BIOGRAPHICAL SKETCH

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NAME: Payne, Kyle K.

eRA COMMONS USER NAME (credential, e.g., agency login): paynekk2

POSITION TITLE: Assistant Professor, Department of Medicine

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
Indiana University, Bloomington, IN	B.S.	05/2005	Biology
Virginia Commonwealth University, Richmond, VA	Ph.D.	08/2015	Tumor Immunology
The Wistar Institute & The University of Pennsylvania, Philadelphia, PA	Postdoctoral	12/2017	Tumor Immunology
H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL	Postdoctoral	07/2021	Tumor Immunology

A. Personal Statement

I am an Assistant Professor in the Department of Medicine, at the Robert Wood Johnson Medical School, Rutgers University. I am also a resident member at Rutgers Cancer Institute of New Jersey, where I work within the Section of Cancer Immunotherapy. I have extensive experience as an oncoimmunologist, thus far amassing >1,500 citations in work focused on defining the immunobiology of cancer. Since 2015, I have been dedicated to the study of the immunobiology of ovarian cancer, which has cemented the identification and targeting of mechanisms governing the balance between immunosuppression and protective immunity in the ovarian cancer microenvironment as the singular overarching goal of my research program. My group is currently focused on pioneering the impact of mitochondrial and oxidative stress signaling on the deployment of multiple T cell-intrinsic suppressive programs in ovarian cancer, as my vision is the rational design of stress-resistant immunotherapies for high-grade serous ovarian cancer (HGSOC) patients. This focus builds upon my previous work where I have contributed to the identification of mechanisms governing unregulated expression of PD-1 on the T cell surface in cancer beds (***Immunity***, 2017); defining the role of butyrophilin 3A1 as a dynamic T cell regulator in ovarian cancer (***Science***, 2020); elucidating the mechanisms by which ovarian cancer-driven endoplasmic reticulum stress responses paralyze antitumor T cell activity (***Nature***, 2018); and illuminating the role of B cells in driving antitumor humoral immunity against ovarian cancer (***Nature***, 2021). Through my laboratory's approach of combining translational understanding and clinical specimens with mechanistic studies in mouse models, the work proposed here will likely further delineate the dysfunction in orchestrating protective immunity in HGSOC cancer beds, and has a very high potential to open new avenues for additional mechanistic studies as well as clinical therapeutic interventions for ovarian cancer patients.

Ongoing and recently completed projects that I would like to highlight include:

PC 138-22; New Jersey Health Foundation; 02/15/2022-02/14/2023
PI: Kyle K Payne
Elucidating the immunoregulatory role of Butyrophilin-like molecules in Ovarian Cancer

COCR23PDF002; New Jersey Commission on Cancer Research; 07/01/2022 – 06/30/2024
PI: Rinkee Kumari (Kyle K Payne supervising)

Evaluation of mitochondrial stress signaling through UHRF1BP1 as a negative regulator of antitumor CD8$^+$ T cell activity in epithelial ovarian cancer.

V2022-030; V Foundation for Cancer Research; 10/01/2022-10/01/2024
PI: Kyle K Payne
Elucidation of Tumor Cell-Intrinsic Mitochondrial Stress Signaling as a Novel Regulator of Antitumor Immunity

ECIG-2023-3-1007; Ovarian Cancer Research Alliance; 02/01/2023-01/31/2026
PI: Kyle K Payne
Mitochondrial Stress Impairs Protective T cell Immunity in Ovarian Cancer

Citations:

a) **Payne KK**, Mine JA, Biswas S, Chaurio RA, Perales-Puchalt A, Anadon CM, Costich TL, Harro CM, Walrath J, Qianqian M, Tcyganov E, Buras AL, Rigolizzo KE, Mandal G, Lajoie J, Ophir M, Tchou J, Marchion D, Luca VC, Bobrowicz P, McLaughlin B, Eskiocak U, Schmidt M, Cubillos-Ruiz JR, Rodriguez PC, Gabrilovich DI, Conejo-Garcia JR. BTN3A1 governs antitumor responses by coordinating $\alpha\beta$ and $\gamma\delta$ T cells. ***Science***. 2020 Aug 21; 369(6506):942-949. doi: 10.1126/science.aay2767. PMCID: PMC7646930.

b) Stephen TL*, **Payne KK***, Chaurio RA, Allegrezza MJ, Zhu H, Perez Sanz J, Perales-Puchalt A, Nguyen JM, Vara-Ailor AE, Eruslanov EB, Borowsky ME, Zhang R, Laufer TM, Conejo-Garcia JR. Satb1 expression governs epigenetic repression of PD-1 in tumor-reactive T cells. ***Immunity***. 2017 Jan 17;46(1):51-64. PMCID: PMC5336605. ***equal contribution**

c) Song M, Sandoval TA, Chae CS, Chopra S, Rutkowski MR, Raundhal M, Chaurio RA, **Payne KK**, Konrad C, Bettigole SE, Shin HR, Crowley MJ, Cerliani JP, Kossenkov AV, Motorykin I, Zhang S, Manfredi G, Zamarin D, Holcomb K, Rodreguez PC, Rabinovich GA, Conejo-Garcia JR, Glimcher LH, Cubillos-Ruiz J. IRE1a-XBP1 controls T cell function in ovarian cancer by regulating mitochondrial activity. ***Nature***. 2018 Oct; 562(7727): 423-428. PMCID: PMC6237282.

d) Biswas S, Mandal G, **Payne KK**, Anadon CM, Gatenbee CD, Chaurio RA, Costich TL, Moran C, Harro CM, Rigolizzo KE, Mine JA, Trillo-Tinoco J, Sasamoto N, Terry KL, Marchion D, Buras A, Wehham RM, Yu X, Townsend MK, Tworoger SS, Rodriguez PC, Anderson AR, Conejo-Garcia JR. IgA transcytosis and antigen recognition govern ovarian cancer immunity. ***Nature***. 2021 Feb 3. doi: 10.1038/s41586-020-03144-0.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023 – Present	Abstract Programming Chair – American Association of Immunologists
2023 - Present	Faculty Search Committee Member – Rutgers Cancer Institute of New Jersey
2023 – Present	Admissions Committee Member – Rutgers University; Molecular Biosciences Program
2022	Department of Defense – Breast Cancer Review Panel; *ad hoc* reviewer
2022	Department of Defense – Ovarian Cancer Review Panel; full reviewer
2021 - Present	Assistant Professor, Department of Medicine, Rutgers RWJ Medical School
2021 - Present	Faculty Director, Immune Monitoring & Advanced Genomics Shared Resource, Rutgers Cancer Institute of New Jersey
2021	Journal Referee, Seminars in Cancer Biology
2020	Journal Referee, Journal of Leukocyte Biology
2020	Journal Referee, ACS Nano
2020	Journal Referee, Cancer Immunology, Immunotherapy
2019	Symposium Chair, Novel Tumor Targets/Therapies, Annual Meeting of the American Association of Immunologists, San Diego, CA
2018	Journal Referee, Cancer Immunology Research
2017	Grant reviewer, The Dutch Cancer Society, KWF Kankerbestrijding
2017 - 2018	Journal Referee, Cancer Research
2017, 2019	Journal Referee, PLOS One

2017 - 2021	Postdoctoral Fellow, Tumor Immunology, Moffitt Cancer Center, Tampa, FL (with Jose R. Conejo-Garcia)
2016 - Present	Member, European Academy of Tumor Immunology
2016	Journal Referee, Immunological Research
2016	Journal Referee, Immunological Investigations
2015 - 2018	Journal Referee, Frontiers in Immunology
2015 - 2017	Postdoctoral Fellow, Tumor Immunology, The Wistar Institute, Philadelphia, PA (with Jose R. Conejo-Garcia and Dmitry I. Gabrilovich)
2015 - 2016	Guest Editor, Immunological Investigations, Thematic issue: Contribution of Tregs in disease
2015	Journal Referee, Pathology – Research and Practice
2015	Journal Referee, Frontiers in Oncology
2014 - Present	Member, The American Association of Immunologists
2012 - 2015	Invited Instructor, Tumor Immunology, Dept. of Microbiology & Immunology, Virginia Commonwealth University, Richmond, VA
2011 - Present	Member, Society for Immunotherapy of Cancer (SITC)
2011 - Present	Scientific Meeting Organizer, Early Career Scientist Committee, Society for Immunotherapy of Cancer
2011 - Present	Member, International Society for Translational Medicine
2010 - Present	Associate Member, American Association for Cancer Research
2005 - 2007	Research Technician, Transplantation Immunology, Center for Immunobiology Indiana University, Bloomington, IN

Honors

2019	The American Association of Immunologists – 2019 AAI Trainee Abstract Award
2018 – 2020	Postdoctoral Fellowship – The American Cancer Society
2017	The American Association of Immunologists – 2017 AAI Trainee Abstract Award
2017	Invited Speaker – SLB annual meeting
2017	The Society of Leukocyte Biology – Highest JLB citations honoree
2015	The American Association of Immunologists – 2015 AAI Trainee Abstract Award
2014 – 2015	The American Association of Immunologists – Careers in Immunology Fellowship
2014	Virginia Commonwealth University – Nominated to attend the 64th Lindau Nobel Laureate Meeting
2012	Adaptive Biotechnologies Corporation – Young Investigator Award
2011, 2012	Virginia Commonwealth University Graduate Student Travel Award

C. Contributions to Science

1. My early contributions to the field of tumor immunology focused on delineating mechanisms of immune suppression driven by myeloid cells in tumor beds. I co-1st-authored the original manuscript that mechanistically defined how reprogramming tumor-reactive lymphocytes with cytokines, *ex vivo*, abrogated pathological myelopoiesis and promoted a phenotypic switch to of a functional antigen presenting cell. The key findings of this work illustrate the plasticity of the tumor microenvironment and, for the first time suggests that cellular therapeutic approaches can substantially reprogram immune activity in tumor beds to facilitate effective antitumor immunity. Additionally, my work contributed to the identification of potential mechanisms which lead adaptive immunity to induce tumor cell immunoediting and subsequent relapse; these findings led to a study investigating manifestations of tumor cell dormancy and the suitability of these cells as immunological targets. This work is illustrated in these representative publications:
   a. **Payne KK**, Graham L, Idowu MO, Wan W, Toor AA, Bear HD, Wang XY, Manjili MH. Gr1-/low CD11b-/low MHCII^{+} myeloid cells boost T cell anti-tumor efficacy. *J Leukoc Biol.* 2018 Dec; 104(6):1215-1228. PMCID: PMC6258302.
   b. **Payne KK**, Keim RC, Graham L, Idowu MO, Wan W, Toor AA, Bear HD, Wang XY, Manjili MH. Tumor- reactive immune cells protect against metastatic breast cancer while immunoediting indolent but not quiescent dormant cells. *J Leukoc Biol* 2016 Sept; 100(3):625-35. PMCID: PMC4982610.
   c. **Payne KK**, Zoon CK, Wan W, Marlar K, Borelli CA, Keim RC, Kenari MN, Kazim AL, Bear HD, Manjili MH. Peripheral blood mononuclear cells of patients with breast cancer can be reprogrammed to enhance anti-HER-2/neu reactivity and overcome myeloid-derived suppressor cells. *Breast Cancer Res Treat.* 2013 Nov; 142(1):45-57. PMCID: PMC4844228.

d. Kmieciak M*, Basu D*, **Payne KK***, Toor A, Yacoub A, Graham L, Sale L, Bear HD, Manjili MH. (2011). Activated NK T cells and NK cells render T cells resistant to MDSC and result in an effective adoptive cellular therapy against breast cancer in the FVBN202 transgenic mouse. *J Immunol.* 2011 Jul; 15;187(2):708-17. PMCID: PMC3131490. ***equal contribution**.

2. Subsequent studies at the Wistar Institute and Moffitt Cancer Center focused on understanding mechanisms of T cell regulation mediated by checkpoint molecules in cancer beds. The first study, which I co-1st-authored, described the genomic organizer, SATB1, functions as a repressor of PD-1 through orchestration of NuRD complexes within Pdcd1 regulatory regions. In contrast, tumor-derived TGF-β signaling was found to decrease SATB1 expression through SMAD occupancy of the *Satb1* promoter, thus defining tumor microenvironmental TGF-β as a driver of PD-1 expression in tumor beds. This work, for the first time, delineated the molecular events culminating in the loss of antitumor T cell effector function mediated by unrelenting expression of PD-1 within tumor beds. Additionally, our work defined a novel mechanism of T cell regulation by BTN3A1 in ovarian cancer beds. We found that homodimers of BTN3A1 mediate suppression against αβ T cells by binding to the T cell surface protein CD45 and impairing its ability to segregate from the immune synapse, which ultimately blunted T cell receptor signaling. Importantly, we found that BTN3A1-targeting antibodies abrogated this suppressive effect by stabilizing BTN3A1:BTN2A1 heterodimers, which also, paradoxically, drove the activation of Vγ9 Vδ2 T cells. This work thus defined the rationale to therapeutically target BTN3A1 to unleash both antitumor αβ T cells as well as γδ T cells in ovarian tumor beds.
   a. **Payne KK**, Mine JA, Biswas S, Chaurio RA, Perales-Puchalt A, Anadon CM, Costich TL, Harro CM, Walrath J, Qianqian M, Tcyganov E, Buras AL, Rigolizzo KE, Mandal G, Lajoie J, Ophir M, Tchou J, Marchion D, Luca VC, Bobrowicz P, McLaughlin B, Eskiocak U, Schmidt M, Cubillos-Ruiz JR, Rodriguez PC, Gabrilovich DI, Conejo-Garcia JR. BTN3A1 governs antitumor responses by coordinating αβ and γδ T cells. ***Science***. 2020 Aug 21; 369(6506):942-949. doi: 10.1126/science.aay2767. PMCID: PMC7646930.
   b. Stephen TL*, **Payne KK***, Chaurio RA, Allegrezza MJ, Zhu H, Perez Sanz J, Perales-Puchalt A, Nguyen JM, Vara-Ailor AE, Eruslanov EB, Borowsky ME, Zhang R, Laufer TM, Conejo-Garcia JR. Satb1 expression governs epigenetic repression of PD-1 in tumor-reactive T cells. *Immunity.* 2017 Jan 17;46(1):51-64. PMCID: PMC5336605. ***equal contribution**

3. Independent investigations in my laboratory are now mostly focused on understanding novel mechanisms which dictate protective antitumor immunity. Currently we are focused on identifying molecular mechanisms functioning in response to environmental stress as a driver of T cell paralysis in tumor beds. These investigations have been launched through collaboration with Juan Cubillos-Ruiz of Weill Cornell Medicine, in which we identified ER stress signaling through the IRE1a-XBP1 pathway as a driver of impaired T cell responsiveness in tumor beds through regulation of the abundance of glutamine carriers, which ultimately impaired mitochondrial respiration. An additional collaboration with Paulo Rodriguez of Moffitt Cancer Center investigated the role of the ER-stress associated kinase PERK in the immunosuppressive function of tumor- resident myeloid-derived suppressor cells. We found that PERK drove NRF2 antioxidant function within the mitochondria to suppress type I IFN production while maintaining the suppressive capacity of these cells. Future studies in my laboratory will delineate, for the first time, the impact of mitochondrial stress on the function and efficacy of antitumor T cells in ovarian cancer beds. It is expected this knowledge will drive T cell engineering approaches to silence deleterious mitochondrial stress induced signaling events, and will promote protective antitumor T cell activity.
   a. Song M, Sandoval TA, Chae CS, Chopra S, Rutkowski MR, Raundhal M, Chaurio RA, **Payne KK**, Konrad C, Bettigole SE, Shin HR, Crowley MJ, Cerliani JP, Kossenkov AV, Motorykin I, Zhang S, Manfredi G, Zamarin D, Holcomb K, Rodreguez PC, Rabinovich GA, Conejo-Garcia JR, Glimcher LH, Cubillos-Ruiz J. IRE1a-XBP1 controls T cell function in ovarian cancer by regulating mitochondrial activity. *Nature*. 2018 Oct; 562(7727): 423-428. PMCID: PMC6237282.
   b. Mohamed, E, Sierra RA, Trillo-Tinoco J, Cao Y, Innamarato P, **Payne KK**, de Ming Pulido A, Mandula J, Zhang S, Thevenot P, Biswas S, Abdalla SK, Costich TL, Hanggi K, Anadon CM, Flores ER, Haura EB, Mehrotra S, Pilon-Thomas S, Ruffell B, Munn DH, Cubillos-Ruiz JR, Conejo-Garcia JR Rodriguez PC. The Unfolded Protein Response Mediator PERK Governs Myeloid Cell-Driven Immunosuppression in Tumors through Inhibition of STING Signaling. *Immunity*. 2020 Apr 14;52(4):668-682.e7. PMCID: PMC7207019.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/kyle.payne.1/bibliography/public/