

PERSONAL INFORMATION

Martina Cesani

WORK EXPERIENCE

- March 2022- Present **CMC Regulatory Affairs and Quality Assurance Manager**
Fondazione Telethon ETS (Italy)
Strategic management of CMC (Chemistry, Manufacturing, and Controls) regulatory activities and Quality Assurance for Gene Therapy products, from the development stage to commercialization
- October 2019-March 2022 **Quality Assurance Manager**
AGC Biologics S.p.A. (former MolMed S.p.A.) (Italy)
Guaranteeing the GMP compliance of an ATMP manufacturing facility; Management of regulatory inspections and client audits; Management of Quality Agreements and of interactions with clients for quality-related matters.
- April 2019-March 2022 **Qualified Person**
AGC Biologics S.p.A. (former MolMed S.p.A.) (Italy)
QP oversight and batch certification and release of investigational and approved ATMPs.
- December 2014-October 2019 **Quality Control Supervisor Molecular Biology Area**
MolMed S.p.A. (Italy)
Planning and management of the release and stability tests for drug products, product intermediates and starting materials; Planning and management of the transfer and validation of analytical methods.
- February 2011-November 2014 **Post-Doctoral Fellow**
San Raffaele Telethon Institute for Gene Therapy (SR-TIGET) (Italy)
Research projects: 1) Identification and characterizations of biomarkers for the monitoring and treatment of patients affected by Metachromatic Leukodystrophy.
2) Gene expression and clonal population follow-up in patients affected by Metachromatic Leukodystrophy upon gene therapy
- October 2009-January 2011 **Post-Doctoral Fellow**
Laboratory of Developmental and Stem Cell Biology, Harvard Medical School and Joslin Diabetes Center (United States)
Research project: Role of EGR1 transcription factor on hematopoietic stem cell fate and function.
- August 2008-February 2009 **PhD Exchange student**
Laboratory of Neurogenomics at Center for Neurological Disorders, Harvard Medical School and Brigham and Womens Hospital (United States)
Research project: Gene expression analysis of patients affected by Metachromatic Leukodystrophy.
- April 2004-August 2009 **Research fellow and PhD student**
San Raffaele Telethon Institute for Gene Therapy (SR-TIGET) (Italy)
Research projects: 1) Biochemical and molecular characterization of patients affected by Metachromatic Leukodystrophy; 2) Development of a safe and efficient protocol of hematopoietic stem cells transduction for gene therapy of Metachromatic Leukodystrophy

EDUCATION AND TRAINING

- December 2017-April 2018 **Master in Quality by Design**
Tartari & Partners (Italy)

February 2006-April 2009

Ph.D. in Molecular Medicine (section of Experimental Neurology)

Vita-Salute San Raffaele University (Italy)

Title of Ph.D. thesis: Metachromatic Leukodystrophy: new insights into genotype-phenotype correlation and pathological mechanisms.

October 1998-October 2003

M.Sc. (Laurea) in Pharmaceutical Biotechnology

University of Milan (Italy)

Title of experimental thesis: Molecular analysis through denaturing HPLC (DHPLC) of the gene coding for periaxin in patients affected by hereditary peripheral neuropathies.

ADDITIONAL INFORMATION

Expertise

Writing and revision of QMS policy and Site Master File

Quality Risk Management

QMS continuous implementation

Management of deviations, out of specifications, CAPAs, analytical non conformities and change controls.

Management of aseptic process validation and environmental monitoring for sterile productions

Management of the activities of computer system validation for the instrument-related softwares

Batch approval and release of investigational and approved ATMPs

QP certification of investigational and approved ATMPs

Regulatory inspections and client audits management

Writing and revision of CMC sections of Regulatory documents for investigational and marketed ATMPs

Writing and revision of Quality Technical Agreements with clients

Writing and revision of SOPs, Master Batch Records and Analytical Methods.

Supervision of validation/qualification protocols and reports

Planning and management of the release and stability tests for drug products, product intermediates and starting materials.

Planning and management of the validation of analytical methods in compliance with the relevant legislation.

Deep knowledge of molecular biology, protein analysis and cell biology standard laboratory techniques

Publications

Fumagalli F, Zambon A, Rancoita P, Baldoli C, Canale S, Spiga I, Medagliani S, Penati R, Facchini M, Ciotti F, Sarzana M, Lorioli L, Cesani M, Natali Sora MG, Del Carro U, Cugnata F, Antonioli G, Recupero S, Calbi V, Di Serio V, Aiuti A, Biffi A, Sessa M. Metachromatic Leukodystrophy: a single-center longitudinal study of 45 patients. *AJ Inherit Metab Disl* 2021 44(5):1151-64. PMID: 33855715. DOI: 10.1002/jimd.12388

Cavalca E, Cesani M, Gifford JC, Sena-Esteves M, Terreni MR, Leoncini G, Peviani M, Biffi A. Metallothioneins are neuroprotective agents in lysosomal storage disorders. *Ann Neurol* 2018 83(2):418-32. PMID: 29369397. DOI: 10.1002/ana.25161

Cesani M, Lorioli L, Grossi S, Amico G, Fumagalli F, Spiga I, Filocamo M, Biffi A. Mutation Update of ARSA and PSAP genes causing Metachromatic Leukodystrophy. *Hum Mutat* 2016 37(1):16-27. PMID: 26462614. DOI: 10.1002/humu.22919

Cesani M, Plati T, Lorioli L, Benedicenti F, Redaelli D, Dionisio F, Biasco L, Montini E, Naldini L, Biffi A. Shedding of clinical-grade lentiviral vectors is not detected in a gene therapy setting. *Gene Ther* 2015 22(6):496-502. PMID: 25762283. DOI: 10.1038/gt.2015.10

Cesani M, Cavalca E, Macco R, Leoncini G, Terreni MR, Lorioli L, Furlan R, Comi GC, Doglioni C, Zacchetti D, Sessa M, Scherzer CR, Biffi A. Metallothioneins as dynamic markers for brain disease in Lysosomal Disorders. *Ann Neurol* 2014 75(1):127-37. PMID: 24242821. DOI: 10.1002/ana.24053

Lorioli L, Cesani M, Regis S, Morena F, Grossi S, Fumagalli F, Acquati S, Redaelli D, Pini A, Sessa M, Martino S, Filocamo M, Biffi A. Critical issues for the proper diagnosis of Metachromatic Leukodystrophy. *Gene* 2014 537(2):348-51. PMID: 24334127. DOI: 10.1016/j.gene.2013.11.062

Biffi A, Montini E, Lorioli L, Cesani M, Fumagalli F, Plati T, Baldoli C, Martino S, Calabria A, Canale S, Benedicenti F, Vallanti G, Biasco L, Leo S, Kabbara N, Zanetti G, Rizzo WB, Mehta NAL, Cicalese MP, Casiraghi M, Boelens JJ, Del Carro U, Dow DJ, Schmidt M, Assanelli A, Neduva V, Di Serio C,

Stupka E, Gardner J, von Kalle C, Bordignon C, Ciceri F, Rovelli A, Roncarolo MG, Aiuti A, Sessa M, Naldini L. Lentiviral hematopoietic stem cell gene therapy benefits metachromatic leukodystrophy. *Science* 2013 341(6148):1233158. PMID: 23845948. DOI: 10.1126/science.1233158

Biffi A, Bartolomae CC, Cesana D, Cartier N, Aubourg P, Ranzani M, Cesani M, Benedicenti F, Plati T, Rubagotti E, Merella S, Capotondo A, Sgualdino J, Zanetti G, von Kalle C, Schmidt M, Naldini L, Montini E. Lentiviral-vector common integration sites in preclinical models and a clinical trial reflect a benign integration bias and not oncogenic selection. *Blood* 2011 117(20):5332-9. PMID: 21403130. DOI: 10.1182/blood-2010-09-306761

Marchesi C, Milani M, Morbin M, Cesani M, Lauria G, Scaioli V, Piccolo G, Fabrizi GM, Cavallaro T, Taroni F, Pareyson D. Four novel cases of periaxin-related neuropathy and review of the literature. *Neurology* 2010 75(20):1830-8. PMID: 21079185. DOI: 10.1212/WNL.0b013e3181fd6314

Visigalli I, Ungari S, Martino S, Park H, Cesani M, Gentner B, Sergi Sergi L, Orlacchio A, Naldini L, Biffi A. The galactocerebrosidase enzyme contributes to the maintenance of a functional hematopoietic stem cell niche. *Blood* 2010 116(11):1857-66. PMID: 20511539. DOI: 10.1182/blood-2009-12-256461

Cesani M, Capotondo A, Plati T, Sergi Sergi L, Fumagalli F, Roncarolo MG, Naldini L, Comi G, Sessa M, Biffi A. Characterization of new Arylsulfatase A gene mutations reinforces genotype-phenotype correlation in Metachromatic Leukodystrophy. *Hum Mutat* 2009 30(10):E936-45. PMID: 19606494. DOI: 10.1002/humu.21093

Biffi A, Cesani M, Fumagalli F, Del Carro U, Baldoli C, Canale S, Gerevini S, Amadio S, Falautano M, Comi G, Roncarolo MG, Sessa M. Metachromatic Leukodystrophy - mutation analysis provides further evidences of genotype-phenotype correlation. *Clin Genet* 2008 74(4):349-57. PMID: 18786133. DOI: 10.1111/j.1399-0004.2008.01058.x

Biffi A and Cesani M. Human hematopoietic stem cells in gene therapy: pre-clinical and clinical issues. Review. *Curr Gene Ther* 2008 8(2):135-46. PMID: 18393833. DOI: 10.2174/156652308784049381

Capotondo A*, Cesani M*, Pepe S, Fasano S, Gregori S, Tononi L, Venneri MA, Brambilla R, Quattrini A, Ballabio A, Cosma MP, Naldini L, Biffi A. Safety of arylsulfatase A overexpression for gene therapy of metachromatic leukodystrophy. *Hum Gene Ther*. 2007 18(9):821-36. PMID: 17845130. DOI: 10.1089/hum.2007.048

*these authors equally contributed to this work

Projects Listed as Co-Inventor on the Patent "Metallothioneins as Biomarkers for Lysosomal Storage Disorders" held by Ospedale San Raffaele Srl, Fondazione Telethon and The Brigham and Women's Hospital Inc. (International Patent Application No. PCT/IB2012/054469).

Memberships Memberships:
Italian Order of Biologists, 2019-present
AFI (Italian Associazione Farnaceutici Industria, Societa Scientifica), 2019-present
ARM (Alliance for Regenerative Medicine), 2020-present
TOPRA (The Organization for Professionals in Regulatory Affairs), 2022-present
Scientific meeting attendance:
Advanced Therapies Congress 2022, London 24-15 May 2022
10th Annual WORLD Symposium, San Diego 10-13 February 2014
6th Meeting on Molecular Mechanisms in Neuroscience, Rome 3-4 October 2011.
8th Annual Meeting of the International Society for Stem Cell Research, San Francisco 16th-19th June 2010.
Genetic and metabolic diseases in pediatrics: diagnosis, prevention and aid, Rome 28-30 November 2007.
3rd Annual CONSERT Meeting, Leukerbad 1-3 February 2007.
10th Annual Meeting of the American Society of Gene Therapy, Seattle 30 May-3 June 2007.
9th Annual Meeting of the American Society of Gene Therapy, Baltimore 31 May-4 June 2006.

Other Relevant Information Certifications:

Eligibility to perform the function of Qualified Person in ATMP manufacturing facilities (AIFA, May 2018).

Italian State Exam for the habilitation to the profession of Biologist (Insubria University of Varese, July 2013).

Teaching:

Scientific, technical and thesis-writing mentorship for B.Sc, M.Sc and MD students

Teaching at II level Master classes.