

BIOGRAPHICAL SKETCH

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 Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Offin, Michael

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

POSITION TITLE: Assistant Attending, Thoracic Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center

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
Rutgers The State University of New Jersey	BA	06/2009	Biological Sciences
Rutgers New Jersey Medical School	MD	06/2013	Medicine
Hospital of the University of Pennsylvania	Residency	06/2016	Internal Medicine
Memorial Sloan Kettering Cancer Center, NY	Fellowship	01/2019	Medical Oncology
Memorial Sloan Kettering Cancer Center, NY	Attending	01/2019	Thoracic Oncology

A. Personal Statement

I am an Assistant Attending Physician in the Thoracic Oncology Service in the Department of Medicine at Memorial Sloan Kettering (MSK). I am the primary/co-primary investigator of several ongoing prospective clinical trials evaluating novel treatment paradigms for patients with mesothelioma and lung cancers. My research focuses on translational studies evaluating predictors of response to therapy in thoracic cancers, including expertise in next-generation sequencing (NGS; DNA-seq, RNA-seq, quantitative proteomic analyses) and modeling (cell line and patient-derived xenografts (PDX)).

B. Positions and Honors

Positions and Employment

- 2013-2014 Intern, Internal Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA
- 2013-2016 Resident, Internal Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA
- 2016-2019 Fellow, Medical Oncology, Memorial Sloan Kettering Cancer Center, New York, NY
- 2019- Assistant Attending, Thoracic Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Honors

- 2009 Valedictorian (Dean's Award), Rutgers University Livingston Campus, New Brunswick, NJ
- 2009 Summa Cum Laude, Rutgers University, New Brunswick, NJ
- 2009 S. Oakley Vander Poel Award for Achievement in Biological Sciences, Rutgers University, New Brunswick, NJ
- 2011 Loran and Klara Korek Scholarship, Rutgers University, New Brunswick, NJ
- 2011, 2012 Abdol H Islami MD Foundation Scholarship, Rutgers University, New Brunswick, NJ
- 2013 Dr. Harold J Jeghers Future Internist Award, Rutgers New Jersey Medical, Newark, NJ
- 2013 Dr. Ruy V. Lourenco Dean's Achievement Award, Rutgers New Jersey Medical, Newark, NJ
- 2013 Thomas Eck and Emily Fay Mentoring Award, Rutgers New Jersey Medical, Newark, NJ

2013	Outstanding Medical Student Award (Student of the Year), Rutgers New Jersey Medical, Newark, NJ
2018	ASCO Conquer Cancer Merit Award
2018	AACR/ASCO Methods in Clinical Research Workshop Attendee
2019	National Institutes of Health Loan Repayment Program: National Cancer Institutes
2021	International Mesothelioma Interest Group Young Investigator Award

Professional Memberships

2012-	Member	American College of Physicians
2012-	Member	American Medical Association
2013-	Member	Alpha Omega Alpha
2013-	Member	Gold Humanism Honor Society
2016-	Member	American Society of Clinical Oncology
2016-	Member	American Society of Hematology
2017-	Member	American Association for Cancer Research
2017-	Member	International Association for the Study of Lung Cancer
2017-	Member	European Society of Medical Oncology
2021-	Member	Society for Immunotherapy of Cancer
2021-	Member	Mesothelioma Applied Research Foundation Scientific Advisory Board

C. Contributions to Science

1. Exploring the application of precision medicine in mesothelioma

Despite recent advances in the treatment of patients with MPM with the integration of first line dual immune checkpoint inhibition as a treatment option, outcomes remain unacceptably poor. There is clear differential response by histologic subtype and our understanding of potential predictors of response remains elusive. Therapeutic progress has largely plateaued and defining the biologically different subtypes of mesothelioma will facilitate our ability to give patients tailored prognostic information, propel drug development, and improve outcomes. I am spearheading efforts to develop rationally designed strategies to improve outcomes as well as our understanding of the biology of response/resistance for patients with this devastating illness.

- Offin M**, Yang SR, Egger J, Jayakumaran G, Spencer RS, Lopardo J, Nash GM, Cercek A, Travis WD, Kris MG, Ladanyi M, Sauter JL, Zauderer MG. Molecular Characterization of Peritoneal Mesotheliomas. *J Thorac Oncol*. 2021:S1556-0864(21)03215-9. PMID: 34648949.
- Zauderer MG, Martin A, Egger J, Rizvi H, **Offin M**, Rimner A, Adusumilli PS, Rusch VW, Kris MG, Sauter JL, Ladanyi M, Shen R. The use of a next-generation sequencing-derived machine-learning risk-prediction model (OncoCast-MPM) for malignant pleural mesothelioma: a retrospective study. *Lancet Digit Health*. 2021;3(9):e565-e576. PMID: PMC8459747.
- Chintala NK, Restle D, Quach H, Saini J, Bellis R, **Offin M**, Beattie J, Adusumilli PS. CAR T-cell therapy for pleural mesothelioma: Rationale, preclinical development, and clinical trials. *Lung Cancer*. 2021;157:48-59. PMID: PMC8184643.
- Ghosn M, Cheema W, Zhu A, Livshitz J, Maybody M, Boas FE, Santos E, Kim D, Beattie JA, **Offin M**, Rusch VW, Zauderer MG, Adusumilli PS, Solomon SB. Image-Guided Interventional Radiological Delivery of Chimeric Antigen Receptor (CAR) T Cells for Pleural Malignancies in a Phase I/II Clinical Trial. *In review*.
- Offin M**, Rusch VW, Rimner A, Adusumilli PS, Zauderer MG. Evolving Landscape of Initial Treatments for Patients with Malignant Pleural Mesotheliomas: Clinical Trials to Clinical Practice. *In review*.
- Offin M**, Sauter JL, Egger JV, Chavan S, Shah NS, Ventura K, Allaj V, de Stanchina E, Travis W, Ladanyi M, Rimner A, Rusch VW, Adusumilli PS, Poirier JT, Zauderer MG, Rudin CM, Sen T. Genomic and transcriptomic analysis of a library of patient-derived xenografts established from patients with diffuse pleural mesothelioma. *In review*.

2. Identification of mechanisms of differential response to therapy in thoracic malignancies

With the integration of NGS into the care of patients with advanced non-small cell lung cancers (NSCLC), the understanding of the importance of the computational landscape of cancer on differential response to

therapy is growing. My translational portfolio has led to several investigations into novel resistance pathways in oncogene-addicted subsets of lung cancer leading to several *in vivo* experiments and proposed/ongoing clinical trials. Leveraging this experience, I am exploring co-alterations and mutational signatures in mesothelioma as novel prognostic and predictive indicators.

- a. **Offin M**, Chan JM, Tenet M, Rizvi HA, Shen R, Riely GJ, Rekhtman N, Daneshbod Y, Quintanal-Villalonga A, Penson A, Hellmann MD, Arcila ME, Ladanyi M, Pe'er D, Kris MG, Rudin CM, Yu HA. Concurrent RB1 and TP53 Alterations Define a Subset of EGFR-Mutant Lung Cancers at risk for Histologic Transformation and Inferior Clinical Outcomes. *J Thorac Oncol*. 2019;14:1784-1793. PMID: PMC6764905
- b. **Offin M**, Rizvi H, Tenet M, Ni A, Sanchez-Vega F, Li BT, Drilon A, Kris MG, Rudin CM, Schultz N, Arcila ME, Ladanyi M, Riely GJ, Yu H, Hellmann MD. Tumor Mutation Burden and Efficacy of EGFR-Tyrosine Kinase Inhibitors in Patients with EGFR-Mutant Lung Cancers. *Clin Cancer Res*. 2019;25:1063-1069. PMID: PMC6347551
- c. **Offin M**, Somwar R, Rekhtman N, Benayed R, Chang JC, Plodkowski A, Lui AJW, Eng J, Rosenblum M, Li BT, Riely GJ, Rudin CM, Kris MG, Travis W, Drilon A, Arcila ME, Ladanyi M, Yu HA. Acquired ALK and RET Gene Fusions as Mechanisms of Resistance to Osimertinib in EGFR-Mutant Lung Cancers. *JCO Precis Oncol*. 2018;2. PMID: PMC6447364.
- d. Suzawa K, **Offin M [co-first]**, Schoenfeld AJ, Plodkowski AJ, Odintsov I, Lu D, Lockwood WW, Arcila ME, Rudin CM, Drilon A, Yu HA, Riely GJ, Somwar R, Ladanyi M. Acquired MET Exon 14 Alteration Drives Secondary Resistance to Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor in EGFR-Mutated Lung Cancer. *JCO Precis Oncol*. 2019;3. PMID: PMC6541452.
- e. Suzawa K., **Offin M. [co-first]**, Liu D., Kurzatkowski C., Tai H., Vojnic M., Smith R.S., Sabari J.K., Mattar M., Khodos I., de Stanchina E., Arcila M.E., Lockwood W.W., Drilon A., Ladanyi M., Somwar R. Oncogenic KRAS mediates resistance to MET targeted therapy in non-small cell lung cancer (NSCLC) with MET mutations that induce exon14 skipping. *Clin Cancer Res*. 2019;25(4):1248-1260. PMID: 30352902.

3. Evaluation of safety, efficacy, and predictors of response to immunotherapy

Through my strong collaborations with the Radiation Oncology Service, I have studied factors predicting local-control, failure patterns, and immune related adverse events. We have several ongoing projects exploring predictors of response and resistance to the addition of immunotherapy, including correlation of outcomes with genomic, immunologic, and pathologic correlates. Through these prior and ongoing collaborations, I have now opened clinical trials evaluating the role of immunotherapy combinations in mesothelioma including two investigator-initiated trials: 1) neoadjuvant trial of chemo-immunotherapy and 2) combination immunotherapy and cryoablation in the later line setting.

- a. **Offin M.**, Shaverdian N., Rimner A., Lobaugh S., Shepherd AF., Simone CB., Gelblum DY., Wu AJ., Lee N., Kris MG., Rudin CM., Zhang Z., Hellmann MD., Chaft JE., Gomez DR. Clinical outcomes, local-regional control and the role for metastasis-directed therapies in stage III non-small cell lung cancers treated with chemoradiation and durvalumab. *Radiother Oncol*. 2020; 149:205-211. PMID: 32361014.
- b. Shaverdian N., Thor M., Shepherd AF., **Offin MD.**, Jackson A., Wu AJ., Gelblum DY., Yorke ED., Simone CB., Chaft JE., Hellmann MD., Gomez DR., Rimner A., Deasy JO. Radiation pneumonitis in lung cancer patients treated with chemoradiation plus durvalumab. *Cancer Med*. 2020;9(13):4622-4631. PMID: PMC7333832
- c. Shaverdian N., **Offin M. [co-first]**, Rimner A., Shepherd AF., Wu AJ., Rudin CM., Hellmann MD., Chaft JE., Gomez DR. Utilization and factors precluding the initiation of consolidative durvalumab in unresectable stage III non-small cell lung cancer. *Radiother Oncol*. 2019; 144:101-104. PMID: 31786421.

4. Leveraging novel strategies to sequence patient blood and tissue specimens at diagnosis and at resistance to understand tumoral evolution during treatment

I study the use of cell-free DNA (cfDNA) in the care of lung cancer patients as a diagnostic and therapeutic biomarker. Through this work, I am exploring the use of cfDNA (liquid biopsy) technologies to ascertain

driver mutations, acquired resistance mechanisms, and molecular responses as measured by dynamic changes in gene specific variant allele frequency (VAF). We are now conducting a pilot study to assess the utility of cfDNA analyses off of pleural effusions and ascites in patients with mesothelioma. Furthermore, I am also involved with the development and integration of targeted RNA-based sequencing techniques into the routine assessment of patients with lung cancer and exploring its use in patients with mesothelioma.

- a. **Offin M**, Chabon JJ, Razavi P, Isbell JM, Rudin CM, Diehn M, Li BT. Capturing Genomic Evolution of Lung Cancers through Liquid Biopsy for Circulating Tumor DNA. *J Oncol.* 2017;2017:4517834. PMID: PMC5368362.
- b. Sabari J.K., **Offin M.** [co-first], Stephens D., Ni A., Lee A., Pavlakis N., Clarke S., Diakos C.I., Datta S., Tandon N., Duboff M., Simpronio J., Martinez A., Ladanyi M., Arcila M.E., Isbell J., Rusch V., Jones D., Rimmer A., Hernandez J., Henderson S., Garg K., DiPasquo D., Raymond C.K., Lim L.P., Li M., Riely G.J., Rudin C.M., Li B.T. A Prospective Study of Circulating Tumor DNA to Guide Matched Targeted Therapy in Lung Cancers. *J Natl Cancer Inst.* 2019;111(6):575-583. PMID: 30496436.
- c. Mondaca S, **Offin M**, Borsu L, Myers M, Josyula S, Makhnin A, Shen R, Riely GJ, Rudin CM, Ladanyi M, Yu HA, Li BT, Arcila ME. Lessons learned from routine, targeted assessment of liquid biopsies for *EGFR* T790M resistance mutation in patients with *EGFR* mutant lung cancers. *Acta Oncol.* 2019;58:1634-1639. PMID: 31347936.
- d. Benayed R., **Offin M.**, Mullaney K., Sukhadia P., Rios K., Desmeules P., Ptashkin R., Won H., Chang J., Halpenny D., Schram A.M., Rudin C.M., Hyman D.M., Arcila M.E., Berger M.F., Zehir A., Kris M.G., Drilon A., Ladanyi M. High yield of RNA sequencing for targetable kinase fusions in lung adenocarcinomas with no mitogenic driver alteration detected by DNA sequencing and low tumor mutation burden. *Clin Cancer Res.* 2019;25(15):4712-4722. PMID: 31028088.

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Druckenmiller Foundation: AWD-GC-259578

Offin (PI)

11/2020-11/2022

An Efficacy and Safety Study of Pembrolizumab plus Cryoablation in Mesothelioma

The goal of this project is to conduct a trial of combination cryoablation and pembrolizumab in patients with mesothelioma to determine safety and evaluate mechanisms of response.

Role: PI

