Curriculum vitae

Mónica Joana Pinto dos **Santos**

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PERSONAL DATA

Identification

Name: **Mónica** Joana Pinto dos **Santos**

Birthplace: Santa Maria da Feira

Birthday: 4th February, 1978

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Academic degrees

Sep. 1996 – Jul. 2000: B.Sc. (Biology), Faculty of Sciences, University of Porto, Portugal

Sep. 1990 – Jul. 1996: Secondary school in Colégio Liceal de Santa Maria de Lamas, Portugal

2006: PhD in Health Sciences, Abel Salazar Biomedical Sciences Institute (ICBAS), University of Porto, Portugal (prevision date for defense: December 2006).

Profissional positions

- **Present position**

Since Jan. 2004: PhD student at Life and Health Sciences Research Institute (ICVS)/ School of Health Sciences, University of Minho, Portugal.

Supervision: Prof. Patrícia Maciel, PhD

Co-supervision: Prof. Jorge Sequeiros and Prof. Amélia Tavares

- **Previous positions**

Dez. 2002 – Dez. 2003: PhD student at UnIGENe – Institute for molecular and cellular biology (IBMC), University of Porto, Portugal.
Supervision: Prof. Patrícia Maciel, PhD
Co-supervision: Prof. Jorge Sequeiros and Prof. Amélia Tavares

Aug. 2002 – Sep. 2002: Visitant researcher at Unicamp with the theme "Molecular diagnostic methods in Rett syndrome". University of Campinas, Campinas, Brasil.
Supervision: Prof. Iscia Lopes-Cendes, MD, PhD

Jul. 2001 – Oct. 2001: Participation in the Genetic Analysis of Multiple sclerosis in EuropeanS (GAMES) project. Genetic study of multiple sclerosis in Europe through genomic screen of 6000 markers in the pooled Portuguese sample. Neurology unit, Addenbroke's Hospital, University of Cambridge, UK.
Supervision: Doctor Stephen Sawcer, MD, PhD
Lab Director: Professor Alastair Compston, MD, PhD

May 2001 - April 2002: Professional trainee fellowship from "Centro de Emprego" (Portuguese government)/IBMC
Supervision: Prof. Patrícia Maciel, PhD
Lab Director: Prof. Jorge Sequeiros, MD, PhD

Nov. 2000 – Nov. 2002: Research assistant at UnIGENe – Institute for Molecular and Cell Biology (IBMC), University of Porto, Portugal.
Supervision: Prof. Patrícia Maciel, PhD
Lab Director: Prof. Jorge Sequeiros, MD, PhD

Sep. 1999 – Oct. 2000: Training course in Human Genetics in the Abel Salazar Biomedics Sciences Institute (ICBAS), University of Porto, Portugal.
Supervision: Prof. Beatriz Porto, PhD
Lab Director: Prof. Isabel Malheiro, PhD

Main scientific area of research

Rett syndrome is a neurodevelopmental disorder, affecting mainly girls, that is caused by mutations in the MECP2 gene. This gene encodes for the MeCP2 protein which is involved in the co-repression of target genes. Presently I am involved in the clinical, epidemiological and genetic study of the Portuguese population with Rett syndrome and perturbations of the autistic spectrum. I am also using a knock out mouse model for the *MECP2* gene, which mimics the

disorder in certain aspects, to study the brain malfunctions that are responsible for the presented pathogenesis in this model.
Multiple sclerosis is a complex neurological disorder in which multiple genes must have a role in its genetic determination. An association study, in which 6,000 microsatellite markers spanning the entire genome were genotyped, was carried out and presently we are refining the highlighted areas to proceed with the study.

Other scientific areas of interest

I am interested in the field of neurosciences, neurogenetics and particularly the study of the molecular basis underneath mental retardation and cognitive impairments.

Participation in financiered projects

- PhD project with the theme: "Study of Rett syndrome pathogenesis and the role of MeCP2 protein in the neuronal function". Supported by FCT, grant SFRH/BD/9111/2002.

- Clinical, epidemiological and genetic study of Rett syndrome in Portugal. Supported by FSE/FEDER and FCT, grant POCTI 41416/2001.
PI: Patrícia Maciel

- Genetic Analysis of Multiple sclerosis in EuropeanS (GAMES). Genomic screen of 6000 markers in the pooled Portuguese sample. Collaboration between Neurology unit, Addenbroke's Hospital, University of Cambridge (UK) and UnIGENe/ IBMC. Supported by Wellcome Trust (UK), grant 057097.
PI: Stephen Sawcer

Prizes

- 2003: Serono award *"Doenças Desmielinizantes"*, in *execuo*, with the studies:
"Study of the *APOE* and *SCA2* loci in multiple sclerosis patients of Portuguese origin".
"Association study of multiple sclerosis in Portuguese patients: whole genome screen using 6,000 microsatellite markers".

Complementary education

- Basic course in informatics (Windows, Word, Excel, PowerPoint, Access, Internet)

- Fluent speaking and reading of English, Spanish and French languages

COMMUNITY SERVICES

- Involvement in the creation of ANPAR (National association of parents and friends of Rett)

- Establishment of the method and routine test of molecular diagnosis of Rett syndrome. Life and Health Sciences Research Institute (ICVS)/ School of Health Sciences, University of Minho, Portugal.

EXPERIENCE IN SUPERVISING

- Oct. 2002 - Jul. 2003: Co-supervision of the trainee student **Eurico** Duarte **Coelho,** Biology course, Faculty of Sciences, University of Madeira, Portugal, with the theme *"Establishment of molecular techniques for the diagnosis of Rett syndrome"*.

- Oct. 2001 - Sep. 2002: Co-supervision of the trainee student **Inês** Fonseca de Almeida **Ramos,** Biology course, Faculty of Sciences, University of Porto, Portugal, with the theme "*Molecular Analysis of MECP2 gene in patients with Rett syndrome*".

- Jun. 2004 - Jul. 2004: Co-supervision of the trainee student **Ana Moutinho**, degree in Medicine, "Projecto de opção 3", School of Health Sciences, University of Minho, Portugal, with the theme "*Rett syndrome*".

- Jul. 2006 - Aug. 2006: Co-supervision of the trainee student **Ana Franky**, degree in Medicine, MD-PhD program, School of Health Sciences, University of Minho, Portugal, with the theme "*Characterization of a Mecp2-null mice*".

EXPERIENCE IN TEACHING

2005 - Seminar on the theme "Molecular diagnostic methods: application to Rett syndrome" as part of the "Molecules and Cells" module, degree in Medicine, School of Health Sciences, University of Minho. Invited by Fernando Rodrigues and Isabel Palmeirim

2004 - Seminar on the theme "Molecular diagnostic methods: application to Rett syndrome" as part of the "Molecules and Cells" module, degree in Medicine, School of Health Sciences, University of Minho. Invited by Patrícia Maciel

SCIENTIFIC EXPERIENCE

Courses and workshops

- 14-16 Feb 2007: "Behaviour pathologies: Biological Approaches". IGC workshop series, Calouste Gulbenkian Foundation, Lisbon, Portugal.

- 17-21 Jul 2007: "Cognition: From Genes to Function". Neurosciences summer seminar, Duques de Soria Foundation, Soria, Spain.

- 2-13 May 2005: "Laboratory Animal Science" 2nd IBMC/ ICVS course. The course curriculum followed the FELASA recommendations on the education and training of persons working with laboratory animals Category C.

- 19-23 Jul 2004: *"Genes and Neurons"* Postgraduate courses, Life and Health Sciences Research Institute (ICVS), University of Minho, Portugal. Sponsored by the European Science Foundation.

- 3-4 Jun 2004: *"Introduction to rodent behaviour testing", Professors* Hanno Würbel, David Wolfer, Rui Costa. Institute for Molecular and Cellular Biology (IBMC), University of Porto, Portugal.

- 29-31 Oct 2003: *"Segurança laboratorial: Biológica, Química e Radiológica".* Life and Health Sciences Research Institute (ICVS), Universty of Minho, Braga, Portugal.

- 25-27 Jun 2003: *"Cell and Tissue culture techniques"*. Postgraduate courses, Life and Health Sciences Research Institute (ICVS), University of Minho, Portugal.

- 29-30 May 2003: "Light microscopy and advanced imaging, principles and good practice", Professors Peter Evennett and Paul Robinson. Postgraduate courses, Life and Health Sciences Research Institute (ICVS), University of Minho, Portugal.

- 15-22 Sep. 2002: "Anatomy and Embryology of the Mouse". EMBO practical course, Croatian Institute for Brain Research, Zagreb University School of Medicine, Zagreb, Croatia.

- 5-7 Jun. 2002: "Light microscopy and analysis: principles and good practice, including recording images from the microscope", Professor Peter Evennett. Postgraduate courses, Life and Health Sciences Research Institute (ICVS), University of Minho, Portugal.

- 1 Mar 2002: "Ciência Responsável: Experimentação animal hoje e no futuro", IBMC – Friday workshops, Porto, Portugal.

- 13 – 31 Aug. 2001: "Erasmus Summer Programme". *Erasmus Medical Center, Rotterdam, The Netherlands.*
Scientific program: "Principles of Research in Medicine and Epidemiology" (Albert Hofman), "Bioinformatics in Medicine" (Peter Raeymaekers and Bertram Muller), "Searching Genes for Complex Disorders" (Peter Heutink and Ben Oostra), "Genetic Epidemiology" (Lodewijk Sandkuijl and Cornelia Van Duijn), "Genetics of Complex Diseases" (Lodewijk Sandkuijl and Cornelia Van Duijn).

- 21–25 May 2001: Course of "Human Disease Gene Mapping". UnIGENe-IBMC, Porto, Portugal. Professors: Peter Heutink and Cisca Wijmenga

- 25-31 Mar. 2001: *"14th Course in Medical Genetics"*. Sestri Levante – Genoa, Italy. European School of Genetic Medicine. Prof. G. Romeo, Prof. S. Antonarakis and Prof. V.A. Mckusik.
Scientific program: *"Introduction to Genetic Analysis", "Genetics of Complex Traits", "Molecular Genetics of Mendelian Disorders", "Neurogenetics", "Human Disease Gene Identification and Model Systems"* and *"Post-Genome Research".*

Scientific meetings

- 16-18 Apr 2007: Participation in the "1st European Research group in Rett syndrome", Lago Maggiori, Italy.

- 26-28 Jun 2006: Participation in the "7th Annual Rett syndrome symposium", Chicago, USA

- 12-16 Nov 2005: Participation in the "Society for Neuroscience 35th Annual Meeting", Washington, DC, USA

- 10-14 Jul 2004: Participation in the **"**4th Forum of European Neuroscience", Lisbon, Portugal.

Presentations in scientific meetings

- **Invited presentations**

- **Santos M** and Maciel P. "Síndrome de Rett: O que nos dizem os genes". Associação Nacional de Pais e Amigos de Rett (ANPAR), Amadora, **19 February 2005**.

- **Santos M**, Costa MC, Matamá MT, Ferro A, Pinto-Basto J, Sequeiros J, Maciel P. "Candidate gene studies in Portuguese patients". G.A.M.ES. Meeting, Istanbul, Turkey, **12-13 April 2002**.

- **Oral presentations**

- **Santos M**, Silva-Fernandes A, Oliveira P, Sousa N and Maciel P. "*Delayed achievement of developmental milestones in a mouse model of Rett syndrome"*. Society for Neuroscience, 35th Annual Meeting. Washington DC, **12-16 November 2005**.

- Maciel P, **Santos M**, Barbot C, Medeira A, Cabral H, Cabral P, Carrilho I, Gaspar I, Lobo-Antunes N, Moreira A, Temudo T. *"Rett syndrome-like male patients: study of the MECP2, NLGN3 and NLGN4 genes"*. 2ª Reunião Ibérica de Neuropediatria. IV Congresso da Sociedade Portuguesa de Neuropediatria. Estoril, **13-15 October 2005**.

- **Santos M**, Silva-Fernandes A, Oliveira P, Sousa N and Maciel P. *"Study of postnatal neurodevelopmental hallmarks in a mouse model of Rett syndrome"*. 2ª Reunião Ibérica de Neuropediatria. IV Congresso da Sociedade Portuguesa de Neuropediatria. Estoril, **13-15 October 2005**.

- Pinto-Basto J, **Santos M**, Rio ME, Sá MJ, Valença A, Sá A, Dinis J, Figueiredo J, Bigotte de Almeida L, Coelho I, Sequeiros J, Maciel P. *"Rastreio do genoma e identificação de loci associados à esclerose múltipla em doentes Portugueses"*. Sociedade Portuguesa de Neurologia, Espinho, **7-10 November 2002**.
Sinapse 2 (2): P-39 96, 2002

- **Santos M**, Costa MC, Rio ME, Sá MJ, Monteiro M, Valença A, Sá A, Dinis J, Figueiredo J, Bigotte de Almeida L, Coelho I, Pinto-Basto J, Matamá MT, Ferro A, Sequeiros J, Maciel P. *"Susceptibilidade e progressão da esclerose múltipla em doentes Portugueses – estudo do papel dos loci APOE e SCA2"*. Sociedade Portuguesa de Neurologia, Espinho, **7-10 November 2002**.
Sinapse 2 (2): P-40 96, 2002

- Pinto-Basto J., **Santos M.**, Rio ME, Valença A, Sequeiros J, Maciel P. "*Association study of multiple sclerosis in Portuguese patients: whole genome screen using 6,000 microsatellite markers"*. 52nd Meeting of American Society of Human Genetics, Baltimore, USA, **15-19 October 2002**.
The American Journal of Human Genetics 71 (4) suppl. Oral presentation (#145)

- Temudo T, Dias K, Barbot C, Oliveira G, **Santos M**, Sequeiros J, Maciel P. *"Estudo Clínico, Epidemiológico e Genético da Síndrome de Rett em Portugal"*. Sociedade Portuguesa de Neurologia, Lisboa, **16-18 November 2001.**
Sinapse P-66 (P37), 2001

- **Poster presentations**

- **Santos M**, Coutinho AM, Yan J, Yang C, Feng J, Vicente A, Temudo T, Sommer SS, Maciel P. "Analysis of the 3' UTR of the *MECP2* gene in patients with clinical diagnosis of Rett syndrome and mental retardation." The American Society of Human Genetics, 56th annual meeting, New Orleans, USA **9-13 October 2006** (submitted).

- **Santos M**, Temudo T, Carrilho I, Gaspar I, Barbot C, Medeira A, Cabral H, Oliveira G, Gomes R, Lourenço MT, Venâncio M, Calado E, Moreira A and Maciel P. "Genetic study of boys with a Rett syndrome-like phenotype: analysis of the *MECP2*, *NLGN3* and *NLGN4* genes". 7th Annual Rett syndrome symposium. Chicago, USA **26-28 June 2006**.

- **Santos M**, Venâncio M, Barbot C, Medeira A, Cabral H, Cabral P, Carrilho I, Gaspar I, Lobo-Antunes N, Moreira A, Temudo T, Maciel P. *"Genetic study of boys with a Rett syndrome-like phenotype: analysis of the MECP2, NLGN3 and NLGN4 genes"* **P56**. 9ª Reunião Anual da Sociedade Portuguesa de Genética Humana. Cascais, **10-12 November 2005.**

- **Santos M**, Temudo T, Barbot C, Medeira A, Cabral H, Cabral P, Carrilho I, Gaspar I, Lobo-Antunes N, Moreira A, Sequeiros J, Maciel P. *"Male patients with Rett-like phenotype do not present mutations in the MECP2, NLGN3 and NLGN4 genes"* **P2727**, 489. The American Society of Human Genetics, 54th annual meeting, Toronto, **26-30 October 2004**.

- Temudo T, **Santos M**, Dias K, Barbot C, Cabral P, Moreira A, Carrilho I, Lobo-Antunes N, Oliveira G, Sequeiros J, Maciel P. *"Genotype-phenotype correlations in Portuguese patients with Rett syndrome"*. **P2728**, 489. The American Society of Human Genetics, 54th annual meeting, Toronto, **26-30 October 2004**.

- Ferro A, Castro MJ, Sousa A, Lemos C, **Santos M**, Silveira I, Pereira-Monteiro J, Sequeiros J, Maciel P. *"The C677T MTHFR polymorphism is not a genetic risk factor for migraine in the Portuguese population".* P16 Genetics of complex traits and isolated populations, Tortoli', Sardinia, Italy, **23–30 May 2003**

- **Santos M**, Costa MC, Rio ME, Sá MJ, Monteiro MC, Valença A, Sá A, Dinis J, Figueiredo J, Almeida LB, Valongueiro A, Coelho I, Pinto-Basto J, Matamá MT, Sequeiros J, Maciel P. "*Susceptibility and disease progression in Portuguese patients with multiple sclerosis - study of the role of APOE and SCA2 loci".* P-0913, European Society of Human Genetics, Strasburg, **25-28 May 2002**.
Eur J Hum Genet 10, suppl. 1: P-0913, 267, 2002

- **Santos M**, Costa MC, Rio ME, Sá MJ, Monteiro MC, Valença A, Sá A, Dinis J, Figueiredo J, Almeida LB, Valongueiro A, Coelho I, Ferro A, Pinto-Basto J, Matamá MT, Sequeiros J, Maciel P. *"Study of the APOE and SCA2 loci in multiple sclerosis patients of Portuguese origin".* P01.138, American Academy of Neurology 54th Annual Meeting, Denver, **13-20 April 2002.**
Neurology 58(7), suppl. 3: P01-138, A71, 2002

- Costa MC, Santos C, Ferro A, **Santos M**, Sequeiros J, Maciel P. *"Identificação de três novos polimorfismos intragénicos no gene MJD1 e estudo da sua frequência numa população Portuguesa"*. Poster, 5ª reunião da Sociedade Portuguesa de Genética Humana, Aveiro, **24-26 October 2001**.

- Costa MC, Santos C, Ferro A, **Santos M**, Sequeiros J, Maciel P. *"Identification of three novel polymorphisms in the MJD1 gene and their frequency study in a Portuguese population"*. The American Society of Human Genetics, 51st Annual meeting, San Diego, **12-16 Ocober 2001**.

The American Journal of Human Genetics 69(4): P-1373, 417, 2001.

Scientific publications

- **Articles in international journals with referees**

- **Santos M**, Yan J, Temudo T, Fen J, Sommer S and Maciel P. "Analysis of highly conserved regions of the 3' UTR of the *MECP2* gene in patients with clinical diagnosis of Rett syndrome and mental retardation". (Submitted to Disease Markers).

- **Santos M**, Temudo T, Kay T, Carrilho I, Gaspar I, Barbot C, Medeira A, Cabral H, , Gomes R, Lourenço MT, Venâncio M, Calado E, Moreira A, Oliveira G and Maciel P. "*Mutations in the MECP2 gene are not a major cause of Rett-like phenotype in male patients*". (Submitted to Genetic Testing)

- Ferro A, Castro MJ, **Santos M**, Lemos C, Sousa A, Pereira-Monteiro J, Sequeiros J, Maciel P. "*The C677T polymorphism in MTHFR is not associated with migraine in the Portuguese population*". (Submitted to Headheach)

- Carvalho A, **Santos M**, Maciel P and Rodrigues F. "T-1237C polymorphism of TLR9 gene is not associated with multiple sclerosis in the Portuguese population".Multiple Sclerosis **2007** (in press)

- Venâncio M, **Santos M**, Pereira SA, Maciel P, Saraiva. An explanation for another familial case of Rett syndrome: maternal germline mosaicism. Eur J Hum Genet. **2007** Apr 18.

- Coutinho AM, Oliveira G, Katz C, Feng J, Yan J, Yang C, Marques C, Ataíde A, Miguel TS, Temudo T, **Santos M**, Maciel P, Sommer SS and Vicente AM. *"MECP2 coding sequence and 3'UTR variation in 172 unrelated autistic patients".* Am J Med Genet – Part B Neuropsychiatr Genet **2007** April 10.

- Temudo T, Oliveira P, **Santos M**, Dias K, Vieira JP, Moreira A, Calado E, Carrilho I, Oliveira G, Levy A, Barbot C, Fonseca MJ, Cabral A, Dias A, Lobo Antunes N, Cabral P, Monteiro JP, Borges L, Gomes R, Barbosa C, Santos M, Mira G, Andrada G, Freitas P, Figueiroa S, Sequeiros J and

Maciel P. "*Stereotypies in Rett Syndrome: analysis of 83 patients with and without detected MECP2 mutations*". Neurology **2007** April 10; 60(15):1183-7.

- **Santos M**, Silva-Fernandes A, Oliveira P, Sousa N and Maciel P. "Evidence for abnormal early development in a mouse model of Rett syndrome". Genes Brain & Behavior, **2007** Apr 6(3): 277-86.

- The GAMES Collaborative Group. "*Linkage disequilibrium screening for multiple sclerosis implicates JAG1 and POU2AF1 as susceptibility genes in Europeans*". J Neuroimmunol **2006** 179:108-116.

- Burwick R, Ramsay P, Haines J, Hauser S, Oksenberg M, Pericak-Vance M, Schmidt S, Compston A, Sawcer S, Cittadella R, Savettieri G Quattrone A, Polman C, Uitdehaag B, Zwemmer J, Hawkins C, Ollier W, Weatherby S, Enzinger C, Fazekas F, Schmidt H, Schmidt R, Hillert J, Thomas Masterman T, Hogh P, Niino M, Kikuchi S, Maciel P, **Santos M**, Rio ME, Kwiecinski H, akrzewska-Pniewska B, Evangelou N, Palace J, Barcellos L. "APOE epsilon variation in multiple sclerosis susceptibility and disease severity: some answers" Neurology **2006** 66: 1373-1383.

- **Santos M**, Coelho PA, Maciel P: *"Chromatin remodelling and neuronal function: exciting links".* Genes Brain and Behavior **2006** 5(suppl. 2): 80-91.

- Shi J, Shibayama A, Liu Q, Nguyen VQ, Feng J, **Santos M**, Temudo T, Maciel P, Sommer SS: *"Detection of heterozygous deletions and duplications in the MECP2 gene in Rett syndrome by Robust Dosage PCR (RD-PCR)".* Hum Mutat **2005** May;25(5):505.

- **Santos M**, Costa MC, Rio ME, Sá MJ, Monteiro MC, Valença A, Sá A, Dinis J, Figueiredo J, Almeida LB, Valongueiro A, Coelho I, Pinto-Basto J, Matamá MT, Sequeiros J, Maciel P: *"Genotypes at the APOE and SCA2 loci do not predict the course of multiple sclerosis in patients of Portuguese origin".* Mult Scler **2004** Apr;10 (2): 153-7.

- **Santos M**, Pinto-Basto J, Rio ME, Sá MJ, Valença A, Sá A, Dinis J, Figueiredo J, Bigotte de Almeida L, Coelho I, Sawcer S, Setakis E, Compston A, Sequeiros J, Maciel P. "A whole genome screen for association with multiple sclerosis in Portuguese patients". J Neuroimmunol **2003** Oct; 143 (1-2): 112-5.