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Date of Birth: 15 July 1990

■ Place of birth: Palermo, Italy

Nationality: Italian

Languages: Italian, English

EDUCATION AND RESEARCH TRAINING

Karolinska Institutet

PhD STUDENT

January 2014 – September 2018

- Project title: "Building blocks of the brain Systematic mapping of cell types of the brain by single-cell transcriptomics"
- Relevant PhD Courses and Schools: Computational Dynamic Analysis of Biological Processes, Machine Learning, Microfluidic Flows # Department of Medical Biochemistry and Biophysics (MBB), Molecular Neurobiology Division, Sten Linnarsson lab.

Karolinska Institutet

RESEARCH ASSISTANT

June - December 2013

Project title: "Developing a microfluidic based single cell RNA-seq approach"
 # Department of Medical Biochemistry and Biophysics(MBB), Molecular Neurobiology Division, Sten Linnarsson lab.

Karolinska Institutet

BIOMEDICINE MASTERS PROGRAM (120 ECTS)

August 2011 - June 2013

- ◆ Comprehensive mark: VG (highest grade)
- Final research project: "Preserving cellular state for single-cell RNA sequencing" PI: Sten Linnarsson, MBB Karolisnka Institutet
- Other Projects: "Functional analysis of distinct Lgr6+ stem cell populations of murine skin" PI: Maria Kasper, BioNut Karolinska Institutet "Identification of fusogenic cytokines in vitro and ex vivo" PI: Clas Johansson, CMM Karolinska Institutet
- Doctoral Courses: Developmental Biology for Regenerative Medicine; Cellular Reprogramming; Stem cell Engineering and Regenerative Medicine
- Characterizing Courses: Frontiers in Translational Medicine (22 ECTS); Bioinformatics (5.5 ECTS); Biostatistics (6 ECTS);

University of Palermo

BACHELOR DEGREE IN BIOTECHNOLOGY (180 ECTS)

Autumn 2008 - July 2011

- ◆ Comprehensive mark: 110/110 with distinction and special mention (equiv. 'magna cum laude')
- Final project: "Over-expression and silencing of p63 in breast cancer stem cells" PI: Giorgio Stassi, Dep. of Surgical and Oncological Sciences UNIPA

COMPETENCES AND TECHNICAL SKILLS

- I have extensive experience in data analysis and the development and implementation of bioinformatics algorithms.
- I master python programming language and a wide selection of scientific libraries (including *numpy*, *scipy*, *pandas*, *matplotlib*), I have a good knowledge of Matlab, R and I use C/C++ for high performance computing.
- Beyond my canonical education I extended my theoretical knowledge on many topics studying Linear Algebra, Dynamical Systems,
 Applied Statistics, Statistical Mechanics, Principles of Algorithms, Convex Optimization and Machine learning.
- I worked extensively at the development of single cell RNA sequencing from the early days of the technology, developing new protocols and adapting preexisting one for clinical applications (i.e. myocardial endovascular micro-biopsies and glioblastoma samples).
- I gained a wide wet-lab experience within the molecular biology field including classical techniques (Real Time PCR; Cloning; Genotyping; Stem cell culture techniques; Immunofluorescence; Flow Cytometry) and more modern high throughput techniques (RNA sequencing library preparation; High throughput protocol design; Barcoded beads synthesis).
- I spent time in the core facility-grade automation of lab protocols use of liquid handling robots (in particular with Beckman robots).
- I have experience in the design of simple custom microfluidics apparatuses including micro well arrays, T-junctions droplet generators and usage of commercial ones (Fluidigm C1, Dolomite Systems).

SCHOLARSHIPS AND GRANTS

- 2014-2017 KID Doctoral Grant. 270000 SEK per year for a total of 4 years.
- 2012/13 Swedish Institute Scholarship (within the Bilateral Scholarship Program for research and education). 72000 SEK

SUPERVISION AND TEACHING

- As part of my departmental responsibilities I assisted the teaching Organic Chemistry labs to Undergraduates (for 4 years)
- I was invited to contribute lectures to several bioinformatics courses (inviters include Piero Carninci director of genomics at RIKEN)
- Day-to-day supervision of masters students: Johanna Stergiadou (Greece) Leonie Von Berlin (Germany)
- Training in molecular biology of PhD student with Medicine background: Arvin Chireh (Sweden)
- Training in computational analysis of postdoc with molecular biology background: Yizhou Hu (China)

PUBLICATIONS

Original research articles: 12 Citations: 1206 h-index: 7

Neuronal atlas of the dorsal horn defines its architecture and links sensory input to transcriptional cell types.

Nature Neuroscience. (In press)

Häring M, Zeisel A, Hochgerner H, Rinwa P, Jakobsson JET, Lönnerberg P, **La Manno G**, Sharma N, Borgius C, Kiehn O, Lagerström MC, Linnarsson S*, Ernfors P*.

Spatial organization of the somatosensory cortex revealed by cyclic smFISH.

bioRxiv. 2018 March 4

Codeluppi S, Borm LE, Zeisel A, La Manno G, van Lunteren JA, Svensson CI, Linnarsson S

STRT-seq-2i: dual-index 5' single cell and nucleus RNA-seq on an addressable microwell array.

Scientific reports. 2017 Nov 27

Hochgerner H, Lönnerberg P, Hodge R, Mikes J, Heskol A, Hubschle H, Lin P, Picelli S, **La Manno G**, Ratz M, Dunne J, Husain S, Lein E, Srinivasan M, Zeisel A, Linnarsson S.

RNA velocity in single cells.

bioRxiv. 2017 Oct 19

La Manno G, Soldatov R, Hochgerner H, Zeisel A, Petukhov V, Kastriti M, Lonnerberg P, Furlan A, Fan J, Liu Z, van Bruggen D, Guo J, Sundstrom E, Castelo-Branco G, Adameyko I, Linnarsson S, Kharchenko P

Molecular analysis of the midbrain dopaminergic niche during neurogenesis

bioRxiv. 2017 Jun 26

Toledo EM, La Manno G, Rivetti di Val Cervo P, Gyllborg D, Islam S, Villaescusa S, Linnarsson S, Arenas E

Induction of functional dopamine neurons from human astrocytes in vitro and mouse astrocytes in a Parkinson's disease model.

Nature Biotechnology. 2017 Oct 10

Rivetti di Val Cervo P, Romanov RA, Spigolon G, Masini D, Martín-Montañez E, Toledo EM, La Manno G, Feyder M, Pifl C, Ng YH, Sánchez SP, Linnarsson S, Wernig M, Harkany T, Fisone G, Arenas E.

Visceral motor neuron diversity delineates a cellular basis for nipple- and pilo-erection muscle control.

Nature Neuroscience 2016 Oct 19

Furlan A, La Manno G, Lübke M, Häring M, Abdo H, Hochgerner H, Kupari J, Usoskin D, Airaksinen MS, Oliver G, Linnarsson S, Ernfors P.

Molecular Diversity of Midbrain Development in Mouse, Human, and Stem Cells.

Cell. 2016 Oct 6

La Manno G, Gyllborg D, Codeluppi S, Nishimura K, Salto C, Zeisel A, Borm LE, Stott SR, Toledo EM, Villaescusa JC, Lönnerberg P, Ryge J, Barker RA, Arenas E, Linnarsson S.

Single-Cell Transcriptomics Reveals that Differentiation and Spatial Signatures Shape Epidermal and Hair Follicle Heterogeneity.

Cell Systems. 2016 Sep 28

Joost S, Zeisel A, Jacob T, Sun X, La Manno G, Lönnerberg P, Linnarsson S, Kasper M

Oligodendrocyte heterogeneity in the mouse juvenile and adult central nervous system.

Science. 2016 June 10

Marques S, Zeisel A, Codeluppi S, van Bruggen D, Mendanha Falcão A, Xiao L, Li H, Häring M, Hochgerner H, Romanov RA, Gyllborg D, Muñoz-Manchado AB, **La Manno G**, Lönnerberg P, Floriddia EM, Rezayee F, Ernfors P, Arenas E, Hjerling-Leffler J, Harkany T, Richardson WD, Linnarsson S, Castelo-Branco G.

Cell types in the mouse cortex and hippocampus revealed by single-cell RNA-seq.

Science 2015 March 6

Zeisel A, Muñoz-Manchado AB, Codeluppi S, Lönnerberg P, **La Manno G**, Juréus A, Marques S, Munguba H, He L, Betsholtz C, Rolny C, Castelo-Branco G, Hjerling-Leffler J, Linnarsson S.

Quantitative single-cell RNA-seq with unique molecular identifiers.

Nature Methods 2014 February

<u>Islam S, Zeisel A,</u> Joost S, **La Manno G**, Zajac P, Kasper M, Lönnerberg P, Linnarsson S.

PATENTS

- I contributed to "Method that allows pooling down from chip to the 96 well device" and "Method for dual end barcoding chemistry" (Filed Patent WAFER-34667/US-1 62/256,968 and WAFER-34667/US-2). Patent licensed to Wafergen Bio-Systems Inc.
- I co-invented and patented a "Method for capturing and encoding nucleic acid from a plurality of single cells" (Filed Patent PCT/EP2014/070824). Legal rights sold to Fluidigm Corp. in 2015.

INVITED TALKS AND LECTURES

"Introduction to data analysis and machine learning" *lecture at* <u>Bioinformatics analysis of gene regulation in omics data and its application in medical problems</u> RIKEN/KI 8th International PhD Course

March 2018, Stockholm, Sweden

"Differentiation and branching of neural cell types unveiled by RNA velocity" selected for a contributed talk at <u>Single Cell Analysis Meeting</u> at Cold Spring Harbor Laboratory

November 2017, New York, USA

"Machine learning for single cell transcriptomics" invited *lecture at* Single Cell Data Analysis Course, University of Helsinki September 2017, Helsinki, Finland

"A single cell atlas of brain development" *invited talk at* <u>Single cell symposium, University of Helsinki</u> September 2017, Helsinki, Finland

"Introduction to Machine learning" *lecture at EMBnet COST.CHARME training school "Big Data for Life Sciences"* September 2017, Uppsala, Sweden

"Single cell RNA-seq unveils the molecular diversity of midbrain development in human, mouse and stem cells". *Invited talk at* ESHG (European Society of Human Genetics Conference)

May 2017, Copenhagen, Denmark

"Single-cell RNA-seq: a high throughput technology to explore cell type diversity" *invited seminar for the* <u>international seminar series of the Masters Programme in Medical Biotechnology and Molecular Medicine</u> of University of Palermo March 2017, Palermo, Italy

"Machine learning: introduction and applications" *lecture at* <u>Bioinformatics analysis of gene regulation in omics data and its application in medical problems</u> RIKEN/KI 7th International PhD Course February 2017, Yokohama, Japan

"Molecular diversity of midbrain development: from cell type homologies to replacement therapies". *Invited talk at* Annual Meeting of the Computational and Molecular Methodologies for Life Sciences Research Programme

December 2016, Turku, Finland

"Single-cell transcriptomics of the nervous system" *invited talk at* <u>SciLifeLab Medical and Population Genetics and Genomics</u> <u>Workshop</u>

October 2015, Uppsala, Sweden

"Conserved principles of brain development revealed by comparative single-cell RNA-seq in mouse and human ventral midbrain" *selected for a contributed talk at* Single Cell Genomics Conference,
September 2015, Utrecht, Netherlands

OTHER PRESENTATIONS

"Constructing gene expression atlases by RNA tomography" poster at Quantitative Principles of Biology EMBO Conference November 2017, Heidelberg. Germany

"RNA velocity in single cells reveals differentiation directionality and dynamics" poster at Single Cell Genomics Conference October 2017, Weizmann Institute, Rehovot. Israel

"Cell Type Learning: From The Conservation Of The Ventral Midbrain To Replacement Therapies" *poster at* <u>Single Cell genomics Conference</u>

September 2016, Hinxton, Cabridge, UK

"Comparative single-cell RNA-seq in mouse and human ventral midbrain reveals conserved principles of brain development" lightning talk and poster presentation at the 3rd Human Brain Project Education Workshop December 2015, Manchester, UK

OPEN SOURCE SCIENTIFIC SOFTWARE

I implemented and maintain the following software (available at https://github.com/linnarsson-lab):

velocyto: a package for the analysis of expression dynamics in single cell RNA seq data

loompy: core implementation of loom file format, the standard format to store and work with single-cell RNA-seq data

ceftools: an older file format designed to store smaller single-cell RNA-seq datasets

BackSPIN: official implementation of the clustering algorithm described in Zeisel et al. 2015

cmdstan-py: an alternative, lightweight, python interface to the Bayesian Modeling language Stan

nbregression: negative binomial generalized linear model for single cell expression data

POULAR SCIENCE AND OUTREACH

- Our paper on visceral motor neuron diversity had important media outreach, at least a dozen newspapers featured our discoveries (including the Guardian)
- I gave popular science talks for high school students: in occasion of UniStem day, an European event for the dissemination and outreach of stem cell science dedicated to high school students and for Klubb Bierkan, a Swedish organization that focuses on intellectual growth of teenagers.
- "DDPDGenes Parkinson's open day" a dissemination meeting with patients and families.