



Name: João Ramalho-Santos

Current Positions:

Associate Professor at the University of Coimbra (Department of Zoology) since July 2005.
 Visiting Scientist at the Pittsburgh Development Center, Magee-Womens Research Institute, University of Pittsburgh, Pittsburgh, Pennsylvania, USA, since 2002.
 Researcher at the Center for Neuroscience and Cell Biology of Coimbra since 1989; and Principal Investigator since 2001.

Research Areas:

Reproductive Biology, stem cell biology.

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Education

Postdoctoral fellow at the Oregon National Primate Research Center (Oregon Health Sciences University), Portland, Oregon, USA, 1997-2000.
 Ph.D. in Cell Biology at the University of Coimbra, Portugal (1997). Research conducted at the Center for Neuroscience and Cell Biology.
 Visiting Graduate Student, Laboratory of Physiological Chemistry, University of Groningen, The Netherlands (1989)
 B.Sc. in Biology at the University of Coimbra, Portugal (1984/1988).

Previous positions

Postdoctoral fellow at the Oregon National Primate Research Center (Oregon Health Sciences University), Portland, Oregon, USA, 1997-2000.
 Teaching assistant at the University of Coimbra (Department of Zoology) from 1989 to 1996.

Research activities

Determinants of male gamete formation.
 Molecular mechanisms involved in the acrosome reaction
 Sperm quality control mechanisms in mammalian systems
 Reproduction in endangered species.
 Putative diagnosis of sperm and oocyte quality for Assisted Reproduction and Human infertility
 Molecular diagnosis of human failed fertilization following Assisted Reproductive Technologies.
 The effect of diabetes on spermatogenesis and sperm function.
 Metabolic regulation of the pluripotency and differentiation of embryonic stem cells

Teaching activities

B. Sc. in Biology at the University of Coimbra (Classes in Cell and Developmental Biology).

Masters in Cell Biology at the University of Coimbra (Classes in Reproductive Biology and stem cell biology)

Ph.D. in Biomedicine and Experimental Biology at the Center for Neuroscience and Cell Biology (Advanced Courses in Reproductive Biology and Stem cell biology).

Current supervision of Student Projects:

Undergraduate (4)

Masters (3)

Ph.D. (6)

SELECTED ORIGINAL CONTRIBUTIONS IN ISI JOURNALS (total of 53 papers)

1- Fusion mechanisms involved in the entry of influenza virus into host cells. Main publications:

A common mechanism for influenza virus fusion activity and inactivation (1993) **João Ramalho-Santos**, Shlomo Nir, Nejat Düzgünes, Arsélio Pato de Carvalho & Maria da Conceição Pedroso de Lima, **Biochemistry**, 32: 2771-2779.

Target membrane sialic acid modulates both binding and fusion activity of influenza virus (1995) Maria da Conceição Pedroso de Lima, **João Ramalho-Santos**, Diana Flasher, Vladimir A. Slepshkin, Shlomo Nir & Nejat Düzgünes, **Biochimica et Biophysica Acta: Biomembranes**, 1236: 323-330.

Partial fusion activity of influenza virus towards liposomes and erythrocyte ghosts is distinct from viral inactivation (1996) **João Ramalho-Santos**, Maria da Conceição Pedroso de Lima & Shlomo Nir, **The Journal of Biological Chemistry**, 271: 23902-23906.

The influenza virus hemagglutinin: A model protein in the study of membrane fusion (1998) **João Ramalho-Santos** & Maria da Conceição Pedroso de Lima, **Biochimica et Biophysica Acta: Reviews in Biomembranes**, 1376:147-154.

2- SNARE proteins and the acrosome reaction in mammalian sperm. Main publications:

SNAREs in mammalian sperm: Possible implications for fertilization (2000) **João Ramalho-Santos**, Ricardo D. Moreno, Peter Sutovsky, Anthony Wing-Sang Chan, Laura Hewitson, Gary M. Wessel, Calvin R. Simerly & Gerald Schatten, **Developmental Biology**, 223: 54-69.

Control of membrane fusion during spermiogenesis and the acrosome reaction (2002), **João Ramalho-Santos**, Gerald Schatten & Ricardo D. Moreno, **Biology of Reproduction**, 67: 1043-1051.

SNARE proteins and caveolin-1 in the acrosome of equine sperm: Possible implications for stallion fertility (2005) Sandra Gamboa & **João Ramalho-Santos**. **Theriogenology** 64: 275-291

3- Genetic modifications of primates using Assisted Reproduction techniques. Main publications:

Foreign DNA transmission by ICSI: Injection of spermatozoa bound with exogenous DNA results in embryonic GFP expression and live rhesus monkey births (2000) Anthony Wing-San Chan, C. Marc Luetjens, Tanja Dominko, **João Ramalho-Santos**, Calvin Simerly, Laura Hewitson & Gerald Schatten, **Molecular Human Reproduction**, 6: 26-33.

TransgenICSI reviewed: Foreign DNA transmission by intracytoplasmic sperm results in embryonic GFP expression and live rhesus births (2000) Anthony Wing-San Chan, C. Marc

Luetjens, Tanja Dominko, **João Ramalho-Santos**, Calvin Simerly, Laura Hewitson & Gerald Schatten, **Molecular Reproduction and Development**, 56(S2):325-328.

4- Mechanisms involved in vesicular transport during acrosome biogenesis. Main publications:

The Golgi apparatus segregates from the lysosomal/acrosomal vesicle during rhesus spermiogenesis: Structural alterations (2000) Ricardo D. Moreno, **João Ramalho-Santos**, Edward K. L. Chan, Gary M. Wessel, & Gerald Schatten, **Developmental Biology**, 219: 334-349.

Membrane trafficking machinery components associated with the mammalian acrosome during spermiogenesis (2001) **João Ramalho-Santos**, Ricardo D. Moreno, Gary M. Wessel, Edward K. L. Chan & Gerald Schatten, **Experimental Cell Research**, 267: 45-60.

5- Molecular mechanisms for the removal of paternal mitochondria in mammalian embryos. Main publications:

Ubiquitin tag for sperm mitochondria (1999) Peter Sutovsky, Ricardo D. Moreno, **João Ramalho-Santos**, Tanja Dominko, Calvin Simerly & Gerald Schatten, **Nature**, 402: 371-372.

Ubiquitinated sperm mitochondria: Selective proteolysis and the regulation of mitochondrial inheritance in mammalian embryos (2000) Peter Sutovsky, Ricardo D. Moreno, **João Ramalho-Santos**, Tanja Dominko, Calvin Simerly & Gerald Schatten, **Biology of Reproduction**, 63: 582-590.

6- Sperm structures during Assisted Reproduction techniques. Main publications:

Unique checkpoints during the first cell cycle of fertilization after intracytoplasmic sperm injection in rhesus monkeys (1999) Laura Hewitson, Tanja Dominko, Diana Takahashi, Crista Martinovich, **João Ramalho-Santos**, Peter Sutovsky, John Fanton, Darla Jacob, Daymond Monteith, Martha Neuringer, David Battaglia, Cal Simerly & Gerald Schatten, **Nature Medicine**, 5: 431-433.

ICSI choreography: Fate of sperm structures after monospermic ICSI and first cell cycle implications (2001) **João Ramalho-Santos**, Peter Sutovsky, Calvin R. Simerly, Richard Oko, Gary M. Wessel, Laura Hewitson & Gerald Schatten, **Human Reproduction**, 15: 2610-2620.

7- Mechanisms for mammalian sperm quality control. Main publications:

Ubiquitin-dependent epididymal mechanism for the recognition and elimination of defective spermatozoa in mammals (2001) Peter Sutovsky, Ricardo D. Moreno, **João Ramalho-Santos**, Tanja Dominko, Winston E. Thompson & Gerald Schatten, **Journal of Cell Science**, 114: 1665-1675.

Comparison between different markers for sperm quality in the cat: Diff-Quik as a simple optical technique to assess changes in the DNA of feline epididymal sperm (2005) Paula C. Mota & **João Ramalho-Santos**. **Theriogenology** 65:1360-1375.

Effects of hyperglycemia on sperm and testicular cells of Goto-Kakizaki and Streptozotocin-treated rat models for Diabetes (2006) Sandra Amaral, António J. Moreno, Maria Sancha Santos, Raquel Seça and **João Ramalho-Santos**. **Theriogenology** 66: 2056-2067.

Characterization of human sperm populations using conventional parameters, surface ubiquitination and apoptotic markers (2007) Sandra Varum, Carla Bento, Ana Paula M. Sousa, Carina Gomes-Santos, Paula Henriques, Teresa Almeida-Santos, Cristina Teodósio, Artur Paiva & **João Ramalho-Santos**. **Fertility and Sterility** (in press).

The expression of polymerase gamma and mitochondrial transcription factor A and the regulation of mitochondrial DNA content in mature human sperm (2007) Alexandra Amaral, **João Ramalho-Santos** & Justin St. John. **Human Reproduction** (in press).

8-Mitochondrial dynamics during nuclear transfer stem cell differentiation. Main publications:

The expression of mitochondrial DNA transcription factors during early cardiomyocyte *in vitro* differentiation from human embryonic stem cells (2005) Justin St. John*, **João Ramalho-Santos***, Heather Gray, Christopher Navara, Vanesa Y. Rawe, Patti Petrosko, Calvin Simerly & Gerald Schatten (*Co-first authors). **Cloning & Stem Cells** 7:141-153

Aberrant nucleo-cytoplasmic cross-talk results in donor cell mtDNA persistence in cloned embryos (2006) Rhiannon E. Lloyd, Jon-Hee Lee, Ramiro Alberio, Emma J. Bowles, **João Ramalho-Santos**, Keith H.S. Campbell & Justin C. St. John. **Genetics** 172: 2515-2527.

Book Chapters

Fertilization: Fate of sperm components after ICSI

Laura Hewitson, **João Ramalho-Santos**, Calvin Simerly & Gerald Schatten

In **Biology and Pathology of the Oocyte: Its Role in Fertility and Reproductive Medicine** (Alan O. Trounson & Roger G. Gosden, editores). Cambridge University Press, pp.133-140. 2003.

Confocal imaging of structural molecules in mammalian gametes

Calvin R. Simerly, Ricardo Moreno, **João Ramalho-Santos**, Laura Hewitson & Gerald Schatten

In **A Laboratory Guide of the Mammalian Embryo** (David K. Gardner & Michelle Lane, editores). Oxford University Press, pp. 165-183. 2003.

The analysis of mitochondria in human embryonic stem cells

Justin St. John, Alexandra Amaral, Emma Bowles, João Facucho, Rhiannon Lloyd, Mariana Freitas, Heather L. Gray, Christopher Navara, Gisela Oliveira, Gerald Schatten, Emma Thomas & **João Ramalho-Santos**

In **Human Embryonic Stem Cells: Methods and Protocols**. Methods in Molecular Biology Series, (Kurshad Turksen, editor). Humana Press. pp 323-350. 2006.