BIOGRAPHICAL SKETCH

NAME: **Francesco Ciscato**

POSITION TITLE: Researcher (PI) at National Research Council of Italy, Institute of Neuroscience

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Padua	Bachelor Degree	2006	Molecular Biology
University of Padua	Master Degree	2008	Health Biology
Venetian Oncology Institute - IOV	Post-Grad fellow	2009	T-ALL (Leukemia)
University of Padua – Dept. Medicine	PhD	2010-2013	Medical, Clinical and Experimental Sciences
University of Padua – Dept. of Biomedical Sciences	Post-Doc Fellow	2013-2022	Tumor metabolism and new chemotherapeutic approaches design and development
National Research Council of Italy, Institute of Neuroscience	PI, permanent position	Nov. 2022	New chemotherapeutic approaches design and development in NF1-derived tumors

A. Personal Statement

Since when I was a student, I was very interested in the development of new chemotherapeutic approaches grounded on new discoveries in cancer biology. I started my career studying molecules involved in chemotherapeutic resistance in leukemia and hepatocellular carcinoma. Now I am developing new molecules that can potentially overcome cell death resistance that characterizes many cancer types. In parallel, I am dissecting their mechanism of action and the signaling pathways they are affecting.

I am particularly focused on tumor metabolism and on the study of its molecular basis in order to develop new anti-neoplastic treatments. More in detail, I am interested in the role of two metabolic key proteins: the glycolytic enzyme Hexokinase 2 (HK2) and the mitochondrial chaperone TRAP1. I am actively participating in the study of the role of TRAP1 in cancer. After the publication of our data that define TRAP1 as a key molecule in NF1-derived tumors onset and progression, my main interest is to develop and test new molecules that can inhibit TRAP1 and induce cell death *in vivo* in plexiform neurofibromas and malignant peripheral nerve sheath tumor models.

I am in charge of a project that developed a novel HK2-targeting peptide to induce death selectively in tumor cells and I am trying to tailor this approach to NF1-related tumors and in particular to MPNSTs. My goal for the next years is try to identify new classes of effective anticancer molecules in pre-clinical tumor models and try to

further developing these new technologies for the application in the field of MPNST treatment, which urgently needs long awaited therapeutic approaches.

B. Positions, Scientific Appointments, and Honors

AWARDS

- July 2020 **Young Investigator Award 2020** conferred by Children Tumor's Foundation, USA

- **Intellectual Property Award MedTech** (Oct 2024) for the best Italian Patent conferred by the Italian Ministry of Enterprises and Made in Italy

- **Elena Cappannini Award** (Oct 2021) for the best Italian research paper on: "Novel and innovative antitumoral approaches" conferred by the Italian Society of Cancer (SIC)

PATENT

Italian - titled: Peptides with anti-tumoral activity, No. IT 102019000002321.
Presently filed for a PCT extension (PCT/IB2020/051329).
Owned by University of Padua, I am one of the three inventors.

RESEARCH SUPPORT

Young Investigator Award 2020 recipient: personal founding of 108'000$ from Children Tumor's Foundation (USA)

Positions

2009 post graduate fellowship to IOV (Venetian Oncology Institute)
2010-2013 PhD student in Medical, Clinical and Experimental Sciences - Dept. Medicine Univ. of Padua (Italy) - PhD student fellowship was founded by Italian University and Research Ministry
2013-2014 FIRB Post-Doctoral fellowship - Dept. Biomedical Sciences Univ. of Padua (Italy)
2015-2016 AIRC Post-Doctoral fellowship - Dept. Biomedical Sciences Univ. of Padua (Italy)
2017 NTAP Post-Doctoral fellowship - Dept. Biomedical Sciences Univ. of Padua (Italy)
2018 AIRC Post-Doctoral fellowship - Dept. Biomedical Sciences Univ. of Padua (Italy)
2019 NTAP Post-Doctoral fellowship - Dept. Biomedical Sciences Univ. of Padua (Italy)
2020 AIRC Post-Doctoral fellowship - Dept. Biomedical Sciences Univ. of Padua (Italy)
2020 (July) Children Tumor's Foundation fellow - Dept. Biomedical Sciences Univ. of Padua (Italy)
2022 (July) AIRC Post-Doctoral fellowship - Dept. Biomedical Sciences Univ. of Padua (Italy)
2022 (Nov) permanent position - Researcher - Neuroscience Institute, CNR (Italian National Research Council)

C. Contributions to Science

SELECTED PUBLICATIONS

Hexokinase 2 displacement from mitochondria-associated membranes prompts Ca^{2+}-dependent death of cancer cells. **Ciscato F**, Filadi R, Masgras I, Pizzi M, Marin O, Damiano N, Pizzo P, Gori A, Frezzato F, Trentin L, Bernardi P, Rasola A. ***EMBO Rep***. 2020 Jul 3;21(7):e49117. doi: 10.15252/embr.201949117. Epub 2020 May 8

The Use of Hexokinase 2-Displacing Peptides as an Anti-Neoplastic Approach for Malignant Peripheral Nerve Sheath Tumors. **Ciscato F**, Masgras I, Gori A, Fantuz M, Bergamaschi G, Komarov D, La Spina M, Ghasemi-Firouzabadi S, Pizzi M, Dei Tos AP, Chiara F, Carrer A, Rasola A. ***Cells***. 2024 Jul 8;13(13):1162. doi: 10.3390/cells13131162

Hexokinase 2 in Cancer: A Prima Donna Playing Multiple Characters. **Ciscato F**, Ferrone L, Masgras I, Laquatra C, Rasola A. ***Int J Mol Sci***. 2021 Apr 29;22(9):4716. doi: 10.3390/ijms22094716.

Tumor growth of neurofibromin-deficient cells is driven by decreased respiration and hampered by NAD+ and SIRT3. Masgras I, Cannino G, **Ciscato F**, et. al, ***Cell Death Differ***. 2022 Oct;29(10):1996-2008. doi: 10.1038/s41418-022-00991-4.

N-terminal cleavage of cyclophilin D boosts its ability to bind F-ATP synthase. Coluccino G, Negro A, Filippi A, Bean C, Muraca VP, Gissi C, Canetti D, Mimmi MC, Zamprogno E, **Ciscato F**, Acquasaliente L, De Filippis V, Comelli M, Carraro M, Rasola A, Gerle C,Bernardi P, Corazza A, Lippe G. ***Commun Biol*** 2024 Nov 11;7(1):1486. doi:10.1038/s42003-024-07172-8.

Design and Test of Molecules that Interfere with the Recognition Mechanisms between the SARS-CoV-2 Spike Protein and Its Host Cell Receptors. Scantamburlo F, Masgras I, **Ciscato F**, Laquatra C, Frigerio F, Cinquini F, Pavoni S, Triveri A, Frasnetti E, Serapian SA, Colombo G, Rasola A, Moroni E. ***J Chem Inf Model***. 2024 Nov 11;64(21):8274-8282. doi: 10.1021/acs.jcim.4c01511. Epub 2024 Oct 23. PMID: 39440601

Absence of neurofibromin induces an oncogenic metabolic switch via mitochondrial ERK-mediated phosphorylation of the chaperone TRAP1. Masgras I, **Ciscato F**, et al. ***Cell Reports***. 2017 Jan 17;18(3):659-672

The mitochondrial chaperone TRAP1 regulates F-ATP synthase channel formation. Cannino G, Urbani A, Gaspari M, Varano M, Negro A, Filippi A, **Ciscato F**, Masgras I, Gerle C, Tibaldi E, Brunati AM, Colombo G, Lippe G, Bernardi P, Rasola A. ***Cell Death Differ***. 2022 Dec;29(12):2335-2346. doi: 10.1038/s41418-022-01020-0.

Defining the molecular mechanisms of the mitochondrial permeability transition through genetic manipulation of F-ATP synthase. Carrer A, Tommasin L, Šileikytė J, **Ciscato F**, Filadi R, Urbani A, Forte M, Rasola A, Szabò I, Carraro M, Bernardi P. ***Nat Commun***. 2021 Aug 10;12(1):4835. doi: 10.1038/s41467-021-25161-x.

Analysis of the Effects of Hexokinase 2 Detachment from Mitochondria-Associated Membranes with the Highly Selective Peptide HK2pep. **Ciscato F**, Chiara F, Filadi R, Rasola A. ***Bio Protoc***. 2021 Jul 20;11(14):e4087

Metabolic Plasticity of Tumor Cell Mitochondria. **Ciscato F**, Cannino G, Masgras I, Sánchez-Martín C, Rasola A. ***Front Oncol***. 2018 Aug 24;8:333. doi: 10.3389/fonc.2018.00333. eCollection 2018. Review.

SERPINB3 protects from oxidative damage by chemotherapeutics through inhibition of mitochondrial respiratory complex I. **Ciscato F**, Sciacovelli M, Villano G, Turato C, Bernardi P, Rasola A, Pontisso P. ***Oncotarget***. 2014 May 15;5(9):2418-27.

Plasma small-extracellular vesicles enriched in miR-122-5p promote disease aggressiveness in pediatric anaplastic large-cell lymphoma. Damanti CC, Ferrone L, Gaffo E, Garbin A, Tosato A, Contarini G, Gallingani I, Angioni R, Molon B, Borile G, Carraro E, Pillon M, Scarmozzino F, Dei Tos AP, Pizzi M, **Ciscato F**, Rasola A, Biffi A, Bortoluzzi S, Lovisa F, Mussolin L. ***Cancer Commun (Lond)***. 2023 May;43(5):630-634.

16 publications in international peer reviewed journals. Citations: 704 (573 from 2020); h-index 10; i10-index 11

More than 20 accepted abstracts with poster presentations and/or oral communications in various international congresses

Editor for Frontiers in Cell and Developmental Biology;

Reviewer for Biochemical Pharmacology and Cell Death & Discovery

Teaching activity: Molecular Biology and Genetic (lab - 2023 and 2024), degree in Biology of Human and Environmental Health (University of Padua)