**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contr butors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Stefano Cagnin

[redacted]

POSITION TITLE: Professor of Genetics

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 | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| University of Padova, Padova, Italy | B.S. | 07/2003 | Biology |
| University of Padova, Padova, Italy | Ph.D. | 04/2007 | Cellular and molecular biology and pathology of skeletal and cardiac muscle and circulatory system |
| University of Padova, Padova, Italy | PostDoc | 01/2012 | Biology in skeletal muscle |

**A. Personal Statement**

I am an Associate Professor of Genetics, and my research focuses on the pathophysiology of skeletal and cardiac muscle and the cardiovascular system, particularly evaluating the role of RNAs in the modulation of studied conditions. During my PhD in early 2000, I developed methods to assess gene expression using genome-wide approaches, starting with Sanger sequencing of EST libraries, and later adopting cDNA and oligonucleotide microarrays and next generation sequencing. In the past two decades, I have developed research expertise on gene expression alterations in various pathophysiological conditions of skeletal and cardiac muscles and the cardiovascular system, applying multiple-scale systems biology approaches. I used transcriptomic analysis of individual myofibers to demonstrate the regulatory networks involved in maintaining muscle trophism and the importance of microRNAs in modulating myofiber metabolism. I have also evaluated transcriptomic alterations associated with endoplasmic reticulum-mitochondrial tethering in skeletal muscle and neurological disorders. Recently, my research group has developed interest in the functional analysis of long non-coding RNAs at the single cell level. We demonstrated the importance of non-coding RNAs in the maintenance of mitochondrial function in skeletal muscle in the context of aging processes and subsequent frailty.

The ongoing and recently completed projects (last 5 years) that I would like to highlight include:

EU Framework Programme
Elena Reddi (PI) (University of Padova). Role: co-investigator.
01/02/2020-2023
Light4Lungs

University of Padova Research Support
Cagnin (PI)
07/01/2020-06/01/2022
Alterations in single cell gene expression induced by glucosyl-β-sitosterol in rat and mice neurons: hints about molecular mechanisms of Parkinson's and ALS disease

Cariplo: MAYBE
Enzo Nisoli (PI) (University of Milan). Role: co-investigator
04/15/2018-05/15/2022
Multicomponent Analysis of phYsical frailty BiomarkErs: focus on mitochondrial health.

Cariparo: SIGMI
Luca Scorrano (PI) (University of Padova). Role: co-investigator
04/01/2018-01/01/2021.
Elucidating signals of mitochondrial shape changes.

European Foundation for the Study of Diabetes (EFSD).
Nina Kaludercic (PI) (University of Padova). Role: co-investigator
03/01/2015-01/01/2018.
Monoamine oxidase inhibition as a new therapeutic strategy for the treatment of diabetic cardiomyopathy.

Citations

1. **Cagnin S**, Alessio E, Bonadio RS, Sales G. Single-Cell RNAseq Analysis of lncRNAs. Methods Mol Biol. 2021;2348:71-90. doi: 10.1007/978-1-0716-1581-2_5. PMID: 34160800.
2. Peggion C, Massimino ML, Bonadio RS, Lia F, Lopreiato R, **Cagnin S**, Calì T, Bertoli A.Regulation of Endoplasmic Reticulum-Mitochondria Tethering and Ca2+ Fluxes by TDP-43 via GSK3β. Int J Mol Sci. 2021 Nov 1;22(21):11853. doi: 10.3390/ijms222111853. PMID: 34769284.
3. Stella R, Bonadio RS, **Cagnin S**, Massimino ML, Bertoli A, Peggion C. Perturbations of the Proteome and of Secreted Metabolites in Primary Astrocytes from the hSOD1(G93A) ALS Mouse Model. Int J Mol Sci. 2021 Jun 29;22(13):7028. doi: 10.3390/ijms22137028. PMID: 34209958.
4. Grespi F, Vianello C, **Cagnin S**, Giacomello M, De Mario A. The Interplay of Microtubules with Mitochondria-ER Contact Sites (MERCs) in Glioblastoma. Biomolecules. 2022 Apr 12;12(4):567. doi: 10.3390/biom12040567. PMID: 35454156.

## B. Positions, Scientific Appointments, and Honors

### Positions and Scientific Appointments

| | |
|---|---|
| 2019–now | Associate Professor, Genetics, University of Padova, Padova, Italy |
| 2012–2019 | Assistant Professor, Genetics, University of Padova, Padova, Italy |
| 2012–now | Co-Director of Gene Expression Facility, University of Padova, Padova, Italy |
| 2008–2012 | Research Fellow, Genetics, University of Padova, Padova, Italy |
| 2004–2007 | PhD Fellow, Genetics, University of Padova, Padova, Italy |
| 2002-2003 | Telethon Research Fellow, Genetics, University of Padova, Padova, Italy |

### Honors

| | |
|---|---|
| 2021 | National Academic qualification as Full Professor of Genetics. |
| 2022 | Member of the Musculo-Skeletal Gene & Cell Therapy committee of American Society of Gene and Cell Therapy. |
| 2009 | BMC Genomics highly accessed articles: “Reconstruction and functional analysis of altered molecular pathways in human atherosclerotic arteries” and “Meta-analysis of expression signatures of muscle atrophy: gene interaction networks in early and late stages”. |

### Professional Memberships and Services

**Member.** Italian Genetic Society (AGI, 2012-now), American Society of Gene and Cell Therapy (2019-now), Interuniversity Institute of Myology (IIM, 2020-now), Myology Center of University of Padova (2016-now), RNA Society (2022-now).
**Editor.** Biochemical Genetics, Frontiers in Oncology, Academia Biology.
**Leader Guest Editor.**
- Guest editor for BioMed Research International on research topic: “Mediators of Heart Failure and Metabolic Consequences: Improvements in the Prevention or Treatment of Heart Failure”
- Guest editor for International Journal of Genomics on research topic: “Improvements in the comprehension of multicellular organisms by the analysis of single cells”
- Guest editor for Genes on research topic: “Non-coding RNA functions in Prokaryotes and Eukaryotes”
- Guest editor for Genes on research topic: “Long non-coding RNA: new insight in Aging and Disease”

**Journal reviewer.** Ad hoc reviewer for Biochemical Genetics, Cells, International Journal of Molecular Science, Nucleic Acids Research, Journal of Developmental Biology, Biology Open, Genes, Cancers,

Biotechniques, Life, Non coding RNA, Cell Regeneration, The FEBS Journal, Clinical and Experimental Pharmacology and Physiology, Biomolecules, Molecular Therapy-Nucleic Acids.
**Grant and career progression *Ad hoc* reviewer:** Universidad Complutense de Madrid (UNA4CAREER), Academic Council King Saud University, AFM Telethon, REPRISE (Italian University and Research Minister)

**C. Contributions to Science**

1. Analysis of single-cell non-coding RNAs. Tissues are composed of different cells, and their functional and structural properties are related to their different gene expression. The ability to amplify RNA in conjunction with the isolation of single cell or nuclei makes it possible to distinguish gene expression in each individual cell of a tissue or cell culture. This approach allows the identification of groups of cells otherwise unidentifiable by bulk sequencing, and we have used it to distinguish the importance of non-coding RNAs in the skeletal muscle.
   a. Alessio E, Bonadio RS, Buson L, Chemello F, **Cagnin S**. A Single Cell but Many Different Transcripts: A Journey into the World of Long Non-Coding RNAs. Int J Mol Sci. 2020 Jan 1;21(1):302. doi: 10.3390/ijms21010302. PMID: 31906285.
   b. Corso D, Chemello F, Alessio E, Urso I, Ferrarese G, Bazzega M, Romualdi C, Lanfranchi G, Sales G, **Cagnin S**. MyoData: An expression knowledgebase at single cell/nucleus level for the discovery of coding-noncoding RNA functional interactions in skeletal muscle. Comput Struct Biotechnol J. 2021 Jul 26;19:4142-4155. doi: 10.1016/j.csbj.2021.07.020. PMID: 34527188.
   c. Chemello F, Grespi F, Zulian A, Cancellara P, Hebert-Chatelain E, Martini P, Bean C, Alessio E, Buson L, Bazzega M, Armani A, Sandri M, Ferrazza R, Laveder P, Guella G, Reggiani C, Romualdi C, Bernardi P, Scorrano L, **Cagnin S***, Lanfranchi G*. Transcriptomic Analysis of Single Isolated Myofibers Identifies miR-27a-3p and miR-142-3p as Regulators of Metabolism in Skeletal Muscle. Cell Rep. 2019 Mar 26;26(13):3784-3797.e8. doi: 10.1016/j.celrep.2019.02.105. PMID: 30917329.
   d. Alessio E, Buson L, Chemello F, Peggion C, Grespi F, Martini P, Massimino ML, Pacchioni B, Millino C, Romualdi C, Bertoli A, Scorrano L, Lanfranchi G, **Cagnin S**. Single cell analysis reveals the involvement of the long non-coding RNA Pvt1 in the modulation of muscle atrophy and mitochondrial network. Nucleic Acids Res. 2019 Feb 28;47(4):1653-1670. doi: 10.1093/nar/gkz007. PMID: 30649422.

2. Genome wide analyses. Cells activate or repress different genes in response to environmental changes. For example, apoptosis is induced by the activation of a specific pathway composed of several proteins. Therefore, to understand the regulation of cellular processes, it is important to have a broad approach (genomic, transcriptomic, proteomic, or metabolomic). In my research, I have used genomic and transcriptomic approaches to dissect different aspects of cell biology. For example, I have used previously mentioned approaches to identify alterations associated with thrombosis or Alstrom syndrome, deoxynucleotides imbalance, or environment action on gene expression.
   a. Bonadio RS, Nunes LB, Moretti PNS, Mazzeu JF, **Cagnin S**, Pic-Taylor A, de Oliveira SF. Insights into how environment shapes post-mortem RNA transcription in mouse brain. Sci Rep. 2021 Jun 21;11(1):13008. doi: 10.1038/s41598-021-92268-y. PMID: 34155272.
   b. Simioni P, **Cagnin S**, Sartorello F, Sales G, Pagani L, Bulato C, Gavasso S, Nuzzo F, Chemello F, Radu CM, Tormene D, Spiezia L, Hackeng TM, Campello E, Castoldi E. Partial F8 gene duplication (factor VIII Padua) associated with high factor VIII levels and familial thrombophilia. Blood. 2021 Apr 29;137(17):2383-2393. doi: 10.1182/blood.2020008168. PMID: 33275657.
   c. Dassie F, Lorusso R, Benavides-Varela S, Milan G, Favaretto F, Callus E, **Cagnin S**, Reggiani F, Minervini G, Tosatto S, Vettor R, Semenza C, Maffei P. Neurocognitive assessment and DNA sequencing expand the phenotype and genotype spectrum of Alstrom syndrome. Am J Med Genet A. 2021 Mar;185(3):732-742. doi: 10.1002/ajmg.a.62029. PMID: 33410256.
   d. Franzolin E, Coletta S, Ferraro P, Pontarin G, D'Aronco G, Stevanoni M, Palumbo E, **Cagnin S**, Bertoldi L, Feltrin E, Valle G, Russo A, Bianchi V, Rampazzo C. SAMHD1-deficient fibroblasts from Aicardi-Goutieres Syndrome patients can escape senescence and accumulate mutations. FASEB J. 2020 Jan;34(1):631-647. doi: 10.1096/fj.201902508R. PMID: 31914608.

3. Skeletal muscle and cardiovascular system. Since 2008, I have used human, mouse and pig models to better analyze the relationship between skeletal and cardiac muscle and the vascular system at the biosystem level. I also used in vitro models of skeletal muscle satellite cells and biological scaffolds to

monitor the ability of pluripotent cells to repopulate them. I used genome-wide expression analyses to assess alterations in different skeletal muscle pathological conditions (e.g. FSHD, DMD) to identify mechanisms involved in fiber switching and determinants of disease severity.

a. Martini P, Sales G, Calura E, Brugiolo M, Lanfranchi G, Romualdi C, **Cagnin S**. Systems biology approach to the dissection of the complexity of regulatory networks in the S. scrofa cardiocirculatory system. Int J Mol Sci. 2013 Nov 21;14(11):23160-87. doi: 10.3390/ijms141123160. PMID: 24284405.
b. Pegoraro E, Hoffman EP, Piva L, Gavassini BF, **Cagnin S**, Ermani M, Bello L, Soraru G, Pacchioni B, Bonifati MD, Lanfranchi G, Angelini C, Kesari A, Lee I, Gordish-Dressman H, Devaney JM, McDonald CM; Cooperative International Neuromuscular Research Group. SPP1 genotype is a determinant of disease severity in Duchenne muscular dystrophy. Neurology. 2011 Jan 18;76(3):219-26. doi: 10.1212/WNL.0b013e318207afeb. PMID: 21178099.
c. **Cagnin S**, Biscuola M, Patuzzo C, Trabetti E, Pasquali A, Laveder P, Faggian G, Iafrancesco M, Mazzucco A, Pignatti PF, Lanfranchi G. Reconstruction and functional analysis of altered molecular pathways in human atherosclerotic arteries. BMC Genomics. 2009 Jan 9;10:13. doi: 10.1186/1471-2164-10-13. PMID: 19134193.
d. Calura E, **Cagnin S**, Raffaello A, Laveder P, Lanfranchi G, Romualdi C. Meta-analysis of expression signatures of muscle atrophy: gene interaction networks in early and late stages. BMC Genomics. 2008 Dec 23;9:630. doi: 10.1186/1471-2164-9-630. PMID: 19108710.

4. Mitochondrial activity and muscle alterations. In collaboration with Profs. Luca Scorrano, Sarino Rizzuto or Paolo Bernardi of the University of Padova, who are leaders in mitochondrial biology, I have recently focused our analysis of gene expression to understand how the alteration due to pathological conditions or stress can affect mitochondrial activity, with the goal of better elucidating the relationship between nucleus and mitochondria. We have shown that by altering mitochondrial calcium homeostasis, gene expression of coding genes is impaired as well as skeletal muscle tropism. Recently, we have also shown that non-coding RNAs impact mitochondrial functions and that these transcriptional elements play an important role in maintaining muscle homeostasis. We also found that coronary artery diseases can be monitored based on the expression of mitochondrial genes.
   a. Grespi F, Vianello C, **Cagnin S**, Giacomello M, De Mario A. The Interplay of Microtubules with Mitochondria-ER Contact Sites (MERCs) in Glioblastoma. Biomolecules. 2022 Apr 12;12(4):567. doi: 10.3390/biom12040567. PMID: 35454156.
   b. Mammucari C, Gherardi G, Zamparo I, Raffaello A, Boncompagni S, Chemello F, **Cagnin S**, Braga A, Zanin S, Pallafacchina G, Zentilin L, Sandri M, De Stefani D, Protasi F, Lanfranchi G, Rizzuto R. The mitochondrial calcium uniporter controls skeletal muscle trophism in vivo. Cell Rep. 2015 Mar 3;10(8):1269-79. doi: 10.1016/j.celrep.2015.01.056. PMID: 25732818.
   c. Holvoet P, Klocke B, Vanhaverbeke M, Menten R, Sinnaeve P, Raitoharju E, Lehtimski T, Oksala N, Zinser C, Janssens S, Sipido K, Lyytikainen LP, **Cagnin S**. RNA-sequencing reveals that STRN, ZNF484 and WNK1 add to the value of mitochondrial MT-COI and COX10 as markers of unstable coronary artery disease. PLoS One. 2019 Dec 10;14(12):e0225621. doi: 10.1371/journal.pone.0225621. PMID: 31821324.
   d. Chemello F, Grespi F, Zulian A, Cancellara P, Hebert-Chatelain E, Martini P, Bean C, Alessio E, Buson L, Bazzega M, Armani A, Sandri M, Ferrazza R, Laveder P, Guella G, Reggiani C, Romualdi C, Bernardi P, Scorrano L, **Cagnin S***, Lanfranchi G*. Transcriptomic Analysis of Single Isolated Myofibers Identifies miR-27a-3p and miR-142-3p as Regulators of Metabolism in Skeletal Muscle. Cell Rep. 2019 Mar 26;26(13):3784-3797.e8. doi: 10.1016/j.celrep.2019.02.105. PMID: 30917329.

5. Epigenetic alterations in skeletal muscle atrophy, cardiocirculatory system and macrophages. After the evidence of pervasive transcriptional activity of different tissues in mammals, I focused my attention on non-coding RNAs showing that through their epigenetic action they can modulate different aspects of the biology of skeletal muscle, the cardiovascular system, and macrophages.
   a. Codolo G, Toffoletto M, Chemello F, Coletta S, Soler Teixidor G, Battaggia G, Munari G, Fassan M, **Cagnin S***, de Bernard M.* Helicobacter pylori Dampens HLA-II Expression on Macrophages via the Up-Regulation of miRNAs Targeting CIITA. Front Immunol. 2020 Jan 8;10:2923. doi: 10.3389/fimmu.2019.02923. PMID: 31969878.
   b. Martini P, Sales G, Brugiolo M, Gandaglia A, Naso F, De Pitt√† C, Spina M, Gerosa G, Chemello F, Romualdi C, **Cagnin S***, Lanfranchi G*. Tissue-specific expression and regulatory networks of pig

microRNAome. PLoS One. 2014 Apr 3;9(4):e89755. doi: 10.1371/journal.pone.0089755. PMID: 24699212.

c. Soares RJ, **Cagnin S**, Chemello F, Silvestrin M, Musaro A, De Pitta C, Lanfranchi G, Sandri M. Involvement of microRNAs in the regulation of muscle wasting during catabolic conditions. J Biol Chem. 2014 Aug 8;289(32):21909-25. doi: 10.1074/jbc.M114.561845. PMID: 24891504.

d. Pagliari M, Munari F, Toffoletto M, Lonardi S, Chemello F, Codolo G, Millino C, Della Bella C, Pacchioni B, Vermi W, Fassan M, de Bernard M*, **Cagnin S***. Helicobacter pylori Affects the Antigen Presentation Activity of Macrophages Modulating the Expression of the Immune Receptor CD300E through miR-4270. Front Immunol. 2017 Oct 12;8:1288. doi: 10.3389/fimmu.2017.01288. PMID: 29085364.

**Complete List of Published Works in**

- **My Bibliography:**

https://www.ncbi.nlm.nih.gov/myncbi/1TAHAjCIEoHkv/bibliography/public/

- **Scopus**

https://www.scopus.com/authid/detail.uri?authorId=6506384365

- **Google scholar**

https://scholar.google.com/citations?user=3SsbBC0AAAAJ&hl=en

**D. Teaching activity**

Teaching activity is described in the following webpage: https://www.biologia.unipd.it/people/?tx_wfqbe_pi1%5Baccount%5D=stefano-cagnin