

BIOGRAPHICAL SKETCH

NAME: Valentina Salsi

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
University of Modena	MSc equivalent in Biological Sciences (with honors)	07/2002	Molecular Biology
University of Modena	PhD (with honors)	03/2006	Molecular Biology/ Human Genetics

A. Personal Statement

I have a long-standing interest in the molecular basis of genetic diseases, which I have pursued through a multidisciplinary approach combining molecular biology, functional genomics, and cellular models. Over the years, I have contributed to understanding the regulation and misregulation of transcription factors in development and disease, with a special focus on chromatin dynamics and gene expression in rare disorders. My recent research has centered on facioscapulohumeral muscular dystrophy (FSHD), where I investigate the pathogenic mechanisms linked to the 4q35 locus, including the role of repetitive elements and non-coding RNAs in gene regulation.

Throughout my career, I have been involved in several national and international projects and have collaborated with both academic and clinical groups. I have developed strong technical expertise in molecular cloning, gene expression profiling, epigenetics, genomics and genome editing. I have also mentored students and young researchers at different levels, fostering a collaborative and supportive lab environment.

Currently, I am working on innovative models to study chromatin domains and transcriptional regulation in FSHD, aiming to uncover new therapeutic targets and to understand how repetitive DNA sequences contribute to interindividual variability and disease susceptibility. My goal is to integrate these findings into a broader framework that can inform personalized approaches to diagnosis and treatment.

B. Positions, Scientific Appointments, and Honors**Academic and Research Positions**

2019–Present Assistant Professor (RTDa), Medical Genetics (SSD: MED/03), University of Modena and Reggio Emilia, Italy

2017–2019 Research Fellow, Medical Genetics, University of Modena and Reggio Emilia, Italy

2015–2017 Research Fellow, Struttura Complessa di Medicina II, azienda ospedaliera Policlinico, Modena

2007–2015 Postdoctoral Research Fellow, Department of Biomedical Sciences, University of Modena and Reggio Emilia, Italy

Honors

2024_ Best Poster Award, Human Genome Meeting - HUGO International, Rome, May 2024.

2010_ Research Fellow, Azienda Ospedaliero-Universitaria di Modena, for the project: "Next-generation sequencing and gene therapy to diagnose and cure rare diseases in Regione Emilia Romagna (RER)" at the Struttura Complessa di Medicina II, funded by the Programma di Ricerca Regione-Università

2005_Advanced Research and Training Fellowship, AIRC project "Study of Hox proteins in transcriptional regulation"

2003_Advanced Research and Training Fellowship, AIRC project "Identification of genomic targets of Hox genes"

C: Contributions to Science

1. Regulation of HOX genes in development and leukemia:

My early research focused on the transcriptional and epigenetic regulation of HOX clusters, particularly their role in hematopoietic differentiation and leukemogenesis. By studying leukemic models harboring MLL rearrangements, I contributed to elucidating how altered chromatin topology and enhancer-promoter interactions lead to aberrant HOX gene activation, thereby supporting leukemic transformation.

- a. **Salsi V***, Fantini S, Zappavigna V. NUP98 fusion oncoproteins interact with the APC/C(Cdc20) as a pseudosubstrate and prevent mitotic checkpoint complex binding. *Cell Cycle*. 2016 Sep; 15(17):2275-87. *Co-Corresponding author.
- b. **Salsi V**, Ferrari S, Gorello P, Fantini S, Chiavolelli F, Mecucci C, Zappavigna V. NUP98 fusion oncoproteins promote aneuploidy by attenuating the mitotic spindle checkpoint. *Cancer Res*. 2014 Feb 15; 74(4):1079-90.
- c. **Salsi V**, Ferrari S, Ferraresi R, Cossarizza A, Grande A, Zappavigna V. HOXD13 binds DNA replication origins and promotes origin licensing and DNA replication in antagonism with Geminin. *Mol. Cell. Biol*. 2009 Nov; 29:5775-88.
- d. **Salsi V**, Vigano MA, Cocchiarella F, Mantovani R, Zappavigna V. Hoxd13 binds in vivo and regulates the expression of genes acting in key pathways for early limb and skeletal patterning. *Dev Biol*. 2008 May 15;317(2):497-507.
- e. **Salsi V**, Zappavigna V. Hoxd13 and Hoxa13 directly control the expression of the EphA7 Ephrin tyrosine kinase receptor in developing limbs. *J Biol Chem*. 2006 Jan, 27; 281(4):1992-9.

2. Chromatin organization and gene regulation at the 4q35 locus in FSHD:

I have extensively studied the 4q35 region implicated in facioscapulohumeral muscular dystrophy (FSHD), proposing the existence of a functional chromatin domain encompassing the most telomeric genes. My work suggests that reduction of the D4Z4 array alters the domain's structure and gene regulation, contributing to disease susceptibility even in the absence of canonical DUX4 expression. This includes identifying chromatin-based regulatory mechanisms and long-range interactions affected by repeat contraction.

- a. **Salsi V**, Magdinier F, Tupler R. Does DNA Methylation Matter in FSHD? *Genes* 2020 Mar; 11,3, 258.
- b. Nikolic A, Jones T, Govi M, Mele F, Maranda L, Sera F, Ricci G, Ruggiero L, Vercelli L, Portaro S, Villa L, Fiorillo C, Maggi L, Santoro L, Antonini G, Filosto M, Moggio M, Angelini C, Pegoraro E, Berardinelli A, Maioli M, D'Angelo G, Di Muzio A, Siciliano G, Tomelleri G, D'Esposito M, Della Ragione F, Brancaccio A, Piras R, Rodolico C, Mongini T, Magdinier F, , Jones P , **Salsi V**, Tupler R. Interpretation of the Epigenetic Signature of Facioscapulohumeral Muscular Dystrophy in Light of Genotype-Phenotype Studies. *Int. J. Mol. Sci*. 2020, 21, 2635;

3. Repetitive Elements as Regulatory Components in Genome Function and Disease

My current research investigates the functional impact of repetitive sequences, including macrosatellite repeats and endogenous retroelements, on nuclear architecture, gene expression, and disease. I have demonstrated that the transcription of these elements can produce regulatory non-coding RNAs with roles in stress response, chromatin dynamics, and disease-specific cellular states. By integrating genomic, epigenomic, and 3D chromatin data (such as RNA-seq, ChIP-seq, ATAC-seq, Hi-C, and 4C-seq), I explore how large-scale chromatin organization and repetitive elements shape gene regulation, particularly at disease-relevant loci like 4q35. This integrative approach has led to the identification of

novel regulatory domains and mechanisms that are crucial for understanding complex genetic conditions, including muscular dystrophies.

- a. **Salsi V**, Losi F, Salani M, Kaufman PD, Tupler R. Posttranscriptional RNA stabilization of telomeric RNAs FRG2, DBE-T, D4Z4 at human 4q35 in response to genotoxic stress and D4Z4 macrosatellite repeat length. *Clin Epigenetics*. 2025 May 4;17(1):73. doi: 10.1186/s13148-025-01881-5. PMID: 40320530.
- b. **Salsi, V**. Losi, F. Fosso, B. Ferrarini, M. Pini, S. Mafredi, M. Vattermi, G. Mongini, T. Maggi, L. Pesole, G. Henras, A. Kaufman, P. McStay, B. Tupler, R. A novel family of lncRNAs relate facioscapulohumeral muscular dystrophy to nucleolar architecture and protein synthesis. *bioRxiv* 2024.06.29.600824; doi: <https://doi.org/10.1101/2024.06.29.600824>
- c. **Salsi V**, M. Chiara, S. Pini, P. Kuś, L. Ruggiero, S. Bonanno, C. Rodolico, S. C. Previtali, M. G. D'Angelo, L. Maggi, D. Lopercolo, M. Kimmel, F. M. Santorelli, G. Pesole, R. G. Tupler, A human pan-genomic analysis reconfigures the genetic and epigenetic make up of facioscapulohumeral muscular dystrophy. *medRxiv [Preprint]* (2023). <https://doi.org/10.1101/2023.06.13.23291337>.

Modena, May 5th, 2025