BIOGRAPHICAL SKETCH

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NAME: Prateek (Pat) Gulhati, M.D., Ph.D.

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POSITION TITLE: Assistant Professor, GI Medical Oncology, Rutgers Cancer Institute of New Jersey

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	COMPLETION DATE	FIELD OF STUDY
University of British Columbia, Vancouver, BC	B.Sc.	05/2006	Physiology (Honors)
University of Texas Medical Branch, Galveston, TX	M.D.	06/2013	Medicine
University of Texas Medical Branch, Galveston, TX	Ph.D.	06/2013	Cancer Biology
The Mount Sinai Hospital, New York, NY	Residency	06/2015	Internal Medicine
The University of Texas MD Anderson Cancer Center, Houston, TX	Fellowship	12/2019	Medical Oncology

A. Personal Statement

I am a Physician-Scientist and Assistant Professor (Tenure-Track) in the Department of Gastrointestinal Medical Oncology at Rutgers Cancer Institute of New Jersey and Robert Wood Johnson Medical School. My clinical practice focuses on management of gastrointestinal cancers including pancreatic cancer. My research interests include basic and translational laboratory-based research in pancreatic cancer with the goal of developing novel therapeutic strategies targeting the tumor microenvironment (TME). After completing undergraduate studies in Physiology, I graduated from the Combined MD/PhD program at the University of Texas. During my PhD studies under the mentorship of Dr. B. Mark Evers, I characterized the role of the mammalian Target Of Rapamycin (mTOR) signaling pathway in tumorigenesis, metastasis and therapeutic resistance of colorectal cancer (CRC). In human biospecimens and mouse models of CRC, we demonstrated for the first time the role of mTOR signaling in mediating invasion and metastasis of CRCs via the RhoA and Rac1 pathway. Another project demonstrated synergistic activity between sorafenib and the first-generation mTOR inhibitor, rapamcyin, in preclinical models of CRC harboring oncogenic *KRAS* and *PIK3CA*. Subsequently, I designed a phase I/II clinical trial for patients with metastatic CRC based on these preclinical findings. These experiences stimulated my interest in using animal models of cancer along with human cancer biospecimens to evaluate novel therapeutic strategies in GI malignancies, and to delineate biomarkers of response as well as mechanisms of therapeutic resistance with the goal of developing innovative clinical trials to improve patient outcomes. During subspecialty fellowship training at MD Anderson Cancer Center, I focused my efforts on building a strong foundation in the clinical management of patients with GI cancers, concentrating on pancreatic ductal adenocarcinoma (PDAC). I also continued to build my expertise in laboratory based basic/translational research during my post-doctoral fellowship under the mentorship of Dr. Ronald DePinho, where I investigated the dynamics of the TME including the immune system in growth and therapeutic resistance of PDAC using genetically engineered mouse models and human PDAC specimens. I have been blessed with the full spectrum of training for understanding, researching and treating pancreatic cancer and I hope to improve outcomes for PDAC patients by 1) understanding the mechanisms by which the immunosuppressive TME contributes to therapeutic resistance, and 2) activating the host immune system to target tumors and achieve durable remissions and cures. Through this work, I have learnt that there is a need to identify and validate the rationale for immunotherapeutic and stromal targeting therapies as well as the sequencing of such therapies in preclinical models. Hypotheses generated from preclinical studies can be validated in human biospecimens and phase I/II clinical trials for PDAC patients including analysis of longitudinal PDAC patient samples to study immune, stromal and genomic determinants of response and resistance, as well as to identify actionable targets to inform future therapeutic vulnerabilities. In addition to laboratory based research, I am also actively engaged in clinical trials evaluating

novel treatment strategies for PDAC patients, and serve as principal investigator for several investigator-initiated clinical trials incorporating the use of circulating tumor DNA into the treatment algorithm for PDAC patients.

B. Positions and Honors

Positions and Scientific Appointments:

2013-2015	Intern and Resident, Internal Medicine, Icahn School of Medicine at Mount Sinai, The Mount Sinai Hospital, New York, NY
2015-2018	Fellow, Hematology and Medical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX
2018-2019	Instructor, Gastrointestinal Medical Oncology, Division of Cancer Medicine, University of Texas MD Anderson Cancer Center, Houston, TX
2020-Present.	Assistant Professor (Tenure-Track) and Principal Investigator, Gastrointestinal Medical Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ

Honors:

2002	Undergraduate Entrance Scholarship, University of British Columbia
2002-2005	Undergraduate Academic Scholarship, University of British Columbia
2003-2005	Golden Key Honor Society Nomination, University of British Columbia
2003-2005	Dean's Honor List, University of British Columbia
2005	Faculty of Medicine Summer Research Studentship, University of British Columbia
2005	Summer Academic Scholarship, University of British Columbia
2006	British Columbia Cancer Studentship Award, Canadian Breast Cancer Foundation
2006-2013	MD/PhD Fellowship Award, University of Texas Medical Branch
2008	Sealy Center for Cancer Biology Pre-Doctoral Fellowship, University of Texas Medical Branch
2009	Osler Award in Translational Medicine, National Student Research Forum
2009	Cancer Day Student Poster Presentation Award, University of Texas Medical Branch
2009	Shirley Patricia Parker Oncology Scholarship, University of Texas Medical Branch
2010	Poster of Distinction at Digestive Diseases Week, American Gastroenterological Association
2010	Scholar-in-Training Award, American Association for Cancer Research
2010	Margaret Saunders Travel Award, University of Texas Medical Branch
2010	Robert Harrison M.D. Memorial MD/PhD Scholarship, University of Texas Medical Branch
2012	Kay and Cary W. Cooper Scholarship Award, University of Texas Medical Branch
2012	Katherine Siebert Award for Oncology Research, University of Texas Medical Branch
2016	American Board of Internal Medicine Certification
2017	Selected for Society of Translational Oncology Fellows Forum
2018	Conquer Cancer Foundation Merit Award, American Society of Clinical Oncology
2018	Conquer Cancer Foundation Merit Award, Gastrointestinal Cancers Symposium
2018	American Board of Internal Medicine, Medical Oncology Certification
2020	Pardee Foundation Award
2021	New Jersey Health Foundation Award

C. Contributions to Science

1. The role of Wnt proteins secreted from stromal myofibroblasts on colorectal cancer stem cell differentiation and self-renewal.

Antigen presenting cells play a critical role in maintaining the balance between tolerance and inflammation in the gut by modulating T cell activity. Dr. Don Powell's group has pioneered the study of human colonic stromal CD90+ myofibroblasts and their role as non-professional antigen presenting cells in the pathogenesis of inflammatory bowel diseases and CRC. As a medical student, I studied the effect of Wnt 5a secreted from stromal myofibroblasts on CRC stem cell differentiation and self-renewal. These studies identified a potential mechanism by which stromal myofibroblasts contribute to initiation and progression of CRC. These findings also provided the rationale for targeting this stromal compartment to inhibit CRC growth and progression.

a. Mifflin RC; DiMari J; Qiu S; Pinchuk IV; Saada JI; **Gulhati P** and Powell DW. Phenotypic Characterization of Human Myofibroblasts Isolated from Sporadic Colonic Adenocarcinomas. Abstract and Poster presented at 'Digestive Diseases Week', Washington D.C., May 19-24, 2007.

b. Powell DW, Mifflin R, DiMari J, Adegboyega P, Pinchuk I, Saada J, **Gulhati P**, Shao J and Sheng H. Role of myofibroblasts in colonic inflammation and cancer. Abstract and Poster presented at the 'Stem Cells in Gastrointestinal Development, Regeneration and Neoplasia Conference', Tyson's Corner, Virginia, September 8-9, 2006.

2. The role of mTOR signaling in tumorigenesis, metastasis and therapeutic resistance of colorectal cancer.

During graduate studies, I continued to build on my interest in GI cancers given the limited number of treatment options that are available to patients and universally poor outcomes associated with advanced GI malignancies. For my doctoral thesis, under the mentorship of Dr. B. Mark Evers, I studied the role played by the mTOR signaling pathway in CRC growth, metastasis and therapeutic resistance. Although mTOR had previously been known to contribute to growth of several cancers, including prostate and hepatocellular cancer, among others, it had not been associated with invasion and metastasis of cancers previously. In one of the most highly cited articles of 2011 in *Cancer Research*, we demonstrated for the first time the role played by mTOR and its interaction partners in regulating the motility, EMT and metastasis of CRC via downstream RhoA and Rac 1 signaling. In another study, we delineated synergistic activity between targeted therapy against mTOR and the multi-kinase inhibitor, sorafenib. I subsequently developed a phase I/II clinical trial involving multiple pharmaceutical companies with the aforementioned combination in patients with refractory metastatic CRC.

a. **Gulhati P**, Bowen KA, Liu J, Stevens PD, Rychahou PG, Chen M, Lee EY, Weiss HL, O'Connor KL, Gao T and Evers BM. mTORC1 and mTORC2 regulate motility, EMT and metastasis of colorectal cancer via RhoA and Rac1 signaling pathways. *Cancer Research*. 2011. 71(9): 3246-3256.
b. **Gulhati P**, Cai Q, Li J, Liu J, Rychahou PG, Qiu S, Lee EY, Silva SR, Bowen K, Gao T and Evers BM. Targeted inhibition of mTOR signaling inhibits tumorigenesis of colorectal cancer. *Clinical Cancer Research.* 2009. 15(23): 7207-16
c. **Gulhati P**, Zaytseva YY, Valentino JD, Stevens PD, Kim JT, Sasazuki T, Shirasawa S, Lee EY, Weiss HL, Dong J, Gao T and Evers BM. Sorafenib enhances the therapeutic efficacy of rapamycin against colorectal cancers harboring oncogenic *KRAS* and *PIK3CA*. *Carcinogenesis.* 2012. 33(9): 1782-90.
d. Wang X, **Gulhati P**, Li J, Dobner PR, Weiss HL, Townsend CM and Evers BM. Characterization of promoter elements regulating expression of the human neurotensin/neuromedin N gene. *Journal of Biological Chemistry.* 2011. 286(1): 542-554.

3. Development of small bowel adenocarcinoma research and clinical trials program.

I am the lead author for two clinical trials evaluating the efficacy of targeted therapies against vascular endothelial growth factor (Avastin) and epidermal growth factor receptor (Panitumumab) in patients with small bowel adenocarcinoma (SBA) and ampullary adenocarcinoma (AAC). There are no randomized clinical trials comparing the efficacy of various chemotherapy regimens in patients with SBA/AAC given their rare nature, however there have been four prospective studies, all of them used chemotherapy backbones. We conducted the first prospective clinical trial evaluating the efficacy of targeted therapy in this rare malignancy. I am also leading the analysis of a large genomic dataset for this rare cancer demonstrating that this cancer is molecularly unique in comparison to other intestinal cancers, such as CRC.

a. **Gulhati P**, Raghav K, Shroff R, Varadhachary G, Kopetz S, Javle M, Qiao W, Wang H, Morris J, Wolff R, Overman MJ. Bevacizumab Combined with Capecitabine and Oxaliplatin in Patients with Advanced Adenocarcinoma of the Small Bowel or Ampulla of Vater: a Single Center, Open-label, Phase 2 Study. *Cancer*. 2017. 123(6): 1011-1017.
b. **Gulhati P**, Raghav K, Shroff R, Varadhachary G, Javle M, Qiao W, Wang H, Morris J, Wolff R, Overman MJ. Phase II Study of Panitumumab in RAS wild-type Metastatic Adenocarcinoma of the Small Bowel or Ampulla of Vater. *The Oncologist.* 2018. 23(3): 277-e26.
c. **Gulhati P**, Shen JP, Raghav K, Overman MJ. Small Bowel Cancer and Appendiceal Tumors in MD Anderson Manual of Medical Oncology, 4th edition. McGraw-Hill. 2022.
d. Pandya K, Overman MJ, **Gulhati P**. Molecular landscape of small bowel adenocarcinoma. *Cancers (Basel)* 2022; 14(5): 1287.

4. Non-invasive biomarkers of therapeutic response/resistance and minimal residual disease in CRC and PDAC.

Circulating tumor DNA (ctDNA) carrying tumor-specific molecular alterations are found in the cell-free fraction of blood from the majority of PDAC and CRC patients. This technology allows non-invasive, real-time assessment

of treatment response in the metastatic setting and patients who remain ctDNA positive after completion of standard treatments have higher risk of recurrence and worse outcomes in the localized setting. I am currently leading two investigator-initiated clinical trials evaluating the use of ctDNA in the neoadjuvant and adjuvant (NCT05415917) setting for localized PDAC. Another recent study published in *Journal of the National Cancer Institute* evaluated the utility of changes in carcinoembryonic antigen (CEA) to monitor response to systemic chemotherapy in patients with metastatic CRC. This study represents the largest dataset to date correlating CEA levels with disease responses for metastatic CRC, providing benchmarks for future clinical trials of novel tumor monitoring approaches, such as circulating tumor cells or ctDNA.

a. **Gulhati P**, Yin J, Pederson L, Schmoll HJ, Hoff P, Douillard JY, Hecht JR, Tournigand C, Tebbutt N, Chibaudel B, De Gramont A, Shi Q, Overman MJ. Threshold Change in CEA as a Predictor of Non-Progression to First-Line Systemic Therapy in Metastatic Colorectal Cancer Patients with Elevated CEA. *Journal of the National Cancer Institute*. 2020. 112(11): 1127-1136.
b. **Gulhati P**, Prakash L, Katz MHG, Wang X, Javle M, Shroff R, Fogelman D, Lee JE, Tzeng CWD, Lee JH, Weston B, Tamm E, Bhosale P, Koay EJ, Maitra A, Wang H, Wolff RA, Varadhachary GR. First-Line Gemcitabine and Nab-Paclitaxel Chemotherapy for Localized Pancreatic Ductal Adenocarcinoma. *Annals of Surgical Oncology*. 2019. 26(2): 619-627.
c. Neibart SS, Mamidanna S, Chundury A, Sayan M, Alexander HR, August DA, Berim LD, Boland PM, Grandhi MS, **Gulhati P**, Hochster HS, Langan RC, Spencer KR, Kennedy TJ, Deek MP, Jabbour SK. Outcomes of patients with borderline resectable and resectable pancreatic adenocarcinoma treated with neoadjuvant three-week course chemoradiotherapy using capecitabine-based versus gemcitabine-based concurrent chemotherapy. *Journal of Gastrointestinal Oncology* 2021;12(6):2557-2566.

5. Targeting the immunosuppressive microenvironment to enhance the efficacy of immunotherapy in pancreatic ductal adenocarcinoma.

Recent progress in immune checkpoint therapy (ICT) has transformed the treatment of a number of advanced cancers, including melanoma and lung cancer among others. However, PDAC has been considered “non-immunogenic” since multiple trials have shown that PDAC is recalcitrant to currently available ICT agents, including anti-CTLA4 and anti-PD1 antibodies. Based on current knowledge, these findings may be related to the immunosuppressive TME whereby interactions between cancer cells, stromal fibroblasts and immune cells enhance PDAC growth. These findings support a model whereby heterotypic interactions across the dense fibrotic stroma, regulatory T cells, myeloid derived suppressor cells and tumor associated macrophages, among other cell types in the PDAC TME, cooperate to form a suppressive barrier against effective immunotherapy. Understanding these cellular interactions will help identify novel regimens that convert non-immunogenic PDAC into an immunogenic tumor by effecting the induction and trafficking of tumor specific cytotoxic T cells, as well as decreasing immunosuppressive myeloid cells. Our work has focused on the role of oncogenic KRAS in the tumor epithelial compartment in establishment of the immunosuppressive microenvironment in PDAC tumors, including recruitment of myeloid immune cells, in concert with stromal fibroblasts, likely through induction of cytokines which facilitate crosstalk among the various compartments. Another recent study published in *Nature Cancer* focused on understanding the recalcitrance to currently available ICTs in PDAC, using genetically engineered mouse models and human PDAC biospecimens. Our findings form the basis for an investigator-initiated multicenter clinical trial which is in the preliminary stages of development.

a. **Gulhati P**, Schalck A, Jiang S, Shang X, Wu CJ, Hou P, Ruiz SH, Soto LS, Parra E, Ying H, Han J, Dey P, Li J, Deng P, Sei E, Maeda DY, Zebala JA, Spring DJ, Kim M, Wang H, Wang YA, Maitra A, Moore D, Dwyer K, Navin NE, DePinho RA. Targeting T cell checkpoints 41BB and LAG3 and myeloid cell CXCR1/2 results in antitumor immunity and durable response in pancreatic cancer. *Nature Cancer*. 2023. 4(1): 62-80.
b. Dey P, Li J, Zhang J, Chaurasiya S, Strom A, Wang H, Liao WT, Cavallaro F, Denz P, Bernard V, Yen EY, Genovese G, **Gulhati P**, Liu J, Chakravarti D, Deng P, Zhang T, Carbone F, Chang Q, Ying H, Shang X, Spring D, Ghosh B, Putluri N, Maitra A, Wang YA, DePinho RA. Oncogenic KRAS driven metabolic reprogramming in pancreas cancer cells utilizes cytokines from the tumor microenvironment. *Cancer Discovery*. 2020. 10(4): 608-625.

Complete list of published articles in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1DWt55Ug7cckt/bibliography/53244712/public/?sort=date&direction=ascending.