

Luca Tottone, PhD

Senior Scientist - Molecular Medicine

 Phone:
 +1(732)3221411

 Email:
 luca.tottone@gmail.com

 LinkedIn:
 https://www.linkedin.com/in/luca-tottone

 Address:
 138 Montgomery Street - APT2J, Highland Park (NJ), 08904, USA

A. Summary

Scientist with 8+ years of hands-on experience conducting *in vivo* and *in vitro* pre-clinical and translational research in immunology and blood malignancies, with particular focus on Acute Leukemias. Passionate about science and medicine I have mastered, optimized and upgraded current top-notch technology in genomics, drug development and cancer modeling to dissect the molecular mechanisms driving aberrant T-cell proliferation and transformation. Rigorous, self-motivated and inclined to problem solving, I rely on my solid scientific background to serve as a versatile resource in academia or private innovative biotechnological work environments.

B. Selected Technical Skills

- In vitro/In vivo modelling and cell culture: Genetically engineered rodent colonies management In/Ex vivo cancer allo/xenografts modelling In vivo drug administration, cancer treatment In vitro culturing, drug screening, treatment In vitro BSL3 lenti/retrovirus cell engineering
 - Molecular Biology: CRISPR/Cas9 gene editing NGS libraries preparation DNA/RNA/Protein/Metabolites assays Molecular Cloning Luciferase reporting assays designing

- Flow Cytometry:
 Populations enrichment (+/- selection)
 Multicolor panel design
 Cell proliferation evaluation
 Cell death and apoptosis evaluation
 Fluorescent proteins tracking
- In silico analysis: Raw data analysis (ImageJ, FlowJo, IGV) Molecular analysis (Genome Browser, STRING) Statistical significance (Prism 8, Excel) Figures refinement (Photoshop, Illustrator) Data presentation (PowerPoint)

C. Education/Training

•

07/2010 Bachelor D. (Magna cum Laude) in Biotechnology, <u>"UniTE" University of Teramo</u> – Teramo, Italy 07/2013 Master D. (Magna cum Laude) in Medical Biotechnology, <u>Sapienza University of Rome</u> – Rome, Italy 12/2016 PhD (Commission Honors) in Molecular Medicine, <u>Sapienza University of Rome</u> – Rome, Italy

D. Positions and Honors

Positions and Employment

- 2022- Assistant Scientist, UM Sylvester Comprehensive Cancer Center, Miami, FL
 - Performing epigenetic studies to identify novel therapeutical targets in multiple leukemias

2018-22 Post-Doctoral Fellow, Rutgers Cancer Institute of New Jersey (CINJ), New Brunswick, NJ

- Performed and optimized in vivo cancer modeling, drug treatment and genetic engineering
- Developed novel/unique transgenic (germinal/conditional KO) leukemias in vivo via BMT*
- Optimized mouse thymic/splenic/peripheral blood FACS panels
- Derived, stabilized and characterized novel primary leukemias ex vivo
- Optimized NGS protocols for human and mouse custom targets (promoters/enhancers)
- Developed NEON transient CRISPR/Cas9 transfection protocols for multiple gene targets
- Developed new luciferase reporters for enhancer potency evaluation in T-ALL
- Developed novel GFP/luciferase leukemic models for in vitro fast TFs screening

- Published high-impact research paper featured on three major media outlets
- 2017-18 Researcher, CLNS, Italian Institute of Technology (IIT), Rome (RM), Italy
 - Screened, optimized and refined novel chalcone-derived drug with anti-leukemic activity, which lead to the establishment of the patent US011104657B2
 - Implemented rapid anti-Notch drug screening protocol through 12XCSL luciferase reporter
 - Developed and introduced GFP/luciferase leukemic models for in vivo xenografts tracking
- 2016-17 Post-Doctoral Fellow, Dep. of Molecular Medicine Sapienza University, Rome (RM), Italy
 - Designed and optimized *in vitro* drug treatment conditions for multiple applications (ChIP, washout assays, epigenetic genome modulations, cell proliferation)
 - Optimized lenti/retroviral oncogene overexpression in vitro for cell-based assays
- 2013-16 Molecular Medicine Doctorate, Dep. of Molecular Medicine Sapienza University, Rome (RM), Italy
 - Developed new luciferase reporters for expression evaluation
 - Optimized NEON nucleofection for plasmids and small RNAs in hard-to-transfect models
 - Derived and stabilized primary medulloblastoma cancer stem cell (CSS) spheroids ex vivo
 - Optimized cell co-culture (suspension cells on adherent cells) conditions for Notch activation *in vitro*

<u>Honors</u>

- 2014 <u>PON01_02464</u> (Research Training Fellowship) <u>Sapienza University</u>, Rome (RM), Italy
- 2014 Progetti Avvio alla Ricerca (Research Startup Award) Sapienza University, Rome (RM), Italy
- 2014 Innovative Research Award <u>SIPMeT</u> ASIP Palermo (PM), Italy
- 2016 Post-Doctoral fellowship from Pasteur Institute in Italy: Cenci Bolognetti
- 2017 Post-Doctoral fellowship from Pasteur Institute in Italy: Cenci Bolognetti
- 2020 Post-Doctoral fellowship from <u>New Jersey Commission on Cancer Research</u> (DCHS20PPC010)
- 2021 Outstanding Abstract Award Federation of American Societies for Experimental Biology (FASEB)
- 2021 <u>Fellow Scholar Award</u> from <u>American Society of Hematology (ASH)</u>

E. Contribution to Science

Patents

a. Botta B, Screpanti I, Tottone L, Zhdanoskaya N, Ingallina C, Giulimondi F, Quaglio D, Palermo R, Moril M, Ghirga F. (2019) <u>Notch inhibitors for use in the treatment of t-cell acute lymphoblastic</u> <u>leukemia.</u> US011104657B2

Selected Publications

- a. Mori M*, Tottone L*, Quaglio D*, Zhdanovskaya N, Ingallina C, Fusto M, Ghirga F, Peruzzi G, Crestoni ME, Simeoni F, Giulimondi F, Talora C, Botta B, Screpanti I, Palermo R. (2017) <u>Identification of a novel chalcone derivative that inhibits Notch signaling in T-cell acute</u> <u>lymphoblastic leukemia</u>. Sci Rep. Vol 7, Article number: 2213 (*) Equal Contribution (PMID: 28526832)
- b. Tottone L*, Zhdanovskaya N*, Carmona Pestaña Á, Zampieri M, Simeoni F, Lazzari S, Ruocco V, Pelullo M, Caiafa P, Felli MP, Checquolo S, Bellavia D, Talora C, Screpanti I, Palermo R. (2019) <u>Histone Modifications Drive Aberrant Notch3 Expression/Activity and Growth in T-ALL</u>. Front Oncol. Vol 9, Article number: 198 (*) Equal Contribution (PMID: 31001470)
- c. Tottone L, Lancho O, Loh JW, Singh A, Kimura S, Roels J, Kuchmiy A, Strubbe S, Lawlor MA, Da Da Silva-Diz V, Luo S, Gachet S, García-Prieto CA, Hagelaar R, Esteller M, Meijerink JPP, Soulier J, Taghon T, Van Vlierberghe P, Mullighan CG, Khiabanian H, Rocha PP, Herranz D. (2021) <u>A</u> <u>Tumor Suppressor Enhancer of PTEN in T-cell development and leukemia</u>. Blood Cancer Discov. Vol 2, pp 92–109

Complete List of Published Work and Citations

Luca Tottone Google Scholar

Appendix: Technical Skills - Extended

• Molecular Biology:

CRISPR/Cas9 mutagenesis/deletion, CRISPR/dCas9 gene activation/inhibition, sgRNAs design/synthesis/purification, Illumina libraries preparation for DNA/RNA sequencing, ChIP/ChIP-Seq, Reverse ChIP, Chromosome Conformation Capture (3C/4C/Capture-C), DNA/RNA/Protein/Metabolites isolation/purification from cells/tissues, Western/Northern/Southern Blotting, PCR/RT-qPCR, blunt/sticky ends cloning (gDNA/cDNA/plasmids), Transcriptional (Promoters/Enhancers) luciferase reporter assays, genotyping, optical/fluorescence microscopy.

• In vitro/In vivo modelling, drug treatment and culturing:

In vivo leukemia generation via BMT* (bone marrow transplant), *in vivo* tumor transplantation (xenografts/allografts retro-orbital/tail-vein injections), *in vivo* cell tracking (IVIS), *ex vivo* tissue culturing, *ex vivo* tumor stabilization/modelling, mouse dissection/tissue harvest, mouse bleeding, mouse intraperitoneal/gavage drug administration, *in vivo* and *in vivo* drug dosing/IC50 evaluation, *in vivo* (mouse) intraperitoneal/gavage drug administration, *in vivo* and *in vitro* toxicity evaluation, mouse gamma irradiation, transgenic mouse models care/monitoring/breeding, immunodeficient mice handling/care, suspension cells *in vitro* handling/culturing (T-ALL/AML/Medulloblastoma/Spheroids/Cancer Stem Cells), adherent cells *in vitro* handling/culturing (HEK293T/Cervical Cancer/Hepatocarcinoma/Breast Cancer), lenti/retroviral gene overexpression/silencing, transient cell transfection (NEON nucleoporation/chemical transfection) single-cell clones development/screening, viable count (trypan blue staining/fluorescence).

• Flow Cytometry:

Extensive use/setting of Attune NxT Flow Cytometer, multicolor panel design (fluorescent proteins and superficial/intracellular staining), cell proliferation (PI), cell death and apoptosis (AnnexV/7AAD), live-dead staining (Sytox), Populations enrichment (+/- column selection).

• Data analysis, statistics, bioinformatics and data presentation:

Prism 8, ImageJ, FlowJo, IGV, BLAST, Genome Browser, STRING, SnapGene, MS Excel, MS PowerPoint, Adobe Photoshop, Adobe Illustrator, Biorender.