellas Pharma Europe, Ltd. , Middlesex, UK.* 2012. Detection of *Clostridium difficile* spores. NB: the research agreement includes funds for research as well as for salaries ; to be signed this year (30.000 €).

Current

Sub-contract/Research Agreement from *Adisseo France* S.A.S. 2011. Screening and identification of sporeforming bacteria with anti-*Clostridium perfringens* activity. NB: the research agreement includes funds for research as well as for salaries (50.000 €).

Project Title: "Proteomics of bacterial cell division". Project Reference: PTDC/BIA-MIC/098637/2008; FCT ("Fundação para a Ciência e a

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Tecnologia"). P.I.: D.-J. Scheffers/Adriano O. Henriques. Start date: January 1st, 2009; duration: 3 years (190.991 k€).

Project ERA-PTG/SAU/0002/2008 (ERA-NET PathoGenoMics): "PathoGenoMics of increased *Clostridium difficile* virulence". PI: Maja Rupnik (Public Health Institute Maribor, Slovenia). Start date: January 1st, 2009; duration: 3 years (181.800 k€).

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Sub-contract/Research Agreement from *DSM Nutritional Products AG*, Wurmisweg 576, CH-4303 Kaiseraugust, Switzerland. 2007. Isolation, identification, and characterization of *Sporolactobacilli* spp. NB: the research agreement includes funds for research on the characterization of wild isolates of *Sporolactobacilli* spp., as well as for salaries (20.000 €).

Project Title: Site-specific labeling of proteins by a novel type of transglutaminase isolated from spores of *Bacillus subtilis*. Project Reference: PTDC/BIO/73946/2006; FCT ("Fundação para a Ciência e a Tecnologia"). PI: Adriano O. Henriques. Start date: January 1st, 2009; duration: 3 years (end 31 de Dezembro de 2011) (87.550 €).

Current funding: 560.341 €

Previous

Project POCI/BIA-BCM/60855/2004 (FCT, "Fundação para a Ciência e a Tecnologia"): Interactions between proteins in adjacent sister cells that signal activation of RNA polymerase in response to cellular morphogenesis. P.I.: Adriano O. Henriques. (106.560 €).

Project POCTI/BCI/48647/2002 (FCT, "Fundação para a Ciência e a Tecnologia"): Dissection of a checkpoint linking chromosome segregation to asymmetric cell division at the onset of endospore development in *Bacillus subtilis*. P.I.: Dr. Adriano O. Henriques. (63.274 €).

Project PBICT/P/BIO/2003/95 ("Junta Nacional de Investigação Científica e Tecnológica"): Genetic and biochemical characterization of bioluminescence-related functions in *Bacillus subtilis* and studies on their role during sporulation. P.I.: Adriano O. Henriques. (31.424 €).

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e Biológica
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F (+351) 214411277
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Project PRAXIS/PCNA/P/BIO/61/96: Genetic and biochemical characterization of bacteriophage SPP1 portal protein function in viral morphogenesis. P.I.: Dr. Paulo E. Tavares. (67.986 €).

Project PRAXIS /P/BIO/13201/98 (FCT, "Fundação para a Ciência e a Tecnologia"): On the mechanisms governing the compartment-specific activation of σ^G during development in *Bacillus subtilis*. P.I.: Adriano O. Henriques. (99.759 €).

Project PRAXIS/PCNA/P/BIO/12306/98 (FCT, "Fundação para a Ciência e a Tecnologia"): Protein-protein and protein-DNA interactions of bacteriophage SPP1 portal protein during viral morphogenesis. P.I.: Dr. Paulo E. Tavares. (139.663 €).

Sub-contract/Research Agreement from Roche Vitamins Ltd., Grenzacherstrasse 124, CH-4070 Basel, Switzerland. (20.000 €).

Project QRLT-2000-01729 (EU, European Union): Sporebiotics, an alternative to antibiotics. Project Coordinator: Prof. Martin J. Woodward, Veterinary Laboratories Agency, Surrey, UK. (303.444 €).

Project B-41/04: Development of improved vaccination strategies against Anthrax (Anglo-Portuguese Joint Research Program, Treaty of Windsor). Dr. Adriano O. Henriques (ITQB) and Dr. Simon M. Cutting (Royal Holloway University of London).

Project POCTI/1999/BIO/BME/35109 (FCT, "Fundação para a Ciência e a Tecnologia"): Analysis of an intercellular signaling pathway coupling gene expression to morphogenesis in *Bacillus subtilis*. P.I.: Dr. Adriano O. Henriques. (124.699 €).

Subcontractor on grant **5 U19 AI056510-03** from the National Institutes of Health/ General Medical Sciences, to Prof. Vincent Fischetti (principal investigator; Rockfeller University). Project Title: Pathogen-specific drug targets for weaponized bacteria; 9/1/2004 – 8/31/2008. (79.925 €).

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Sub-contract/Research Agreement from DSM Nutritional Products AG, Wurmisweg 576, CH-4303 Kaiseraugust, Switzerland. 2006. Isolation and characterization of undomesticated *Bacillus* spp. NB: the research agreement includes funds for research on the characterization of wild isolates of *Bacillus* spp., as well as for salaries. (20.000 €).

Collaborator on grant **5 R01 GM54395-21** from the National Institutes of Health/ General Medical Sciences, to Prof. Charles P. Moran Jr. (principal investigator; Emory University, School of Medicine). Project Title: RNA Polymerase and Bacterial Differentiation; 9/1/2004 – 8/31/2008.

Project REEQ/692/BIO/2005 (FCT, "Fundação para a Ciência e a Tecnologia"): A Platform for protein expression profiling, cell mapping, and the analysis of biomolecular interactions. Re-equipment program: 1/1/2005-1/1/2006. NB: the proposal was submitted by and granted to Prof. H. de Lencastre (November 2003), and the responsibility transferred to myself at a later stage (12/4/2005). (240.000 €).

European Synchrotron Radiation Facility. Application for beam time at ESRF, Grenoble, France; C. Romão and A. O. Henriques. Project title: analysis of a bacterial synapse-like signalling complex. April, 2008.

PATENTS*:

1 - Schyns, G., A. O. Henriques, J. W. Thibaut, and S. Potot. Spore Surface Display of Bioactive Molecules. International patent with DSM Nutritional Products, Basel, Switzerland. Publication number: US2010055244 (A1); also published as: WO2008017483 (A2), WO2008017483 (A3), EP2049669 (A2). Publication date: 2010-03-04. Application number: US20070375976 20070809. Priority numbers: EP20060016599 20060809; WO2007EP07052 20070809.

2 - Henriques, A.O., C. R. Serra, G. Schyns. Probiotic. International patent with DSM Nutritional Products, Basel, Switzerland. Publication

number: WO2008110325 (A2); also published as WO2008110325 (A3). Publication date: 2008-09-18. Application number: WO2008EP01892 20080310. Priority numbers: EP20070004866 20070309.

3 - Henriques, A.O., G. Schyns. Novel gene useful for growth control of plants. International patent with DSM Nutritional Products, Basel, Switzerland. Publication number: WO2008110303 (A1). Publication date: 2008-09-18. Application number: WO2008EP01827 20080307. Priority numbers: EP20070004868 20070309.

4 - Schyns, A. O. Henriques. Sporeformers and screening for sporeformers. International patent with DSM Nutritional Products, Basel, Switzerland. Publication number: WO2008089970 (A1). Publication date: 2008-07-31. Application number: WO2008EP00498 20080123. Priority numbers: EP20070001671 20070126.

*http://v3.espacenet.com

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RESEARCH COLLABORATIONS:

1. Professor Charles P. Moran Jr. Emory University School of Medicine, Department of Microbiology and Immunology, Atlanta GA, USA. On the checkpoint that links morphogenesis to the cell type-specific activation of RNA polymerase sigma factor σ^G, and on the macromolecular assembly of the *B. subtilis* spore coat structure.
17 joint publications, 1 manuscript submitted for publication, 3 manuscripts in preparation.

2. Professor Jeffery Errington, Sir William Dunn School of Pathology, Oxford University, Oxford, UK. On the analysis of the function of the essential cell division protein DivIB in the activation of the Spo0A response regulator, the key transcription factor that governs entry into sporulation; on the link between chromosome segregation and asymmetric cell division at the onset of sporulation.
1 joint publication, 1 manuscript in preparation.

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3. Dr. Ezio Ricca, Department of General and Environmental Physiology, University Federico II, Naples, Italy. On the protein-protein interactions underlying assembly of the CotB and CotC spore coat proteins, and on the isolation and characterization of new sporeforming *Bacillae*.
4 joint publications, 1 manuscript submitted for publication, 1 manuscript in preparation.

4. Dr. Simon M. Cutting, Reader in Molecular Microbiology, School of Biological Sciences, Royal Holloway University of London, Egham, Surrey, UK**.** On the isolation and characterization of new sporeforming *Bacillae* with potential uses as Probiotics, and on the development of a new vaccine against anthrax.
2 joint publications; 1 manuscript in preparation.

5. Dr. Paulo Tavares, Laboratoire de Virologie Moléculaire et Structurale, CNRS, Gif-sur-Yvette, France. On the genetic analysis of the role of bacteriophage SPP1 portal protein at different stages in viral morphogenesis. We have obtained the first high resolution functional map of a portal protein, and in combination with the crystal structure of the portal oligomer, proposed mechanistic models for its involvment in DNA packaging and viral morphogenesis.
3 joint publications.

6. Prof. Maria Arménia Carrondo, Protein Crystallography Group, Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Oeiras, Portugal. On the structural characterization of bacterial spore coat proteins. Together, we have described the first crystal structure of a bacterial spore coat component.
3 joint publications.

7. Dr. Cláudio M. Soares, Protein Modelling Group, Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Oeiras, Portugal. On the modeling of: i) structural components of the bacterial endospore coat structure; ii) the cell wall-binding domain of the SafA and

SpoVID morphogenetic proteins; iii) complexes between the SpoIIAB anti-sigma factor and the σ^G transcription factor.
2 joint publications; 1 manuscript submitted for publication.

8. Dr. Uwe Völker, Philipps-Universität Marburg and Max Planck Institut für Terrestrische Mikrobiologie, Marburg, Germany. On the use of DNA arrays to characterize the transcriptome of sporulating cells of *B. subtilis*, and on the structural proteomics of the spore coat organelle. Prof. Völker has been involved in the identification of proteins isolated from 1D and 2D gels (including those present in protein complexes) by MALDI-TOF and LC-MS/MS.
4 joint publications.

9. Prof. M. J. Woodward, Veterinary Laboratories Agency, Addlestone, Surrey, UK. On the isolation and characterization of gut sporeformers with potential uses as Probiotics. The Laboratory of Prof. Woodward performs in vivo tests to evaluate the safety and efficacy of spore preparations.
1 joint publication.

10. Prof. Manuel J. T. Carrondo/António Cunha, Director and CEO, Instituto de Biologia Experimental e Tecnológica (IBET)/Director, IBET's Pilot Plant. On the optimization of methods for the large-scale production of *Bacillus subtilis* spores.
1 joint publication.

11. Dr. Elizabeth J. Harry, Department of Biochemistry. The University of Sydney, Sydney, Australia. On the function of *B. subtilis* cell division protein DivIB during both vegetative (medial), and sporulation (asymmetric) cell division.
2 joint publication; 1 manuscript submitted for publication.

12. Prof. Alexander Tomasz, Microbiology Laboratory, The Rockefeller University, New York, USA. On the functional analysis of genes coding for peptidoglycan deacetylases in pathogenic *Bacillus cereus*. To formalize

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our collaboration, Prof. Tomasz has kindly proposed my appointment as an Adjunct Assistant Professor at the Rockefeller University.
2 joint publication; 1 manuscript in preparation.

13. Dr. Ghislain Schyns and Dr. John B. Perkins, DSM Nutritional Products AG, Wurmisweg 576, CH-4303 Kaiseraugust, Switzerland. On the genetic mapping of mutations causing increased production of thiamin; on the characterization of *Bacillus* spp. strains with potential uses as Probiotics.
2 joint publications; 1 manuscript submitted; 4 patents.

14. Dr. Kit Pogliano, University of California, San Diego, CA, USA. On the analysis of analysis of the coupling between the phagocytic-like process of prespore engulfment and the cell-type specific activation of a developmental transcription factor of *Bacillus subtilis*.
1 manuscript in preparation.

15. Dr. Jonathan Dworkin, Columbia University, New York, NY, USA. On the sub-cellular localization and interactions of a developmental-specific SEDS protein of *Bacillus subtilis*.
1 publication.

16. Dr. David M. Rudner, Harvard Medical School, Department of Microbiology and Molecular Genetics University, Boston, MA, USA. On the mother cell to prespore siganling during development in *Bacillus subtilis*.
1 manuscript in preparation.

17. Dr. Jan Maarteen van Dijl, Groningen University Medical Center, Department of Microbiology and Molecular Genetics University, Boston, MA, USA. On the mother cell to prespore siganling during development in *Bacillus subtilis*.
1 manuscript in preparation.

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18. Dr. Philippe Noirot, INRA Medical School, Department of Microbiology and Molecular Genetics University, Boston, MA, USA. On the mother cell to prespore siganling during development in *Bacillus subtilis*.
1 manuscript in preparation.

19. Dr. Patrick Eichenberger, Center for Genomics and Systems Biology, Department of Biology, New York University, New York, N.Y., USA. Systems biology of spore coat assembly in *Bacillus subtilis* and related organisms.
1 manuscript published; 1 manuscript in preparation.

20. Murielle Salomé, European Synchrotron Radiation Facility, Grenoble, France, and Dr. Célia Romão, INRA Medical School, Department of Microbiology and Molecular Genetics University, Boston, MA, USA. X-ray microscopy of Bacillus spores.
1 manuscript in preparation.

21. Dr. José Pereira-Leal. Computational Biology Group, Instituto Gulbenkian de Ciência. Oeiras, Portugal. On the origin of the endosporulation program, and on the structure, function and evolution of the spore surface layers.
2 manuscripts in preparation; 1 public database (SporedB) on the structure, function and composition of the bacterial spore surface layers.

22. Dr. Célia Romão. ITQB. On the characterization of the metal content of bacterial spores by X-ray microscopy.

23. Dr. Manolis Matzaptakis. NMR Group, ITQB. On the characterization of protein-protein interactions and protein structures by NMR spectroscopy.

24. Dr. Cláudio Gomes. Protein Folding and Stability, ITQB. On the characterization of Flavin-containing spore surface proteins, and on the

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F (+351) 214411277
E: aoh@itqb.unl.pt
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thermal stability of key surface components of the bacterial spore surface layers.
2 manuscripts in preparation.

25. Dra. Rita Abranches. Plant Genome stability and Plant Biotechnology, ITQB. On the production of spore surface components in plant cells.
2 manuscripts in preparation

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26. Dra. Christine Jacobs-Wagner. Department of Cellular and Molecular Biology, Yale University. Hew Have, CT, USA. On the characterization of a core component (RodZ) of the bacterial morohogenetic apparatus.
1 paper published; 2 manuscripts in preparation.

27. Dr. Maja Rupnik. Institute of Public Health Maribor, Centre for Microbiology, Maribor, Slovenia. Consortium on the characterization of the sporulation and germination properties, in vitro and in vivo, of *Clostridium difficile* strains with increased virulence potential.

28. Dr. Bruno Dupuy. Institut Pasteur, Paris, France. Consortium on the characterization of the sporulation and germination properties, in vitro and in vivo, of *Clostridium difficile* strains with increased virulence.

29. Dr. Frederic Barbut. Faculté de Médecine Pierre et Marie Curie, Paris, France. Consortium on the characterization of the sporulation and germination properties, in vitro and in vivo, of *Clostridium difficile* strains with increased virulence potential.

30. Dr. Alexander Indra. Austrian Agency for Health and Food Safety, Vienna, Austria. Consortium on the characterization of the sporulation and germination properties, in vitro and in vivo, of *Clostridium difficile* strains with increased virulence potential.

31. Prof. Wolfgang Liebl. Technische Universität München, Munich, Germany. Consortium on the characterization of the sporulation and

germination properties, in vitro and in vivo, of *Clostridium difficile* strains with increased virulence potential.

32. Dr. Ralf Möller. German Aerospace Center, Institute of Aerospace Medicine, Radiation Biology Division, Research Group 'Astrobiology', Köln, Germany. On the survival of bacterial spores in simulated extraterrestrial conditions.

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F (+351) 214411277
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SUPERVISION OF RESEARCH PROJECTS:

Undergraduate Thesis

Gonçalo Bruno Ferreira Real Rodrigues de Carvalho. "Structure-function studies of the *B. subtilis* cell-shape determinant SpoVE". November, 1999. G.R. was the recipient of a PRODEP fellowship (nº1/3.2/PRODEP/99).

Rita Leonor Álvares Cabral de Figueiredo Fior. "Characterization of the *ybcS* locus of *B. subtilis* and its role in the compartment-specific activation of σ^G during spore development". November, 2000. R.F. was the recipient of a PRODEP fellowship (nº1/3.2/PRODEP/2000). R.F. is now a PhD Student at School of Medicine, University of Lisbon.

Alexandre Alves Neves. "Isolation and molecular characterization of mutations in the *spoIIIG* gene of *Bacillus subtilis*". November, 2001. A.N. was the recipient of a PRODEP fellowship (nº1/3.2/PRODEP/2001). A.N. is now a PhD student at the Fred Hutchinson Cancer Research Center, Seattle, W.

Susana Faleiro Leal. (Erasmus Student, Université Paris VII, Paris, France). "Role of the *yocH* locus in the macromolecular assembly of the *Bacillus subtilis* endospore coat structure". S.L. was the recipient of fellowships from the "Conseil Régional de L´Ile de France", and from the ERASMUS Program (2001). Co-supervision with Dr. Rita Zilhão, Laboratory of Microbial Development.

Nguyen Huy Hoang. "Characterization of a reticulline oxidase and a patatin-like phospholipase associated with the *Bacillus subtilis* endospore coat structure". February, 2003. N.H.H. was the recipient of a BTI fellowship (010A/BIC/2002). N.H.H. is currently head of the Laboratory of Soil Microbiology, Institute of Biotechnology, Vietnam Academy of Science and Technology, Hanoi, Vietnam.

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Cláudia Serra. "Characterization of gut sporeformers". March, 2003. C.S. was the recipient of a BIC fellowship (008/BIC/2003). Co-supervision with Dr. Teresa Barbosa, Laboratory of Microbial Development.

Filipe Jorge Garrett Vieira. "The σ^G checkpoint: the functional interaction between the *spoIIIA* and *spoIIIJ* loci of *Bacillus subtilis*". September 2003-September 2004. S.P. is presently a PhD student in the Department of Genetics, University of Barcelona, Barcelona, Spain.

Sérgio Filipe Morgado Pinto. "The functional map of a SEDS (shape, elongation, division, and sporulation) protein from *Bacillus subtilis*". October 2003-October 2004. S.P. is presently a PhD student in the Laboratory of Prof. Michael Hengartner, at the Institute for Molecular Biology, University of Zurich, Zurich, Switzerland.

Ana Margarida Almeida. "Requirement for the GTPase activity of morphogenetic protein SpoIVA in spore coat assembly". Volunteer. October 2006-December 2006. A.M.A. is currently a PhD student at the Pasteur Institute, Paris, France, in the Laboratory of Dr. Philippe Sansonetti.

Catarina Fernandes. "Site-specific labeling of proteins in vitro and at the cell surface by a transglutaminase isolated from the *Bacillus subtilis* spore coat". Diploma Student. October 2006-December 2006.

João Paulo Gonçalves de Almeida. "Interactions among integral membrane components of a *Bacillus subtilis* cell-cell signaling complex". Volunteer. October 2007-December 2008.

Joana Rodrigues. "Control of cell shape in *Bacillus subtilis*: over-production, purification and analysis of the cytoplasmic and extra-cytoplasmic domains of morphogenic protein RodZ". Diploma Student, Escola Superior Agrária, Coimbra, Portugal. December 2008-December 2009.

2010 (Jan-Jun) - Curso Extensão Universitária. Project: Control of cellular morphogenesis by a conserved cytoskeletal-associated bacterial component.

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Joana Lopes. "Functional analysis of the genes for a sortase and a collagen-binding adhesin in a gut isolate of *Bacillus subtilis*". BII Fellowship. September 2009-September 2010.

Lia Domingues. "The interaction between the SpoIVA NTPase and the tropomyosin-like protein SpoVID of *Bacillus subtilis*". Volunteer. September 2007-September 2008.

Carolina Pissarra Cassona. "Functional analysis of the conserved core of bacterial endosporulation genes". BII Fellowship. September 2009-September 2010.

Tomás Cruz. "Cloning and overproduction of the cell type-specific sporulation sigma factors of *Clostridium difficile*". Visiting student from the University of Newcastle, UK. July-September, 2011.

Maria Teresa Ribeiro Maio. "Functional analysis of the conserved core of bacterial endosporulation genes". BII Fellowship (ref. 043/BI-BI/2011; Project in collaboration with Adisseo France, SA). July - December, 2011.

Lluis FausCortes. "Probing the genetic circuitry that restricts the ectopic activation of a cell type-specific auto-regulatory sigma factor of *B. subtilis*". Visiting student from the University of Valencia, Spain. July-September, 2011.

Gabriela Azevedo Pires Drabek. "Activity of Tgl variants". Diploma student, Universidade Lusófona, Lisbon, Portugal. October 2011-July 2012.

Master Degree Thesis

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Joana Santos. "Protein-protein interactions that signal activation of RNA polymerase in response to cellular morphogenesis". Master in Medical Microbiology, IHMT/FM/ITQB. September 2004-September 2005 (ISBN 978-989-20-0304-7). J.S. defended her Thesis on October 26th, 2006. J. S. is presently a PhD student in the Laboratory of Dr. E. J. Harry, at the Department of Microbiology, Technical University of Sydney, Sydney, Australia.

Pedro Gonçalo Alves da Costa Rodrigues. "Role of the Sec translocon in cell-cell communication during spore development in *Bacillus subtilis*". Master in Medical Microbiology, IHMT/FM/ITQB. September 2006-September 2007. P.R. defended his Master Degree Thesis on June 17, 2010. P.R is presently a technician of Pathologic Anatomy, at the Department of Molecular Biology, Hospital de Santa Maria, Lisbon, Portugal.

Carla Graciete Ribeiro Esteves. "Interactions of DivIB at the onset of spore development in *Bacillus subtilis*". Master in Medical Microbiology, IHMT/FM/ITQB. September 2006-September 2007.

Lia Domingues. "Interactions in the assembly of a molecular machine that drives assembly of the spore coat structure in *Bacillus subtilis*". Master in Medical Microbiology, IHMT/FM/ITQB. September 2008-September 2009. L.D. defended her Thesis on November 25th, 2009. She is presently a PhD student in the Laboratory of Dr. Jaime Mota, Laboratory of Infection Biology, ITQB-UNL.

João Pedro Vieira Bota. "Role of Transcription/repair coupling factor in the cell type-specific activation of a transcription factor during development in *Bacillus subtilis*". Master in Medical Microbiology, IHMT/FM/ITQB. July 2010-September 2011.

Ana Margarida Oliveira Paiva. "Function and interactions of a the core cytoskeletal component RodZ in *Bacillus subtilis*". Master in Medical Microbiology, IHMT/FM/ITQB. July 2010-September 2011.

Carolina Freitas. "Enforcing compartmentalized gene expression in *Bacillus subtilis*". Volunteer, 1st year Master in Microbiology and Genetics, FCT-UNL. September 2012-September 2013.

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Ph.D Thesis

Anabela Lopes Isidro. "Caracterização da função da proteína portal do bacteríofago SPP1 de *Bacillus subtilis* na formação do pro-capsídeo e durante a encapsidação o DNA". A.I. holded a Ph.D fellowship (PRAXIS XXI/BD/13345/97) from "Fundação para a Ciência e a Tecnologia" (FCT). Co-supervision with Dr. Paulo Tavares, Gif-sur-Yvette.

A.I. got her Ph.D degree from the ITQB-UNL on June 7th, 2002. She was a post-doctoral fellow at the Unité de Virologie Molécularie et Structurale, CNRS, Gif-sur-Yvette, France, and is now a post-doc at the Gulbenkian Institute of Science.

Mónica Paula Fernandes Serrano. "Genetic analysis of the σ^G checkpoint during development in *Bacillus subtilis*". M.S. holds a Ph.D fellowship (PRAXIS XXI/BD/18251/98) from the FCT.

M.S. got her Ph.D degree (from the ITQB) on July 12th, 2004 (ISBN 972-9119-07-4). M.S. is currently a post-doctoral fellow at the Microbial Development Laboratory, ITQB.

Gonçalo Bruno Ferreira Real Rodrigues de Carvalho. "Role of cell division protein DivIB in the activation of the response regulator Spo0A at

the onset of sporulation in *Bacillus subtilis*". G.R. holds a fellowship (SFRH/BD/21560/99) from the FCT.

G.R. got his PhD Degree from the ITQB-UNL on December 15, 2005 (ISBN 972-9119-07-4). He is presently a post-doc in the Microbial Development Group at the ITQB.

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F (+351) 214411277
E: aoh@itqb.unl.pt
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Teresa Parente Madureira de Vasconcelos Costa. "Role of the CotE and SpoVID morphogenetic proteins in the macromolecular assembly of the *B. subtilis* endospore coat structure". T.C. holds a Ph.D fellowship (SFRH/BD/1167/00) from the FCT.

T.C. got her PhD Degree from the ITQB-UNL, on December 13, 2005 (ISBN 989-20-0073-0). T.C. did a post-doc in the Laboratory of Dr. Christine Jacobs-Wagner at the Department of Molecular, Cellular, and Developmental Biology, Yale University, USA.

Maria Luísa Gouveia e Freitas Côrte. "Convergent signalling of σ^G activation in *Bacillus subtilis*". L.C. holds a Ph.D fellowship (SFRH/BD/6489/01) from the FCT.

Sandro Filipe Fernandes Pereira. Penicillin-binding proteins in the cell cycle of *Staphylococcus aureus*". S.P. holds a Ph.D fellowship (SFRH/BD/9185/02) from the FCT. S.P. was also funded, for part of the time, by a Grant (79108) from the Gulbenkian Foundation. Co-supervision with Prof. Alexander Tomasz, and Prof. Hermínia de Lencastre, ITQB and The Rockfeller University.

S.P. got his PhD Degree from the ITQB-UNL, on December 2, 2008. He is currently a post-doctoral fellow in the Laboratory of Prof. J. Dworkin, Columbia University, New York, N.Y., U.S.A.

Alexandre Alves Neves, ITQB Internal supervisor. "Identification and characterization of Notch downstream effectors that act in pharynx induction in *C. elegans*". Thesis supervisor: Prof. James Priess, Fred Hutchinson Cancer Research Center, Seattle, USA.

Cláudia Serra. "Extra- and intracellular signaling governing sporulation initiation in undomesticated *Bacillus subtilis*". C.S. holds a Ph.D fellowship (SFRH/BD/29397/06) from the FCT.

Diana Plácido. "Structural characterization of a *B. subtilis* spore coat-associated transglutaminase". D.P. holds a Ph.D fellowship (SFRH/BD/14384/03) from the FCT. Co-supervision with Prof. Maria Arménia Carrondo, and Dr. Margarida Archer, Protein Crystalography Group, ITQB.

D.P. got her PhD Degree from the ITQB-UNL, on February 26, 2008 (ISBN 978-989-1003-8). She is presently working for the McKinsey consultancy and IP company in Madrid, Spain.

Patrícia Inácio. vvvvvv vvvv vvvv vvvvvvvv vvvvv vvvvvv vvvvv vvvvvv vvvvv vvvvv vvv.

Catarina Fernandes. "Biology and applications of a bacterial protein cross-linking enzyme". October 1st, 2008. C.F. holds a Ph.D fellowship (SFRH/BD/29397/06) from the FCT. Start date: October 1st, 2008.

Assunta Pelosi. "Mapping the interaction between CotB and CotG during their assembly onto the surface layers of *Bacillus subtilis* spores". A.P. was a visiting scientist from the University Federico II, Naples, Italy.

Fátima Pereira. "Sporulation as a virulence factor in *Clostridium difficile*". October 1st, 2008. F.P. holds a Ph.D fellowship (SFRH/BD/45459/08) from the FCT.

Filipa Nunes. "Analysis of a membrane-associated tripartite molecular machine that drives assembly of the bacterial spore surface layers". Start date: October 1st, 2009. Co-supervision with Dr. Mónica Serrano. F.N. holds a Ph.D. fellowship (SFRH/BD/64470/2009) from the FCT.

Wilson Antunez. "Analysis of the *Clostridium difficile* spore surface layers". W.A. joins the Microbial Development Group to conduct his PhD studies under a cooperation protocol with the Microbiology Laboratory of

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the Portuguese Army. Co-supervision with Dr. Mónica Serrano. Start date: January 1st, 2012.

Patrícia Cátia Isidoro de Amaral. "Genes expressed in vivo in probiotic, undomesticated strains of *Bacillus subtilis*". P.A. joins the Microbial Development Group in the framework of a collaboration with *Lallemand* Inc. Co-supervision with Dr. Teresa Costa. Start date: January 1st, 2012.

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Post-doctoral fellows and senior researchers of the Laboratory

Dr. Leonor Oliveira. "Function of bacteriophage SPP1 portal protein during DNA packaging". Post-doctoral fellowship (044/BPD/2000) from "Fundação para a Ciência e a Tecnologia" (FCT). Co-supervisor with Dr. Paulo Tavares, Gif-sur-Yvette. L.O. is presently a post-doctoral researcher at the Unité de Virologie Molécularie et Structurale, CNRS, Gif-sur-Yvette, France.

Dr. Teresa Barbosa. "Isoaltion and characterization of aerobic gut sporeformers". Post-doctoral fellowship (031/BPD/2002) from "Fundação para a Ciência e a Tecnologia" (FCT). T. B. is since October 2006, a Lecturer in Microbiology at the University of Cork, Cork, Ireland.

Dr. Rita Zilhão. "Mechanism of assembly of spore coat protein CotB of *Bacillus subtilis*". Dr. R. Zilhão is a Professor of Molecular Biology in the Department of Plant Biology, Universidade de Lisboa, Lisbon, Portugal.

Dr. Lígia O. Martins. "Studies on the characterization of the spore coat-associated CotA laccase of *Bacillus subtilis*". Dr. L. Martins is Professor of Microbiology at Universidade Lusófona de Humanidades e Tecnologias, Lisbon, Portugal.

Dr. Rachele Isticato. "The developmentally-regulated transglutaminase-dependent cross-linking of *B. subtilis* spore coat protein components". Dr. R. Isticato got her PhD degree from the Universitá Federico II, Naples, Italy. Co-supervision with Dr. R. Zilhão (ITQB).

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Dr. Mónica Serrano. 2004-2007 - "Functional analysis of the genes for peptidoglycan deacetylases in pathogenic *Bacillus*, and their roles in sporulation and virulence". Post-doctoral fellowship (SFRH/BPD/14966/2004) from "Fundação para a Ciência e a Tecnologia" (FCT). Project in collaboration with Prof. Alexander Tomasz, Laboratory of Microbiology, The Rockfeller University, New York, NY. 2007-present - "Dissection of a cell-cell synapse-like signaling complex in developing cells of *Bacillus subtilis*". Post-doctoral fellowship (SFRH/BPD/36328/200) from the FCT.

Dr. Anabela Lopes Isidro. "Structure and function of the LysM domain in relation to spore morphogenesis in *Bacillus subtilis*". A.I. holds a post-doctoral fellowship (SFRH/BPD/8967/2002) from "Fundação para a Ciência e a Tecnologia" (FCT). Start date: February 2005 (until June 2009). A.I. presently holds a Ciência 2008 position at the Laboratory of Virology, School of Veterinary Sciences, Technical University of Lisbon, Lisbon, Portugal.

Dr. Gonçalo Bruno Ferreira Real Rodrigues de Carvalho. "Role of cell division protein DivIB in the activation of the response regulator Spo0A at the onset of sporulation in *Bacillus subtilis*". G.R. holds a post-doctoral fellowship (SFRH/BPD/20668/2004) from the FCT. G.R. is presently a Program Manager at the Antibodies Unit, IBET, Oeiras, Portugal.

Dr. Ana Filipa Valente. "Molecular architecture and function of cell-cell signaling complexes that coordinate *Bacillus subtilis* spore development". A.F.V. holds a post-doctoral fellowship (SFRH/BPD/26470/2006) fom the FCT. F.V. is presently a post-doctoral fellow in the Department of Biology, University of Minho, Portugal. P.I.: Dr. Margarida Casal.

Teresa Parente Madureira de Vasconcelos Costa. "Identification and characterization of novel factors controlling asymmetric cell division during *Bacillus subtilis* sporulation". T.C. holds a Post-doctoral fellowship (SFRH/BPD/26232/06) from the FCT. Start date: July 15th, 2008.

Tiago dos Vultos Santos. "Analysis of the sporulation and germination pathways of the nosocomial pathogen *Clostridium difficile*". T.V.S. holds a Post-doctoral fellowship from the ITQB. Start date: July 23rd, 2008.

Tiago Vasconcelos Duarte Moreira Pais. "*The role of hub proteins in the macromolecular assembly of a bacterial organellar structure*". Post-doctoral fellowship applied for (FCT, refª. SFRH/BPD/92006/2012). 27/06/2011.

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THESIS EXAMINATIONS

2000 – Examiner of the Ph.D Thesis Dissertation presented by Ivo Gomperts Boneca to the ITQB, entitled "Cell wall biosynthesis and β-lactam resistance in *Staphylococcus aureus*". August, 2000.

2000 – Examiner of the Ph.D Thesis Dissertation presented by Luís Jaime Mota to the ITQB, entitled "Molecular mechanism of induction of the arabinose regulon in *Bacillus subtilis*". May, 2000.

2000 – Examiner of the Ph.D Thesis Dissertation presented by Maria Margarida Dias Duarte to the ITQB, entitled "Molecular basis of virulence and hemadsorption in the portuguese isolates Lisboa 60 and Lisboa 689 of the African swine fever vius". October, 2000.

2001 – Main Examiner of the Ph.D Thesis Dissertation presented by Gabriela de Medeiros Silva to the ITQB, entitled "Genes contained in two DNA fragments of *Desulfovibrio gigas* genome: molecular characterization of the metalloproteins rubredoxin-oxygen oxidoreductase and neelaredoxin". October, 3.

2001 – Main Examiner of the Ph.D Thesis Dissertation presented by Gabriela Gomes de Pinho to the ITQB, entitled "Methicillin resistance in *Staphylococcus aureus*". October, 12.

2001 – External examiner of the Ph.D Thesis Dissertation presented by Gabriella Casula to the Royal Holloway University of London, entitled "Use of *Bacillus subtilis* spores as vaccines". October, 21.

2001 – Main examiner of the Master Thesis Dissertation presented by Helena da Conceição Pereira Albano to the Instituto Superior Técnico, Universidade Técnica de Lisboa, Portugal, entitled "Cloning and functional analysis of the *gelC* and *gelE* genes involved in the biosynthesis of gelan by *Sphingomonas paucimobilis*". March, 6.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

2002 – Examiner of the Ph.D Thesis Dissertation presented by Anabela Lopes Isidro to the ITQB, entitled "Characterization of the function of *Bacillus subtilis* bacteriophage SPP1 portal protein in viral assembly and DNA encapsidation". June, 7.

2003 – Examiner of the Ph.D Thesis Dissertation presented by Luís Jorge Camilo Maranga to the ITQB, entitled "Engineering challenges in the production of VLPs". February, 28.

2004 – External examiner of the Ph.D Thesis Dissertation presented by Tran Cat Dong to the Royal Holloway University of London, entitled "Intercompartmental Signaling of Pro-σ^K processing in *Bacillus subtilis*". March, 19.

2004 – Examiner of the Ph.D Thesis Dissertation presented by Dulce Alexandra Alves Lobo da Costa Azevedo to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Sensing thiol-reactive compounds by the bZIP transcription factors Yap2 and Yap1 in the yeast *Sacharomyces cerevisae*". July, 7.

2004 – Examiner of the PhD Thesis Dissertation presented by Nuno Formiga Borges to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Role of Mannosylglycerate in Thermo- and Osmo-Adaptation of *Rhodothermus marinus*: biosynthesis, regulation and applications". July 9.

2004 – Examiner (supervisor) of the PhD Thesis Dissertation presented by Mónica Paula Fernandes Serrano to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Analysis of the σ^G checkpoint during development in *Bacillus subtilis*". July 12.

2004 – External examiner of the Ph.D Thesis Dissertation presented by Mattew J. Johnson to the University of Sheffield, entitled "The function of ExsY and CotY, two structural proteins of the *Bacillus cereus* exosporium". July, 27.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

2005 – Examiner (supervisor) of the PhD Thesis Dissertation presented by Mónica Paula Fernandes Serrano to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Analysis of the σ^G checkpoint during development in *Bacillus subtilis*". December, 13.

2005 – Examiner (supervisor) of the PhD Thesis Dissertation presented by Teresa Costa to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Assembly of the *Bacillus subtilis* spore coat". Dec., 13.

2005 – Examiner (supervisor) of the PhD Thesis Dissertation presented by Gonçalo Real to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Cell division and chromosome segregation in *Bacillus subtilis*". December, 15.

2005 – Member of the Juri of the Ph.D Thesis Dissertation presented by Tracy Nevitt to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Towards understanding the functional role of Yap4 in the yeast response to hyper osmolarity". December, 20.

2006 – Examiner (supervisor) of the Juri of the Master Thesis Dissertation presented by Joana Santos to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "A region in *Bacillus subtilis* transcription factor σ^G targeted by a negative regulator that prevents its ectopic expression". November, 14.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

2006 – Member of the Juri of the PhD Thesis Dissertation presented by Susana Gardete to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Towards the understanding of the mechanism of methicillin resistance in *Staphylococcus aureus*". June, 20.

2006 – Member of the Juri of the PhD Thesis Dissertation presented by Rita Sobral to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Modulating *Staphylococcus aureus* cell physiology through a murein ligase". November, 22.

2007 – President of the Juri of the PhD Thesis Dissertation presented by Clara Correia dos Reis to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Study of Trf4 and Trf5 in *Sacharomyces cerevisae*: poly(A) polymerases with a function in histone homeostasis". January, 12.

2007 – Member of the Juri of the PhD Thesis Dissertation presented by Lénia Marisa Pereira Rodrigues to the School of Medicine, Universidade de Lisboa, entitled "Modulação de factores celulares de troca de nucleótidos da família VAV por Gama-herpesvírus". January, 22.

2008 – President of the Juri, Master Degree Thesis Dissertation presented by Natália Faria to the School of Medicine, Universidade de Lisboa, entitled "Modulação de factores celulares de troca de nucleótidos da família VAV por Gama-herpesvírus". January, 22.

2008 – President of the Juri, Master Degree Thesis Dissertation presented by Joana Filipa da Silva Costa to the School of Medicine, Universidade de Lisboa, entitled "Infecção nosocomial por *Legionella pneumophila* serogrupo 1: estudo epidemiológico". September, 26.

2008 – Member of the Juri, PhD Degree Thesis Dissertation presented by Catarina de Certima Fernandes Homem to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Regulation of Cadherin-based cell adhesion and its interaction with the cytoskeleton". October, 17.

2008 – President of the Juri, Master Degree Thesis Dissertation presented by Joana Filipa da Silva Costa to the Instituto de Tecnologia Química e Biológica, Universidade de Lisboa, entitled "Infecção Nosocomial por *Legionella pneumophila* serogrupo 1: Estudo Epidemiológico". September, 26th.

2008 – President of the Juri, Master Degree Thesis Dissertation presented by Ana Catarina Heitor Martins Cardoso to the Instituto de Tecnologia Química e Biológica, Universidade de Lisboa, entitled "Efluxo de substâncias fluorescentes através da parade de Escherichia coli: correlação com a resistência fenotípica aos antibióticos em estirpes de origem clínica". December, 3rd.

2008 – President of the Juri, Master Degree Thesis Dissertation presented by Maria Margarida Horta Soares Lobão Serejo to the Instituto de Tecnologia Química e Biológica, Universidade de Lisboa, entitled "Detecção de *Legionella* spp. em amostras clínicas por reacção em cadeia da polimerase em tempo real". November, 17th.

2009 – President of the Juri, Master Degree Thesis Dissertation presented by Helena Isabel Ribeiro Nunes to the Instituto de Tecnologia Química e Biológica, Universidade de Lisboa, entitled "*Chlamydia trachomatis* em populações de risco: detecção de anticorpos e de DNA". February, 27th.

2009 – Member of the Juri, PhD Degree Thesis Dissertation presented by Nuno Moreno to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Oscillatory behavior in pollen tubes: the biophysical and biochemical fundamental basis of cell grwoth and morphogenesis". July 30th.

2009 - Member of the Juri, PhD Degree Thesis Dissertation presented by Rute de Almeida Ferreira de Castro to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled "Sugar Metabolism in Lactococcus lactis: Glucose Transporters and a Novel α-Phosphoglucomutase". September, 18th.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

2009 – Main examiner, Master Degree Thesis Dissertation presented by Mário José Rodrigues Ferreira to the School of Sciences and Technology, Universidade Nova de LIsboa, entitled: “Utilization of arabinose-containing polysaccharides by *Bacillus subtilis*: transport and metabolism”. November, 24th.

2009 - Member of the Juri (supervisor) of the Master Thesis Dissertation presented by Lia Domingues Santos to the Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, entitled “Interactions in the assembly of a molecular machine that drives assembly of the spore coat structure in *Bacillus subtilis*”. Master in Medical Microbiology, IHMT/FM/ITQB. November, 25th.

2010 - Member of the Juri of the PhD Thesis Dissertation presented by Paulo Durão to the Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, entitled “CotA-laccase from *Bacillus subtilis*: stucture-function studies of catalytic copper centers". ITQB-UNL, Oeiras, April 12st.

2010 - Member of the Juri of the PhD Thesis Dissertation presented by Ana Almeida (Pasteur Institute, Paris) to the Universidade de Lisboa, entitled “Role of carbon catabolite repression (CCR) in the pathogenicity of *Clostridium difficile*". UL, Lisbon, May 3rd.

2010 - Member of the Juri (supervisor) of the Master Thesis Dissertation presented by Pedro Gonçalo Alves da Costa Rodrigues to the Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, entitled “Role of the Sec translocon in cell-cell communication during spore development in *Bacillus subtilis*”. Master in Medical Microbiology, IHMT/FM/ITQB. June, 17th.

2010 - Member of the Juri (supervisor) of the PhD Thesis Dissertation presented by Sébastien Potot to the ITQB, Universidade Nova de Lisboa, entitled “Metabolic and morphogenetic engineering of *Bacillus subtilis*: biotechnology for industry” (ISBN 978-989-96988-1-9). November, 5th.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

S.P. is currently a principal investigator at DSM Nutritional Products, Basel, Switzerland.

2010 - Member of the Juri (supervisor) of the PhD Thesis Dissertation presented by Zita Carvalho dos Santos to the ITQB, Universidade Nova de Lisboa, entitled “Integrative study on centrosome biogenesis and function”. November, 12th. Supervisor: Dra. Mónica Bettencourt Dias, Instituto Gulbenkian de Ciência.

2010 - Main examiner, "Estágio de Investigação Científica”, Daniela Isidoro (Supervisors: Cláudio Gomes, Bárbara Henriques). Studies on ETF clinical mutants. Instituto de Tecnologia Química e Biológica. December, 10.

2010 - Member of the Juri, "Bolsa de Integração na Investigação, BII”, Carolina Cassona (Supervisors: Mónica Serrano, Adriano O. Henriques). “Function and Intercations of two lipases of the *Bacillus subtilis* spore surface”. Instituto de Tecnologia Química e Biológica. Outubro, 29.

2010 - Member of the Juri, "Curso de Extensão Universitária”, Joana Rodrigues (Supervisors: Teresa Costa, Adriano O. Henriques). “Estudo da ologomerização dos domínios citoplasmático e extra-celular da proteína morfogenética RodZ”. Instituto de Tecnologia Química e Biológica. December, 10.

2011 - External examiner, PhD Thesis presented by Rok Lenarcic to the University of Newcastle, U.K., entitled “Role of MinD and related proteins in chromosome partitioning during sporulation in *Bacillus subtilis*”. Supervisors: Dr. Ling Wu and Dr. Leendert Hamoen. Center for Bacterial Cell Biology, Institute for Cell and Molecular Biosciences, University of Newcastle, UK. February, 12th.

2011 - Main examiner, Master Degree Thesis presented by Ana Rita Ladeira Courelas da Silva, to the School of Sciences and Technology, Universidade Nova de Lisboa (FCT-UNL), entitled “Importância do complexo mediador na actividade transcricional do Yap8”. Supervisors: Dr. Regina Menezes and Prof. Dra. Claudina Rodrigues-Pousada. October, 31th.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

2011 - Member of the Juri, PhD Thesis presented by Alexandra Simões, to the ITQB, Universidade Nova de Lisboa, entitled "Insights into the epidemiology of drug-resistant *Streptococcus pneumonia* and closely-related streptococci in the era of conjugate vaccines". Supervisors: Dra. Raquel Sá-Leão and Prof. Dra. Hermínia de Lencastre. December, 6.

2012 - Member of the Juri, PhD Thesis presented by Ana Lúcia Carvalho Machado, to the ITQB, Universidade Nova de Lisboa, entitled "Metabolic Engineering of *Lactococcus lactis* for Improved Tolerance to Acid Stress: guidelines from *in vivo* NMR analysis of glucose metabolism". Supervisor: Prof. Dra. Helena Santos. January, 30.

2012 - Member of the Juri, PhD Thesis presented by Ana Lúcia Carvalho Machado, to the ITQB, Universidade Nova de Lisboa, entitled "Metabolic Engineering of *Lactococcus lactis* for Improved Tolerance to Acid Stress: guidelines from *in vivo* NMR analysis of glucose metabolism". Supervisor: Prof. Dra. Helena Santos. January, 30.

2012 - Member of the Juri, PhD Thesis presented by Inês Manuel Bento Mendes Pinto, to the ITQB, Universidade Nova de Lisboa, entitled "Spatiotemporal mechanisms for actomyosin ring assembly and contraction in budding yeast cell division". Supervisor: Prof. Rong Li (Stowers Institute for Medical Research, Kansas City, USA). March, 19.

2012- Member of the Juri, PhD Thesis presented by Liliana S. Batista Nascimento, to the ITQB, Universidade Nova de Lisboa, entitled "Yeast as a model system to study genetic and post-translational regulation of metabolic pathways in mammals". Supervisors: Prof. Claudina Rodrigues-Pousada (ITQB-UNL) and Dennis J. Thiele (Duke University Medical Center, USA). June, 19.

2012 - Main examiner, PhD Thesis presented by Filipa Bravo Nunes, to the School of Medicine, Universidade de Lisboa, entitled "Modulação da activação da célula T *helper* $CD4^+$ na sinapse imunológica por gamaherpesvírus". Supervisor: Prof. Pedro Simas (SM-UL). September, 18.

2012 - Member of the Juri, PhD Thesis presented by Pedro Arêde Rei, to the School of Sciences, Universidade Nova de Lisboa, entitled "On the track of β-lactam resistance: Studies on the regulation of methicillinresistance in *Staphylococcus aureus*". Supervisors: Dr. Duarte Oliveira (FCT-UNL) and Prof. H. de Lencastre (ITQB-UNL and the Rockefeller University, USA). November, 16.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

PhD THESIS COMMITTEES

2006 – Catarina Sim-Sim Pereira (BD/28543/06). AI-2 Quorum sensing: its function in bacterial inter-species communication. Supervisor: Karina Xavier (ITQB/IGC). C.P. obtained her PhD degree from the ITQB, on July 8th, 2011.

2007 – Teresa Carla de Almeida Figueiredo (BD/36843/07). Exploring the lipid phase of peptidoglycan synthesis and cell wall turnover in *Staphylococcus aureus*. Supervisors: Hermínia de Lencastre (ITQB/ Rockefeller), Ana Madalena Ludovice (FCT-UNL), Rita Sobral (Rockefeller), Alexander Tomasz (Rockefeller).

2009 – Sofia Venceslau (BD/30648/06). Study of the novel membrane proteins and cofactors involved in sulphate respiration. Supervisors: Inês Cardoso Pereira (ITQB), Lígia Saraiva (ITQB). S.V. obtained a PhD degree from the ITQB, on December 15, 2011.

2009 – Liliana Sofia Batista-Nascimento (BD/39389/07). Characterization of the roles played by Yap1 and Yap2 in the detoxification of the metalloid arsenic in *Saccharomyces cerevisiae*. Supervisors: Claudina Rodrigues-Pousada (ITQB), Dennis Thiele (Duke University). L.N. obtained her PhD degree from the ITQB, on June 18th, 2012.

2009 – Ana Maria da Silva Esteves (BD/61742/09). Unravelling the regulatory mechanisms in thermo-adaptation of hyperthermophilic *archae*. Supervisors: Helena Santos (ITQB), Nuno Borges (ITQB).

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

2009 – Diego de Oliveira Hartmann (BD/66396/09). Bioelectricity production for accelerated bioremediation. Supervisors: Ricardo Louro (ITQB), Cristina Silva Pereira (ITQB).

2010 – Maria Isabel Lopes Correia (BD/29469/06). Assembly of AraR-DNA complexes and gene regulation in *Bacillus subtilis*. Supervisor: Isabel Sá Nogueira (FCT-UNL).

2011 - Maria Inês Ramos Grilo (SFRH/BD/70162/2010). Extracellular DNA in *S. aureus* - roles and mechanisms. Supervisor: Hermínia de Lencastre (ITQB/UNL, The Rockefeller University); co-supervisors**:** Ana Madalena Ludovice (ITQB/UNL, FCT/UNL), Rita Sobral (ITQB/UNL, CREM-FCT/UNL).

2012 - Débora Alexandra Tavares (SFRH/BD/70147/2010). The nasopharyngeal ecosystem: studies on the nature of bacterial intersepcies competion. in *S. aureus* - roles and mechanisms. Supervisors: Hermínia de Lencastre (ITQB/UNL, The Rockefeller University); Raquel Sá-Leão (ITQB/UNL).

ORGANIZATION OF SEMINARS AND MEETINGS:

2001 – Scientific Committee, Meeting of the Portuguese Society for Microbiology, Micro´2001. Póvoa do Varzim, Portugal. December, 5-8.

2001 – FEBS Forum of Young Scientists. Protein Structure-Function, Trafficking, and Signaling. Instituto de Tecnologia Química e Biológica, Oeiras, Portugal. June 28-30.

2003 – Organizing and Scientific Committees, Meeting of the Portuguese Society for Microbiology, Micro´2003. Tomar, Portugal, November 2003.

2004 – Organizing and scientific Committee, 1st European Spores Conference, Bratislava, Slovakia, June 17-21.

2006 – Organizing and scientific Committee, 2nd European Spores Conference, Bratislava, Slovac Republic, June 17-21.

2006 – Scientific Committee, and co-chair of the Symposium on Microbial Physiology and Genetics, XV National Congress of Biochemistry, Universidade de Aveiro, Aveiro Portugal, December 8-10.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

2008 – Organizing and Scientific Committees, 3rd European Spores Conference. Naples, Italy, April 21-23.

2011 - Organizing and Scientific Committee, European Science Foundation (ESF) Networking Program "Functional Dynamics in Complex Chemical and Biological Systems"; Theme School on "Basic Experimental Techniques in Biological Dynamics". ITQB, Oeiras, September 5-9.

2011 - Local Organizing Committee, The Great Wall Meeting. Cascais, Portugal, September 9-12.

2012 - Scientific Committee. XXXVII Jornadas Portuguesas de Genética. Lisbon. May 28-30.

2000-2012 – Organization of several research seminars at the ITQB. Invited speakers included: Prof. Charles P. Moran Jr. (Emory University, Atlanta, GA, USA), Dr. Ezio Ricca (University Federico II, Naples, Italy), Dr. Simon M. Cutting (Royal Holloway University of London, London, UK), Prof. Marion Hullet (University of Chicago, Chicago, IL, USA), Prof. Phil Matsumura (University of Chicago, Chicago, IL, USA), Prof. Kelly Hughes (University of Washington, Seattle, WA), Dr. Leonor Oliveira (CNRS, Gif-sur-Yvette, France), Prof. Mike Manson (Texas A&M University, TX, USA), Prof. Liz Harry (University of Sydney, Sydney, Australia), Dr. Uwe Voelker and Dr. Leif Steil (Max Planck Institut for Terrestrial Microbiology and University of Marburg, Marburg, Germany), Dr. Christophe Quétard (Biacore AG, Sweden), Dr. Ghislain Schyns (DSM Nutritional Products, Basel, Switzerland); Prof. Philippe Sansonetti (Institut Pasteur, Paris); Prof. Corné Pieterse (Utrecht University).

RESEARCH INTERESTS

Several bacteria can form specialized cell types to cope with harsh environmental conditions including extreme starvation. Endospores (herein referred to as spores) formed by ancient lineages of bacteria such as those of the Clostridium and Bacillus genera are the most resistant of these cell types. Bacterial spores can survive most environmental challenges that would promptly kill vegetative (undifferentiated) cells of the same species, or other bacterial forms. Moreover, they can remain in a dormant stage by periods in excess of millions of years.

Spore formation is the result of a developmental process initiated by the asymmetric division of the sporangial cell, followed by the engulfment of the smaller compartment, or prespore, by the larger mother cell. The mother cell then altruistically directs the assembly of several protective layers that encase the developing spore, and lyses at the end of the process to release a free mature spore into the environment. At the onset of the process, the bacterial chromosome is replicated and one copy segregated into the prespore compartment. Soon after the asymmetric partitioning of the sporangium, compartment-specific gene expression ensues, first in the prespore, and shortly after in the mother cell chamber.

Differential gene expression is maintained by a cascade of RNA polymerase sigma (σ) subunits, specifically activated in either the prespore or the mother cell, which direct the core enzyme to specific classes of promoters. The compartment-specific activation of each σ factor alternates between the two cell types, in a criss-cross pattern, as it relies on signals that emanate from the sibling cell. These cell-cell signaling pathways ensure that the programs of gene expression in the mother cell and in the prespore are kept in register. Moreover, the activation of the successive σ factors also responds to morphological cues that signal the completion of key intermediate cellular structures in spore morphogenesis. As the result, the prespore and mother cell lines of gene expression are tightly coupled to the course of morphogenesis. The regulatory circuits that couple gene expression to morphogenesis are called checkpoints, and are essential for the fidelity of the morphogenetic process.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
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Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
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The study of asymmetric cell division and the concomitant establishment of compartment-specific gene expression, cell-cell communication, checkpoint regulation, and morphogenesis of complex cellular structures are central to cellular and developmental biology. In the model organism *B. subtilis*, for which the genome sequence is known since 1997, the study of these problems is facilitated by the involvement of only two cell types in the developmental process, as well as by the existence of a plethora of highly sophisticated genetic tools. The genetic approach is complemented by biochemical and cell biological methodologies, to produce an integrated view of the developmental process. Cell biology methods (e.g., fluorescence deconvolution or confocal microscopy) are particularly important, as they allows us to unravel the dynamic behaviour of proteins or other cellular components, as well as the mechanisms underlying their targeting to specific subcellular localizations during the cell and developmental cycles. Our two main lines of fundamental research deal with the study of **developmental checkpoints**, and the control of **cellular morphogenesis**. Specifically, we are interested in the study of two checkpoints, one linking chromosome segregation to asymmetric cell division at the onset of sporulation, and the other coupling the activation of the late prespore-specific transcription regulator σ^G to the complete engulfment of the prespore by the mother cell.

Activation of σ^G following engulfment completion triggers the morphogenesis of the main protective structures of the spore. The outermost of these structures is the spore coat, formed by the ordered assembly of over 30 protein components. Coat biogenesis is a model system for the assembly of complex multiprotein structures during a developmental process, but it also allows the study of the mechanisms by which proteins or protein assemblies are targeted to specific sub-cellular locations, in this case to the surface of the developing spore.

Other lines of work in the Laboratory have a more applied angle. For example, the identification of domains of coat proteins that contain the determinants for assembly permits the construction of chimaeras for the display of enzymes or heterologous antigens at the spore surface. One Project in course deals with the use of *Bacillus subtilis* spores (non-pathogenic) for the display of subunits of the anthrax toxins, and the potential use of the recombinant **spores as vaccines**. In another example, we have isolated a large collection of aerobic sporeforming bacteria associated with the gastrointestinal tract of various animals, and are characterizing them in view of a potential application in **probiosis**. We

found undomesticated isolates of *Bacillus subtilis* to differ greatly from the Laboratory strains currently in use, and to produce a wide array of antimicrobial compounds, including several with bacteriolytic activity against important pathogens. We have been actively characterizing some of the B. subtilis undomesticated isolates, and one in particular, whose genome was sequenced in collaboration with the Swiss company DSM. These studies have illuminated several previously unrecognized aspects of the biology of B. subtilis, because many important traits have been attenuated through domestication. Our work has produced insight into a biphasic life-style, in which the organism cycles between the gut and the soil, as well as into the genomic and regulatory alterations that have accompanied the process of domestication.

Several *Bacillus* and *Clostridium* species are important pathogens, and the ability to form highly resistant spores is a key component of their pathogenic behaviour, as the spore is often the infectious vehicle. One line of work in the group deals with the characterization of key aspects of the biology of *B. cereus*, namely the functional characterization of the genes coding for **peptidoglycan (PG) deacetylases**. These enzymes are potential virulence factors, since deacetylated PG is more resistant to the hydrolytic action of host lysozyme. In work to be published we have shown that the inactivation of a forespore expressed gene in a strain of ***B. cereus*** that is an accepted surrogate for ***B. anthracis*** results in normal-looking and fully resistant spores that nevertheless are unable to germinate and resume active growth. The protein coded for by this gene, *pdaA*, is therefore a potential target for spore inactivation. More recently, we have begun manipulating ***C. difficile*** in the laboratory. This organism has emerged as one of the major causes of nosocomial infections and is also increasingly represented in community-acquired infections. Some of the most damaging epidemic clones of *C. difficile* show an augmented frequency of sporulation, which is presumably associated with their persistance in the environment (including hospitals settings), and infection ability. Taking advantage of recently developed tools for the genetic manipulation of *C. difficile*, and specifically the use of **type II introns** for the construction of insertional mutants, we have initiated a program to examine in detail the factors governing entry into sporulation and the function of the main effectors of spore morphogenesis in this organism.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

PUBLICATIONS:

Citation Indexes:

Citations for '**Adriano O. Henriques**' (all/since 2007): **2278/1435**
Cited Publications/total: **49/71**
H-Index: **25/18**
i10-Index: **48/37**

Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

1 - Carvalho, A. P., M. S. Santos, A. O. Henriques, P. Tavares, and C. M. Carvalho. 1988. **Calcium Channels and Na^{+}/Ca^{2+} exchange in synaptosomes**. **In "Cellular and Molecular Basis of Synaptic Transmission" (Zimmermann, H., *ed.*), pg. 264-284. Springer-Verlag, Berlin and Heidelberg.**

2 - Henriques, A. O., P. Tavares, and C. A. M. Carvalho. 1988. Measurement of membrane potentials in synaptosomes. *Ciência Biológica*, 13:15-25.

3 - Joris, B., G. Dive, A. O. Henriques, P. J. Piggot, and J.-M. Ghuysen. 1990. The life-cycle proteins RodA of *Escherichia coli* and SpoVE of *Bacillus subtilis* have very similar primary structures. *Mol. Microbiol.*, 4:513-517.

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F (+351) 214411277
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New University of Lisbon

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F (+351) 214411277
E: aoh@itqb.unl.pt
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T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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F (+351) 214411277
E: aoh@itqb.unl.pt
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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

(*) by invitation.

Presenting author is underlined.

ABSTRACTS:

Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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Instituto de Tecnologia Química
e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

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e Biológica
New University of Lisbon
T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
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F (+351) 214411277
E: aoh@itqb.unl.pt
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F (+351) 214411277
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F (+351) 214411277
E: aoh@itqb.unl.pt
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F (+351) 214411277
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F (+351) 214411277
E: aoh@itqb.unl.pt
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Presenting author is underlined.

Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

Microbial Development Group
ITQB-UNL

REFERALS

PROFESSOR Hermínia de Lencastre

Instituto de Tecnologia Química e Biológica
Universidade Nova de Lisboa
Avenida da Republica, Apartado 127
2781-901 Oeiras Codex, Portugal

and Laboratory of Microbiology
The Rockefeller University
1230 York Avenue
New York, NY 10021-6399, USA

Tel: + 01 212 327 8278
Fax: + 01 212 327 8688
Email: lencash@mail.rockefeller.edu

Instituto de Tecnologia Química
e Biológica
New University of Lisbon

T (+351)214469522
F (+351) 214411277
E: aoh@itqb.unl.pt
www.itqb.unl.pt

PROFESSOR Charles P. Moran Jr.

Emory University School of Medicine
Department of Microbiology
and Immunology
3010 Rollins Research Center
Atlanta GA 30322, USA

Tel: + 01 404-727 5969
Fax: + 01 404-727 3659
Email: moran@microbio.emory.edu

PROFESSOR Patrick J. Piggot

Temple University School of Medicine
Department of Microbiology
and Immunology
1400 North Broad Street
Philadelphia, PA 19140, USA

Tel: + 01 212-327 8278
Fax: + 01 212-327 8688
Email: piggot@astro.temple.edu