

Matteo Ligorio, MD, PhD

University of Texas Southwestern, Medical Center
 Department of Surgery
 Harold C. Simmons Comprehensive Cancer Center
 5323 Harry Hines Blvd.
 Dallas, Texas 75390, USA

Phone: +1 (617)-583-3640
 E-mail: matteo.ligorio@utsouthwestern.edu

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Education, Training and Professional Positions

Assistant Professor <i>University of Texas Southwestern, Medical Center</i>	1/2020 – Present
Instructor <i>Massachusetts General Hospital, Harvard Medical School</i>	1/2018 – 12/2019
Post-Doctoral Research Fellow <i>Massachusetts General Hospital, Harvard Medical School, Boston</i>	6/2014 – 12/2017
Ph.D in Molecular Epidemiology and Biostatistics <i>Harvard Medical School, Boston - University of Genova, Italy</i>	1/2011 - 4/2014
Residency in General Surgery <i>University of Genova, Italy</i>	1/2005 - 12/2010
Medical School with honors (<i>Summa cum laude</i>) <i>University of Genova, Italy</i>	9/1998 - 7/2004

Laboratory Research Experience

David T. Ting MD (mentor), Daniel A. Haber MD PhD (co-mentor), and Shyamala Maheswaran PhD (co-mentor): Cancer Center, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Post-Doctoral Research Fellow

(1) Defining the role of tumor stroma on single cell heterogeneity and tumor progression in pancreatic cancer; (2) Characterization of circulating tumor cells; (3) Generation of human xenografts in zebrafish as a novel animal model for cancer research.

Andrew L. Warshaw MD FACS FRCSE (Hon), Cristina R. Ferrone MD, Carlos Fernandez Del Castillo MD: Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Ph.D. Student - Clinical Research Fellow

(1) Development of a new drug-eluting platform to treat pancreatic cancer; (2) Discovery of novel prognostic biomarkers for gastrointestinal tumors.

Silvio De Flora, MD, PhD, and Roberto Gasparini, MD: University of Genova, Public Health Department, Genova, Italy

Ph.D. Student

(1) Mechanisms of mutagenesis in human cancer; (2) Epigenetic alterations in solid tumors.

Clinical Research Experience

Department of Surgery: University of Genova, Italy

Resident - MD student

(1) Robotic surgical anastomosis (MD Thesis); (2) Physio-Pathology of outlet obstruction syndrome; (3) Regenerative medicine to improve wound healing.

Awards and Honors

MGH ECOR Fund for Medical Discovery (FMD) Postdoctoral Fellowship Award	01/2018
Hirshberg Foundation for Pancreatic Cancer Research - Seed Grant Award	11/2017
Best Research Annual Award, MGH, Cancer Center	09/2016
American-Italian Cancer Foundation Post-Doctoral Fellowship Award	07/2015
MIT \$100K Award Finalist, PanTher Therapeutics	05/2015
Medal for academic achievements (MD Thesis)	07/2004

Board Certification

Board Certified in General Surgery	12/2010
Board Certificated in Emergency Territorial Medicine	07/2010
Medical Doctor License	10/2004

Entrepreneurship & Patents

Launching a Biotech Company, Panther Therapeutics® (http://www.panthertx.com/)	05/2015
Co-inventor (Patent Number: <i>US9301926 B2</i>) of a novel drug delivery device to treat pancreatic cancer	04/2014

Invited Speaker (selected): Meetings and Seminars

- Weill Cornell, Seminar, NYC, USA. October 21st, 2019
- UT Southwestern, Seminar. TX, USA. August 1st, 2019
- Pancreatic Diseases Gordon Conferences. Sunday River. ME, USA. June 20th, 2019
- Broad Institute. Epigenomic Seminar. Cambridge. MA, USA. April 29th, 2019
- Humanitas University. Seminar, Milan, Italy. December 21th, 2018.
- Memorial Sloan Kettering Cancer Center. Seminar, NYC, USA. July 17th, 2018
- University of Nebraska Medical Center, Special Seminar, NE, USA July 10th, 2018
- American Pancreatic Association (APA), Annual Meeting. San Diego, (CA). November 11th, 2017
- MGH Cancer Center Retreat, Waterville Valley, NH, USA. September 26th, 2017.
- American college of Surgeon, Annual Meeting. Washington, D.C. USA. October 7th, 2013.
- American college of Surgeon, Annual Meeting, Chicago, IL, USA. October 1st, 2012.

List of Peer-Reviewed and Under-Submission Publications

1. Porter RL, Magnus NKC, Thapar V, Morris R, Szabolcs A, Neyaz A, Kulkarni AS, Tai E, Chougule A, Hillis A, Golczer G, Guo H, Yamada T, Kurokawa T, Yashaswini C, **Ligorio M**, Vo KD, Nieman L, Liss AS, Deshpande V, Lawrence MS, Maheswaran S, Fernandez-Del Castillo C, Hong TS, Ryan DP, O'Dwyer PJ, Drebin JA, Ferrone CR, Haber DA, Ting DT. Epithelial to mesenchymal plasticity and differential response to therapies in pancreatic ductal adenocarcinoma. *PNAS* (2020) Jan 21;117(3):1818.

2. **Ligorio M***, Sil S*, Malagon-Lopez J, Nieman LT, Misale S, Di Pilato M, Ebright RY, Karabacak M, Kulkarni A, Liu A, Vincent Jordan N, Franses JW, Philipp J, Kreuzer J, Desai N, Arora KS, Rajurkar M, Horwitz E, Neyaz A, Tai E, Magnus NKC, Vo KD, Yashaswini CN, Marangoni F, Boukhali M, Fatherree JP, Damon LJ, Xega K, Desai R, Choz M, Bersani F, Langenbucher A, Thapar V, Morris R, Wellner UF, Schilling O, Lawrence MS, Liss AS, Rivera MN, Deshpande V, Benes CH, Maheswaran S, Haber DA, Fernandez-Del-Castillo C, Ferrone CR, Haas W, Aryee MJ, Ting DT. Stromal Microenvironment Shapes the Intratumoral Architecture of Pancreatic Cancer. *Cell* (2019) Jun 27;178(1):160-175.

***Equal Contribution**

3. Di Pilato M, Kim EY, Cadilha BL, Misale S, Zappulli V, Pruessmann JN, Usmani SM, Carrizosa E, Mani V, Seruggia D, **Ligorio M**, Warner R, Medoff BD, Marangoni F, and Mempel TR. Targeting the CBM signalosome induces Treg to prime the tumor environment 2 for effective immune checkpoint therapy. *Nature* (2019).
4. Yan C, Brunson DC, Tang Q, Do D, Iftimia NA, Moore JC, Hayes MN, Welker AM, Garcia EG, Dubash TD, Benjamin XH, Drapkin BJ, Myers DT, Phat S, Volorio A, Marvin DL, **Ligorio M**, Dershowitz L, McCarthy KM, Karabacak MN, Fletcher JA, Sgroi DC, Iafrate AJ, Maheswaran S, Dyson NJ, Haber DA, Rawls FJ, Langenau DM. Imaging tumor heterogeneity and therapy responses at single cell resolution using human xenografts grown in immune deficient zebrafish. *Cell* (2019)
5. Rajurkar M, Parikh A, Solovyov A, Kulkarni AS, Vo KD, Tai E, Lu C, Nieman LT, Desai N, Arora KS, **Ligorio M**, Thapar V, Deshpande V, Ferrone CR, Rivera MN, Hong TS, Greenbaum BD, Ting DT. Inhibition of Cancer Repeat RNA Retroviral Mimicry Triggers Necroptotic Immunosurveillance. (*Manuscript under submission*).
6. Potter RL, Magnus NC, Morris R, Thapar V, Szabolcs A, Tai E, Hillis A, Kulkarni AS, Chougule A, Yashaswini C, **Ligorio M**, Vo KD, Deshpande V, Fernandez-Del Castillo C, Ferrone CR, Lawrence MS, O'Dwyer PJ, Bebrin J, Ting D. Differential Effects of Vitamin D on Pancreatic Cancer Subtypes. (*PNAS - manuscript submitted*).
7. Franses JW, Philipp J, Missios P, Liu A, Yashaswini C, Kulkarni AS, **Ligorio M**, Zhu H, Maheswaran S, Haber DA, Daley GQ, Ting DT. LIN28B directly contributes to pancreatic cancer pathogenesis via a let-7/HMGA2 pathway. (*Nature Cancer - manuscript submitted*).
8. Geller L T, Barzily-Rokni M, Danino T, Jonas O H, Shental N, Nejman D, Gavert N, Zwang Y, Cooper Z A, Shee K, Thaiss C A, Reuben A, Livny J, Avraham R, Frederick D T, **Ligorio M**, Chatman K, Johnston S E, Mosher C M, Brandis A, Fuks G, Gurbatri C, Gopalakrishnan V, Kim M, Hurd M, Katz M, Fleming J, Maitra A, Smith D A, Skalak M, Bu J, Michaud M, Trauger S A, Barshack I, Golan T, Sandbank J, Flaherty K T, Mandinova A, Garrett W S, Thayer S P, Ferrone C R, Huttenhower C, Bhatia S N, Gevers D, Wargo J A, Golub T R, Straussman R. Intra-tumor bacteria elicit drug resistance in pancreatic ductal adenocarcinoma. *Science* (2017). Sep 15;357(6356):1156-1160
9. Villani* V, Mahadevan* K, **Ligorio* M**, Fernandez-del Castillo C, Ting D, Sabbatino F, Zhang I, Vangel M, Ferrone S, Warshaw A, Lillemoe K, Wargo J, Deshpande# V, Ferrone# C. Phosphorylated histone H3 (PHH3) is a superior proliferation marker for prognosis of pancreatic neuroendocrine tumors. *Annals of Surgical Oncology* (2016). Dec; 23(Suppl 5):609-617

***Equal Contribution.**

10. Vincent N, Bardia A, Wittner B, Benes C, **Ligorio M**, Zheng Y, Yu M, Sundaresan T, Desai R, O'Keefe R, Ebright R, Boukhali M, Sil S, Kapur R, Sgroi D, Ting D, Toner M, Ramaswamy S,

Haas W, Maheswaran S, Haber D. Heterogeneity of HER2 expression in circulating breast cancer cells identifies functionally distinct populations. *Nature* (2016). Sep 1;537(7618):102-106

11. Indolfi* L, **Ligorio* M**, Ting* D, Bersani F, Aceto N, Deshpande V, Ferrone C, Haber D, Langer R[#], Clark J[#], Edelman E[#]. A Tunable Delivery Platform to Provide Local Chemotherapy for Pancreatic Ductal Adenocarcinoma. *Biomaterials* (2016). Jul; 93:71-82

***Equal Contribution.**

12. Ting D, Wittner B, **Ligorio M**, Vincent Jordan N, Shah A, Miyamoto D, Aceto N, Bersani F, Brannigan B, Xega K, Ciciliano J, Zhu H, MacKenzie O, Trautwein J, Arora K, Shahid M, Ellis H, Qu N, Bardeesy N, Rivera M, Deshpande V, Ferrone C, Kapur R, Ramaswamy S, Shioda T, Toner M, Maheswaran S, Haber D. Single Cell RNA-sequencing Identifies Extracellular Matrix Gene Expression by Pancreatic Circulating Tumor Cells. *Cell Reports* (2014) Sep.; 25;8(6):1905-18.
13. Son J, Lyssiotis CA, Ying H, Wang X, Hua S, **Ligorio M**, Perera RM, Ferrone CR, Mullarky E, Shyh-Chang N, Kang Y, Fleming JB, Bardeesy N, Asara JM, Haigis MC, DePinho RA, Cantley LC, Kimmelman AC. Glutamine supports pancreatic cancer growth through a KRAS-regulated metabolic pathway. *Nature* (2013) Apr; 496(7443): 101-5.
14. Cecchini S, Correa-Gallego C, Deshpande V, **Ligorio M**, Dursun A, Wargo J, Fernández-del Castillo C, Warshaw AL, Ferrone CR. Superior prognostic importance of perineural invasion vs. lymph node involvement after curative resection of duodenal adenocarcinoma. *J Gastrointest Surg* (2012) Jan; 16(1): 113-20.
15. **Ligorio M**, Izzotti A, Pulliero A, Arrigo P. Mutagens interfere with microRNA maturation by inhibiting DICER. An *in silico* biology analysis. *Mutat Res.* (2011) Dec 1; 717(1-2): 116-28.
16. Reboa G, Gipponi M, **Ligorio M**, Marino P, Lantieri F. The impact of stapled transanal rectal resection on anorectal function in patients with obstructed defecation syndrome. *Dis Colon Rectum* (2009) Sep; 52(9): 1598-604.
17. Scala M, Gipponi M, Pasetti S, Dellachá E, **Ligorio M**, Villa G, Margarino G, Giannini G, Strada P. Clinical applications of autologous cryoplatelet gel for the reconstruction of the maxillary sinus. A new approach for the treatment of chronic oro-sinusal fistula. *In Vivo* (2007) May-Jun; 21(3): 541-7.

Research Support

Active

Cancer Prevention & Research Institute of Texas

CPRIT

Ligorio (PI)

02/2020-12/2023

Principal Investigator

\$2,000,000

Targeting tumor architecture as a novel therapeutic strategy for pancreatic cancer.

Targeting therapies against tumor architecture (stroma compartment) have proven efficacy in preclinical studies and have led to ongoing clinical trials. This is the proof-of-concept of the existence of tissue-specific properties that regulate tumor architecture during tumor progression. This proposed study aims at identifying the mechanisms that regulate tumor tissue homeostasis (e.g. the multicellular dynamics during tumor evolution) to find novel therapeutic strategies for patient with pancreatic cancer.

Role: **Principal Investigator (PI)**

Re-Submitted (03/05/2020)

NIH, RO1 Grant **Ligorio (PI)** 09/2020-09/2025
Principal Investigator \$1,750,000

Targeting tumor architecture as a novel therapeutic strategy for pancreatic cancer.

Targeting therapies against tumor architecture (stroma compartment) have proven efficacy in preclinical studies and have led to ongoing clinical trials. This is the proof-of-concept of the existence of tissue-specific properties that regulate tumor architecture during tumor progression. This proposed study aims at identifying the mechanisms that regulate tumor tissue homeostasis (e.g. the multicellular dynamics during tumor evolution) to find novel therapeutic strategies for patient with pancreatic cancer.

Role: ***Principal Investigator (PI)***

Completed

MGH ECOR Fund for Medical Discovery (FMD) **Ligorio (PI)** 01/2018-12/2018
Postdoctoral Fellowship Award \$75,000

Targeting an Aggressive Cancer Cell Subpopulation in Pancreatic Adenocarcinoma.

The overall goal of this project is to eliminate the DP cells (Ki67⁺/FN1⁺) by simultaneously targeting MAPK and STAT3 knocking out via CRISPR or by pharmacologically inhibiting these pathways with trametinib (MAPK) and pyrimethamine (STAT3). Moreover, we will define the role of the DP phenotype in PDAC chemoresistance (primary vs. acquired chemoresistance).

Role: ***Principal Investigator (PI)***

Hirshberg Foundation for Pancreatic Cancer Research **Ligorio (PI)** 11/2017-12/2018
Seed Grant \$50,000

Discovering Novel Therapeutic Strategies for Patients with Pancreatic Cancer.

The overall goal of this project is to eliminate the DP cells (Ki67⁺/FN1⁺) by simultaneously targeting MAPK and STAT3 knocking out via CRISPR or by pharmacologically inhibiting these pathways with trametinib (MAPK) and pyrimethamine (STAT3). Moreover, we will define the role of the DP phenotype in PDAC chemoresistance (primary vs. acquired chemoresistance).

Role: ***Principal Investigator (PI)***

American-Italian Cancer Foundation **Ligorio (PI)** 8/2015-7/31/2017
Postdoctoral Fellowship Award \$80,000

Role of Cancer Associated Fibroblasts (CAFs) in Pancreatic Cancer Progression

The overall goal of this project is to understand how CAFs affect pancreatic cancer circulating tumor cells (CTCs) and metastasis. A deeper understanding of the cancer-stroma interaction will help elucidate the major determinants implicated in tumor progression and identify novel molecular vulnerabilities that can be therapeutically targeted to improve the dismal prognosis of patients with pancreatic cancer.

Role: ***Principal Investigator (PI)***

Warsaw Institute for Pancreatic Cancer Research Ting (PI) 8/2016-8/2017
 Andrew L. Warsaw, M.D., Institute for Pancreatic Cancer Research \$50,000

Understanding the Heterogeneous Response of Pancreatic Cancer to Stroma

The goal of this project is to better define the different biological behavior of epithelial vs. mesenchymal pancreatic subtypes to stroma, which determine tumor growth and dissemination.

Role: ***Co-Investigator***

Warsaw Institute for Pancreatic Cancer Research Ting (PI) 7/2014-6/2015
 Andrew L. Warsaw, M.D., Institute for Pancreatic Cancer Research \$50,000

CURRICULUM VITAE

Role of Cancer Associated Fibroblasts in Pancreatic Cancer Progression

The goal of this project is to understand the contribution of cancer associated fibroblasts in tumor growth and dissemination.

Role: **Co-Investigator**

Bridge Project

Langer, Edelman & Clark (PIs)

3/2012-6/20

MIT Koch Institute & DF/HCC

\$650,000

Development of a Pancreatobiliary Chemotherapy Eluting Stent for Pancreatic Adenocarcinoma

This is a multi-disciplinary project involving researchers at MIT Koch Institute and Dana-Farber/Harvard Cancer Center to develop a controlled released chemotherapy local delivery platform with a polymer-coated pancreatobiliary stent scaffold. My role is in the overall coordination of PIs and researchers between MIT and MGH as well as execution of mouse model experiments at the MGH Cancer Center.

Role: **PhD Student**

Warsaw Institute for Pancreatic Cancer Research

Ferrone (PI)

5/2012-5/2013

Andrew L. Warsaw, M.D., Institute for Pancreatic Cancer Research

\$50,000

Epithelial-to-mesenchymal transition (EMT) as a prognostic factor for survival and chemosensitivity in pancreatic adenocarcinoma (PDAC)

To evaluate EMT status as a prognostic factor in PDAC patients, and analyze the role of EMT in response to gemcitabine, 5-FU, oxaliplatin, irinotecan and FOLFIRINOX in a panel of PDAC cell lines.

Role: **PhD Student**

References

David T. Ting, MD

Associate Clinical Director for Innovation
Massachusetts General Hospital Cancer Center
Assistant Professor of Medicine
Harvard Medical School
Building 149, Thirteenth Street
Charlestown, Massachusetts 02129
e-mail: dting1@mgh.harvard.edu
Tel: 617-240-9402 Fax: 617 724-3676
PhD and Post Doctoral Mentor

Daniel A. Haber, MD, PhD

Director, Cancer Center
Massachusetts General Hospital Cancer Center
Kurt J. Isselbacher Professor of Oncology
Harvard Medical School
Howard Hughes Medical Institute (HHMI)
Investigator
Building 149, Thirteenth Street
Charlestown, Massachusetts 02129
e-mail: dhaber@mgh.harvard.edu
Tel: 617-726-7805 Fax: 617-724-6919
Post Doctoral Co-Mentor

Andrew L. Warsaw, MD, FACS, FRCSEd (Hon)

Surgeon-in-Chief Emeritus
Massachusetts General Hospital
W. Gerald Austen Distinguished
Professor of Surgery
Harvard Medical School
Director, The Warsaw Institute for
Pancreatic Cancer Research
55 Fruit Street, BUL370
Boston, MA, 02114, USA
e-mail: awarshaw@partners.org
Tel: +1 617-726-8254
PhD and Post Doctoral Co-Mentor

Cristina R. Ferrone, MD

Massachusetts General Hospital
Associate Professor of Surgery
Harvard Medical School
General and Gastrointestinal Surgery
Surgical Oncology
Department of Surgery
15 Parkman Street, WACC 460
Boston, MA, 02114, USA
Email: cferrone@mgh.harvard.edu
Tel: +1 617-643-6189
Fax: +1 617-643-6116
PhD Mentor

Shyamala Maheswaran, PhD

Scientific Director, Center for Cancer Risk Management
 Massachusetts General Hospital
 Associate Professor
 Harvard Medical School
 Building 149, Thirteenth Street
 Charlestown, Massachusetts 02129
 e-mail: smaheswaran@mgh.harvard.edu
 Tel : 617-724-6552 Fax: 617-724-6919
Post Doctoral Co-Mentor

Wilhelm Haas, PhD

Massachusetts General Hospital
 Assistant Professor
 Harvard Medical School
 Building 149, Thirteenth Street
 Charlestown, Massachusetts 02129
 e-mail: WHAAS@mgh.harvard.edu
 Tel: 617-726-0538
Post Doctoral Collaborator

Roberto Gasparini, MD

Full Professor
 Department of Health Sciences
 University of Genova, Italy
 Director of the Center of Research on Influenza
 Medical School, via Pastore, 1 – 16132 – Genova
 e-mail: gasparini@unige.it
PhD Mentor

Maurizio Scaltriti, PhD

Memorial Sloan Kettering Cancer Center
 Associate Attending Molecular Biologist
 Human Oncology & Pathogenesis Program
 Associate Director of Translational Science
 Center for Molecular-Based Therapies
 Room Z-1702
 1275 York Avenue, Box 20
 e-mail: scaltrim@mskcc.org
 Tel 6468883519
Post Doctoral Collaborator

Martin Aryee, PhD

Assistant Professor of Pathology
 Massachusetts General Hospital
 Assistant Professor Department of Biostatistics
 Harvard T.H. Chan School of Public Health
 Associate Member, Broad Institute of
 MIT & Harvard
 Charlestown, Massachusetts 02129
 Email: aryee.martin@mgh.harvard.edu
Post Doctoral Co-Mentor

Elazer R. Edelman, MD, PhD, FACC

Thomas D. and Virginia W. Cabot Professor,
 Health Sciences and Technology
 Massachusetts Institute of Technology
 Professor of Medicine, Harvard Medical School
 Senior Physician, Brigham and Women's Hospital
 Director, Biomedical Engineering Center
 Director, Clinical Research Center
 Institute for Medical Engineering and Science
 77 Massachusetts Avenue, E25-438
 Cambridge, MA 02139
 e-mail: ere@mit.edu
 Tel: 617-253-1569 Fax: 617-253-2514
PhD Mentor

Mario L. Suva, MD, PhD

Massachusetts General Hospital
 Assistant Professor
 Harvard Medical School
 Building 149, Thirteenth Street
 Charlestown, Massachusetts 02129
 e-mail: Suva.Mario@mgh.harvard.edu
Post Doctoral Collaborator