BIOGRAPHICAL SKETCH

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NAME: Franco Izzo

eRA COMMONS USER NAME (credential, e.g., agency login): FRI2002

POSITION TITLE: Assistant Professor

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 *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Icahn School of Medicine at Mount Sinai	Assistant Professor	01/01/2024 - Present	Molecular epigenetics of hematological cancers
Weill Cornell Medicine and the New York Genome Center	Instructor	12/2023	Molecular biology of myeloproliferative neoplasms
Weill Cornell Medicine and the New York Genome Center	Postdoctoral Fellow	05/2022	Single cell genotype-to-phenotype mapping in clonal hematopoiesis
Institute of Biology and Experimental Medicine	Posdoctoral Fellow	05/2016	Molecular oncology of breast cancer
University of Buenos Aires - Institute of Biology and Experimental Medicine	Ph.D.	03/2015	Molecular oncology of breast cancer
University of Buenos Aires - Institute of Biology and Experimental Medicine	Undergrad Student	03/2010	Molecular oncology of breast cancer
University of Buenos Aires - Instituto de Química Física de los Materiales, Medio Ambiente y Energía	Undergrad student	12/2008	Characterization of axonal migration in differential substrates

A. Personal Statement

I am a an Assistant Professor with a Ph.D. with a strong background in molecular biology, oncology, and computational biology. As a blood cancer researcher, I am committed to provide fundamental insights into a key aspect of blood cancer onset, progression and resistance to therapy - how clonal evolution and epigenetic plasticity shapes the phenotype of the cancer cell, promoting resistance to therapy and disease recurrence. In the past, I have approached this challenge by coupling model organisms and human patient samples with cutting-edge single cell sequencing technologies, allowing for integration of the genome, epigenome and transcriptome information.

I recognize that our understanding of the underlying mechanisms through which deregulation of the epigenome leads to a cancer phenotype is incomplete. Therefore, we need to gain insight into the processes that maintain

and shape cell identity and clonal fitness, to effectively develop new alternatives to decrease the probabilities of cancer initiation and progression. To this end, my long-term career goal is to establish a robust scientific research program in the interphase between the genome, epigenome and phenotypic output to unveil how these features are deregulated and interact to foster cancer onset, progression and resistance to therapy. I aim to study this question directly in primary patient samples, using newly developed sequencing techniques allowing to simultaneously interrogate epigenetic and genetic features simultaneously from the same single cell. **Beyond the basic science aspects, I seek to use this knowledge to identify targetable molecular mechanisms that would render an improvement in the therapeutic options to address hematological malignancies.**

B. Positions, Scientific Appointments, and Honors

Positions

2024-present – **Assistant Professor**, Department of Oncological Sciences at Icahn School of Medicine at Mount Sinai

2022-2024 - **Instructor of Molecular Biology in Medicine**, Weill Cornell Medicine and the New York Genome Center

2016-2022 - **Post-Doctoral Fellow**, Weill Cornell Medicine and the New York Genome Center Single cell genotype-to-phenotype mapping in clonal hematopoiesis

2015-2016 - **Postdoctoral Fellow**, Institute of Biology and Experimental Medicine

2010-2015 - **Ph.D. Student**, Institute of Biology and Experimental Medicine. Dissertation: https://bibliotecadigital.exactas.uba.ar/collection/tesis/document/tesis_n5710_Izzo

2008-2010 - **Undergraduate Research**, Institute of Biology and Experimental Medicine

2005-2008 - **Undergraduate Research**, INQUIMAE. University of Buenos Aires

Honors

2024 – Leukemia Research Foundation New Investigator Award.

2024 - Paul Calabresi Award in Clinical Oncology Research - K12 Program - (*selected*)

2023 - Emergent Leaders in Computational Oncology Award – Memorial Sloan Kettering Cancer Center

2022 - Innovation and Discovery Award – New York Genome Center

2021 - American Society of Hematology Fellow-to-Faculty Scholar Award

2017 - Outstanding Achievement Abstract Award, 59th American Society of Hematology.

2015 - Endocrine Society Outstanding Abstract Award

2013 - Institute Pasteur Fellowship: Granted to the top three foreign candidates for attendance to the Molecular Biology of the Cell course at the Pasteur Institute in Paris, France.

2013 - Jorge Oster Fellowship: For specialization in advanced research techniques and knowledge in oncology, by performing the proposed research: “Modification of GATA3 cistrome by progestins and its impact in endocrine therapy in breast cancer” at the Department of Hematology and Medical Oncology at Weill Cornell Medical College, New York, NY, USA.

2011 - Avon Scholar-in-training travel award: Granted to early-career scientists presenting a meritorious proffered paper at the American Association for Cancer Research (AACR) annual meeting.

C. Contributions to Science

A - During the initial years of my career as a Ph.D. student, I focused on understanding the function and molecular mechanisms behind hormone-dependent breast cancer. In particular, I studied the regulation of the transcription factor GATA3 by activation of the progesterone receptor and its involvement in tumor growth. In line with this research, I also explored the development of molecular tools to reduce the expression levels of STAT3, a key factor in breast cancer growth. These efforts resulted in the following publications:

1 - Izzo F, Mercogliano F, Venturutti L, Tkach M, Inurrigarro G, Schillaci R, Cerchietti L, Elizalde PV, Proietti CJ. Progesterone receptor activation downregulates GATA3 by transcriptional repression and increased protein turnover promoting breast tumor growth. **Breast Cancer Res**. **2014** Dec 6;16(6):491. doi: 10.1186/s13058-014-0491-x. PubMed PMID: 25479686; PubMed Central PMCID: PMC4303201.

2 - Robaldo L, **Izzo F**, Dellafiore M, Proietti C, Elizalde PV, Montserrat JM, Iribarren AM. Influence of conformationally restricted pyrimidines on the activity of 10-23 DNAzymes. **Bioorg Med Chem**. **2012** Apr 15;20(8):2581-6. doi: 10.1016/j.bmc.2012.02.047. Epub 2012 Feb 28. PubMed PMID: 22429508.

B - In the next stage of my career, I switched to the study of blood malignancies and clonal hematopoieis. One of the main challenges when studying these diseases in human samples, is the lack of clear cell surface markers to resolve the admixture of wild type and mutated cells. To address this challenge, I was involved in the development of new single cell sequencing technologies that allowed to jointly capture the genotype and an additional feature (i.e., transcriptional profiles, chromatin accessibility profiles or cell surface proteins) from the same single cell. In this manner, by analytically identifying the genotypes, comparisons between wild type and mutated cells can be performed within the same patient sample. This approach has the advantage of circumventing common confounders that are present in population studies, such as genetic background and microenvironment. Thus, by applying these technologies we can uncover the cell-intrinsic changes that occur in the presence of the mutations. This line of work lead to several publications:

1 - Izzo F[*,#], Myers RM*, Ganesan S*, Mekerishvili L*, Kottapalli S, Prieto T, Eton EO, Botella T, Dunbar A, Bowman RL, Sotelo J, Potenski C, Mimitou EP, Stahl M, Ghaity-Beckley SE, Arandela J, Raviram R, Choi D, Hoffman R, Chaligné R, Abdel-Wahab O, Smibert P, Ghobrial IM, Scandura JM, Marcellino B, Levine RL, and Landau DA[#]. Mapping Genotypes to Chromatin Accessibility Profiles in Single Cells. **Nature. 2024** May 8. doi: 10.1038/s41586-024-07388-y. Online ahead of print.PMID: 38720070
Corresponding authors; * First authors

2 – Nam,A.*, Dusaj, N.*, **Izzo, F.***, Murali, R.*, Myers, R.M.*, Mouhieddine, T., Sotelo, J., Benbarche, S., Waarts, M., Gaiti, F., Tahri, S., Levine, R., Abdel-Wahab, O., Godley, L.A., Chaligne, R., Ghobrial, I., Landau, D.A. Single-cell multi-omics of human clonal hematopoiesis reveals that DNMT3A R882 mutations perturb early progenitor states through selective hypomethylation. **Nat Genet. 2022** Sep 22. doi: 10.1038/s41588-022-01179-9. Online ahead of print. PMID: 36138229
* First authors

3 - Izzo F*, Lee SC*, Poran A, Chaligne R, Gaiti F, Gross B, Murali RR, Deochand SD, Ang C, Jones PW, Nam AS, Kim KT, Kothen-Hill S, Schulman RC, Ki M, Lhoumaud P, Skok JA, Viny AD, Levine RL, Kenigsberg E, Abdel-Wahab O, Landau DA. DNA methylation disruption reshapes the hematopoietic differentiation landscape. **Nat Genet**. **2020** Apr;52(4):378-387. doi: 10.1038/s41588-020-0595-4. Epub 2020 Mar 23. PubMed PMID: 32203468.
* First authors

4 - Nam AS*, Kim KT*, Chaligne R*, **Izzo F**, Ang C, Taylor J, Myers RM, Abu-Zeinah G, Brand R, Omans ND, Alonso A, Sheridan C, Mariani M, Dai X, Harrington E, Pastore A, Cubillos-Ruiz JR, Tam W, Hoffman R, Rabadan R, Scandura JM, Abdel-Wahab O, Smibert P, Landau DA. Somatic mutations and cell identity linked by Genotyping of Transcriptomes. **Nature**. **2019** Jul;571(7765):355-360. doi: 10.1038/s41586-019-1367-0. Epub 2019 Jul 3. PubMed PMID: 31270458.
* First authors

C - During this time, I was also involved in fruitful collaborations involving single cell sequencing analysis, in both hematopoiesis and development. In these projects, we defined the role of the transcription factor c-MAF in the generation and differentiation of liver vasculature during embryonic development. On another project, I identified the effects of the epitranscriptomic modification m6A in hematopoietic stem cell biology through the use of mouse models coupled with single cell sequencing. Finally, I developed a new molecular biology technique to simultaneously measure chromatin accessibility and DNA methylation. These projects resulted in the following publications:

1 - Gómez-Salinero JM*, **Izzo F***, Lin Y, Houghton S, Itkin T, Geng F, Bram Y, Adelson RP, Lu TM, Inghirami G, Xiang JZ, Lis R, Redmond D, Schreiner R, Rabbany SY, Landau DA, Schwartz RE, Rafii S. Specification of fetal liver endothelial progenitors to functional zonated adult sinusoids requires c-Maf induction. **Cell Stem Cell**. **2022** Apr 7;29(4):593-609.e7. doi: 10.1016/j.stem.2022.03.002. Epub 2022 Mar 31. PubMed PMID: 35364013.
* First authors

2 - Cheng Y*, Luo H*, **Izzo F***, Pickering BF, Nguyen D, Myers R, Schurer A, Gourkanti S, Brüning JC, Vu LP, Jaffrey SR, Landau DA, Kharas MG. m6A RNA Methylation Maintains Hematopoietic Stem Cell Identity and Symmetric Commitment. **Cell Rep**. **2019** Aug 13;28(7):1703-1716.e6. doi: 10.1016/j.celrep.2019.07.032. PubMed PMID: 31412241.
* First authors

3 - Lhoumaud P, Sethia G, **Izzo F**, Sakellaropoulos T, Snetkova V, Vidal S, Badri S, Cornwell M, Di Giammartino DC, Kim KT, Apostolou E, Stadtfeld M, Landau DA, Skok J. EpiMethylTag: simultaneous detection of ATAC-seq or ChIP-seq signals with DNA methylation. **Genome Biol**. **2019** Nov 21;20(1):248. doi: 10.1186/s13059-019-1853-6. PubMed PMID: 31752933.

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