

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Pylayeva-Gupta, Yuliya

Persistent Identifier (PID) of the Senior/Key Person: <https://orcid.org/0000-0003-4458-9091>

Position Title: Associate Professor

Organization and Location: UNIV OF NORTH CAROLINA CHAPEL HILL, Chapel Hill, North Carolina, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
NYU School of Medicine, New York City, New York, United States	Postdoctoral Fellow	06/2008	12/2014	Tumor Immunology
Weill Graduate School of Medical Sciences at Cornell University, New York, New York, United States	DOCTOR OF PHILOSOPHY	08/2001	05/2008	Cell Biology and Genetics
SUNY at Stony Brook, Stony Brook, NY, United States	Bachelor of Science (BS)/Bachelor of Arts (BA)	08/1996	05/2000	Biochemistry/Russian Language and Literature

Appointments and Positions

2021 - present	Associate Professor, UNIV OF NORTH CAROLINA CHAPEL HILL, Chapel Hill, North Carolina, United States
2025 - present	Co-Director, Cancer Cell Biology Training Program (T32), University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2022 - present	Co-leader, Immunology Program, Lineberger Comprehensive Cancer Center, Chapel Hill, North Carolina, United States
2022 - 2025	Associate Director, Cancer Cell Biology Training Program (T32), Lineberger Comprehensive Cancer Center, Chapel Hill, North Carolina, United States
2020 - present	Member, Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2016 - present	Member, Curriculum in Cell Biology and Physiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2015 - present	Member, Curriculum in Genetics and Molecular Biology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States
2015 - 2020	Assistant Professor, Department of Genetics, Lineberger Comprehensive Cancer Center, Chapel Hill, North Carolina, United States
2008 - 2014	Postdoctoral Fellow, Department of Biochemistry, NYU School of Medicine, Laboratory of Dr. Dafna Bar-Sagi, PhD, Professor of Biochemistry, New York, New York, United States

Products**Products Closely Related to the Proposed Project**

1. Li S, Mirlekar B, Johnson BM, Brickey WJ, Wrobel JA, Yang N, Song D, Entwistle S, Tan X, Deng M, Cui Y, Li W, Vincent BG, Gale M Jr, Pylayeva-Gupta Y, Ting JP. STING-induced regulatory B cells compromise NK function in cancer immunity. *Nature*. 2022 Oct;610(7931):373-380. PubMed Central PMCID: [PMC9875944](https://pubmed.ncbi.nlm.nih.gov/39875944/).
2. Mirlekar B, Wang Y, Li S, Zhou M, Entwistle S, De Buysscher T, Morrison A, Herrera G, Harris C, Vincent BG, Ting JP, Rashid N, Kim WY, Yeh JJ, Pylayeva-Gupta Y. Balance between immunoregulatory B cells and plasma cells drives pancreatic tumor immunity. *Cell Rep Med*. 2022 Sep 20;3(9):100744. PubMed Central PMCID: [PMC9512696](https://pubmed.ncbi.nlm.nih.gov/39512696/).
3. Mirlekar B, Michaud D, Lee SJ, Kren NP, Harris C, Greene K, Goldman EC, Gupta GP, Fields RC, Hawkins WG, DeNardo DG, Rashid NU, Yeh JJ, McRee AJ, Vincent BG, Vignali DAA, Pylayeva-Gupta Y. B cell-Derived IL35 Drives STAT3-

Dependent CD8(+) T-cell Exclusion in Pancreatic Cancer. Cancer Immunol Res. 2020 Mar;8(3):292-308. PubMed Central PMCID: [PMC7056532](#).

4. Pylayeva-Gupta Y, Das S, Handler JS, Hajdu CH, Coffre M, Koralov SB, Bar-Sagi D. IL35-Producing B Cells Promote the Development of Pancreatic Neoplasia. Cancer Discov. 2016 Mar;6(3):247-55. PubMed Central PMCID: [PMC5709038](#).
5. Mirlekar B, Michaud D, Searcy R, Greene K, Pylayeva-Gupta Y. IL35 Hinders Endogenous Antitumor T-cell Immunity and Responsiveness to Immunotherapy in Pancreatic Cancer. Cancer Immunol Res. 2018 Sep;6(9):1014-1024. PubMed Central PMCID: [PMC6125203](#).

Other Significant Products Highlighting Contributions to Science

1. Green WD, Gomez A, Plotkin AL, Pratt BM, Merritt EF, Mullins GN, Kren NP, Modliszewski JL, Zhabotynsky V, Woodcock MG, Green JM, Cannon G, Pipkin ME, Dotti G, Thaxton JE, Pylayeva-Gupta Y, Baldwin AS, Morris JP 4th, Stanley N, Milner JJ. Enhancer-driven gene regulatory networks reveal transcription factors governing T cell adaptation and differentiation in the tumor microenvironment. Immunity. 2025 Jul 8;58(7):1725-1741.e9. PubMed Central PMCID: [PMC12240711](#).
2. Sturdevant C, Pylayeva-Gupta Y. B cell heterogeneity in cancer comes of age. Cancer Cell. 2024 Oct 14;42(10):1650-1652. PubMed PMID: [39406185](#).
3. Pylayeva-Gupta Y. Molecular Pathways: Interleukin-35 in Autoimmunity and Cancer. Clin Cancer Res. 2016 Oct 15;22(20):4973-4978. PubMed PMID: [27582486](#).
4. Michaud D, Mirlekar B, Bischoff S, Cowley DO, Vignali DAA, Pylayeva-Gupta Y. Pancreatic cancer-associated inflammation drives dynamic regulation of p35 and Ebi3. Cytokine. 2020 Jan;125:154817. PubMed Central PMCID: [PMC6876557](#).
5. Michaud D, Mirlekar B, Steward C, Bishop G, Pylayeva-Gupta Y. B Cell Receptor Signaling and Protein Kinase D2 Support Regulatory B Cell Function in Pancreatic Cancer. Front Immunol. 2021;12:745873. PubMed Central PMCID: [PMC8761795](#).

Certification:

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§ 287, 1001, 1031 and 31 U.S.C. §§ 3729-3733 and 3802.

Certified by Pylayeva-Gupta, Yuliya in SciENcv on 2026-03-04 17:49:54

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Pylayeva-Gupta, Yuliya

Persistent Identifier (PID) of the Senior/Key Person: <https://orcid.org/0000-0003-4458-9091>

Position Title: Associate Professor

Organization and Location: UNIV OF NORTH CAROLINA CHAPEL HILL, Chapel Hill, North Carolina, United States

Personal Statement

I have a broad background in cancer cell biology and tumor immunology, and my laboratory research focuses on understanding the mechanisms by which tumors co-opt the immune system and stroma to facilitate emergence and progression of cancer, with a particular focus on pancreatic ductal adenocarcinoma (PDAC). My laboratory investigates how oncogenic KRAS, mutant p53, and other tumor-derived cues reshape the immune system and stroma to drive tumor initiation, progression, and metastatic spread. Using non-animal models and genetically engineered mouse models of PDAC, we dissect the immunological mechanisms that underlie tumor-immune crosstalk in both primary and metastatic disease.

A major emphasis of my work is understanding how B cells contribute to immunosuppression in cancer. Our research identified B-cell-derived IL-35 as a key mediator that suppresses T-cell activation and trafficking in PDAC, and we demonstrated that IL-35 blockade enhances responses to checkpoint inhibitors. We also discovered that B-cell dysfunction in cancer can be initiated at the naïve B-cell stage through an active suppression program that skews away from productive plasma cell generation. In a landmark Nature study, we further showed that systemic activation of inflammatory pathways—specifically via STING agonists—can paradoxically induce potent B-cell-driven immunosuppression that limits both T- and NK-cell immunity. Most recently, we have begun defining how tumor antigens shape B and T cell-driven immune responses in PDAC.

Current efforts in my laboratory aim to identify regulators of B-cell differentiation in cancer, define therapeutic gene targets, and develop B-cell and/or antibody directed strategies to enhance immunotherapy. We are also pursuing development of novel cell-penetrating antibodies capable of targeting intracellular oncoproteins such as mutant KRAS, reversing immunosuppression, and synergizing with neoantigen-directed B- and T-cell responses. Beyond B-cell biology, our work extends to broader mechanisms of tumor-microenvironment interactions, including myeloid cells and fibroblasts, with the goal of informing rational therapeutic strategies for this highly lethal cancer.

Honors

2022	Hettelman Prize for Outstanding Scholarly Achievement, University of North Carolina at Chapel Hill
2022	Emerging Leader Award, Mark Foundation for Cancer Research
2021	Cancer Research Fund Innovation Award, University of North Carolina at Chapel Hill
2019	V Scholar Plus Award, V Foundation
2019	Cancer Research Fund Innovation Award, University of North Carolina at Chapel Hill
2018	Conquer Cancer Now Award, Concern Foundation
2017	Career Enhancement Award, NIH
2016	V Scholar Award, V Foundation
2013	Pathway to Leadership Award, American Association for Cancer Research (AACR) and Pancreatic cancer Action Network (PanCAN)
2010	Young Investigator Travel Award, American Pancreatic Association
2009	Postdoctoral Fellowship in Cancer Immunology, Cancer Research Institute
1999	Summer undergraduate research fellowship, HHMI

Contributions to Science

1. Integrin signaling in breast cancer. My early work interrogated the role of cell adhesion signaling in the initiation and progression of breast cancer. Although perturbations in cancer cell interactions with extracellular matrix are recognized to be associated with aggressive tumor phenotypes, it was not known whether downstream signaling via integrins was also an important determinant of cancer growth. My work demonstrated that integrin and focal adhesion kinase signaling contribute to

breast tumorigenesis, and delineated contributions of specific FAK signaling domains to the processes of cell proliferation, cell death, invasion and ultimately tumor maintenance. This work provided insights into the contribution of integrin-mediated adhesion and signaling to breast cancer pathogenesis and identified FAK inhibitors as promising agents for clinical investigation.

a. Guo W et al., Cell, 2006.

b. Pylyayeva Y et al., Methods Enzymology, 2007

c. Pylyayeva Y et al., J Clin Invest., 2009

2. Role of myeloid cells in pancreatic cancer and metastasis. I have a longstanding interest in understanding the contribution of non-cell autonomous pathways of cancer pathogenesis. During my postdoctoral work, I have developed an experimentally tractable, transplant-based mouse model of pancreatic cancer and used it to study mechanisms of immunomodulation. I have demonstrated that oncogenic Kras in pancreatic epithelium via GM-CSF drives myeloid cell-mediated immunosuppressive program, which suppresses T cell mediated immune responses. We have recently investigated the role of myeloid cell contribution to metastatic outgrowth in pancreatic cancer, and we continue to use innovative mouse models as platform to mechanistically understand how cancer cells engage host-dependent immune and inflammatory responses in cancer growth and metastasis.

a. Kren N et al., Sci Rep., 2020

b. Pylyayeva-Gupta Y et al., Cancer Cell, 2012

c. Ochi A et al., J Exp Med., 2012

3. Mechanisms of B cell responses in cancer. A major focus of my lab has been the identification and dissection of pathways that mediate and control regulatory B cell function. We have identified that B cell-derived IL-35 is a major factor suppressing anti-tumor T-cell activity in pancreatic cancer. We showed that IL-35 inhibits T-cell activation and migration, contributing to immune evasion by tumors. We found that B cells can be derailed from their normal plasma cell function at the naïve B cell stage, even in the presence of tumor-specific antigens, providing potential therapeutic opportunities for re-programming B cell function in cancer. Our study published in Nature showed how systemic administration of pro-inflammatory stimuli, specifically STING agonists can lead to profound B cell-driven immunosuppression that contributes to suppression of T and NK cell mediated immunity. Most recently, we have tackled the role of tumor antigens in stimulating productive immune response in PDAC.

a. Sturdevant C. and Pylyayeva-Gupta Y. Cancer Cell., 2024

b. Li S et al., Nature, 2022

c. Mirlekar B et al., Cell Reports Medicine, 2022

d. Pylyayeva-Gupta Y et al., Cancer Discovery, 2016

Certification:

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§ 287, 1001, 1031 and 31 U.S.C. §§ 3729-3733 and 3802.

Certified by Pylyayeva-Gupta, Yuliya in SciENcv on 2026-03-0417:49:54