Matthew Philip Mulè PhD

Website and online CV | Google Scholar | GitHub
Permanent email: mpm63@cantab.ac.uk | phone: US: +1(860) 882-3843 | UK: +44 07766 153007

Education & Training

University of Cambridge	Doctor of Philosophy (PhD) 2023 NIH Oxford-Cambridge Scholars Program Supervisors: John Tsang (NIAID), Ken Smith (Cambridge)
University of North Carolina	Doctor of Medicine (MD) in progress, expected 2025 UNC Chapel Hill Medical Scientist Training Program
National Institutes of Health	Postbaccalaureate IRTA Fellowship 2014–2016 Supervisor: Chris Hourigan (NHLBI)
Tufts University	Bachelor of Science in Biology 2014 *Cum Laude with Highest Thesis Honors* Honors thesis supervisor: Andrew Camilli

Doctoral Thesis: Systems immunology frameworks link multicellular immune perturbation phenotypes and setpoints to response outcomes [pdf] *Examiners: Sarah Teichmann, Petter Brodin*

Peer reviewed publications & preprints by research theme

Computational methods for analysis of multimodal single cell data

Normalizing and denoising protein expression data from droplet-based single cell profiling
Mulè MP#, Martins AJ#, Tsang JS
Nature Communications (2022) PDF | R package on CRAN

Identifying multicellular molecular immune networks that predict clinical responses

Integrating population and single-cell variations in vaccine responses identifies a naturally adjuvanted human immune setpoint.
Mulè MP, Martins AJ, Cheung F, Farmer R, Sellers BA, Quiel JA, Jain A, Kotliarov Y, Bansal N, Chen J, Schwartzberg PL, Tsang JS.
Immunity (2024) PMID: 38697118 PDF | editorial coverage

Contrasting autoimmune and treatment effects reveals baseline setpoints of immune toxicity following checkpoint inhibitor treatment
Mulè MP, Martins AJ, Pinal-Fernandez I, Donahue RN, Chen J, Schlom J, Gulley JL, Mammen A, Rajan A, Zhao C, Tsang JS
bioRxiv (2022) https://doi.org/10.1101/2022.06.05.49459 PDF

Iron dysregulation and inflammatory stress erythropoiesis associates with long-term outcome of COVID-19
Hanson AL, **Mulè MP**, Ruffieux H, Mescia F, Bergamaschi L, Pelly VS, Turner L, Kotagiri P; CITIID–NIHR, COVID BioResource Collaboration; Göttgens B, Hess C, Gleadall N, Bradley JR, Nathan JA, Lyons PA, Drakesmith H, Smith KGC.
Nature Immunology (2024) PMID: 38429458 PDF | editorial coverage

Broad mmune activation underlies shared set point signatures for vaccine responsiveness in

healthy individuals and disease activity in patients with lupus.
Kotliaov Y[#], Sparks R[#], Martins AJ[†], **Mulè MP[†],** Lu Y[†], Goswami M, Kardava L, Banchereau R, Pascual V, Biancotto A, Chen J, Schwartzberg PL, Bansal N, Liu CC, Cheung F, Moir S, Tsang JS. (#equal contribution, +equal contribution)
NatureMedicine (2020) PMID: 32094927 PDF | editorial coverage

Comparative systems immunology studies of infection and vaccination / vaccine engineering

Dynamic response patterns elicited by H5N1 vaccination reveal adjuvant-dependent and -independent functional impacts on the human immune system.
Apps R, Candia J, Kotliarov Y, Pearl S, Cheung F, Farmer R, **Mulè MP**, Rachmaninoff N, Chen J, Martins AJ, Rongye S, Zhou H, Bansal N, Schum P, Olnes MJ, Milanez-Almeida P, Han K, Kyu L, Sellers B, Cortese M, Hagan T, Rouphael N, Pulendran B, King L, Manischewitz J, Khurana S, Golding H, Van Der Most RG, Dickler HB, Germain RN Schwartzberg PL, Tsang JS
Cell Reports *(in press).* (2024).

Pan-vaccine analysis reveals innate immune endotypes predictive of antibody responses to vaccination.
Fourati S, Tomalin LE, **Mulè MP**, Chawla DG, Gerritsen B, Rychkov D, Henrich E, Miller HER, Hagan T, Diray-Arce J, Dunn P; Human Immunology Project Consortium (HIPC); Levy O, Gottardo R, Sarwal MM, Tsang JS, Suárez-Fariñas M, Pulendran B, Kleinstein SH, Sékaly RP.
Nature Immunology PMID: 36316476 (2022) PDF

Transcriptional atlas of the human immune response to 13 vaccines reveals a common predictor of vaccine-induced antibody responses.
Hagan T, Gerritsen B, Tomalin LE, Fourati S, **Mulè MP**, Chawla DG, Rychkov D, Henrich E, Miller HER, Diray-Arce J, Dunn P, Lee A; Human Immunology Project Consortium (HIPC); Levy O, Gottardo R, Sarwal MM, Tsang JS, Suárez-Fariñas M, Sékaly RP, Kleinstein SH, Pulendran B.
Nature Immunology (2022) PMID: 36316475 PDF

Time-resolved systems immunology reveals a late juncture linked to fatal COVID-19
Liu C, Martins AJ, Lau WW, Rachmaninoff N, Chen J, Imberti L, Mostaghimi D, Fink DL, Burbelo PD, Dobbs K, Delmonte OM, Bansal N, Failla L, Sottini A, Quiros-Roldan E, Han KL, Sellers BA, Cheung F, Sparks R, Chun TW, Moir S, Lionakis MS; NIAID COVID Consortium: Abers MS, Apps R, Bosticardo M, Milanez-Almeida P, **Mulè MP**, Shaw E, Zhang. Y; COVID Clinicians; Rossi C, Su HC, Kuhns DB, Cohen JI, Notarangelo LD, Tsang JS.
Cell (2021) PMID: 33713619 PDF

The Immune Signatures data resource, a compendium of systems vaccinology datasets.
Diray-Arce J, Miller HER, Henrich E, Gerritsen B, **Mulè MP**, Fourati S, Gygi J, Hagan T, Tomalin L, Rychkov D, Kazmin D, Chawla DG, Meng H, Dunn P, Campbell J; Human Immunology Project Consortium (HIPC); Sarwal M, Tsang JS, Levy O, Pulendran B, Sekaly R, Floratos A, Gottardo R, Kleinstein SH, Suárez-Fariñas M.
Scientific Data (2022) PMID: 36266291 PDF

Intravenous nanoparticle vaccination generates stem-like TCF1+ neoantigen-specific CD8+ T cells
Baharom F, Ramirez-Valdez RA, Tobin KKS, Yamane H, Dutertre CA, Khalilnezhad A, Reynoso GV, Coble VL, Lynn GM, **Mulè MP**, Martins AJ, Finnigan JP, Zhang XM, Hamerman JA, Bhardwaj N, Tsang JS, Hickman HD, Ginhoux F, Ishizuka AS, Seder RA.
Nature Immunology (2021) PMID: 33139915 PDF

Clinical molecular diagnostics, pathology in clinical immunology and hematologic malignancies

Multigene measurable residual disease assessment improves acute myeloid leukemia relapse risk stratification in autologous hematopoietic cell transplantation

Mulè MP, Mannis GN, Wood BL, Radich JP, Hwang J, Ramos NR, Andreadis C, Damon L, Logan AC, Martin TG, Hourigan CS.
Biology of Blood and Marrow Transplantation (2016) PMID: 27544285 PDF

Advancing the minimal residual disease concept in acute myeloid leukemia
Hokland P, Ommen HB, **Mulè MP**, Hourigan CS.
Seminars in Hematology (2015) PMID: 26111465 PDF

MDS-associated mutations in germline GATA2 mutated patients with hematologic manifestations
McReynolds LJ, Yang Y, Yuen Wong H, Tang J, Zhang Y, **Mulè MP**, Daub J, Palmer C, Foruraghi L, Liu Q, Zhu J, Wang W, West RR, Yohe ME, Hsu AP, Hickstein DD, Townsley DM, Holland SM, Calvo KR, Hourigan CS.
Leukemia Research (2019) PMID: 30578959 PDF

Rapid progression to AML in a patient with germline GATA2 mutation and acquired NRAS Q61K mutation.
McReynolds LJ, Zhang Y, Yang Y, Tang J, **Mulè M**, Hsu AP, Townsley DM, West RR, Zhu J, Hickstein DD, Holland SM, Calvo KR, Hourigan CS.
Leukemia Research Reports (2019) PMID: 31245276 PDF

Molecular measurable residual disease testing of blood during AML cytotoxic therapy for early prediction of clinical response
Wong HY, Sung AD, Lindblad KE, Sheela S, Roloff GW, Rizzieri D, Goswami M, **Mulè MP**, Ramos NR, Tang J, Thompson J, DeStefano CB, Romero K, Dillon LW, Kim DY, Lai C, Hourigan CS.
Frontiers in Oncology (2019) PMID: 30697529 PDF

Bacterial transcriptional dynamics in infection

The core promoter of the capsule operon of Streptococcus pneumoniae is necessary and sufficient for colonization and invasive disease.
Shainheit MG, **Mulè M**, Camilli A.
Infection and Immunity (2014) PMID: 24478084 PDF

Iron dependent gene expression in Actinomyces oris
Mulè MP, Giacalone D, Lawlor K, Golden A, Cook C, Lott T, Aksten E, O'Toole GA, Bergeron LJ
Journal of Oral Microbiology (2015)PMID: 26685151 PDF

Open source software

I created and continue to maintain these open source software repositories:
dsb Normalize & denoise droplet single cell protein data. R package on CRAN
scglmmr sample-level single cell generalized linear mixed models & phenotype networks in R GitHub

Clinical Trials

NCT02527447 Biomarkers for personalized early assessment of response during salvage chemotherapy in people with relapsed or refractory acute myeloid leukemia (PEARL15)
Associate investigator
- Role: I optimized custom molecular assays and liquid handling robotics and created laboratory policies/standard operating procedures for this clinical trial at NIH.

Awards

International Biomedical Research Alliance Outstanding Recent Graduate Award (2024)

- Recognizes noteworthy achievements of a graduate of the NIH Oxford-Cambridge Scholars Program who embodies the values of scientific innovation and collaboration leading to seminal biomedical discoveries at an early stage in their career.

NIH Fellows Award for Research Excellence (2022)
- Award based on peer reviewed blind study section competition recognizing outstanding scientific research performed by NIH intramural postdoctoral fellows or graduate students.

NIH Bioinformatics Special Interest Group award (2022)
- Selection by the NIH Bioinformatics special interest group of one winning abstract from the NIH FARE Competition deemed to be of high scientific merit.

NIH Systems Biology Special Interest Group award runner up (2022)
- Selection of abstract from the FARE Competition by the NIH Systems Biology special interest group.

Cambridge Trust NIH Scholarship (August 2018–August 2022)
- The Cambridge Trust grants scholarships to international students to study at Cambridge.

NIH Oxford-Cambridge Scholars program Scholarship (August 2018–August 2022)
- Awarded to pursue PhD in an international collaborative systems immunology project between University of Cambridge (Lab of Ken Smith) and National Institutes of Health (Lab of John Tsang)

University Cancer Research Fund MD/PhD Scholar Award (July 2017-August 2018)
- Funding from UNC Lineberger Comprehensive Cancer Center to support MD-PhD training.

National Institutes of Health Intramural Research Training Award (2014- 2016)
- Funding award to support my two year research fellowship in the lab of of Christopher Hourigan, chief of the Myeloid Malignancies Section at National Institutes of Health (NHLBI).

Tufts Summer Scholars Nathan T. Gantcher Scholarship Award (2013-2014)
- Funding award to support my research with Andrew Camilli at Tufts school of Medicine / HHMI

Tufts Summer Scholars Award (2013-2014)
- Funding award to support my research with Andrew Camilli at Tufts school of Medicine / HHMI

NH-INBRE Undergraduate Research Fellowship (2010-2012)
- Funding award to support my research with Lori Bergeron at New England College.

<u>Invited Seminars and conference talks</u>

Invited Seminars

GlaxoSmithKline Immunology Network Summit: Immunology of Vaccines (Stevenage UK Nov 16, 2022)
Talk title: Systems immunology frameworks link multicellular immune perturbation phenotypes and setpoints to vaccine response outcomes

Cambridge Yale AstraZeneca 2022 (Trinity Hall College, Cambridge UK, Sept 2022)
Talk Title: A longitudinal characterisation of COIVD-19 pathology and long-COIVD risk (with Aimee Hanson)

NIH Bioinformatics Special Interest Group FARE Award Lecture (Nov 18, 2021)
Talk title: An analysis framework for multi-subject CITE-seq perturbation studies

National Cancer Institute DCTD Biometric Research Program Seminar (June 8, 2021)
Talk title: Evaluation of single cell multiomics technologies for human perturbation cohort studies

Invited Refereed Conference Talks

Systems Immunology 2021 – Cold Spring Harbor (April 22, 2021)
Talk title: Pinpointing cell states associated with vaccination response with new computational tools for nested-group CITE-seq analysis [link]

Human Immunology Project Consortium Annual Meeting (March 24, 2021)
Talk title: Experimental and computational noise deconvolution inspires dsb, an open source R package for normalizing and denoising CITE-seq protein data

UNC Chapel Hill John B Graham Research Day (November 11, 2016)
Talk title: Multigene relapse risk prediction in autologous transplantation for acute myeloid leukemia.
*One of six students selected for oral presentation.

Selected Conference Poster Presentations (Presenting / first author)

Systems Immunology 2023 – Cold Spring Harbor (CSHL April 18, 2023)
Talk title: Multicellular immune networks of disease activity and clinical outcome in vasculitis [link]

European Advanced School in the Philosophy of the Life Sciences (Bordeaux, Fr Sept 5-9 2022)
2022 summer school on dealing with complexity in the life sciences
Poster and talk: Avoiding the mind projection fallacy in interpreting complex single cell systems biological data [pdf]

NIH Graduate Student Research Symposium 2021 (NIH, Febuary 21 2021)
Poster: Pinpointing Cell States Induced by Vaccines using New Computational Tools for Multimodal Single Cell Analysis [link]

NIH Global Doctoral Partnerships Research Workshop 2020 (June 15-20 2020)
Talk title: Mapping human immune system variation to clinical outcome with systems immunology

NIH Oxford Cambridge Scholars Program Annual Colloquium, (Oxford, June 25-27 2019)
Poster: Human vaccine response signatures revealed through simultaneous transcriptome and protein profiling in single cells

Cold Spring Harbor Systems Immunology 2019 (CSHL March 14-16 2019)
Poster: Human vaccine response signatures revealed through simultaneous transcriptome and protein profiling in single cells [link]

NHLBI Research Day Festival (Bethesda, MD April 29, 2016)
Talk and poster title: Comprehensive residual disease assessment improves AML relapse risk stratification in autologous hematopoietic cell transplantation.

NIH Postbac Poster Day (Bethesda, MD April 20, 2016)
Poster: High sensitivity personalized residual disease monitoring predicts acute myeloid leukemia relapse. Best poster award

57th American Society of Hematology Annual Meeting (Orlando FL December 5-8 2015)
Poster: (Abstract # 4350) Multigene MRD Assessment Improves AML Relapse Risk Stratification in Autologous Hematopoietic Cell Transplantation. [pdf]

NHLBI Research Day Festival (June 12, 2015. Bethesda, MD)
Oral presentation and poster: Measurable residual disease in patients undergoing autologous stem cell transplant for acute myeloid leukemia.

NIH Postbac Poster Day (April 30, 2015. Bethesda, MD)
Poster: A complementary multigene strategy to quantify residual disease in acute myeloid leukemia patients prior to autologous stem cell transplant.

Tufts University Summer Scholars Annual Research Symposium (October 30, 2013. Somerville MA)
Poster: Characterizing transcriptional regulation of *Streptococcus pneumoniae* capsule in host colonization and disease

Tufts Summer Scholars Biochemistry and Biomedicine Panel (July 17, 2013, Somerville, MA.) Oral Presentation: Characterizing transcriptional regulation of *Streptococcus pneumoniae* capsular polysaccharide.

5th Annual Northeast Undergraduate Research and Development Symposium (Biddeford ME, March 2-3, 2013 Biddeford, ME) Poster: Characterization of AmdR, an iron dependent transcriptional repressor. Best Poster Award

New Hampshire-INBRE 2012 Annual Meeting (July 13-14, 2012. Whitefield, NH) Oral Presentation: Metal Dependent Transcriptional Regulation in *Actinomyces naeslundii* *One of four students state wide selected to give oral presentation

2012 Eastern New England Biology Conference (April 24, 2012. Easton, MA) Poster: *Actinomyces naeslundii* Metal Dependent Repressor Binds to Siderophore Promoters

New England College Undergraduate Research Showcase (April 7, 2012. Henniker, NH)
Poster: *Actinomyces naeslundii* Metal Dependent Repressor Binds to Siderophore Promoters

Other refereed conference presentations (co-author)

Society for Immunotherapy of Cancer (SITC) 36th Anniversary Annual Meeting (2021)
Abstract 540: Baseline mTOR transcriptional signatures in CD8 T cells are associated with immune-related adverse events but not anti-tumor responses in patients receiving immune checkpoint inhibitors [pdf]

Cold Spring Harbor Systems Immunology 2019 (March 14-16 2019) Integrated surface protein and gene expression analysis of cord blood mononuclear cells from pre-term and full-term births. [link]

58th American Society of Hematology Annual Meeting (December 3-6 2016)
Abstract # 1664: Increased Frequencies of PD-1+ CD8+ Marrow-Infiltrating Lymphocytes Associated with Highly Clonal T-Lymphocyte Expansions in Relapsed and Refractory AML Patients but Not Healthy Adults. [pdf]

American Society of Clinical Oncology (ASCO) Annual Meeting (June 1-8 2018)
Abstract 7047: Molecular testing during AML treatment for early prediction of clinical response [pdf]

Academic Service and mentorship

Peer reviewer
Nature Communications (1)
Cell Reports (1)
Bone Marrow Transplant (1)

John B. Graham Research Day organizing committee – UNC Chapel Hill School of Medicine (2017)

Hematology/oncology block focus group – UNC Chapel Hill School of Medicine (2017)

UNC Medical Mentors Program 2016-2017
- Volunteer mentor to pre-health students navigating medical school application

Other Clinical Training

National Institutes of Health Clinical Research Training Course

Medical service and leadership

Open Door Clinic Alamance County Diabetes Management & Prevention Program: (2017-2018)
Clinic Coordinator
- Responsible for physician recruiting / scheduling and patient continuity of care for this clinic providing free diabetes care to uninsured patients in North Carolina.

Timmy Global Health, Tufts University Chapter (September 2012-May 2014)
Trip Leader and Executive Board Member
- 2014 Guatemala Trip Leader: recruited medical professionals and organized January 2014
- Integrated mobile electronic medical record for better continuity of care between volunteer groups.
- 2013 Volunteered in an 18-person mobile medical relief trip in Guatemala.

The Sharewood Project of Tufts Medical School, Boston, MA (June 2013-January 2014)
Demographics Project Leader and public health commite member
- Volunteered in free medical clinic serving uninsured in the greater Boston area.
- Helped integrate EMR in the clinic and ran a demographics tracking project to secure funding.
- Public Health Committee: oversaw public health interventions for the local community.