

BIOGRAPHICAL SKETCH

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NAME: MARCO BARCHI

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POSITION TITLE: ASSOCIATE PROFESSOR, UNIVERSITY OF ROME TOR VERGATA, ITALY

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Rome La Sapienza, Italy	B.S	1995	Molecular Biology
University of Rome Tor Vergata, Italy	Ph.D.	2000	Medical Embryology
Columbia University, NY, USA	Post-doc	2001	Biological Science
MSKCC, NY, USA	Post-doc	2006	Developmental Biology
University of Rome Tor Vergata, Italy	Assistant Professor	2021	Developmental Biology
University of Rome Tor Vergata, Italy	Associate Professor	To date	Developmental Biology

A. Personal Statement

I am a researcher with more than 20 years of activity, an expert in basic and biomedical research in the field of reproduction and male germ cell tumor biology, with international and national experience. I was fascinated by the field of developmental biology since I was a Ph.D. student when I decided to study the mechanisms of calcium release after fertilization and molecular players involved in male germ cell differentiation. I subsequently developed these interests during my postdoctoral career in the United States, where I became acquainted with the meiotic recombination field. I am truly fascinated by the mechanisms that control recombination between male sex chromosomes. Autosomal chromosomes are homologous throughout their entire length and are therefore able to pair and recombine from end to end. On the other hand, the X and Y chromosomes are heteromorphic, except for a short segment called the pseudoautosomal region (PAR). Therefore, XY chromosome pairing and recombination can only occur in PAR, which conceivably makes XY segregation particularly difficult. The SPO11 gene plays a key role in the generation of double-strand breaks that initiate meiotic recombination and crossover formation in germ cells. Recently, using animal models, we have shown that the SPO11-*alpha splice isoform* and the *Fus* gene play an important role in the recombination of XY and the formation of the (single obligatory) crossover between male sex chromosomes. If XY recombination fails and chromosomes segregate randomly, germ cells are eliminated by checkpoint mechanisms, causing sterility or subfertility. In some cases, germ cells skip the checkpoint and differentiate into aneuploid spermatozoa. This may predispose to the conception of offspring with sex chromosome aneuploidy, such as Klinefelter (47,XXY), which is often of paternal origin, caused by a lack of recombination at the PAR. Understanding the origin of the XY nondisjunction that causes Klinefelter is the goal of my current research. That is why I am now carrying out a project involving the exome sequencing of fathers of Klinefelter subjects, to identify variants of meiotic-related genes that potentially have an impact on XY recombination proficiency. This approach is complementary to the one proposed in the application to NF, in which, starting from an animal model of XY aneuploidy developed in house, we plan to identify structural variants and gene variants associated with failure of recombination between male sex chromosomes in mice. To date, the mouse PAR is one of those regions with incomplete sequence information. This proposal aims to generate the first haplotype-aware *denovo X chromosomal* optical map with telomere-to-telomere coverage via nanopore sequencing. In the long run, results obtained from these projects could help develop preconception tests for

the risk assessment of nondisjunction-associated XY infertility/subfertility or the conception of a Klinefelter child. In the latter case, parents with risk awareness will be advised to monitor the karyotype of the unborn child and, on medical advice, to subject the child with Klinefelter to hormone replacement therapy, at the earliest convenient time. Early diagnosis of Klinefelter still occurs rarely today, with consequent reduced quality of life of Klinefelter individuals, and increased expenditure from the national health system, to compensate for the comorbidity associated with late treatment.

B. Positions, Scientific Appointments, and Honors

- 1993-1995, Ungraduated at the National Institute for Alternative Energy and Environment (E.N.E.A.), Italy;
- 1995-1996, Research Fellow, Physiology, University of Rome "Tor Vergata", Rome, Italy;
- 1996-2000, PhD Student, Anatomy, University of Rome "Tor Vergata", Rome, Italy;
- 2001-2002, Postdoctoral Research Fellow, Biological Sciences, Columbia University;
- 2002-2006, Postdoctoral Research Fellow, Memorial Sloan-Kettering Institute;
- 2006-2021, Assistant Professor (Faculty), University of Rome, "Tor Vergata", Rome, Italy;
- 2021-to date, Associate Professor (Faculty), University of Rome "Tor Vergata", Rome, Italy;
- 1999: Research Fellowship, Italian National Science Council (CNR) Italy. Project: Study of Ca^{++} release at fertilization in *Xenopus* eggs. Supervisor: Prof. Richard Nuccitelli, University of California, Davis, USA;
- 2003-2004: The Lalor Foundation Fellowship, USA. Memorial Sloan-Kettering Cancer Center (MSKCC), New York, NY, 10021, USA;
- 2003-2005: American-Italian Cancer Foundation Fellowship. MSKCC, New York, NY, 10021, USA;
- 2006-2010: "Brain Gain" program (already "Rientro Cervelli") from the Italian Ministry of Education and Research (MUR). Grant of Euro 80,000 for salary and 20,000 for research support.

C. Contributions to Science

Under postdoctoral scholarship at MSKCC, I focused my studies on the study of meiotic checkpoints in female and male germ cells, and I became acquainted with XY recombination issue, providing a key input in identifying the role of SPO11 during meiosis

1. [Collaboration of homologous recombination and nonhomologous end-joining factors for the survival and integrity of mice and cells.](#)
Couëdel C, Mills KD, **Barchi M**, Shen L, Olshen A, Johnson RD, Nussenzweig A, Essers J, Kanaar R, Li GC, Alt FW, Jasin M. *Genes Dev.* 2004 Jun 1;18(11):1293-304. doi: 10.1101/gad.1209204.PMID: 15175261
2. [Surveillance of different recombination defects in mouse spermatocytes yields distinct responses despite elimination at an identical developmental stage.](#)
Barchi M, Mahadevaiah S, Di Giacomo M, Baudat F, de Rooij DG, Burgoyne PS, Jasin M, Keeney S. *Mol Cell Biol.* 2005 Aug;25(16):7203-15. doi: 10.1128/MCB.25.16.7203-7215.2005.PMID: 16055729
3. [Distinct DNA-damage-dependent and -independent responses drive the loss of oocytes in recombination-defective mouse mutants.](#)
Di Giacomo M, **Barchi M**, Baudat F, Edelmann W, Keeney S, Jasin M. *Proc Natl Acad Sci U S A.* 2005 Jan 18;102(3):737-42. doi: 10.1073/pnas.0406212102. Epub 2005 Jan 7. PMID: 15640358
4. [Bub1 maintains centromeric cohesion by activation of the spindle checkpoint.](#)
Perera D, Tilston V, Hopwood JA, **Barchi M**, Boot-Handford RP, Taylor SS. *Dev Cell.* 2007 Oct;13(4):566-79. doi: 10.1016/j.devcel.2007.08.008.PMID: 17925231
5. [ATM promotes the obligate XY crossover and both crossover control and chromosome axis integrity on autosomes.](#)
Barchi M, Roig I, Di Giacomo M, de Rooij DG, Keeney S, Jasin M. *PLoS Genet.* 2008 May 23;4(5):e1000076. doi: 10.1371/journal.pgen.1000076.PMID: 18497861
6. [Distinct properties of the XY pseudoautosomal region crucial for male meiosis.](#)
Kauppi L, **Barchi M**, Baudat F, Romanienko PJ, Keeney S, Jasin M. *Science.* 2011 Feb 18;331(6019):916-20. doi: 10.1126/science.1195774.PMID: 21330546
7. [Numerical constraints and feedback control of double-strand breaks in mouse meiosis.](#)

Kauppi L, **Barchi M**, Lange J, Baudat F, Jasin M, Keeney S. *Genes Dev.* 2013 Apr 15;27(8):873-86. doi: 10.1101/gad.213652.113. Epub 2013 Apr 18. PMID: 23599345

As PI in Italy, I continued my interest in meiotic recombination and broadened my horizons by studying recombinative mechanisms in male germ cell tumors. In the following (selected) list of papers published as PI, myself, as well as, Ph.D. students, technicians and research fellow in my lab are in bold.

1. [Isolation and analyses of enriched populations of male mouse germ cells by sedimentation velocity: the centrifugal elutriation.](#)
Barchi M, Geremia R, **Magliozzi R**, Bianchi E. *Methods Mol Biol.* 2009;558:299-321. doi: 10.1007/978-1-60761-103-5_18. PMID: 19685332
2. [Targeted inactivation of nuclear interaction partner of ALK disrupts meiotic prophase.](#)
Illert AL, Kawaguchi H, **Antinozzi C**, Bassermann F, Quintanilla-Martinez L, von Klitzing C, Hiwatari M, Peschel C, de Rooij DG, Morris SW, **Barchi M**, Duyster J. *Development.* 2012 Jul;139(14):2523-34. doi: 10.1242/dev.073072. Epub 2012 Jun 13. PMID: 22696294
3. [A surge of late-occurring meiotic double-strand breaks rescues synapsis abnormalities in spermatocytes of mice with hypomorphic expression of SPO11.](#)
Faieta M, **Di Cecca S**, de Rooij DG, Luchetti A, Murdocca M, Di Giacomo M, Di Siena S, Pellegrini M, Rossi P, **Barchi M**. *Chromosoma.* 2016 Jun;125(2):189-203. doi: 10.1007/s00412-015-0544-7. Epub 2015 Oct 6. PMID: 26440409
4. [H2AFX and MDC1 promote maintenance of genomic integrity in male germ cells.](#)
Testa E, **Nardozi D**, **Antinozzi C**, **Faieta M**, Di Cecca S, **Caggiano C**, Fukuda T, Bonanno E, Zhenkun L, Maldonado A, Roig I, Di Giacomo M, **Barchi M**. *J Cell Sci.* 2018 Mar 20;131(6):jcs214411. doi: 10.1242/jcs.214411. PMID: 29437857
5. [Mouse ANKRD31 Regulates Spatiotemporal Patterning of Meiotic Recombination Initiation and Ensures Recombination between X and Y Sex Chromosomes.](#)
Papanikos F, Clément JAJ, **Testa E**, Ravindranathan R, Grey C, Dereli I, Bondarieva A, Valerio-Cabrera S, Stanzione M, Schleiffer A, Jansa P, Lustyk D, Fei JF, Adams IR, Forejt J, **Barchi M**, de Massy B, Toth A. *Mol Cell.* 2019 Jun 6;74(5):1069-1085.e11. doi: 10.1016/j.molcel.2019.03.022. Epub 2019 Apr 15. PMID: 31000436
6. [Assessing Homologous Recombination and Interstrand Cross-Link Repair in Embryonal Carcinoma Testicular Germ Cell Tumor Cell Lines.](#)
Cavallo F, **Caggiano C**, Jasin M, **Barchi M**. *Methods Mol Biol.* 2021;2195:113-123. doi: 10.1007/978-1-0716-0860-9_9. PMID: 32852761
7. [Sempervirine inhibits RNA polymerase I transcription independently from p53 in tumor cells.](#)
Caggiano C, Guida E, Todaro F, Bielli P, Mori M, Ghirga F, Quaglio D, Botta B, Moretti F, Grimaldi P, Rossi P, Jannini EA, **Barchi M***, Dolci S*. *Cell Death Discov.* 2020 Oct 28;6(1):111. doi: 10.1038/s41420-020-00345-4. PMID: 33298840; *Co-corresponding authors
8. [Testicular Germ Cell Tumors Acquire Cisplatin Resistance by Rebalancing the Usage of DNA Repair Pathways.](#)
Caggiano C, **Cavallo F**, **Giannattasio T**, **Cappelletti G**, Rossi P, Grimaldi P, Feldman DR, Jasin M, **Barchi M**. *Cancers (Basel).* 2021 Feb 13;13(4):787. doi: 10.3390/cancers13040787. PMID: 33668653
9. [The RNA-binding protein FUS/TLS interacts with SPO11 and PRDM9 and localize at meiotic recombination hotspots.](#) **Giannattasio T**, **Testa E**, Palombo R, Chellini L, Franceschini F, Crevenna Á, Petkov PM, Paronetto MP, **Barchi M**. *Cell Mol Life Sci.* 2023 Mar 26;80(4):107. doi: 10.1007/s00018-023-04744-5. PMID: 36967403
10. [The proper interplay between the expression of Spo11 splice isoforms and the structure of the pseudoautosomal region promotes XY chromosomes recombination.](#)
Giannattasio T, **Testa E**, **Faieta M**, **Lampitto M**, **Nardozi D**, **di Cecca S**, Russo A, **Barchi M**. *Cell Mol Life Sci.* 2023 Sep 8;80(10):279. doi: 10.1007/s00018-023-04912-7. PMID: 37682311
11. [Seeding the meiotic DNA break machinery and initiating recombination on chromosome axes.](#)
Dereli I, Telychko V, Papanikos F, Raveendran K, Xu J, Boekhout M, Stanzione M, Neuditschko B, Imjeti NS, Selezneva E, Tuncay H, Demir S, **Giannattasio T**, Gentzel M, Bondarieva A, Stevense M, **Barchi M**, Schnittger A, Weir JR, Herzog F, Keeney S, Tóth A. *Nat Commun.* 2024 Apr 5;15(1):2941. doi: 10.1038/s41467-024-47020-1. PMID: 38580643

12. [Recent advances in mechanisms ensuring the pairing, synapsis and segregation of XY chromosomes in mice and humans.](#)
Lampitto M, Barchi M. Cell Mol Life Sci. 2024 Apr 23;81(1):194. doi: 10.1007/s00018-024-05216-0. PMID: 38653846