

## MARGARIDA DUARTE AMARAL



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### OVERVIEW

Articles in international peer-reviewed journals	90
Book chapters	4
Average impact factor	5.239
Books edited	2
Total ISI (Web of Knowledge) citations:	1,442
Total Google Scholar citations:	2,318
Organizer of international conferences	26
Invited international conferences/ seminars	> 100
Total no. of grants (as PI)	25 (13)
Total budget in grants	2.8M€
Poster communications (team members)	~300
Published peer-reviewed abstracts	~120
Patents	3
Teaching Experience	43 semesters (average: 9.3h /week)
PhD supervisions (ongoing)	16 (+3)
Post-docs supervisions (ongoing)	15 (+4)
H-Index	22   29 Res ID (E-5748-2012)   Google Scholar
i10 <sup>1</sup> -index	56

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<sup>1</sup> i10-index is the number of publications with at least 10 citations.

## ACADEMIC/SCIENTIFIC BACKGROUND

- Jul 2006 "Habilitation" to the title of "**Professor Agregado**", Area of **Chemistry**, Sub-area of **Biochemistry**, Univ Lisboa, Portugal. Unanimously Approved. Course proposal: "Human Molecular Biology from a Systems Biology Perspective".
- 1993 PhD in **Biochemistry/Molecular Genetics**, Univ Lisboa, Portugal & Gulbenkian Institute of Science (Oeiras, Portugal). Supervisor: Prof Claudina Rodrigues-Pousada. Final mark: *summa cum laude*. Thesis: "Stress Proteins: Induction and Regulation in *Tetrahymena pyriformis*".
- 1986 MSc (equiv) in **Biochemistry**, Univ Lisboa, Portugal & Gulbenkian Institute of Science (Oeiras, Portugal). Supervisor: Prof Claudina Rodrigues-Pousada. Final mark: *summa cum laude*. Thesis: "The Response of the Protozoan *Tetrahymena pyriformis* to a Stress Agent: Sodium Meta-Arsenite".
- 1982 BSc in **Chemistry/Biochemistry**, Univ Lisboa Portugal. Work carried out as undergraduate research student at the Faculty of Medical Sciences, New University of Lisboa, Portugal. Final mark: 17/20. Thesis: "Lipid Content of Liver and Blood Plasma of Hepatomized Rats".

## POSITIONS/TRAINING

- Jul 2013 - Full Professor of Biochemistry/ Molecular Biology. Dept of Chemistry & Biochemistry, Faculty of Sciences, University of Lisboa.
- Sept 2012- - Coordinator of the Research Centre BioFiG- Centre for Biodiversity, Functional and Integrative Genomics.
- Aug 08- Jul 10 - Visiting fellow (2-year sabbatical) at the Pepperkok group, European Molecular Biology Laboratory, Heidelberg (Germany) to coordinate EU project TargetScreen2.
- 2007 - Founding member of Research Centre BioFiG- Centre for Biodiversity, Functional and Integrative Genomics, University of Lisboa (Portugal) and head of Membrane Protein Disorders Unit.
- Since 2006 - Assistant Professor with "Habilitation" (Biochemistry), Fac Sciences, Univ Lisboa.
- 2006-2011 - Coordinator of the Cystic Fibrosis Research Unit, Centre of Human Genetics of the National Institute of Health, Lisboa (Portugal)
- 1993/2006 - Assistant Professor, Faculty Sciences, Univ Lisboa, Portugal (tenure: 1998).  
- Invited Researcher at the Centre Human Genetics, National Institute of Health and Head of Cystic Fibrosis Research Group since May 2005.
- 1986/1993 - Teaching Assistant, Dept. Chemistry & Biochemistry, Faculty of Sciences, University of Lisboa.  
- Graduate student at the Gulbenkian Institute of Science, Oeiras, Portugal.
- 1983/1986 - Trainee Teaching Assistant, Dept. Chem & Biochemistry, Faculty of Sciences, University of Lisboa.  
- Graduate student at the Gulbenkian Institute of Science, Oeiras, Portugal.

## RESEARCH INTERESTS

Study of human disease mechanisms associated with membrane proteins. Particular focus has been on the molecular and cellular mechanisms of the autosomic genetic disease Cystic Fibrosis (CF). Most of my research has been aimed at understanding the molecular mechanisms that retain the CFTR (CF transmembrane Conductance Regulator) protein with the most frequent mutation in patients (F508del) in the endoplasmic reticulum (ER). Indeed, through manipulation of these ER quality control mechanisms, which involve multiple intervenients, namely molecular chaperones, we could enable some mutant protein to escape its ER retention and thus restore (even if partially) Cl<sup>-</sup> transport at the cell membrane, with substantial benefit for CF patients.

My research has also focused on the characterization of other CFTR gene mutations, namely on the effect of CF-causing mutations at the level of: 1) affecting processing of mRNA (splicing and nonsense-mediated decay); 2) intracellular trafficking defects due to protein misfolding and

endoplasmic reticulum (ER) quality control, involving molecular chaperones; and 3) translating knowledge from the basic science into the clinical practice, namely diagnosis, prognosis and therapeutics. A major emphasis has been on the assessment of basic cellular defects in **fresh native tissues** (collected from patients), namely, nasal epithelial cells and rectal biopsies.

**Transcriptomics** and **proteomics** projects have also been underway in the lab to better understand CF pathophysiology and also, in collaboration with nanoelectronics centres, towards the development of novel chips (based on magnetic sensors) for the quick and cheap diagnosis of CF. I am also involved in pharmacological projects (elucidation of the mechanism of action of compounds) and genomic (**human artificial chromosomes**) approaches to CF therapy.

Recent work on **genome-wide functional genomics** has been carried out through EU-project TargetScreen2 (*Novel post-genomics cell-based screens for drug targeting in membrane protein disorders*) in collaboration with EMBL (Heidelberg and other partners, including 4 companies). The goal was to identify and characterize proteins involved in the traffic/function of three model proteins, namely: CFTR, the epithelial Na<sup>+</sup> channel ENaC and the G-protein coupled receptor (GPCR) melanocortin 4 receptor (MC4R) and to identify novel small-molecules that correct the defects associated with these membrane proteins.

## **PUBLICATIONS**

### *Articles in International Peer-Reviewed Journals [impact factor as per 2012]*

1. Beekman JM, Sermet-Gaudelus I, de Boeck K, Gonska T, Derichs N, Mall MA, Mehta A, Martin U, Drumm M, Amaral MD (2014) CFTR Functional Measurements in Human Models For Diagnosis, Prognosis and Personalised Therapy. *J Cyst Fibros.* In Press.
2. Luz S, Cihil KM, Brautigan DL, Amaral MD, Farinha CM, Swiatecka-Urban A (2014) LMTK2 Mediated Phosphorylation Regulates CFTR Endocytosis in Human Airway Epithelial Cells. *J Biol Chem.* Apr 11. Epub ahead of print. [PMID: [24727471](#)]. IF: **4.651**.
3. Xu Z, Pissarra LS, Farinha CM, Liu J, Cai Z, Thibodeau PH, Amaral MD, Sheppard DN (2014) Revertant mutants modify, but do not rescue, the gating defect of the cystic fibrosis mutant G551D-CFTR. *J Physiol.* Mar 31. Epub ahead of print [PMID: [24591578](#)]. IF: **4.384**.
4. Almaça J, Faria D, Sousa M, Uliyakina I, Conrad C, Sirianant L, Clarke LA, Martins JP, Santos M, Hériché JK, Huber W, Schreiber R, Pepperkok R, Kunzelmann K, Amaral MD (2013) High-content siRNA screen reveals global ENaC regulators and potential cystic fibrosis therapy targets. *Cell* **154**, 1390-1400. [PMID: [24034256](#)]. IF: **31.957**.
5. Masvidal L, Igreja S, Ramos MD, Alvarez A, de Gracia J, Ramalho AS, Amaral MD, Larriba S, Casals T (2013) Assessing the residual CFTR gene expression in human nasal epithelium cells bearing CFTR splicing mutations causing Cystic Fibrosis. *Eur J Hum Genet.* Oct 16. doi: 10.1038/ejhg.2013.238. Epub ahead of print. [PMID: [24129438](#)]. IF: **4.319**.
6. Sosnay PR, Siklosi KR, Van Goor F, Kaniecki K, Corey M, Ramalho AS, Amaral MD, Dorfman R, Masica DL, Karchin R, Sharma N, Lewis MH, Yu H, Thomas PJ, Millen L, Zielenski, J Patrinos GP, Castellani C, Rommens JM, Penland CM, Cutting GR (2013) Defining the disease-liability of mutations in the cystic fibrosis transmembrane conductance regulator gene. *Nat Genet* **45**: 1160-7 [PMID: [23974870](#)]. IF: **35.209**.
7. Silva MC, Amaral MD, Morimoto RI (2013) Neuronal Reprogramming of Protein Homeostasis by Calcium-Dependent Regulation of the Heat Shock. *PLoS Genet.* 9(8): e1003711. [PMID: [24009518](#)]. IF: **8.517**.
8. Farinha CM, King-Underwood J, Sousa M, Correia AR, Henriques MJ, Roxo-Rosa M, Da Paula AC, Williams J, Hirst S, Gomes CM, Amaral MD (2013) Revertants, Low Temperature, and Correctors Reveal the Mechanism of F508del-CFTR Rescue by VX-809 and Suggest Multiple Agents for Full Correction. *Chem Biol* **20**, 943-55. [PMID: [23890012](#)]. IF: **6.157**.
9. Farinha CM, Matos P, Amaral MD (2013) Control of CFTR membrane trafficking: not just from the ER to the Golgi. *FEBS J* **280**, 4396-406. [PMID: [23773658](#)]. IF: **4.250**.
10. Amaral MD, Farinha CM (2013) CFTR Post-translational Modifications and Signalling: Lessons from a Model Protein and Roles in Cystic Fibrosis Disease. *FEBS J* **280**, 4396-406. [PMID: [23680006](#)]. IF: **4.250**.
11. Servidoni MF, Sousa M, Vinagre AM, Cardoso SR, Ribeiro MA, Meirelles L, Carvalho RB, Kunzelmann K, Ribeiro AF, Ribeiro JD, Amaral MD (2013) Rectal Forceps Biopsy Procedure in

Cystic Fibrosis: Technical Aspects and Patients Perspective for Clinical Trials Feasibility. *BMC Gastroenterology* **13**, 91. [PMID: [23688510](#)]. IF: **2.110**.

12. Clarke LA, Sousa L, Amaral MD (2013) Transcriptomic changes in native nasal epithelium expressing F508del-CFTR and contrasting data from comparable studies. *Respir Res* **14**, 38. [PMID: [23537407](#)]. IF: **3.642**. ["Highly accessed" article, as defined by the journal].
13. Amaral MD, Farinha CM (2013) Rescuing mutant CFTR: a multi-task approach to a better outcome in treating Cystic Fibrosis. *Curr Pharm Des* **19**, 3497-508. [PMID: [23331027](#)]. IF: **3.311**.
14. Tian Y, Schreiber R, Wanitchakool P, Kongsuphol P, Sousa M, Uliyakina I, Palma M, Faria D, Traynor-Kaplen AE, Fragata JI, Amaral MD, Kunzelmann K (2013) Control of TMEM16A by INO-4995 and other inositolphosphates. *Br J Pharmacol* **168**, 253-65. [PMID: [22946960](#)]. IF: **5.067**.
15. De Boeck K, Kent L, Davies J, Derichs N, Amaral M, Rowe S, Middleton P, de Jonge H, Bronsveld I, Wilschanski M, Melotti P, Danner-Boucher I, Boerner S, Fajac I, Southern K, de Nooijer R, Bot A, de Rijke Y, de Wachter E, Leal T, Vermeulen F, J Hug M, Rault G, Nguyen-Khoa T, Barreto C, Proesmans M, Sermet-Gaudelus I. [On behalf of the European Cystic Fibrosis Society Clinical Trial Network Standardisation Committee] (2013) CFTR biomarkers: time for promotion to surrogate endpoint? *Eur Respir J* **41**, 203-216 [PMID: [22878883](#)]. IF: **6.355**.
16. Tosoni K, Stobart M, Luz S, Cassidy DM, Pagano M, Venerando A, Amaral MD, Kunzelmann K, Pinna L, Farinha CM, Mehta A (2013) CFTR mutations altering CFTR fragmentation. *Biochem J* **449**, 295-305. [PMID: [23067305](#)]. IF: **4.654**.
17. Moniz S, Sousa M, Moraes B, Mendes AI, Palma M, Barreto C, Fragata JI, Jordan P, Amaral MD\*, Matos P\* (2013) HGF stimulation of Rac1 signaling enhances pharmacological correction of the most prevalent Cystic Fibrosis mutant F508del-CFTR. *ACS Chem Biol* **8**, 432-42. \*Shared senior authorship. [PMID: [23148778](#)] IF: **5.442**.
18. Amaral MS (2012) Finding new medicines to fight CF: multiple steps of a success story. *Orphanet J Rare Dis* **7S2**, A19. IF: **5.442**
19. Sousa M, Servidoni MF, Vinagre AM, Ramalho AS, Bonadia LC, Felício V, Ribeiro MA, Uliyakina I, Marson FA, Kmit A, Cardoso SR, Ribeiro JD, Bertuzzo CS, Sousa L, Kunzelmann K, Ribeiro AF, Amaral MD (2012) CFTR-mediated Cl<sup>-</sup> Secretion in Human Rectal Biopsies is a Robust Biomarker for Cystic Fibrosis Diagnosis and Prognosis. *PLoS One* **7**, e47708. [PMID: [23082198](#)]. IF: **3.730**.
20. Mendes F, Farinha CM, Felício V, Alves PC, Vieira I, Amaral MD (2012) BAG-1 Stabilizes Mutant F508del-CFTR in a Ubiquitin-Like-Domain-Dependent Manner. *Cell Physiol & Biochem* **30**, 1120-1133. [PMID: [23178238](#)]. IF: **3.415**.
21. Li H, Yang W, Mendes F, Amaral MD, Sheppard DN (2012) Impact of the cystic fibrosis mutation F508del-CFTR on renal cyst formation and growth. *Am J Physiol Renal Physiol* **303**, F1176-86. [PMID: [22874761](#)]. IF: **3.612**.
22. Faria D, Lentze N, Almaça J, Luz S, Alessio L, Tian Y, Martins JP, Cruz P, Schreiber R, Farinha CM, Auerbach D, Amaral MD, Kunzelmann K (2012) Differential regulation of biogenesis of ENaC and CFTR by the stress response protein SERP1. *Pflügers Arch Eur J Physiol* **463**, 819-27. [PMID: [22526458](#)] IF: **4.866**.
23. Silva MC, Fox S, Thakkar H, Beam M, Amaral MD, Morimoto RI (2011) A Genetic Screening Strategy Identifies Novel Regulators of the Proteostasis Network. *PLoS Genetics* **7**, e1002438. [PMID: [22242008](#)]. IF: **8.517**.
24. Luz S, Kongsuphol P, Mendes AI, Romeiras F, Sousa M, Schreiber R, Matos P, Jordan P, Mehta A, Amaral MD, Kunzelmann K, Farinha CM (2011) The contribution of CK2 and spleen tyrosine kinase (SYK) to CFTR trafficking and PKA-induced activity. *Mol Cell Biol* **31**, 4392-404. [PMID: [21930781](#)]. IF: **5.372**.
25. Roth EK, Hirtz S, Duerr J, Wenning D, Eichler I, Seydewitz HH, Amaral MD, Mall MA (2011) The K<sup>+</sup> Channel Opener 1-EBIO Potentiates Residual Function of Mutant CFTR in Rectal Biopsies from Cystic Fibrosis Patients. *PLoS ONE* **6**, e24445. [PMID: [21909392](#)] IF: **3.730**.
26. Martins JR, Kongsuphol P, Sammels E, Daimène S, Aldehni F, Clarke L, Schreiber R, de Smedt H, Amaral MD, Kunzelmann K (2011) F508del-CFTR increases intracellular Ca<sup>2+</sup> signaling that causes enhanced Ca<sup>2+</sup>-dependent Cl<sup>-</sup> conductance in cystic fibrosis. *Biochim Biophys Acta Mol Basis Dis* **1812**, 1385-92. [PMID: [21907281](#)] IF: **4.910**.

27. Mendes AI, Matos P, Moniz S, Luz S, Amaral MD, Farinha CM, Jordan P (2011) Antagonistic Regulation of CFTR Cell Surface Expression by the Protein Kinases WNK4 and Spleen Tyrosine Kinase. *Mol Cell Biol* **31**, 4076-86. [PMID: [21807898](#)]. IF: **5.372**.
28. De Boeck K, Derichs N, Fajac I, de Jonge HR, Bronsveld I, Sermet I, Vermeulen F, Sheppard DN, Cappens H, Hug M, Melotti P, Middleton PG, Wilschanski M & ECFS Diagnostic Network Working Group. EuroCareCF WP3 Group on CF diagnosis] (2011) New clinical diagnostic procedures for cystic fibrosis in Europe. *J Cyst Fibros* **10 Suppl 2**, S53-66. [PMID: [21658643](#)] IF: **3.190**.
29. Amaral MD, Lukacs GL. (2011) Introduction to Section III: Biochemical Methods to Study CFTR Protein. *Methods Mol Biol* **741**, 213-8. [PMID: [21594787](#)].
30. Ramalho AS, Clarke LA, Amaral MD (2011) Quantification of CFTR Transcripts. *Methods Mol Biol* **741**, 115-35. [PMID: [21594782](#)].
31. Amaral MD (2011) Introduction to section III: resources for CFTR research. In: Cystic Fibrosis Protocols and Diagnosis. *Methods Mol Biol* **742**, 281-3. [PMID: [21547739](#)].
32. Almaça J, Dahimène S, Appel N, Conrad C, Kunzelmann K, Pepperkok R, Amaral MD (2011) Functional genomics assays to study CFTR traffic and ENaC function. In: Cystic Fibrosis Protocols and Diagnosis. *Methods Mol Biol* **742**, 249-64. [PMID: [21547737](#)].
33. Ramachandran S, Clarke LA, Scheetz TE, Amaral MD, McCray PB Jr (2011) Microarray mRNA expression profiling to study cystic fibrosis. *Methods Mol Biol* **742**, 193-212. [PMID: [21547734](#)].
34. Faria D, Dahimène S, Alessio L, Scott-Ward T, Schreiber R, Kunzelmann K, Amaral MD (2011) Effect of Annexin A5 on CFTR: regulated traffic or scaffolding? *Mol Membr Biol* **28**, 14-29. [PMID: [21067452](#)]. IF: **3.130**.
35. Amaral MD (2011) Targeting CFTR: How to Treat Cystic Fibrosis by CFTR-Repairing Therapies. *Curr Drug Targets* **12**, 683-93. [PMID: [21039334](#)]. IF: **3.848**.
36. Da Paula AC, Sousa M, Xu Z, Dawson ES, Boyd AC, Sheppard DN, Amaral MD (2010) Folding and rescue of a CFTR trafficking mutant identified using human - murine chimeric proteins. *J Biol Chem* **85**, 27033-44. [PMID: [20551307](#)]. IF: **4.651**.
37. Rocchi L, Braz C, Cattani S, Ramalho A, Christian S, Edlinger M, Laner A, Kraner S, Amaral MD, Schindelhauer D (2010) *E. coli* cloned CFTR loci relevant for human artificial chromosome therapy. *Hum Gene Ther* **21**, 1-16. [PMID: [20384480](#)]. IF: **4.019**.
38. Ramalho AS, Lewandowska M, Farinha CM, Mendes F, Gonçalves J, Barreto C, Harris A, Amaral MD (2009) Deletion of CFTR translation start site reveals functional isoforms of the protein in CF patients. *Cell Physiol & Biochem* **24**, 335-346. [PMID: [19910674](#)]. IF: **3.415**.
39. Scott-Ward TS, Amaral MD (2009) Deletion of F508 in the first nucleotide binding domain of CFTR increases its affinity to bind the Hsc70 chaperone. *FEBS J* **276**, 7097-7109. [PMID: [19878303](#)]. IF: **4.250**.
40. Almaça J, Kongsuphol P, Hieke B, Ousingsawat J, Viollet B, Schreiber R, Amaral MD, Kunzelmann K (2009) AMPK controls epithelial Na(+) channels through Nedd4-2 and causes an epithelial phenotype when mutated. *Pflügers Arch Eur J Physiol* **458**, 713-721. [PMID: [19333618](#)] IF: **4.866**.
41. Bachhuber T, Almaça J, Aldehni F, Mehta A, Amaral MD, Schreiber R, Kunzelmann K (2008) Regulation of the epithelial Na<sup>+</sup> channel by protein kinase CK2. *J Biol Chem* **283**, 13225-32. [PMID: [18308722](#)]. IF: **4.651**.
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43. Pissarra LS, Farinha CM, Xu Z, Schmidt A, Thibodeau PH, Cai Z, Thomas PJ, Sheppard DN, Amaral MD (2008) Solubilizing mutations used to crystallize one CFTR domain attenuate the trafficking and channel defects caused by the major cystic fibrosis mutation. *Chem Biol* **15**, 62-9. [PMID: [18215773](#)]. IF: **6.157**.
44. Garcia SM, Casanueva MO, Silva MC, Amaral MD, Morimoto RI (2007) Neuronal signaling modulates protein homeostasis in *Caenorhabditis elegans* post-synaptic muscle cells. *Genes Dev* **21**, 3006-16. [PMID: [18006691](#)]. IF: **12.444**.

45. Scott-Ward TS, Dawson ES, Cai Z, Doherty A, Da Paula AC, Davidson H, Porteous DJ, Wainwright BJ, Amaral MD, Sheppard DN, Boyd AC (2007) Chimeric constructs endow the human CFTR Cl<sup>-</sup> channel with the gating behaviour of murine CFTR. *Proc Natl Acad Sci USA* **104**, 16365-70. [PMID: [17913891](#)]. IF: **9.737**.
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47. Amaral MD, Kunzelmann K (2007) Molecular targeting of CFTR as a therapeutic approach to cystic fibrosis. *Trends Pharmacol Sci* **28**, 334-341. [PMID: [17573123](#)]. IF: **9.250**.
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62. Amaral MD (2005) Processing of CFTR – Traversing the cellular maze. How much CFTR needs to go through to avoid Cystic Fibrosis? *Pediatric Pulmonol* **39**, 479-491. [PMID: [15765539](#)]. IF: **2.375**.
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89. Amaral MD, Galego L, Rodrigues-Pousada C (1993) Heat-shock-induced protein synthesis is responsible for the switch-off of *hsp70* transcription in *Tetrahymena*. *Biochim Biophys Acta Gene Strct & Express*\*\* **1174**, 133-142. [PMID: [8357830](#)]. IF: **5.456**. [\*\*currently: - Gene Regul Mech]
90. Amaral MD, Galego L, Rodrigues-Pousada C (1988) Stress response of *Tetrahymena pyriformis* to arsenite and heat shock: differences and similarities. *Eur J Biochem*\* **171**, 463-470. [PMID: [3126063](#)]. IF: **4.250**. [\*currently: - FEBS J]

#### *Book chapters*

1. Amaral MD (2011) In: *Tratado de Fibrose Quística*. Salcedo A, Gartner S, Novo MDG, Girón RM, editores. Editorial Just in Time SL.
2. Kunzelmann K & Amaral MD (2008) "Novas Abordagens Terapêuticas Destinadas a corrigir o Defeito Básico na Fibrose Cística". In: *Fibrose Cística: Enfoque Multidisciplinar*. Neto NL, Coordenador. Secretaria de Estado de Santa Catarina, Florianópolis, SC, Brasil.

3. Freitas PP, Ferreira HA, Graham DL, Clarke LA, Amaral MD, Martins V, Fonseca L, Cabral JS (2004) Magnetoresistive DNA chips. In: *Magnetoelectronics*. Johnson M (Editor). Elsevier-Academic Press, Amsterdam, Netherlands, pp. 331-373.
4. Farinha CM, Amaral MD (2002) Processing and intracellular trafficking of wild-type and mutant CFTR. In: *Proc 25th European Cystic Fibrosis Conference Genova, Italy* (June 20-23). Romano L, Manno G, Galietta LJV, Eds, Monduzzi Editores, Bologna, Italy, pp.1-6. ISBN: 88-323-2622-1.

#### *Other Publications*

1. Amaral MD (2010) Cystic Fibrosis – Translating Basic Science Knowledge into Therapies. *Eur Resp Disease* **6**, 66-9.
2. Amaral MD, Clarke LA, Roxo-Rosa M, Sousa L (2006) Genomics and proteomics approaches to study the genetic disease cystic fibrosis. *Revstat* **27**, 47-54.
3. Amaral MD (2004) Editorial. *J Cyst Fibros* **3(S2)**, 3.
4. Edelman A, Amaral MD (2004) General introduction to section C: biochemistry and biophysics of CFTR. *J Cyst Fibros* **3(S2)**, 67.
5. Freitas PP, Freitas H, Graham D, Clarke L, Amaral M, Martins V, Fonseca L, Cabral JS (2003) Magnetoresistive Biochips. *Europhysics News* **34**, 224-226.

In addition, ~300 abstracts in peer-reviewed international conferences (some published in international journals, 25 in ISI)

#### **PATENTS:**

1. Amaral MD, Almaça J, Faria D, Kunzelmann K, Schreiber R, Conrad C, Pepperkok R (2012) High-content siRNA screen reveals DAG kinase as a key regulator of ENaC and therapeutic target for cystic fibrosis. Patent PPP 46287/12.
2. Matos P, Amaral MD, Moniz S, Moraes B, Mendes AI, Jordan P (2011) Rac1 signalling stimulation rescues F508del-CFTR plasma membrane expression and function in human airway cells: a novel therapeutic approach for cystic fibrosis. Patent US 14/070,533.
3. Amaral MD, Dahimène S, Mendes F, Luz S (2011) Two novel human epithelial cell lines to be used in assays for traffic studies/ screens of CFTR protein (wild-type and with the F508del mutation). Pat Pending PT105697.

#### **CURRENT GRANTS:**

- |      |   |
|------|---|
| 2014 | CF Trust Strategic Research Centre Award (CFT project No. SRC 003) " <i>I NOVCF-Innovative non-CFTR Approaches for Cystic Fibrosis Therapies</i> ". Total budget: £749,666.27. FCUL budget: 178.420 €; 3 years. PI: Dr. Michael Gray, Newcastle (UK). |
| 2014 | Gilead GÉNESE Programme (Ref 002/2013) " <i>Diagnosis, Prognosis and Personalized Treatment of Cystic Fibrosis</i> ". Total budget: 20.000 €, 1 year. PI  |
| 2012 | FCT/POCTI (PTDC/SAU-GMG/122299/2010) " <i>Characterization Of ER-Quality Control for the F508del-CFTR Protein: Potential Therapeutic Targets for Cystic Fibrosis</i> ". Total budget: 170.000 €, 3 years. PI  |
| 2010 | COST (EU) BM1003. " <i>Microbial Cell Surface Determinants of Virulence as Targets for New Therapeutics in Cystic Fibrosis</i> ". Coordinator: Antonio Molinaro, Università di Napoli Federico II, Napoli, Italy. 349.600, €4 years.                  |

Previous grants included 6 EU-funded projects and multiple nationally funded (FCT) projects. Total budget: 2.1 M€

#### **PREVIOUS GRANTS:**

- 2011 CFF-Cystic Fibrosis Foundation, USA (Ref: 7207534) *Identification of Novel Targets Rescuing of F508del-CFTR Traffic: Mechanism of Action*. Total budget: 227.881 US\$, 2 years. PI
- 2009 FCT (PIC/IC/83103/2007); Budget: 170 000€; 3 years. *Diagnosis, Prognosis and Treatment of Cystic Fibrosis*. Principal Investigator.
- 2007/2011 European Union (FP6-2005-LH-7-037365). *TargetScreen2 - Novel post-genomics cell-based screens for drug targeting in membrane protein disorders*. Budget: 3.7 M€; 4 years. Coordinator: MD Amaral. <http://www.targetscreen.eu/>
- 2005/2010 European Union (FP6-2004-LSH-018932). *EuroCareCF – European Coordination Action for Research in Cystic Fibrosis*. Budget: Euro 89,700; 3 years. Coordinator: David Sheppard, University of Bristol, Bristol (UK). Vice-Coordinator and PI for Coordination of Basic Research: MDAmaral. <http://www.eurocarecf.eu/>
- 2005/2008 European Union (FP6-2004-IST-NMP-2-016833). *SNiP2CHIP – Development of a complete integrated SNP analysis system*. Budget: Euro 195,380; 3 years. Coordinator: Paul Galvin, Tyndall National Institute, Cork (Ireland). PI for the FCUL group: MD Amaral. <http://www.tyndall.ie/projects/snip2chip/>
- 2005/2008 European Union (FP6-2003-LSH-512044). *NEUPROCF – Development of New Technologies for Low Abundance Proteomics: Application to Cystic Fibrosis*. Budget: Euro 15,000. 3 years. Coordinator: Aleksander Edelman, Faculté de Médecine Necker – Enfants Malades, Paris (France). PI for the FCUL group: MD Amaral. [http://www.biocompetence.eu/index.php/kb\\_6/io\\_3466/io.html](http://www.biocompetence.eu/index.php/kb_6/io_3466/io.html)
- 2005/2008** BBSRC grant (*Biotechnology and Biological Sciences Research Council*, UK). *Use of Human-Murine CFTR Chimeras to Investigate the Coupling of Permeation and Gating in the CFTR Chloride Channel*. Budget: Euro 10,000. 3 years. Principal Investigator: David Sheppard, University of Bristol, Bristol (UK). PI for the FCUL group: MD Amaral.
- 2005/2008** FCT /POCTI (SAU/MMO/58425/2004). *CFTR Interactome*. Budget: Euro 95,000; 3 years. Principal Investigator: MD Amaral.
- 2005/2008** FCT /POCTI (BIA-BCM/56609/2004). *Caenorhabditis elegans as a model to study folding of CFTR protein*. Budget: Euro 95,000; 3 years. Principal Investigator: MD Amaral.
- 2005/2007** FCT. Budget: Euro 132.000. *Aquisition of a small physiology unit*. Project approved by the *National Programme for Scientific Re-equipament*. Principal Investigator: MD Amaral.
- 2003/2006** FCT /POCTI /MGI/47382/2002. Budget: Euro 86,819; 3 years. *Folding, Processing and Function of Normal and Mutant Cystic Fibrosis Transmembranar Conductance Regulator: Structural Implications*. Principal Investigator: MD Amaral.
- 2002/2005** European Union (FP5-QLRT-2000-0182). *CF-Chip – Novel Genechip Technology for Early Detection of Cystic Fibrosis*. Budget: Euro 147,602; 3 years. Coordinator: Paul Galvin, National Microelectronics Research Centre (NMRC), "Lee Maltings", University College, Cork (Ireland). PI for the FCUL group: MD Amaral. <http://www.nmrc.ie/projects/cf-chip/>
- 2000/2004** European Union (FP5-QLK-1999-00241, Concerted Action). *CF Network – Thematic Network around Cystic Fibrosis and Related Diseases*. Budget: Euro 236,400; 4 years. Coordinator: Jean-Jacques Cassiman, University of Leuven (Belgium). PI for the INSA/FCUL group: MD Amaral. <http://www.cfnetwork.be/> and <http://central.igc.gulbenkian.pt/cftr/>
- 2001/2004** FCT/ POCTI (MGI/35737/1999). *Biogenesis & Function of CFTR Protein with Different Mutations: Molecular Basis for Clinical and Therapeutic of Cystic Fibrosis?* Euro 84,796; 3 years. Principal Investigator: MD Amaral; Co-PI: D Penque (INSA).
- 2002/2004** POCTI (MGI/40878/2001). *In search of New Molecular Targets for the Development of Novel Therapeutic Strategies for Cystic Fibrosis*. Budget: Euro 60,000; 2 years. Principal Investigator: D Penque (INSA); Co-PI: MD Amaral.
- 1997/2000** FCT/ PraxisXXI (PSAU/P/SAU/55/96). *Cystic Fibrosis - Traffic and Cellular Function of CFTR*. Budget: Euro 54,828; 3 years. Principal Investigator: MD Amaral.

- 1995/1997** JNICT (PBIC/C/BIA/2060/95). *Expression Studies of CFTR Gene*. Budget: Euro 37,410; 3 years. Principal Investigator: D Penque (INSA); Team member: MD Amaral.
- 1995/1997** JNICT/ French Embassy (049 C0). *Immortalization of Epithelial Cells in Portuguese Cystic Fibrosis Patients: Models to Study CFTR Gene Expression*. Budget: Euro 998; 1 year. Principal Investigator: MD Amaral.
- 1993/1995** JNICT (PBIC/C/SAU/1587/92). *Molecular Biology of Cystic Fibrosis in the Portuguese Population: Epidemiology, Anthropogenetics and Physiopathology*. Budget: Euro 74 820; 3 years. Principal Investigator: João Lavinha (INSA); Team member: MD Amaral.

#### **VARIOUS:**

- Honours** **Elected member of the Board of ECFS-European Society of Cystic Fibrosis**
- Prizes:** **2010 Award of the European Cystic Fibrosis Society** (jointly with David Sheppard, Bristol, UK).
- Supervision:** currently, 4 post-Docs, 2 PhD stds, 2 MSc stds, 3 junior stds, 1 technician.  
previously: 15 post-Docs; 14 PhD students (Univ of Lisboa, all approved with Honours); 1 MSc (DEA, France, Honours) + 4 MSc theses; 12 BSc (Diploma theses) students, all approved, 1 technician. Supervised 17 junior students (BICs). Member of 36 PhD, 6 MSc and 37 BSc theses committees.
- Grant Reviewer:** NSF- National Science Foundation (USA); DFG-Deutsche Forschungsgemeinschaft (Germany); Wellcome Trust (UK); FWO (Belgium); VLM - Vaincre la Mucoviscidose (French CF Foundation); SFI - Science Foundation Ireland; Canadian CF Foundation; Cystic Fibrosis Trust (UK); US-Israel Binational Science Foundation (BSF); Italian Cystic Fibrosis Foundation.
- Reviewer:** Science Transl Med; Nature Struct & Mol Biol; J Molecular Biology; BBA; Journal of Medical Genetics; Gene Therapy; Molecular and Cell Biology; Journal of Molecular Biology; Proteomics; Human Molecular Genetics, Thorax; Alberts 3<sup>rd</sup>ed - Essentials of Molecular and Cellular Biology (textbook, Garland).
- Conferences organized:** President of the 36<sup>th</sup> Annual ECFS Conference (Lisboa, Portugal); SAC member of the ABC – Special FEBS Meetings on ABC Proteins; Chairman (2004-2009) of the *ECFS Basic Science Conferences- New Frontiers in Basic Science of CF*; Scientific Committee member of various *European Cystic Fibrosis Society Conferences* (Vice-Chairman in 2007); 2<sup>nd</sup> International Congress on Stress Responses in Biology and Medicine (2004); Co-Organizer and Chairman (2000-2003) of the *European CF Network Consensus Meetings Towards Validation of CFTR Gene Expression & Functional Assays*.
- Invited talks:** ~90 international invited talks at conferences and seminars in Europe and USA; ~300 poster communications (team members) at international scientific conferences, (~120 published peer-reviewed abstracts).
- Other:** (since 2012) Elected member of the Board of ECFS-European Society of Cystic Fibrosis; President of the 36th Annual ECFS Conference to be held in 2013, 12-15 June (Lisboa, Portugal); Co-editor (with Karl Kunzelmann) of "Cystic Fibrosis Protocols and Diagnosis" (2011, Humana Press) Series: Methods in Molecular Biology Series; Volume I (Vol. 741): "Approaches to Study and Correct CFTR Defects" ISBN 978-1-61779-116-1 & Volume II (Vol. 742): "Methods and Resources to Understand Cystic Fibrosis" ISBN 978-1-61779-119-2; (since 2010) Member of the Research Advisory Board of Mukoviszidose Institut-the Cystic Fibrosis Patients Association (Germany); (since 2008) Associate Editor Journal of Cystic Fibrosis (Elsevier); (2007-2010) Member of the Award Committee of EMBO/FEBS Women in Science; (2006-2009) Member of the Research Advisory Board of the Cystic Fibrosis Trust (UK). Chief-editor of a special supplement of *J Cystic Fibrosis*. Member of the Award Committee of Fundação Pulido Valente (2011).