# Claus M. Azzalin, PhD

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# ACADEMIC CAREER

#### **October 2016-Present:**

Group Leader at Instituto de Medicina Molecular João Lobo Antunes (iMM) (Lisbon, Portugal).

#### March 2009-Septemebr 2016:

SNF/ETHZ Assistant Professor for Genome Stability at the Institute of Biochemistry (IBC) of ETHZ (Zürich, Switzerland).

#### January 2008-February 2009:

Junior Group Leader at the Institute of Biochemistry (IBC) of ETHZ (Zürich, Switzerland).

#### March 2002-January 2008:

Post-doctoral Fellow at the Swiss Institute for Experimental Cancer Research (Lausanne, Switzerland), laboratory headed by Prof. J. Lingner.

#### July 2001-March 2002:

Post-doctoral Fellow at the Memorial Sloan-Kettering Cancer Center (New York, USA), laboratory headed by Dr. M. Jasin.

## November 2000-July 2001:

European Community fellowship (European Community contract "TeloRad", EC F1S5-1999-00055), Department of Genetics and Microbiology "A. Buzzati Traverso", Molecular and Cellular Biology laboratory headed by Prof. E. Giulotto.

#### December 2000:

PhD in 'Genetics and Molecular Biology' at the University of Pavia (Pavia, Italy).

#### January-April 1997:

Research stage at the University of Oxford (Oxford, UK), Dept. of Biochemistry, CRC Chromosome Molecular Biology Group headed by Prof. E. Southern and Dr. W. Brown (European Community contract "Biomed II", EC BMH4-CT96-0894).

#### November 1996-October 2000:

PhD training at the University of Pavia (Pavia, Italy), Dept. of Genetics and Microbiology "A. Buzzati Traverso", Molecular and Cellular Biology laboratory headed by Prof. E. Giulotto.

#### June 1996:

Degree in Biology *cum laude* at the University of Pavia (Pavia, Italy).

## **MAJOR AWARDS**

EMBO Installation Grant Award (January 2017).

FCT Investigator Programme award (November 2016).

Associate Membership of 'Epigenesys', a FP7 European Community-funded Network of Excellence (July 2013).

EMBO Young Investigator Programme (YIP) Award (November 2012).

Swiss National Science Foundation (SNF) Professorship for 'Genome Stability' associated to the grant '*Transcription of telomeric heterochromatin*' (April 2009 - March 2013).

European Research Council (ERC) starting grant '*BFTERRA*' (October 2009-September 2014).

Renewal of the Swiss National Science Foundation (SNF) Professorship for 'Genome stability' associated to the grant '*Non-coding nuclear RNAs: from telomere integrity to RNA surveillance to pre-mRNA splicing*' (April 2013 - March 2015).

## **MEETING ORGANIZATION**

*January 2015:* co-organizer of the LS2 (Life Science Switzerland) annual meeting '*Light: from the basis of life to life science technologies*', Zurich, Switzerland.

*July 2016:* co-organizer of the symposium '*Non-coding RNAs in health and disease*' within the 12th International Congress of Cell Biology, Prague, Czech Republic.

May 2018: co-organizer of the EMBO workshop '*Telomere biology in health and human disease*', Troia, Portugal

## LANGUAGES

Italian, English, French.

## AREAS OF INTEREST

Telomere structure and telomere length regulation, RNA metabolism, Telomeric Repeatcontaining RNA (TERRA), heterochromatin organization, non-coding RNA, genetic basis of cancer, aging and rare human diseases, DNA-damage recognition and repair, chromosomal rearrangements and their significance in genetic disease and karyotype evolution.

## **TEACHING AND MENTORING ACTIVITY**

I participated in the following courses at ETHZ:

*Cellular Biochemistry I*, course number: 551-0319-00, organizer: Prof. Ulrike Kutay.

Grundlagen der Biologie I (Praktikum), coordinator: Dr. Ruth Kroschewski.

*Current Research Topics in Cellular Biochemistry*, course number: 551-1310-00, organizers: Prof. Vikram Panse and Dr. Alicia Smith.

*Methods in Cellular Biochemistry* Block Course, course number 551-0336-00, organizer: Prof. Paola Picotti.

*MLS Cell Biology* course for PhD students of ETHZ and University of Zürich.

I organized for 3 years the block course '*RNA biology*' at ETHZ, course number: 551-1309-00.

I organized for 1 year the block course *'Cause and Consequences of Unstable Genomes'* at ETHZ, course number: 551-1300-00L.

I supervise directly undergraduate and graduate students working in my laboratory.

I have been or still am part of PhD committee meetings of a total of 15 students from different European Universities.

I regularly give lectures on chromosome stability for medical students of the University of Lisbon (Universidade de Lisboa).

## **REVIEWING ACTIVITY**

I have served as *ad hoc* Reviewer for several international peer-reviewed journals including Cancer Research, Chromosoma, Chromosome Research, The EMBO Journal, EMBO Reports, ELife, Genetics, Journal of Biological Chemistry, Molecular and Cellular Biology, Nature, Nature Cell Biology, Nature Structural and Molecular Biology, Scientific reports, Nature Communications, Nucleic Acids Research, Oncogene, RNA, FEBS Letters, Frontiers in Oncology, PLos ONE, PLos Genetics, and others.

I have served as *ad hoc* Reviewer and evaluation panel member for the assessment of research grant applications and personal fellowships for different funding agencies including ERC (starting, consolidator and advanced grants), EMBO, the Swiss Science Foundation (SNF), the Swiss Cancer League, the French Agence nationale de la recherche (ANR), and the Agency for Science, Technology and Research of Singapore.

I am an Academic Editor for FEBS Letters.

#### **ORAL PRESENTATIONS**

I am regularly invited to present our work at national and international institutions and members of my laboratory regularly give oral presentations at international meetings.

I have also been selected or invited for oral presentation at the following international meetings:

*October 2002:* <u>selected speaker</u> for the CSHL Meeting '*Molecular genetics of Aging*', CSH New York, USA.

April 2003: <u>selected speaker</u> for the CSHL Meeting '*Telomeres & Telomerase*', CSH, New York, USA.

*May 2007:* <u>selected speaker</u> for the CSHL Meeting '*Telomeres & Telomerase*', CSH, New York, USA.

September 2008: invited speaker and chairman for the EMBO conference '*Telomeres and the DNA Damage response*', Villars-sur-Ollon, Switzerland.

*October 2012:* <u>selected speaker</u> for the EMBO conference '*Telomeres and the DNA Damage response*', L'isle-sur-la-Sourge, France.

*December 2012:* <u>invited speaker</u> for the Institute Curie International Course '*The Non-Coding Genome*', Paris, France.

*April 2013:* <u>invited speaker and chairman</u> for the CSHL Meeting '*Telomeres & Telomerase*', CSH, New York, USA.

June 2013: invited speaker for the Swiss Yeast Meeting, Interlaken, Switzerland.

*July 2013:* <u>invited speaker</u> for the 38<sup>th</sup> FEBS Congress '*Mechanisms in Biology*', St. Petersburg, Russia.

May 2014: invited speaker for the 'EMBO Young Scientists Forum 2014', Brno, Czech Republic.

June 2014: invited speaker for the 7<sup>th</sup> 'IMG PhD Conference', Prague, Czech Republic.

October 2014: invited speaker for the EMBO workshop 'Non-coding RNA in genome expression, maintenance and stability', Cargese, France.

*October 2015:* <u>selected speaker</u> for the '*Molecular Biology of Ageing Meeting*', Groningen, The Netherlands.

*April 2016:* <u>invited speaker</u> for the EMBO meeting '*Telomeres, telomerase and disease*', Liege, Belgium.

*July 2016:* <u>invited speaker and chairman</u> for the 'Congress of Cell Biology - Exploring Cellular Structure and Function', Prague, Czech Republic.

July 2017: invited speaker for the GABBA Symposium 'Nano 2 Universe', Porto, Portugal.

*October 2017:* <u>invited speaker and chairman</u> for the EMBO meeting '*Nuclear structure and dynamics*', L'isle-sur-la-Sourge, France.

*December 2017:* <u>invited speaker</u> for the workshop '*Telomeres in Health, Aging and Disease*' UNESP Botucatu, Brazil.

*October 2018:* <u>invited speaker</u> for the EMBO workshop '*RNA and genome maintenance: Cooperation and conflict management*', Mainz, Germany.

# PUBLICATIONS

- **1** "Fluorescence in situ hybridization with a synthetic (T<sub>2</sub>AG<sub>3</sub>)n polynucleotide detects several intrachromosomal telomere-like repeats on human chromosomes". **C.M. Azzalin**, E. Mucciolo, L. Bertoni and E. Giulotto (1997). *Cytogenet Cell Genet* 78: 112-115.
- **2** "The chicken *HPRT* gene: a counter selectable marker for the DT40 cell line". T. Fukagawa, N. Hayward, J. Yang, **C. Azzalin**, D. Griffin, A.F. Stewart and W. Brown (1999). *Nucleic Acids Res* 27: 1966-69.
- **3** "Instability of interstitial telomeric sequences in the human genome". C. Mondello, L. Pirzio, **C.M. Azzalin** and E. Giulotto (2000). *Genomics* 68: 111-117.

- **4** "Human intrachromosomal telomeric-like repeats: genome organization and mechanisms of origin". **C.M. Azzalin**, S.G. Nergadze, L. Bertoni and E. Giulotto (2001). *Chromosoma* 110: 75-82.
- **5** "Molecular organization of interstitial telomeric sequences in Chinese hamster". M. Faravelli, **C.M. Azzalin**, L. Bertoni, O. Chernova, C. Mondello and E. Giulotto (2002). *Gene* 283: 11-16.
- **6** "Distribution of intrachromosomal telomeric sequences (ITS) on Macaca fascicularis (Primates) chromosomes and their implication for chromosome evolution". A. Ruiz-Herrera, F. Garcia, **C. Azzalin**, E. Giulotto, J. Egozcue, M. Ponsa and M. Garcia (2002). *Hum Genet* 110: 578-86.
- 7 "A human homolog of yeast Est1 associates with telomerase and uncaps chromosome ends when overexpressed". P. Reichenbach\*, M. Hoss\*, C.M. Azzalin\*, M. Nabholz, P. Bucher and J. Lingner (2003). *Curr Biol* 13:568-574. [\*shared first authorship]
- **8** "Telomere wedding ends in divorce". **C.M. Azzalin** and J. Lingner (2004). *Science* 304: 60-62.
- **9** "Insertion of telomeric repeats at intrachromosomal break sites during primate evolution". S.G. Nergadze, M. Rocchi, **C.M. Azzalin**, C. Mondello and E. Giulotto (2004). *Genome Res* 14: 1704-1710.
- **10** "A GFP-based reporter system to monitor nonsense-mediated mRNA decay". A. Paillusson, N. Hirschi, C. Vallan, **C.M. Azzalin** and O. Mühlemann (2005). *Nucleic Acids Res* 33: e54.
- **11** "New mammalian cellular systems to study mutations introduced at the break site by nonhomologous end-joining". P. Rebuzzini, L. Khoriauli, **C.M. Azzalin**, E. Magnani, C. Mondello and E. Giulotto (2005). *DNA Repair* 4: 546-555.
- 12 "S. cerevisiae Est1/H. sapiens SMG6 Protein Family Members Function in Telomere Metabolism". C.M. Azzalin, S. Redon and J. Lingner (2005). In the book 'Nonsense-Mediated mRNA Decay' edited by Lynne E. Maquat. Landes Bioscience TX, USA.
- **13** "The human RNA surveillance factor UPF1 is required for S-phase progression and genome stability". **C.M. Azzalin** and J. Lingner (2006). *Curr. Biol* 16: 433-439.
- **14** "The Double Life of UPF1 in RNA and DNA Stability Pathways". **C.M. Azzalin** and J. Lingner (2006). *Cell Cycle* 5: 1496-1498.
- **15** "Molecular biology: damage control". **C.M. Azzalin** and J. Lingner (2007). *Nature* 448: 1001-1002.
- **16** "Telomeric Repeat Containing RNA and RNA surveillance factors at mammalian chromosome ends". **C.M. Azzalin**, P. Reichenback, L. Khoriauli, E. Giulotto and J. Lingner (2007). *Science* 318: 798-801.
- **17** "Saccharomyces cerevisiae Ebs1p is a putative ortholog of human Smg7 and promotes nonsense mediated mRNA decay". B. Luke\*, **C.M. Azzalin**\*, N. Hug, A. Deplazes, M. Peter and J. Lingner (2007). *Nucleic Acids Res* 35: 7688-7697. [\*shared first authorship]
- **18** "Telomeres: the silence is broken". **C.M. Azzalin** and J. Lingner (2008). *Cell Cycle* 7: 1161-1165.
- **19** "The telomeric transcriptome and SMG proteins at the crossroads". R. Chawla and **C.M. Azzalin** (2008). *Cytogenet Genome Research* 122: 194-201.
- **20** "CpG-island promoters drive transcription of human telomeres". S.G. Nergadze, B.O. Farnung, H. Wischnewski, L. Khoriauli, V. Vitelli, R. Chawla, E. Giulotto and **C.M. Azzalin** (2009). *RNA* 15: 2186-2194.

- **21** "Promoting transcription of chromosome ends". B.O. Farnung, E. Giulotto and **C.M. Azzalin** (2010). *Transcription* 1: 140-143.
- 22 "TERRA: Long Noncoding RNA at Eukaryotic Telomeres". R. Arora , C.M. Brun and C.M. Azzalin (2011). *Prog Mol Subcell Biol* 51: 65-94.
- **23** "Human UPF1 interacts with TPP1 and telomerase and sustains telomere leading-strand replication". R. Chawla, S. Redon, C. Raftopoulou, H. Wischnewski, S. Gagos and **C.M. Azzalin** (2011). *EMBO J* 30: 4047-4058.
- **24** "The telomeric transcriptome of *Schizosaccharomyces pombe*". A. Bah, H. Wischnewski, V. Shchepachev and **C.M. Azzalin** (2011). *Nucleic Acids Res* 40: 2995-3005.
- 25 "UPF1: A leader at the end of chromosomes". C.M. Azzalin (2012). Nucleus 3: 16-21.
- **26** "Transcription regulates telomere dynamics in human cancer cells". R. Arora, C.M. Brun and **C.M. Azzalin** (2012). *RNA* 18: 684-693.
- **27** "Telomerase efficiently elongates highly transcribing telomeres in human cancer cells". B.O. Farnung, C.M. Brun, R. Arora, L.E. Lorenzi and **C.M. Azzalin** (2012). *PLoS ONE* 7: e35714.
- **28** "The telomeric transcriptome: from fission yeast to mammals". A. Bah and **C.M. Azzalin** (2012). *Int J Biochem Cell Bio* 44: 1055-1059.
- **29** "Mpn1, mutated in Clericuzio-type poikiloderma with neutropenia protein 1, is a conserved 3'-to-5' RNA exonuclease processing U6 small nuclear RNA". V. Shchepachev, H. Wischnewski, E. Missiaglia, C. Soneson and **C.M. Azzalin** (2012). *Cell Rep* 2: 855-865.
- **30** "The Mpn1 RNA exonuclease: cellular functions and implication in disease". V. Shchepachev and **C.M. Azzalin** (2013). *FEBS Lett* 587:1858-1862.
- **31** "The host nonsense-mediated mRNA decay pathway restricts Mammalian RNA virus replication". G. Balistreri, P. Horvath, C. Schweingruber, D. Zünd, G. McInerney, A. Merits, O. Mühlemann, **C. Azzalin** and A. Helenius (2014). *Cell Host Microbe* 16: 403-411.
- **32** "Telomere functions grounding on TERRA firma". **C.M. Azzalin**\* and J. Lingner\* (2014). *Trends Cell Biol* 25: 29-36. [\*shared corresponding authorship]
- **33** "RNaseH1 regulates TERRA-telomeric DNA hybrids and telomere maintenance in ALT tumor cells". R. Arora, Y. Lee, H. Wischnewski, C. M. Brun, T. Schwarz and **C.M. Azzalin** (2014). *Nat Commun* 5: 5220.
- **34** "Fission yeast Cactin restricts telomere transcription and elongation by regulating Rap1 levels". L.E. Lorenzi, A. Bah, H. Wischnewski, V. Shchepachev, C. Soneson, M. Santagostino and **C. M. Azzalin** (2014). *The EMBO J* 34: 115-129.
- **35** "Telomere elongation chooses TERRA ALTernatives". R. Arora and **C. M. Azzalin** (2015). *RNA Biol* 12: 938-941.
- **36** "Human Mpn1 promotes post-transcriptional processing and stability of U6atac". V. Shchepachev, H. Wischnewski, C. Soneson, A. Arnold and **C.M. Azzalin** (2015). *FEBS Lett* 589: 2417-2423.
- 37 "TERRA promotes telomerase-mediated telomere elongation in *Schizosaccharomyces pombe*". M. Moravec, H. Wischnewski, A. Bah, Y. Hu, N. Liu, L. Lafranchi, M.C. King and C.M. Azzalin (2016). *EMBO Rep* 17: 999-1012.
- **38** "Stem-loop RNA labeling can affect nuclear and cytoplasmic mRNA processing". S. Heinrich, C.L. Sidler, **C.M. Azzalin** and K. Weis (2017). *RNA* 23: 134-141.
- **39** "Human Cactin interacts with DHX8 and SRRM2 to assure efficient pre-mRNA splicing and sister chromatid cohesion". I.M. Zanini, C. Soneson, L.E. Lorenzi and **C.M. Azzalin** (2017). *J Cell Sci* 130: 767-778.

- **40** "Non-targeted metabolomic approach reveals two distinct types of metabolic responses to telomerase dysfunction in *S. cerevisiae*". F. Buettner, K. Jay, H. Wischnewski, T. Stadelmann, S. Saad, K. Jefimovs, M. Mansurova, J. Gerez, **C.M. Azzalin**, R. Dechant and A.J. Ibáñez (2017). *Metabolomics* 13: 53.
- **41** "TRF1 participates in chromosome end protection by averting TRF2-dependent telomeric R loops". Y.W. Lee, R. Arora, H. Wischnewski, **C.M. Azzalin**. *Nat Struct Mol Biol* (2018). 25: 147-153.