# Curriculum Vitae Dr. MARGHERITA GHISI

## PERSONAL INFORMATION

Name & Surname: Margherita Ghisi

Place & date of birth: Milano (Italy) - November 4th, 1982.

Nationality: Italian, Australian.

Languages: Italian (mother language), English and French.

Residential address: 5 Rue Ella Maillart, Résidence "Les Fontaines d'Opale" M-323, 31300 – Toulouse, France.

Affiliation: Team 18 "Equipe METAML: Metabolism and Drug Resistance in Acute Myeloid Leukemia" (JE. Sarry)

Cancer Research Centre of Toulouse (CRCT), UMR5071 (CNRS) / UMR1037 (INSERM)

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## **EDUCATION AND TRAINING**

01/2007–04/2010 PhD in Oncology and Surgical Oncology

University of Padova, Padova (Italy)

09/2004–09/2006 Master Degree in Medical Biotechnology

University of Padova, Padova (Italy) with the mark of 110/110 with Honours

09/2001–09/2004 Bachelor Degree in Health Biotechnology

University of Padova, Padova (Italy)

with the mark of 110/110

#### **WORK EXPERIENCE**

10/2020 - To date Recruited as Chargé de Recherche de Classe Normale (CRCN) at the CNRS (recruited

on the 1<sup>st</sup> October 2020; Commission 24/02 "Physiologie, Vieillissement, Tumorigenèse"), working at the CNRS UMR5071 - INSERM UMR1037 - Cancer Research Center of Toulouse (CRCT, Toulouse, France) in the team "METAML: Metabolism and Drug Resistance in Acute Myeloid Leukemia" (Team 18; Lab Head Dr. Jean-Emmanuel Sarry). Research thematic: *Role of RNA splicing and other non-genetic mechanisms of regulation* 

of AML metabolism and drug resistance.

03/2017–10/2020 Post-doctoral fellow

Cancer Research Centre of Toulouse (CRCT), Toulouse (France)

Lab Head: Prof. Pierre Brousset (Team 7)/ Dr. Jean-Emmanuel Sarry (Team 18)

2017-2018. Project 1: Study of unconventional mechanisms of post-transcriptional regulation of microRNA expression in hematological malignancies. (Team 7,

Brousset).

2018-2020. Project 2: *Investigating molecular determinants of AML chemoresistant phenotype.* (Team 18, Sarry).

05/2015–12/2016 Post-doctoral fellow

Monash University, Australian Centre for Blood Diseases (ACBD);

(Honorary appointment) Peter MacCallum Cancer Centre, Melbourne (Australia)

Lab Head: A/Prof. Ross Dickins

Project: Investigating AML differentiation plasticity.

07/2011–05/2015 Post-doctoral fellow

Peter MacCallum Cancer Centre, Melbourne (Australia)

Lab Head: Prof. Ricky Johnstone

Project 1: Investigating the role of the Id/E protein family of transcription regulators in the

pathogenesis of AML.

Project 2: Dissecting the molecular mechanisms underpinning the anticancer activity of

histone acetylase inhibitors in a mouse model of t(8;21) AML.

04/2010–06/2011 Post-doctoral fellow

University of Padova, Padova (Italy)

Additional year to achieve the publication of my PhD work in the laboratory of Prof. Amadori.

Supervisor: Prof. Alberto Amadori

Project: Study of the role of microRNAs in T cell maturation and leukemogenesis.

01/2007–04/2010 PhD in Oncology and Surgical Oncology

University of Padova, Padova (Italy)

Supervisors: Prof. Alberto Amadori and Prof. Paola Zanovello

Project: Study of the role of microRNAs in T cell maturation and leukemogenesis.

11/2005–09/2006 Internship for Master Degree in Medical Biotechnology

University of Padova, Padova (Italy)

Supervisors: Prof. Alberto Amadori and Dr. Stefano Indraccolo.

Project: Characterization of a side population of ovarian cancer cells with stem cell-like

properties.

03/2004–06/2004 Internship for Bachelor Degree in Health Biotechnology

University of Padova, Padova (Italy)

## PRESENTATIONS AT NATIONAL/ INTERNATIONAL CONFERENCES AND INVITED SEMINARS

#### Selected and invited oral communications

1. Invited Speaker, Session "Jeunes recruté(e)s"; **CHO2021: 27ème congrès du Club Hématopoièse et Oncogenèse**, Giens, France; 29<sup>th</sup> September – 2<sup>nd</sup> October, 2021. "Exploring non genetic mechanisms of resistance to therapy in acute myeloid leukemia: interplay between metabolic reprogramming and RNA splicing".

2. Selected Speaker (International Conference); **NDLR (New Directions in Leukemia Research) 2016**, Noosa, Queensland, Australia; 16-19<sup>th</sup> March, 2016. "The Id2-E protein axis controls MLL-rearranged acute myeloid leukemia initiation and maintenance".

- 3. Selected Speaker; **The Melbourne Acute Myeloid Leukemia (AML) Research Meeting**, Melbourne, Victoria, Australia; 19<sup>th</sup> March **2015.** "Role of the Id2-E protein axis in MLL-rearranged acute myeloid leukemia".
- 4. Selected speaker for short oral presentation (International Conference); **NDLR (New Directions in Leukemia Research, 2014**, Noosa, Queensland, Australia; 30<sup>th</sup> March 30- April 2, 2014. "*Investigating the role of Id2 And E proteins in MLL-rearranged acute myeloid* leukemia".
- 5. Selected Speaker; **Epigenetics 2012**, Melbourne, Victoria, Australia; November 7, 2012. "Mechanisms underpinning the anticancer activity of histone deacetylase inhibitors in a mouse model of t(8;21) acute myeloid leukemia".
- 6. Selected Speaker; **The First Australian Workshop on Cell Death (AWCD)**. Lindeman Island, Queensland, Australia; August 21-25, **2011**. "Modulation of microRNA (miR) expression in human T cell development: targeting of Notch3 by miR-150".

## Selected poster presentations

- 1. Selected poster presentations (National conference); RNAtoul 2017. Toulouse, June, 2017.
- 2. Two selected poster presentations (International Conference); **58**th **ASH (American Society of Hematology) Annual Meeting.** San Diego, USA; December 3-6, **2016**.
- 3. Selected poster presentation (International Conference); **NDLR (New Directions in Leukemia Research).** Sunshine Coast, Queensland, Australia; March 25-28, **2012**.
- 4. Selected poster presentation (International Conference); **Idibell Cancer Conference (ICC)**. Barcelona, Spain, May 26-27, **2011**.
- 5. Selected poster presentation (International Conference); **14th International Congress of Immunology (ICI)**. Kobe, Japan, August 22-27, **2010**.
- 6. Selected poster presentation (International Conference); **International Biomedical Conference "The Notch Meeting 09"**. Athens, Greece, 27 September 1 October, **2009**.

## **Invited seminars**

- Invited seminar at the Centre de Recherche en Cancérologie de Lyon (CRCL) (November 29, 2019).
- Invited seminar at the Institut de Génétique Moléculaire de Montpellier (IGMM) (November 19, 2019).

## **SCIENTIFIC PUBLICATIONS**

## Peer-reviewed research articles:

- 1. Aroua N\*, Boet E\*, Ghisi M\*, Nicolau-Travers ML, Saland E, Gwilliam R, de Toni F, Hosseini M, Mouchel PL, Farge T, Bosc C, Stuani L, Sabatier M, Mazed F, Larrue C, Jarrou L, Gandarillas S, Bardotti M, Picard M, Syrykh C, Laurent C, Gotanègre M, Bonnefoy N, Bellvert F, Portais JC, Nicot N, Azuaje F, Kaoma T, Joffre C, Tamburini J, Récher C, Vergez F, Sarry JE. "Extracellular ATP and CD39 activate cAMP-mediated mitochondrial stress response to promote cytarabine resistance in acute myeloid leukemia". Cancer Discov. 2020 Oct;10(10):1544-1565. \*Co-first author.
- McKenzie MD\*, <u>Ghisi M\*</u>, Oxley EP\*, Ngo S, Cimmino L, Esnault C, Liu R, Salmon JM, Bell CC, Ahmed N, Erlichster M, Witkowski MT, Liu GJ, Chopin M, Dakic A, Simankowicz E, Pomilio G, Vu T, Krsmanovic P, Su S, Tian L, Baldwin TM, Zalcenstein DA, DiRago L, Wang S, Metcalf D, Johnstone RW, Croker BA, Lancaster GI, Murphy AJ, Naik SH, Nutt SL, Pospisil V, Schroeder T, Wall M, Dawson MA, Wei AH, de Thé H, Ritchie ME, Zuber J, Dickins RA. "Interconversion between Tumorigenic and Differentiated States in Acute Myeloid Leukemia". Cell Stem Cell. 2019 Aug 1;25(2):258-272. \*Co-first author.
- 3. Pinazza M, <u>Ghisi M</u>, Minuzzo S, Agnusdei V, Fossati G, Ciminale V, Pezzè L, Ciribilli Y, Pilotto G, Venturoli C, Amadori A and Indraccolo S. *"Histone deacetylase 6 controls Notch3 trafficking and degradation in T-cell acute lymphoblastic leukemia cells"*. *Oncogene*. **2018** Jul;37(28):3839-3851. **Second author**.
- 4. Witkowski MT, Hu Y, Roberts KG, Boer JM, McKenzie MD, Liu GJ, Le Grice OD, Tremblay CS, <u>Ghisi M</u>, Willson TA, Horstmann MA, Aifantis I, Cimmino L, Frietze S, den Boer ML, Mullighan CG, Smyth GK, Dickins RA. "Conserved IKAROS-regulated genes associated with B-progenitor acute lymphoblastic leukemia outcome". J Exp Med. 2017 Mar 6;214(3):773-791.
- 5. Ghisi M<sup>+</sup>, Kats L, Masson F, Li J, Kratina T, Vidacs E, Gilan O, Doyle MA, Newbold A, Bolden JE, Fairfax KA, de Graaf CA, Firth M, Zuber J, Dickins RA, Corcoran LM, Dawson MA, Belz GT, Johnstone RW<sup>+</sup>. "Id2 and E proteins orchestrate the initiation and maintenance of MLL-rearranged acute myeloid leukemia". Cancer Cell. 2016 Jul 11;30(1):59-74. \*Co-corresponding author.

- 6. Gilan O\*, Lam EY\*, Becher I, Lugo D, Cannizzaro E, Joberty G, Ward A, Wiese M, Fong CY, Ftouni S, Tyler D, Stanley K, MacPherson L, Weng CF, Chan YC, <u>Ghisi M</u>, Smil D, Carpenter C, Brown P, Garton N, Blewitt ME, Bannister AJ, Kouzarides T, Huntly BJ, Johnstone RW, Drewes G, Dawson SJ, Arrowsmith CH, Grandi P, Prinjha RK, Dawson MA. "Functional interdependency of BRD4 and DOT1L in MLL leukaemia." Nat Struct Mol Biol. 2016 Jul;23(7):673-81.
- 7. Brumatti G, Ma C, Lalaoui N, Nguyen NY, Navarro M, Tanzer MC, Richmond J, <u>Ghisi M</u>, Salmon JM, Silke N, Pomilio G, Glaser SP, de Valle E, Gugasyan R, Gurthridge MA, Condon SM, Johnstone RW, Lock R, Salvesen G, Wei A, Vaux DL, Ekert PG, Silke J. "*The caspase-8 inhibitor emricasan combines with the SMAC mimetic birinapant to induce necroptosis and treat acute myeloid leukemia." Sci Transl Med.* 2016 May 18;8(339):339ra69.
- Lalaoui N, Hänggi K, Brumatti G, Chau D, Nguyen NY, Vasilikos L, Spilgies LM, Heckmann DA, Ma C, <u>Ghisi M</u>, Salmon JM, Matthews GM, de Valle E, Moujalled DM, Menon MB, Spall SK, Glaser SP, Richmond J, Lock RB, Condon SM, Gugasyan R, Gaestel M, Guthridge M, Johnstone RW, Munoz L, Wei A, Ekert PG, Vaux DL, Wong WW, Silke J. "Targeting p38 or MK2 Enhances the Anti-Leukemic Activity of Smac-Mimetics". Cancer Cell. 2016 Feb 8;29(2):145-58.
- Masson F, <u>Ghisi M</u>, Groom J, Kallies A, Seillet C, Johnstone RW, Nutt SL, and Belz GT. "Id2 represses E2A-mediated activation of IL-10 expression in T cells". Blood. 2014 May 29;123(22):3420-8. Second author.
- 10. Mussolin L, Holmes A, Romualdi C, Sales G, D'Amore E, Ghisi M, Pillon M, Rosolen A, and Basso K. "An aberrant microRNA signature in childhood T-cell lymphoblastic lymphoma affecting CDKN1B expression, NOTCH1 and growth factor signaling pathways". Leukemia. 2014 Sep;28(9):1909-12.
- 11. Bots M, Verbrugge I, Martin BP, Salmon JM, <u>Ghisi M</u>, Baker A, Stanley K, Shortt J, Ossenkoppele GJ, Zuber J, Rappaport AR, Atadja P, Lowe SW, Johnstone RW. "*Differentiation therapy for the treatment of t(8;21) acute myeloid leukemia using histone deacetylase inhibitors"*. *Blood.* 2014 Feb 27;123(9):1341-52.
- 12. Serafin V\*, Persano L\*, Moserle L\*, Esposito G, <u>Ghisi M</u>, Curtarello M, Bonanno L, Masiero M, Ribatti D, Stürzl M, Naschberger E, Croner RS, Jubb AM, Harris AL, Koeppen H, Amadori A and Indraccolo S. "*Notch3 signaling promotes tumor growth in colorectal cancer"*. *J Pathol*. 2011 Aug; 224(4):448-60.
- 13. **Ghisi M**\*, Corradin A\*, Basso K, Serafin V, Frasson C, Mukherjee S, Guffanti A, De Bellis G, Mussolin L, Gerosa G, Stellin G, D'Agostino DM, Bronte V, Indraccolo S, Amadori A and Zanovello P. **"Modulation of microRNA expression in human T cell development: targeting of Notch3 by miR-150". Blood. 2011 Jun 30; 117(26):7053-62. \*Co-first author.**
- 14. Moserle L\*, Indraccolo S\*, <u>Ghisi M</u>, Frasson C, Fortunato E, Canevari S, Miotti S, Tosello V, Zamarchi R, Corradin A, Minuzzo S, Rossi E, Basso G and Amadori A. *"The side population of ovarian cancer cells is a primary target of interferon-α anti-tumor effects". Cancer Res.* 2008 Jul 15;68(14):5658-68.

## **Review articles and book chapters:**

- 1. **Ghisi M** and Johnstone RW. **AML-Deacetylases.** Targeted therapy of Acute Myeloid Leukemia (Part III: Epigenetics), *Springer-Verlag New York* 2015.
- 2. Moserle L\*, <u>Ghisi M</u>\*, Amadori A, Indraccolo S. "Side population and cancer stem cells: therapeutic implications." Cancer Lett. 2010 Feb 1; 288(1):1-9. \*Co-first author.

## **GRANTS, FELLOWSHIPS and AWARDS**

## Fellowships and grants

- 2019: Post-doctoral fellowship from the Fondation de France (Fondation de France « Recherche fondamentale et translationelle sur le cancer appel d'offre 2019 »; duration: 2019-2021).
- 2019 : Career development grant from Gilead Sciences (2019 Gilead International Research Scholars Program in Hematology/Oncology; duration: 2019-2021, 130K USD) as Chief Investigator.
- 2018: Regional Grant of the LRLCC 2018 (Subvention de Recherche Ligue Régional Lutte Contre le Cancer 2018) as Chief Investigator (25K EUR). Duration: 01/01/2019-31/12/2019.
- 2017: Prestige European Co-financing Grant Award. Duration: 09/2017 09/2019.

- 2017: Post-doctoral Fellowship « Fondation ARC » (Association pour la Recherche sur le Cancer). Aides individuelles Postdoctorat en France. Duration: 01/03/2017 28/02/2019.
- 2013: Leukaemia Foundation of Australia Research Grant-in-aid 2013 as Young Chief Investigator (100K AUD). Duration: 01/2013-12/2013.
- 2012: Post-doctoral Fellowship "FIRC" (Italian Foundation for Cancer Research). Fellowship for abroad. Duration: 06/2012-06/2013.
- 2010: University of Padova Early Career Post-doctoral Fellowship. Duration: 01/03/2010-01/03/2012.

## **Awards**

- Winner of the Aspen Australia New Investigator Travel Bursary (amount: 1500 AUD) at the NDLR (New Directions in Leukemia Research) Conference 2014 (Noosa, Australia, 2014).
- Winner of the Qiagen Young Investigator Award (amount: 500 AUD) at Epigenetics 2012 (Melbourne, Australia, 2012)
- Congress Scholarship SIICA (Italian Society of Immunology, Clinical Immunology and Allergology) for attending the 14th International Congress of Immunology (Kobe, Japan, 2010).

#### MENTORING, TEACHING and MANAGEMENT RESPONSABILITIES

## Mentoring and teaching

As a senior PhD student and as a postdoctoral fellow I have been supervising and mentoring undergraduate and PhD students in the laboratory, training them to develop their technical skills in the laboratory, and helping them to improve their critical thinking and writing skills.

- January 2021-June 2021. Supervision of one M2 student (Ms. Gaelle Dormio; M2-Sciences du vivant PT Recherche en Biologie – Santé, University de Lorraine); project: "Role of the splicing factor PTBP1 in the metabolism and survival of acute myeloid leukemia".
- **February 2019-August 2019.** Supervision of one M2 student (Ms. Lea Prevaud; Master Biologie-Santé, parcours BIOTIN: management de projects et innovations en biotechnologies, University of Montpellier); project: "Study of alternative splicing on metabolic flexibility in acute myeloid leukemia".
- **January 2018-March 2018.** Co-supervision of one M1 student (Ms. Manon Nivet, Master Biologie-Santé, University Toulouse III Paul Sabatier); project: "Characterization of a small peptide encoded from the primary transcript of miR-22".
- **February 2016-October 2016.** Co-supervision of one undergraduate Honours (equivalent of master M2) student (Mr. Ethan Oxley; Monash University; Melbourne; Australia); project: "Establishing a platform for identifying functional targets of the tumour suppressor PU.1 in acute myeloid leukaemia". Mr. Oxley was subsequently selected to enter the PhD program at Monash University and I pursued his supervision during the first year of his PhD formation before moving to France.
- **2014-15.** PhD student evaluation committee (member of the commission; Peter MacCallum Cancer Centre, Melbourne; Australia).
- 2010-11. Co-supervision of two undergraduate (equivalent of master M1 and M2) students (Padova University; Italy):

Ms. Irene Zancan (equivalent of Master M1). Project: "Characterization of functional targets of miR-150 in T-ALL cells".

Ms. Marica Pinazza (equivalent of Master M2). Project: "Dissecting the role of histone deacetylases in the regulation of Notch3 stability".

After being awarded an excellent mark for her Master thesis, Ms. Pinazza started her PhD in the same laboratory continuing the work of her undergraduate thesis.

## Management

- **January 2021-To date.** Supervision of one Research Assistant (IE2, Ms. Anais Granjon) in the laboratory of Dr. JE. Sarry at the Cancer Research Centre of Toulouse (CRCT, Toulouse, France).
- **June 2018-January 2019.** Co-supervision of one Research Assistant (IE2, Ms. Mathilde Gotanegre) in the laboratory of Dr. JE. Sarry at the Cancer Research Centre of Toulouse (CRCT, Toulouse, France).
- March 2017-December 2018. Co-supervision of one Research Assistant (AI, Mr. Nicolas Broin) in the laboratory of Prof. P. Brousset at the Cancer Research Centre of Toulouse (CRCT, Toulouse, France).
- **June 2015-November 2016.** Management and co-supervision of one junior Research Assistant (Ms. Emilia Simankowicz) in the laboratory of Prof. R. Dickins at the Australian Centre for Blood Diseases (ACBD) (Monash University, Melbourne, Australia).

# OTHER SCIENCE-RELATED ACTIVITIES

# Journal assessor

Invited to Peer-review research articles for: Scientific Reports, Journal of Hematology and Transfusion.

# **Professional memberships**

Member of the RNA society.