BIOGRAPHICAL SKETCH

NAME:	POSITION TITLE:
Tiziana Vaisitti, Ph.D.	**Associate Professor of Medical Genetics**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Torino, Italy	Post-Doc	2007-2014	Onco-Hematology
University of Torino, Italy	Ph.D.	2003-2006	Oncology
University of Torino, Italy	Master Degree	1998-2003	Biotechnology

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Personal Statement

After obtaining a PhD degree in Immunodiagnostic, I continued my training obtaining a 3-year fellowship from the Italian Association for Cancer Research (AIRC). During this period, I spent several periods in Italian and foreign laboratories as visiting scientist. Over these years, my research, in collaboration with other groups, was focused on the identification and functional characterization of recurrently mutated genes in chronic lymphoproliferative syndromes. These studies led to the recognition of mutations in *NOTCH1*, *SF3B1* and *BIRC3* in CLL patients and of *NOTCH2* in SMZL patients. These mutations were subsequently functionally characterized. Current studies are dedicated to the understanding of the genetic, epigenetic and transcriptomic landscape of Richter's syndrome. From September 2014 to August 2016, I was Visiting Fellow at the Weill Cornell Medicine (New York, NY) working on the set-up of xenograft models of genetically characterized primary cells. These models allow for extensive genetic and molecular characterization of human diseases and can be used as pre-clinical tools to investigate the functional impact of novel drugs. A second topic of the research was the discovery and analysis of host micro-environmental conditions favoring leukemic development and progression, with attention focused on nucleotides/nucleosides and enzymes able to metabolize them, finally creating conditions for tumor progression and immune-escape.

In March 2017, I was appointed Assistant Professor of Medical Genetics at the University of Torino and, as part of the Immunogenetics and Transplant Biology Unit – Città della Salute e della Scienza, I'm part of a multidisciplinary team that works on the identification by NGS of genetic variants responsible for diseases that can lead to organ failure and on the functional validation of selective variants. Specifically, I'm in charge of the technical and analytical parts.

In November 2021, I was appointed Associate Professor of Medical Genetics at the University of Torino, Dept. of Medical Sciences.

Positions and Employment

2002-2003: Internal student, Laboratory of Analytical Chemistry, Dept. of Chemistry, University of Torino, Italy. Supervisor: Prof. G. Giraudi

2003-2006: Ph.D. student, Laboratory of Immunogenetics, Dept. of Genetics, Biology and Biochemistry, University of Torino, Italy. Supervisor: Prof. F. Malavasi, M.D.

2004: Visiting scientist, Dept. of Evolutionary Biology, University of Siena, Italy. Reference: Prof. C.T. Baldari.

2007: Visiting scientist, The Feinstein Institute for Medical Research, North Shore-Long Island Jewish, Manhasset, NY. Reference: Prof. N. Chiorazzi, M.D.

2009: Visiting scientist, Dept. of Medical Biochemistry and Immunology, School of Medicine, Cardiff University. Reference: Drs. C. Pepper, PhD e P. Brennan, PhD.

2007-2009: AIRC/FIRC Fellowship, Laboratory of Immunogenetics, Dept. of Genetics, Biology and Biochemistry, University of Torino, Italy. Supervisor: Prof. S. Deaglio, M.D., Ph.D.

2009-2014: Senior Post-Doc, Dept. of Medical Sciences and Human Genetics Foundation (HuGeF), University of Turin, Italy. Supervisor: Prof. S. Deaglio, M.D., Ph.D.

2014-2016: Visiting Fellow, Dept. of Pathology and Laboratory Medicine, Weill Cornell Medicine, New York, NY. Reference: Prof. D.M. Knowles

2017-2018: Assistant Professor of Medical Genetics (RTD A), Dept. of Medical Sciences, University of Torino, Torino, Italy

2018-2021: Assistant Professor of Medical Genetics (RTD B), Dept. of Medical Sciences, University of Torino, Torino, Italy

2018 -: Abilitazione Scientifica Nazionale professore di seconda fascia (SSD: 06/N1)

*2019 -: National professional qualification as Biologist (*EA_020410)

2020 -: Abilitazione Scientifica Nazionale professore di seconda fascia (SSD: 06/A2)

2021 -: Abilitazione Scientifica Nazionale professore di seconda fascia (SSD: 06/A1)

2021-: Associate Professor of Medical Genetics, Dept. of Medical Sciences, University of Torino, Torino, Italy

Mentoring activity:

- Training of 8 PhD students: PhD program in Biomedical Sciences and Human Oncology, Curriculum in Genetics and curriculum in Immunodiagnostic and PhD in Physiopathology
- Training of 1 MD/PhD student: MD/PhD program, University of Torino
- Training of 4 students: Biomedical Laboratory Technician, University of Torino
- Training of 8 students: Master Degree in Biotechnology, University of Torino

Teaching duties

2004-2006: Tutor in Human Genetics, Graduate programme in Medicine, University of Torino.

2004-2017: Teaching Assistant in Human Genetics, Graduate programme in Biomedical Laboratory Technicians, University of Torino.

2018-: Chair of Human Genetics, Graduate programme in Biomedical Laboratory Technicians, University of Torino.

2018-: Chair of Medical Genetics, Speciality programme in Geriatrics, University of Torino.

2018-: Chair of Medical Genetics, Speciality programme in Orthodontics, University of Torino.

2018-: Chair of Medical Genetics, Speciality programme in Pediatrics Odontology, University of Torino.

2018-: Teaching Member of the Master in “Immunogenetics and transplant biology”, University of Torino.

2018-: Teaching Member of the PhD School in Biomedical Sciences and Oncology, University of Torino.

2019-: Chair of Medical Genetics, Graduate Programme in Nursing (Aosta), University of Torino.
2020-: Chair of Medical Genetics, Graduate programme in Medicine; University of Torino.

Professional Memberships

2006- : SIC Società Italiana di Cancerologia
2006- : EACR European Association for Cancer Research
2009- : EHA European Hematology Association
2012- : ASH American Society of Hematology
2017- : ERIC European Research Initiative on CLL
2019- : SIGU Società Italiana di Genetica Umana

Honors:

2005: Prize for the best graduate student in Biotechnology from the University of Turin
2007: Travel grant by the Società Italiana di Cancerologia, 49° Congress of the Society
2009: Travel grant by the European Hematology Association, 14th Congress of the Society
2011: Mediterranean School of Oncology (MSO) Young Investigator Award (short listed)
2011: AACR-SIC Scholar in Training award from American association for Cancer Research - Società Italiana di Cancerologia
2017: Best abstract presented at the XVII International Workshop on Chronic Lymphocytic Leukemia (iwCLL), May 2017, New York, NY.

Editorial/Reviewer activities:

2019-: Guest Editor Special Issue on Chronic Lymphocytic Leukemia, Cancer_MDPI, https://www.linkedin.com/in/cancers-mdpi-23a2a6a4/
2021-: Reviewer Editor for T cell Biology, Frontiers in Immunology https://loop.frontiersin.org/people/149929/overview
2021-: Reviewer Editor for Hematologic Malignancies, Frontiers in Oncology https://loop.frontiersin.org/people/149929/overview
2019-: Reviewer for Frontiers in Immunology, Frontiers in Oncology, Haematologica, Scientific Reports, PlosOne, Journal of Leukocyte Biology

Contribution to Science

1. Identification by clinical exome sequencing of variants relevant for the diagnosis of genetic diseases responsible for organ failure. The aim of this research and diagnostic area of interest is the identification of variants responsible for genetic diseases resulting in organ failure. The focus is on kidney, liver and cardiac diseases to provide clinicians and patients a genetic diagnosis and confirmation of the clinical phenotype. To this aim we're expoliting next-generation sequencing based on Illumina platforms, using a clinical exome kit (focused on 6700 genes) or a targeted panel (174 genes related to cardiac diseases). This diagnostic service is part of the Regional Transplantation Center (Torino) and is recruiting samples from different regional hospitals. Dr. Vaisitti is responsible for the DNA sequencing and bio-informatic analysis of data.

1. Vaisitti T et al., *Clinical exome sequencing is a powerful tool in the diagnostic flow of monogenic kidney diseases: an Italian experience.* J Nephrol. 2020 Nov 23.
2. Vaisitti T et al., *The role of genetic testing in the diagnostic workflow of pediatric patients with kidney diseases: the experience of a single institution.* Hum Genomics. 2023 Feb 13;17(1):10.

2. Identification of early markers of organ rejection by combining liquid biopsy (cell free DNA) and droplet digital PCR: early detection of cell free DNA from the donor. The aim of this research topic is the identification of early markers of organ rejection. The analysis is based on cell-free DNA, exploiting the droplet digital PCR technology and the donor-recipient mismatch at the locus HLA-DRB1. The preliminary data were obtained analyzing two different cohorts of transplanted patients (heart and lung) and showed that an increase of donor DNA can be detect with high sensitivity in presence of organ rejection.

3. Sorbini M et al., *HLA-DRB1 mismatch-based identification of donor-derived cell free DNA (dd-cfDNA) as a marker of rejection in heart transplant recipients: a pilot single-Institution study.* J Heart Lung Transplant. 2021 Aug;40(8):794-804.
4. Sorbini M et al., *Validation of a Simple, Rapid, and Cost-Effective Method for Acute Rejection Monitoring in Lung Transplant Recipients.* Transpl Int. 2022 Jun 9;35:10546.

3. Set-up and genetic/transcriptomic analyses of patient-derived xenograft models of Richter's syndrome. In the last years, attention has been focused on the set-up of patient-derived xenograft (PDX) models of RS. Once established, PDXs were genetically characterized by whole-exome sequencing or targeted sequencing to identify chromosomal abnormalities and gene mutations. Expression profiling of PDXs were perfomed by RNA sequencing to identify detrimental pathway contributing to disease pathogenesis. These models represent useful tools for pre-clinical testing of novel drugs.

5. Vaisitti T et al., *Novel Richter's syndrome xenograft models to study genetic architecture, biology and therapy responses*. Cancer Res. 2018 Jul 1;78(13):3413-3420.
6. Vaisitti T et al., *ROR1 targeting with the antibody drug-conjugate VLS-101 is effective in Richter syndrome patient-derived xenograft mouse models.* Blood. 2021 Jun 17;137(24):3365-3377. doi: 10.1182/blood.2020008404.
7. Iannello A et al., *Synergistic efficacy of dual PI3Kd/g inhibitor Duvelisib with Bcl2 inhibitor Venetoclax in Richter's Syndrome PDX models.* Blood. 2021 Jun 17;137(24):3378-3389. doi: 10.1182/blood.2020010187.

4. Identification and functional characterization of novel genetic lesions in chronic lymphoproliferative diseases. The topic of this research was the identification of novel genetic lesions characterizing CLL patients and driving the transformation to Richter syndrome, the acute and more aggressive form of CLL. As part of a network of collaborators, we identified several recurrent mutations in CLL patients, characterizing the more aggressive subset of patients. The open question now is to understand the functional impact of these mutations, trying to dissect the signaling pathway and identifying the main players. This topic is quite important in a translational perspective due to the poor responsiveness to conventional chemotherapy and drugs of this subset of patients.

8. Rossi D, et al., *Mutations of the SF3B1 splicing factor in chronic lymphocytic leukemia: association with progression and fludarabine-refractoriness.* Blood, 2011. **118**(26): p. 6904-8.
9. Rossi D, et al., *Disruption of BIRC3 associates with fludarabine chemorefractoriness in TP53 wild-type chronic lymphocytic leukemia.* Blood, 2012. **119**(12): p. 2854-62.
10. Arruga F, et al., *Functional impact of NOTCH1 mutations in chronic lymphocytic leukemia.* Leukemia, 2014. **28**(5): p. 1060-70.

5. Role of nucleotides and nucleotide-metabolizing enzymes in shaping the tumor niche. In addition to the contributions described above, I'm part of a team interested in studying the role of nucleotides and nucleotides-metabolizing enzymes as modifier of the tumor microenvironment. The final aim of this topic is to analyze the expression and understand the role played by nucleotides and their relative enzymes in generating the favorable conditions for the tumor growth, by modifying the host environment and controlling the immune system. This project led to the identification of NAMPT and adenosine as key players in the tumor-host cross-talk and elements favoring the establishment of growth favorable niches.

13. Vaisitti T, et al., *NAD+-metabolizing ecto-enzymes shape tumor-host interactions: the chronic lymphocytic leukemia model.* FEBS letters, 2011. 585(11): p. 1514-20.
14. Serra S, et al., *CD73-generated extracellular adenosine in chronic lymphocytic leukemia creates local conditions counteracting drug-induced cell death.* Blood, 2011. 118(23): p. 6141-52.
15. Arruga F, et al., *Targeting of the A2A adenosine receptor counteracts immunosuppression in vivo in a mouse model of chronic lymphocytic leukemia.* Haematologica, 2020.

6. Analysis of the functional role of CD38 in Chronic lymphocytic leukemia. One of the main focus of my research was the understanding of the role played by CD38, an ectoenzyme of the cell surface, in chronic lymphocytic leukemia (CLL). CD38 is not only a negative prognosticator of the disease, but a pathogenetic element. We deeply analyzed and dissected the signaling pathway driven by CD38 and we identified the molecular partners of this molecule. Indeed, in leukemic cells, CD38 is able to work in association with CXCR4, a chemokine receptor, and CD49d, an integrin, controlling the homing process of neoplastic cells to growth-favorable niches. These effects are mediated by its enzymatic properties.

16. Vaisitti T, et al., *CD38 increases CXCL12-mediated signals and homing of chronic lymphocytic leukemia cells.* Leukemia, 2010. **24**(5): p. 958-69.
17. Vaisitti T, et al., *CD38 signals upregulate expression and functions of matrix metalloproteinase-9 in chronic lymphocytic leukemia cells.* Leukemia, 2013. **27**(5): p. 1177-81.
18. Vaisitti T, et al., *The enzymatic activities of CD38 enhance CLL growth and trafficking: implications for therapeutic targeting.* Leukemia, 2015. **29**(2): p. 356-68.
19. Zucchetto A*, Vaisitti T**, et al., *The CD49d/CD29 complex is physically and functionally associated with CD38 in B-cell chronic lymphocytic leukemia cells* Leukemia. 2012 Jun;**26**(6):1301-12 *These authors equally contributed to the work.

Peer-reviewed publications.
Publication with Impact Factor (2005-2023): 66
Total IF: 630.502
Mean IF: 9.55
H-Index (Scopus): 30
Total citations: 3781

Chapter in a book: 1