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PRINCIPAL INVESTIGATOR: Ping Chi, MD, PhD

CONTRACTING ORGANIZATION: Sloan Kettering Institute for Cancer Research
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14. ABSTRACT
Malignant peripheral nerve sheath tumors (MPNSTs), the most common and lethal malignant tumors in patients with Neurofibromatosis Type 1 (NF1), is characterized by recurrent biallelic inactivation of the NF1, CDKN2A and PRC2 components (EED or SUZ12). PRC2 loss in MPNST results in global loss of H3K27me2/3 and aberrant transcriptional activation of developmentally silenced master regulators, leading to enhanced cellular plasticity. PRC2 loss through epigenomic reprogramming also leads to aberrant activation of multiple signaling pathways (e.g. WNT signaling), an "immune desert" tumor microenvironment (TME), and primary resistance to immune checkpoint blockade (ICB). We hypothesize that PRC2 loss-mediated epigenomic reprograming underlines the molecular mechanisms of aberrant tumor heterogeneity and plastic behaviors in NF1-associated MPNST and represents a fundamental barrier for effective novel therapeutics. We further hypothesize that novel strategies aimed to reprogram the tumor cell epigenome and induces antigen presentation and innate antiviral immune responses may overcome the PRC2 loss tumor cell-specific "cold" TME, elicit anti-tumor immunity, and facilitate the development of novel immunotherapy combination. We proposed two specific aims for focused investigations: 1) Characterize the transcriptional plasticity and tumor heterogeneity and tumor evolution of NF1-associated MPNST under the selective pressure of TME in genetically defined in vitro and in vivo MPNST models. 2) Evaluate the impact of epigenomic reprograming of cancer cells by DNMT1 and bromodomain CBP/P300 inhibitors to elicit antigen presentation and innate immune responses, and to capitalize on cytotoxic T lymphocyte-mediated cancer cell immunotherapy in MPNST.

15. SUBJECT TERMS
NF-1 associated MPNST, tumor heterogeneity, tumor plasticity, epigenetic reprograming, tumor microenvironment, therapeutics

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1. INTRODUCTION:

Malignant peripheral nerve sheath tumors (MPNSTs), the most common and lethal malignant tumors in patients with Neurofibromatosis Type 1 (NF1), is characterized by recurrent biallelic inactivation of the *NF1*, *CDKN2A* and PRC2 components (*EED* or *SUZ12*). PRC2 loss in MPNST results in global loss of H3K27me2/3 and aberrant transcriptional activation of developmentally silenced master regulators, leading to enhanced cellular plasticity. PRC2 loss through epigenomic reprogramming also leads to aberrant activation of multiple signaling pathways (e.g. WNT signaling), an "immune desert" tumor microenvironment (TME), and primary resistance to immune checkpoint blockade (ICB). Using RNAi-based screen, we identified DNMT1 as a top synthetic lethal candidate with PRC2 loss in MPNST. We further demonstrated that DNA methyltransferase (DNMT) inhibitors led to significantly enhanced cytotoxicity and anti-tumor effects in PRC2 loss MPNST cells and tumors, at least in part through augmented activation of viral mimicry and innate immune responses. These observations have led to an investigator-initiated phase II trial of ASTX727 (an oral pan-DNMT inhibitor, recently FDA approved for treatment of myelodysplastic syndrome) in MPNST with PRC2 inactivation (Clinicaltrials.gov NCT04872543). Following these preliminary studies, we have focused our efforts to identify novel epigenetic agents to reprogram the tumor cell epigenome to elicit augmented antiviral innate immune response, and increased proinflammatory cytokine production and antigen presentation. *We hypothesize that PRC2 loss-mediated epigenomic reprograming underlines the molecular mechanisms of aberrant tumor heterogeneity and plastic behaviors in NF1-associated MPNST and represents a fundamental barrier for effective novel therapeutics. We further hypothesize that novel strategies aimed to reprogram the tumor cell epigenome and induces antigen presentation and innate antiviral immune responses may overcome the PRC2 loss tumor cell-specific "cold" TME, elicit anti-tumor immunity, and facilitate the development of novel immunotherapy combination.* We proposed two specific aims for focused investigations: 1) Characterize the transcriptional plasticity and tumor heterogeneity and tumor evolution of NF1-associated MPNST under the selective pressure of TME in genetically defined *in vitro* and *in vivo* MPNST models. 2) Evaluate the impact of epigenomic reprograming of cancer cells by DNMT1 and bromodomain CBP/P300 inhibitors to elicit antigen presentation and innate immune responses, and to capitalize on cytotoxic T lymphocyte-mediated cancer cell immunotherapy in MPNST.

2. KEYWORDS:

NF-1 associated MPNST, tumor heterogeneity, tumor plasticity, epigenetic reprograming, tumor microenvironment, therapeutics.

3. ACCOMPLISHMENTS:

<u>Major goals of the project</u>

Specific Aim 1: Characterize the transcriptional plasticity and tumor heterogeneity and tumor evolution of NF1-associated MPNST under the selective pressure of TME in genetically defined in vitro and in vivo MPNST models.

Major tasks:

1) *Evaluation of clonal evolution in vitro*
2) *Evaluation of clonal evolution in vivo*

Specific Aim 2: Evaluate the impact of epigenomic reprograming of cancer cells by DNMT1 and bromodomain CBP/P300 inhibitors to elicit antigen presentation and innate immune responses, and to capitalize on cytotoxic T lymphocyte (CTL)-mediated cancer cell immunotherapy in MPNST.

Major tasks:

1) *Evaluation of clonal evolution under therapeutic pressure in vitro*
2) *Evaluation of clonal evolution in vivo with drug treatment*
3) *Evaluate the effect of epigenetic drug treatment as a single agent or in combination with immune checkpoint blockade.*

Accomplished goals to date

Specific Aim 1: Characterize the transcriptional plasticity and tumor heterogeneity and tumor evolution of NF1-associated MPNST under the selective pressure of TME in genetically defined in vitro and in vivo MPNST models.

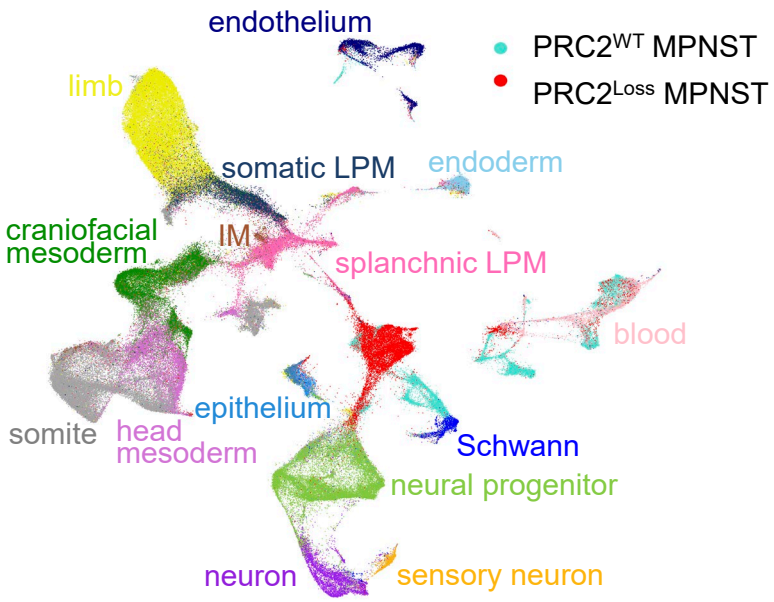

Fig. 1. 2D Umap of single cell analysis of PRC2-wt and PRC2-loss MPNST projected onto publicly available single cell profiles of early (4-6-week-old) human embryos (Xu Y et al., Nature Cell biology, 2023). LPM, lateral plate mesoderm.

We have been characterizing the NF1-associated MPNST tumor heterogeneity with and without PRC2 loss in both human tumor samples and in controlled cellular and transplanted tumor systems using scRNA-seq. To date, we have characterized a total of 5 human MPNST tumor samples, 2 of which are PRC2-wt and 2 of which are PRC2-loss MPNSTs. Comparing to the publicly available early human embryo single cell analysis, PRC2-wt MPNST clustered preferentially with the early Schwann progenitors, consistent with the cell of origin of MPNST (Fig. 1). However, the PRC2-loss MPNSTs have a distinct distribution pattern from any of the tissue lineages in human early embryogenesis, including the Schwann lineage. Instead, the PRC2-loss MPNSTs form "bridges" or "connections" with several tissue lineages, e.g., head mesoderm, neural progenitors, and splanchnic lateral plate mesoderm (LPM). These data indicate that PRC2-loss MPNST has enhanced heterogeneity and plasticity that has the potential to transdifferentiating into any of these tissue lineages when under the appropriate signaling and tumor microenvironment.

Clonal evolution and adaptive homeostasis in normal culture *in vitro*. As a pilot, we have transduced the CellTag system as planned in the proposal to uniquely tag each cell in a PRC2-isogneic *NF1*$^{-/-}$*; CDKN2A*$^{-/-}$ human MPNST cell line with sg*CON* vs. sg*SUZ12*. The cells were propagated for 28 days, and a sample of cells were collected every 5 days and subjected for scRNA-seq and scATAC-seq. We have performed the preliminary QC scRNA-seq analysis. The data demonstrated that we can only track ~10% of CellTag consistently in every single cell transcriptome with each collection. The attrition rate is too high for proposed heterogeneity studies in vitro and in vivo. We have decided to switch to the LARRY (Lineage and RNA Recovery) system with longer and easily trackable and more

diverse tagging system (Weinreb C. et al., Science 2020, PMCID: PMC7608074).

Clonal evolution in TME *in vivo*. The tumor cellular heterogeneity and therapeutic adaptive response are guided by local microenvironment. Since we have decided to switch to the LARRY system, we just piloted the LARRY tag in a PRC2-isogneic AT3 murine mammary model system and just harvested the tumors for LARRY tag detection of the diversity and heterogeneity. If the analysis shows appropriate diversity and heterogeneity, we will use the LARRY system in the murine PRC2-isogneic MPNST systems (SKP603 Nf1-/-; cdkn2a-/-; sgCON vs. sgEed) that has been previously validated (Yan J et al., JCI 2022, PMCID: PMC9433107; Patel A et al., Cancer Discovery 2022, PMCID: PMC9437570).

Specific Aim 2: Evaluate the impact of epigenomic reprograming of cancer cells by DNMT1 and bromodomain CBP/P300 inhibitors to elicit antigen presentation and innate immune responses, and to capitalize on cytotoxic T lymphocyte (CTL)-mediated cancer cell immunotherapy in MPNST.

Evaluate the effect of epigenomic reprograming by GSK862 and GNE049 and clonal evolution in MPNST. Due to the set back with the CellTag system, we will switch to the LARRY system for these drug treatment investigations.

Opportunities for training and professional development

Nothing to Report.

Dissemination of results to communities of interest

A) Invited talks at regional/national/international meetings and conferences:

1) Invited talk, AACR Special Conference in Sarcomas, Montreal, Canada, May 2022.
2) Invited talk, SARC Science Symposium, Chicago, IL, June 2023.
3) Invited talk, Annual Neurofibromatosis Conference by Children Tumor Foundation, Scottsdale, AZ, June 2023
4) Invited talk, Radiation Oncology Grand Rounds, Memorial Sloan Kettering Cancer Center, New York, NY, April 2022
5) Invited talk, Sarcoma Center Translational Science Seminar, Memorial Sloan Kettering Cancer Center, New York, NY, Feb 2022 and March 2023
6) Invited talk, Center for Experimental Therapeutics Symposium, Memorial Sloan Kettering Cancer Center, New York, NY, April 2023
7) Invited talk, Hospital Forum, Memorial Sloan Kettering Cancer Center, New York, NY, May 2023

B) Publications:

1) Nguyen B, Fong C, Luthra A, Smith SA, DiNatale RG, Nandakumar S, Walch H, Chatila WK, Madupuri R, Kundra R, Bielski CM, Mastrogiacomo B, Donoghue MTA, Boire A, Chandarlapaty S, Ganesh K, Harding JJ, Iacobuzio-Donahue CA, Razavi P, Reznik E, Rudin CM, Zamarin D, Abida W, Abou-Alfa GK, Aghajanian C, Cercek A, **Chi P**, Feldman D, Ho AL, Iyer G, Janjigian YY, Morris M, Motzer RJ, O'Reilly EM, Postow MA, Raj NP, Riely GJ, Robson ME, Rosenberg JE, Safonov A, Shoushtari AN, Tap W, Teo MY, Varghese AM, Voss M, Yaeger R, Zauderer MG, Abu-Rustum N, Garcia-Aguilar J, Bochner B, Hakimi A, Jarnagin WR, Jones DR, Molena D, Morris L, Rios-Doria E, Russo P, Singer S, Strong VE, Chakravarty D, Ellenson LH, Gopalan A, Reis-Filho JS, Weigelt B, Ladanyi M, Gonen M, Shah SP, Massague J, Gao J, Zehir A, Berger MF, Solit DB, Bakhoum SF, Sanchez-Vega F,

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5) **Chi P***, Qin LX, Camacho N, Kelly CM, D'Angelo SP, Dickson MA, Gounder MM, Keohan ML, Movva S, Nacev BA, Rosenbaum E, Thornton KA, Crago AM, Francis JH, Martindale M, Phelan HT, Biniakewitz MD, Lee CJ, Singer S, Hwang S, Berger MF, Chen Y, Antonescu CR, Tap WD*. *Phase Ib Trial of the Combination of Imatinib and Binimetinib in Patients with Advanced Gastrointestinal Stromal Tumors*. **Clinical Cancer Research.** 2022;28(8):1507-1517. PMCID: PMC9012681.

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11) D'Angelo SP, Richards AL, Conley AP, Woo HJ, Dickson MA, Gounder M, Kelly C, Keohan ML, Movva S, Thornton K, Rosenbaum E, **Chi P**, Nacev B, Chan JE, Slotkin EK, Kiesler H, Adamson T, Ling L, Rao P, Patel S, Livingston JA, Singer S, Agaram NP, Antonescu CR, Koff A, Erinjeri JP, Hwang S, Qin LX, Donoghue MTA, Tap WD. *Pilot study of bempegaldesleukin in combination with nivolumab in patients with metastatic sarcoma*. **Nature Communications**. 2022;13(1):3477. PMCID: PMC9203519.

12) Janku F, Bauer S, Shoumariyeh K, Jones RL, Spreafico A, Jennings J, Psoinos C, Meade J, Ruiz-Soto R, **Chi P**. *Efficacy and safety of ripretinib in patients with KIT-altered metastatic melanoma*. **ESMO Open**. 2022;7(4):100520. PMCID: PMC9434165.

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16) Yan J, Chen Y, Patel AJ, Warda S, Lee CJ, Nixon BG, Wong EWP, Miranda-Román MA, Yang N, Wang Y, Pachai MR, Sher J, Giff E, Tang F, Khurana E, Singer S, Liu Y, Galbo PM Jr, Maag JL, Koche RP, Zheng D, Antonescu C, Deng L, Li M, Chen Y*, **Chi P*.** *Tumor-intrinsic PRC2 inactivation drives a context-dependent immune-desert*

microenvironment and is sensitized by immunogenic therapeutic viruses. **Journal of Clinical Investigation.** 2022 Sep 1;132(17). pii: e153437. doi: 10.1172/JCI153437. PMCID: PMC9433107.

17) Bartlett EK, Sharma A, Seier K, Antonescu CR, Agaram NP, Jadeja B, Rosenbaum E, **Chi P**, Brennan MF, Qin LX, Alektiar KM, Singer S. *Histology-Specific Prognostication for Radiation-Associated Soft Tissue Sarcoma.* **JCO Precision Oncology.** 2022 Oct;6:e2200087. doi: 10.1200/PO.22.00087. PMCID: PMC9616643.

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19) Dermawan JK, Singer S, Tap WD, Nacev BA, **Chi P**, Wexler LH, Ortiz MV, Gounder M, Antonescu CR. *The genetic landscape of SMARCB1 alterations in SMARCB1-deficient spectrum of mesenchymal neoplasms.* **Modern Pathology.** 2022 Dec;35(12):1900-1909. doi: 10.1038/s41379-022-01148-x. Epub 2022 Sep 10. PMCID: PMC9712236.

20) Mandelker D, Marra A, Mehta N, Selenica P, Yelskaya Z, Yang C, Somar J, Mehine M, Misyura M, Basturk O, Latham A, Carlo M, Walsh M, Stadler ZK, Offit K, Bandlamudi C, Hameed M, **Chi P**, Reis-Filho JS, Ceyhan-Birsoy O. *Expanded genetic testing of GIST patients identifies high proportion of non-syndromic patients with germline alterations*. **NPJ Precision Oncology**. 2023 Jan 2;7(1):1. doi: 10.1038/s41698-022-00342-z. PMCID: PMC9807588.

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22) Kelly CM, Qin LX, Whiting KA, Richards AL, Avutu V, Chan JE, **Chi P**, Dickson MA, Gounder MM, Keohan ML, Movva S, Nacev BA, Rosenbaum E, Adamson T, Singer S, Bartlett EK, Crago AM, Yoon SS, Hwang S, Erinjeri JP, Antonescu CR, Tap WD, D'Angelo SP. *A phase 2 study of epacadostat an pembrolizumab in patients with advanced sarcoma*. **Clinical Cancer Research.** 2023 Mar 27:CCR-22-3911. doi: 10.1158/1078-0432.CCR-22-3911. Online ahead of print. PMID: 36971773.

23) Li D, Zhan Y, Wang N, Tang F, Lee CJ, Bayshtok G, Moore AR, Wong EWP, Pachai MR, Xie Y, Sher J, Zhao JL, Khudoynazarova M, Gopalan A, Chan J, Khurana E, Shepherd P, Navone NM, **Chi P***, Chen Y*. *ETV4 mediates dosage-dependent prostate tumor initiation and cooperates with p53 loss to generate prostate cancer.* **Science Advances.** 2023, in press.

*Corresponding author.

Plans for the next reporting period to accomplish the goals

As described in the above for Aim1, we will continue to benchmark the LARRY system and adapt it to our in vitro and in vivo single cell analysis for tumor evolution and tumor heterogeneity analysis. In

parallel, we will also continue analyze human PRC2-wt and PRC2-loss NF1-associated MPNST samples for discovery of novel biomarkers for novel therapeutic strategy discovery. We have been working with our significant collaborator, Dr. Christina Leslie for computational analysis and evaluation of our single cell analysis along with the CellTag tracking. We have just generated the LARRY-tracking pilot data and will continue working with Dr. Leslie for scRNA-seq and scATAC-seq analysis along with the LARRY-tracking system for tumor evolution evaluation.

For Aim 2, we will continue adapt the LARRY system for tumor evolution studies with drug treatment. In addition, we will begin the in vivo drug treatment with ICB and the characterization of epigenomic reprograming with GSK032 and GNE049 in vivo as planned.

4. IMPACT:

Impact on the development of the principal discipline(s) of the project

Nothing to Report.

Impact on other disciplines

Nothing to Report.

Impact on technology transfer

Nothing to report.

Impact on society beyond science and technology

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to report.

Actual or anticipated problems or delays and actions or plans to resolve them

As described in the above section 3, the previously proposed CellTag system did not provide adequate efficiency for single cell tracking in long-term experiments. We have since switched the system to LARRY and completed the initial pilot experiments, pending analysis.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

Significant changes in use or care of human subjects

N/A

Significant changes in use or care of vertebrate animals

N/A

Significant changes in use of biohazards and/or select agents

N/A

6. PRODUCTS:

Publications, conference papers, and presentations

1) Invited talk, AACR Special Conference in Sarcomas, Montreal, Canada, May 2022.
2) Invited talk, SARC Science Symposium, Chicago, IL, June 2023.
3) Invited talk, Annual Neurofibromatosis Conference by Children Tumor Foundation, Scottsdale, AZ, June 2023
4) Invited talk, Radiation Oncology Grand Rounds, Memorial Sloan Kettering Cancer Center, New York, NY, April 2022
5) Invited talk, Sarcoma Center Translational Science Seminar, Memorial Sloan Kettering Cancer Center, New York, NY, Feb 2022 and March 2023
6) Invited talk, Center for Experimental Therapeutics Symposium, Memorial Sloan Kettering Cancer Center, New York, NY, April 2023
7) Invited talk, Hospital Forum, Memorial Sloan Kettering Cancer Center, New York, NY, May 2023

Journal publications

1) Patel AJ, Warda S, Maag JLV, Misra R, Miranda-Roman MA, Pachai MR, Lee CJ, Li D, Wang N, Bayshtok G, Fishinevich E, Meng Y, Wong EWP, Yan J, Giff E, Pappalardi MB, McCabe MT, Fletcher JA, Rudin CM, Chandarlapaty S, Scandura JM, Koche RP, Glass JL, Antonescu CR, Zheng D, Chen Y*, **Chi P***. *PRC2 Inactivating Mutations in Cancer Enhance Cytotoxic Response to DNMT1 Targeted Therapy via Enhanced Viral Mimicry*. **Cancer Discovery**. 2022 Sep 2;12(9):2120-2139. doi: 10.1158/2159-8290.CD-21-1671. PMCID: PMC9437570. Featured in "In the Spotlight".

2) Yan J, Chen Y, Patel AJ, Warda S, Lee CJ, Nixon BG, Wong EWP, Miranda-Román MA, Yang N, Wang Y, Pachai MR, Sher J, Giff E, Tang F, Khurana E, Singer S, Liu Y, Galbo PM Jr, Maag JL, Koche RP, Zheng D, Antonescu C, Deng L, Li M, Chen Y*, **Chi P*.** *Tumor-intrinsic PRC2 inactivation drives a context-dependent immune-desert microenvironment and is sensitized by immunogenic therapeutic viruses*. **Journal of Clinical Investigation.** 2022 Sep 1;132(17). pii: e153437. doi: 10.1172/JCI153437. PMCID: PMC9433107.

   *Corresponding author.
   Acknowledgement of government support- yes.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

PI: Ping Chi, MD, PhD. (HOPP and Department of Medicine, MSKCC) (1.2 cal mo)
Qalified Collaborator: Christina Leslie, PhD (Computational & Systems Biology Program, Sloan Kettering Institute, MSKCC) (1.2 cal mo)
Juan Yan, PhD, was a postdoc fellow and has been promoted to senior scientist recently and continued the project (3.0 cal mo)
Alli Pine, PhD graduate student in the Leslie lab, who had just graduated. She will be replaced by another graduate student in the Leslie lab in summer 2023. (6 cal mo)
Cindy Lee, a Senior Research Assistant has moved to an industry position and her role has been replaced by Makhzuna Khudoynazarova, an experienced research assistant and continued her responsibilities. (3 cal mo)

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Yes; see updated Previous/Current/Pending Support files in Appendix.

What other organizations were involved as partners?

N/A.

8. SPECIAL REPORTING REQUIREMENTS

Please see section 3. The Qualified Collaborator, Dr. Christina Leslie, and her group was planning to do the computational analysis of the CellTag system for tumor evolution. However, since the CellTag did not work, we have since switched to the LARRY tracking system and the data have just been generated, pending analysis.

9. APPENDICES:

a) Previous/Current/Pending Support: Ping Chi, MD, PhD

b) Previous/Current/Pending Support: Christina Leslie, PhD

CHI, PING

Previous/Current/Pending Support

PREVIOUS

*Title: Novel therapeutic development of NF1-associated malignant peripheral nerve sheath tumor (MPNST)
*Major Goals: The goal of the project is to follow our recent oncogenomics discovery to develop prognostic and therapeutic prediction biomarkers of PRC2 loss (H3K27me3) and to explore therapeutic vulnerabilities of the PRC2 loss in MPNST.
*Status of Support: Complete
Project Number: W81XWH-15-1-0124
Name of PD/PI: Chi, P
Source of Support: Congressionally Directed Medical Research
Contracting Officer: Jamie Shortall, jamie.a.shortall.civ@mail.mil
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 7/15/2015-07/14/2018
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2016	1.20 calendar
2.	2017	1.20 calendar
3.	2018	1.20 calendar

*Title: Main Project 1: Molecular Mechanisms of KIT signaling and Imatinib Resistance in GIST
*Major Goals: The long-term goal of the SPORE in Soft Tissue Sarcoma is to reduce morbidity and mortality from soft tissue sarcoma by developing therapies targeted to the molecular, genetic, epigenetic, and signaling pathway alterations that are specific to sarcoma type and subtype.
*Status of Support: Complete
Project Number: P50 CA140146
Name of PD/PI: Singer, S
Source of Support: NIH/NCI
Contracting Officer: Michael Zarkin, zarkinm@mail.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 11/01/2013-06/01/2018
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2014	0.60 calendar
2.	2015	0.60 calendar
3.	2016	0.60 calendar
4.	2017	0.60 calendar
5.	2018	0.60 calendar

*Title: An Integrative Approach to Target Lineage-Specific Oncogenic Transcription Factor
*Major Goals: This proposal describes a novel integrative approach that combines a high throughput RNAi-based screen with high complexity gene-signature based readout to systematically discover druggable modifiers of oncogenic transcription factors.
*Status of Support: Complete
Project Number: DP2 CA174499-04
Name of PD/PI: Chi, P

Source of Support: NIH/NCI
Contracting Officer: Jason Gil, gilljas@mail.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/13/2012–06/30/2017
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2013	3.00 calendar
2.	2014	3.00 calendar
3.	2015	3.00 calendar
4.	2016	3.00 calendar
5.	2017	3.00 calendar

*Title: Phase2 trial of MEK162 & imatinib combined therapy in GIST, IND119794(09/20/2013)
*Major Goals: Here, we propose to test the clinical efficacy of a novel combination strategy of MEK162 and imatinib to specifically target ETV1 in a phase II clinical trial in advanced GIST patients, with the potential to change our current clinical practice in GIST management.
*Status of Support: Complete
Project Number: R01 FD005731-04
Name of PD/PI: Chi, P
Source of Support: FDA
Contracting Officer: Dan Lukash, daniel.lukash@fda.hhs.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/25/2017 - 8/31/2021
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2018	1.80 calendar
2.	2019	1.80 calendar
3.	2020	1.80 calendar
4.	2021	1.80 calendar

*Title: Immune evasion and immunotherapeutic intervention of PRC2-deficient tumors
*Major Goals: The goals of this project are to further elucidate the mechanism of PRC2-loss and DLK1-mediated immune-exclusion and ICB resistance in MPNST and other murine tumor models, and to test whether intratumoral (IT) delivery of engineered immunogenic Modified Vaccinia Virus Anakara (MVA) can reverse the PRC2-loss mediated immune suppressive environment.
*Status of Support: Complete
Project Number: GC241229
Name of PD/PI: Chi, P
Source of Support: Geoffrey Beene Cancer Research Center
Contracting Officer: Vicky Baudin, Project Portfolio Manager, baudinv@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 10/1/2019 - 9/30/2021
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)

1.	2020	1.20 calendar
2.	2021	1.20 calendar

*Title: Targeting DLK1 in Cancer
*Major Goals: The goals of the proposal is to identify: 1) a single therapeutic agent in DLK1-expressing cancers, including MPNST, HCC, etc) 2) an antibody drug conjugates in DLK1-expressing cancers, 3) an immune modulator that can be combine with immune checkpoint inhibitors in treating DLK1-expressing tumors that lack immune infiltrates, 4) as a "liquid biopsy" for early diagnosis of malignant transformation of neurofibromas in Neurofibromatosis patients, which can be incorporated in clinical trials.
*Status of Support: Active
Project Number: ETC Independent Investigator Research - Chi
Name of PD/PI: Chi, P
Source of Support: Center for Experimental Therapeutics
Contracting Officer: Gloria Hsu, hsug@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2021 - 3/31/2022
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2022	0.60 calendar

*Title: Novel therapeutic development of NF1 associated malignant peripheral nerve sheath tumor (MPNST)
*Major Goals: Aim 1: Harvest an additional 1-2 NF1-patient with either atypical neurofibroma or suspected MPNST for PDX and cell line development. Goal is at least 6 samples (0-2 atypical and at least 4-6 MPNST) and 3 PDXs and 3 cell lines over three years. Aim 2: Test the drug combination (LEE011+trametinib) in additionally procured 1 PRC2-loss MPNST PDX and 1 PRC2-wild type MPNST xenografts. Also, we plan to test a new combination of pan-KIT/PDGFRA inhibitor+trametinib as an exploratory proof of concept study. Aim 3: Based on the candidate list generated in year 1 (milestone 2), start candidate validation with doxycycline inducible separate shRNAs targeting candidates for validation in MPNST cell lines (prioritized candidates 1-3).
*Status of Support: Active
Project Number: 2003518194
Name of PD/PI: Chi, P
Source of Support: The Bloomberg Family Foundation
Contracting Officer: Not Available
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 7/1/2017 - 12/31/2022 NCE
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
5.	2022	0.00 calendar

CURRENT
*Title: Clinical Scholars Biomedical Research Training Program
*Major Goals: Because they function at the interface between the laboratory and the clinic, physician-scientists play a critical role in the translation of scientific discoveries into new diagnostics and therapeutics. This training program is designed to prepare board eligible/qualified physicians to carry out independent laboratory based translational research. These individuals will increase our understanding the origins of cancer and lead the development of new cancer treatments.

*Status of Support: Active
Project Number: 5 T32 CA009512-33
Name of PD/PI: Chi, P
Source of Support: National Cancer Institute
Contracting Officer: Sean Hine, hines@mail.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 7/10/2017 - 6/30/2023 NCE
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
33. 2022	0.00 calendar

*Title: Understanding the role of an aberrant hepatic nuclear transcription circuit in prostate cancer tumorigenesis and castration resistance
*Major Goals: This project will shed light on the molecular mechanisms by which HNF1A and HNF4G regulate transcription, tumorigenesis, and castration resistance.
*Status of Support: Active
Project Number: 5 R01 CA208100-05
Name of PD/PI: Chen, Y
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk, Michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 8/1/2017 - 7/31/2023 NCE
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2023	0.12 calendar

*Title: Epigenetic mechanisms of transcriptional activation of a novel oncogenic ALK variant in cancer
*Major Goals: Here, we proposes systematic and comprehensive investigations focused on understanding the epigenetic mechanisms (e.g. chromatin organization, chromatin context and MAPK signaling crosstalk with chromatin) involved in ALKATI transcriptional activation in melanoma, which may provide mechanistic and therapeutic insights of other oncogene activation through similar epigenetic mechanisms in cancer.
*Status of Support: Active
Project Number: 5 R01 CA228216-05
Name of PD/PI: Chi, P
Source of Support: National Cancer Institute
Contracting Officer: Olivia Paolucci, Olivia.paolucci@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2018 - 3/31/2024 NCE
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2023	0.60 calendar

*Title: SPORE in Soft Tissue Sarcoma (Project 1: Novel therapeutics development and mechanisms of therapeutic resistance in gastrointestinal stromal)

*Major Goals: Although soft tissue sarcomas can be treated surgically, for patients with advanced disease there are few effective systemic therapies. By discovering the molecular alterations that drive the formation and growth of sarcomas, we have an opportunity to identify new types of therapy for these deadly diseases. Insight into the molecular alterations will also allow for more precise diagnosis and prognosis and will identify biomarkers that predict how the tumor will respond to specific treatments.
*Status of Support: Active
Project Number: 5P50CA217694-05
Name of PD/PI: Singer, S
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk, Michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/1/2018 - 8/31/2023
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
5.	2023	1.20 calendar

*Title: Molecular Pathophysiology of Thyroid Cell Growth
*Major Goals: Advanced forms of thyroid cancers acquire mutations of genes that are involved in remodeling chromatin, the DNA and protein material that determines which genes are active and which are not. We discovered that these mutations block the activity of key genes that determine the differentiation state of thyroid tumor cells. We aim to find out how this takes place, and whether we can find ways to reprogram the cells to restore differentiation and improve outcomes.
*Status of Support: Active
Project Number: 5 R01 CA050706-31
Name of PD/PI: Fagin, J
Source of Support: National Cancer Institute
Contracting Officer: Jennifer Meininger, Jennifer.meininger@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 12/1/2018 - 11/30/2023
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
31.	2023	0.60 calendar

*Title: Targeting the epigenetic vulnerability in malignant peripheral nerve sheath tumor (MPNST)with PRC2 inactivation
*Major Goals: Aim 1: Conduct a proof-of-principal investigator-initiated phase II clinical trial (IIT) to evaluate the efficacy of ASTX727 (combination of decitabine and cedazuridine) in patients withPRC2-loss MPNSTs. Aim 2: Elucidate the molecular determinants that regulate the sensitivity and resistance toDNMTis in PRC2-loss MPNST.
*Status of Support: Active
Project Number: Cycle for Survival's Equinox Innovation Award in Rare Cancers
Name of PD/PI: Chi, P
Source of Support: Cycle for Survival
Contracting Officer: Kathleen Bourke, bourkek@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2021 - 12/31/2023 NCE
*Total Award Amount (including Indirect Costs):

Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
2.	2023	0.60 calendar

*Title: Understanding and targeting MAPK pathway activation in NF1-deficient malignant peripheral nerve sheath tumor (MPNST)
*Major Goals: Malignant peripheral nerve sheath tumors (MPNSTs) represent a group of highly aggressive soft tissue sarcomas with poor prognosis that occur in distinct clinical settings: neurofibromatosis 1 (NF1)-associated (45%), sporadic (45%) or radiotherapy (RT)-associated (10%). Most MPNSTs have NF1 loss (>90%hence, NF1- deficient), CDKN2A loss (~80%) and PRC2 loss (~60-80%), but they are resistant to MEK inhibitor alone due to feedback reactivation of PDGFRA/B pathways.
*Status of Support: Active
Project Number: 5U01CA252048-03
Name of PD/PI: Chi, P
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk, Michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2021 - 3/31/2026
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
3.	2024	1.80 calendar
4.	2025	1.80 calendar
5.	2026	1.80 calendar

*Title: Understanding and targeting MYC-mediated tumorigenesis and plasticity in angiosarcoma
*Major Goals: This grant focuses on angiosarcoma, a rare and aggressive sarcoma subtype with poor prognosis. This is a collaborative effort among Drs Antonescu, Chi and Chen with clinical expertise in sarcoma pathology and medical management, and research expertise in genomics, epigenetics/epigenomics, transcription factor regulation, mouse modeling and therapeutic development. Using this genetically relevant preclinical murine model, we propose two aims with translational relevance to 1)characterize the role of MYC overexpression in tumorigenesis and tumor intrinsic epigenetic plasticity, and 2) to evaluate novel therapeutics to target MYC in RAAS.
*Status of Support: Active
Project Number: Sarcoma Research Collector Fund-Chi
Name of PD/PI: Chi, P
Source of Support: Sarcoma Research Collector Fund
Contracting Officer: Sarah Lee, sarah.lee@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/1/2021 - 9/30/2023
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
2.	2023	0.60 calendar

*Title: DLK1-specific monoclonal antibodies (murine) by a TDI exploratory project.
*Major Goals: Aim 1. Evaluation of 89Zr-lableled DLK1-antibody PET imaging in B16 models

Aim 2a. Generation of IgG1 and IgG2a murine DLK1-specific antibodies (2 CDRs per isotype)
Aim 1. Evaluation of 89Zr-labeled DLK1-antibody PET imaging in cancer cell xenograft models and PDX models
Aim 2b. Evaluate the DLK1-specific antibodies (IgG1G265A and IgG2a) for anti-tumor and ADCC/CDC/ADCP effects in vivo
Aim 3. Evaluate the effect of DLK1 antibodies in modulating tumor immune infiltrates in various DLK1-syngeneic transplant model.
*Status of Support: Active
Project Number: ETC Independent Investigator Research - Chi
Name of PD/PI: Chi, P
Source of Support: Center for Experimental Therapeutics
Contracting Officer: David Scheinberg, scheinbd@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2022 - 6/30/2023 NCE
*Total Award Amount (including Indirect Costs):
Overlap: None
Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
1.	2023	0.00 calendar*

**No measurable effort during extension period*

*Title: Elucidating the mechanism of action of second-generation recombinant modified vaccinia virus Ankara for the treatment of malignant peripheral nerve sheath tumor
*Major Goals: In this proposed collaborative research among the laboratories of Ping Chi (epigenetics and MPNST tumor biology), Ming Li (Immunology and tumor microenvironment), and Liang Deng (Innate immunity and novel immunogenic DNA viruses), we plan to elucidate the mechanism of action of MQ833 in MPNST and investigate how PRC2-loss enhances the responsiveness of MPNST to immunogenic DNA virus therapy. These studies will lay a solid foundation for the clinical translation of using novel immunogenic viruses for PRC2-loss MPNST.
*Status of Support: Active
Contracting Officer: Andrew Murphy, murphya3@mskcc.org
Project Number: Cycle for Survival
Name of PD/PI: Deng, L
Source of Support: Cycle for Survival
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2022 - 3/31/2024
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
2.	2024	0.36 calendar

*Title: Reprogram cancer cell and cancer microenvironment for anti-tumor immunity in NF1-associated MPNST
*Major Goals: Aim 1: Characterize the transcriptional plasticity and tumor heterogeneity and tumor evolution of NF1-associated MPNST under the selective pressure of TME in genetically defined in vitro and in vivo MPNST models.
Aim 2: Evaluate the impact of epigenomic reprograming of cancer cells by DNMT1 and bromodomain CBP/P300 inhibitors to elicit antigen presentation and immune-response signature and to capitalize on cytotoxic T lymphocyte-mediated cancer cell immunotherapy in MPNST.
*Status of Support: Active
Project Number: W81XWH22-1-0326
Name of PD/PI: Chi, P

Source of Support: Congressionally Directed Medical Research Programs
Contracting Officer: Joann Martin, joann.1.martin2.civ@health.mil
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 5/15/2022 - 5/14/2025
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
2.	2024	1.20 calendar
3.	2025	1.20 calendar

*Title: Window of opportunity study assessing nivolumab and ipilimumab in people with Neurofibromatosis Type 1 and newly diagnosed malignant and pre-malignant peripheral nerve sheath tumors
*Major Goals: Aim 1: Evaluate the safety, tolerability, and feasibility of neoadjuvant nivolumab and ipilimumab prior to conventional therapy in people with NF1 and biopsy proven newly diagnosed ANNUBP and MPNST. Aim 2: Evaluate the biologic effect of two doses of nivolumab and ipilimumab in ANNUBP or MPNST tissue via assessment of pre-treatment biopsy samples and post-treatment surgical resection samples. Aim 3: Estimate the rate of radiographic response for the target tumor defined by RECIST and iRECIST criteria after two doses of nivolumab and ipilimumab and throughout the course of conventional MPNST treatment compared to baseline.
*Status of Support: Active
Project Number: W81XWH22-1-0580
Name of PD/PI: Blakeley, J
Source of Support: Johns Hopkins University / Congressionally Directed Medical Research Programs
Contracting Officer: Jacquelyn Eubanks-Rudd, jeubank5@jhmi.edu
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 7/15/2022 - 7/14/2025
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
1.	2023	0.24 calendar
2.	2024	0.24 calendar
3.	2025	0.24 calendar

*Title: Defining the role of histone H3K4 mono-methyltransferase dysfunction in urothelial carcinoma
*Major Goals: Components of the epigenetic complex that regulate enhancer function and methylate histone H3 at lysine 4, including KMT2C, KMT2D, and KDM6A are early oncogenic events in urothelial cancer of the bladder and ureters, and can be detected in normal appearing urothelium. We have generated genetic engineered mouse models of urothelial cancers based on mutations of KMT2C and KMT2D. In this proposal, we will characterize the epigenetic mechanisms of tumor suppression.
*Status of Support: Active
Project Number: R01 CA265026-01A1
Name of PD/PI: Chen, Y
Source of Support: National Institutes of Health
Contracting Officer: Olivia Paolucci, Olivia.paolucci@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/1/2022 - 8/31/2027
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2023	1.20 calendar
2. 2024	1.20 calendar
3. 2025	1.20 calendar
4. 2026	1.20 calendar
5. 2027	1.20 calendar

*Title: Phase II Study of ASTX727 in Patients with PRC2 loss Malignant Peripheral Nerve Sheath Tumor (MPNST)
*Major Goals: Aim 1: Conduct a proof-of-concept investigator-initiated phase II trial (IIT) to evaluate the efficacy of ASTX727 (combination of decitabine and cedazuridine) in patients with PRC2-loss MPNST (IRB#21-048, clinicaltrials.gov NCT04872543). Aim 2: Investigate the molecular mechanisms that regulate the sensitivity and resistance to DNMT inhibitors in PRC2-loss MPNST using pre-, on-treatment and at progression biopsy samples and treatment responses from the prospective clinical trial.
*Status of Support: Active
Project Number: 1 R01 FD007544-01
Name of PD/PI: Chi, P
Source of Support: Food and Drug Administration
Contracting Officer: Shashi Malhotra, Shashi.malhotra@fda.hhs.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/15/2022 - 8/31/2026
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2023	1.20 calendar
2. 2024	1.20 calendar
3. 2025	1.20 calendar
4. 2026	1.20 calendar

*Title: Harnessing double stranded-RNA (dsRNA)-response and anti-tumor effect in PRC2-inactivated cancer
*Major Goals: We propose innovative and integrative approaches to dissect the molecular mechanisms and evaluate novel therapeutic strategies (e.g., DNMT1 inhibitors, synthetic dsRNA, second generation of engineered immunogenic viruses) in relevant PRC2-loss cancer models to facilitate future design of biomarker driven clinical trials in PRC2-loss cancers with the goal to improve outcomes in individuals with MPNST and other PRC2-loss cancers.
*Status of Support: Active
Project Number: R01CA280657-01
Name of PD/PI: Chi, P
Source of Support: National Institutes of Health
Contracting Officer: Naydia Rowe, Naydia.rowe@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 3/22/2023 - 2/29/2028
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2024	1.80 calendar
2. 2025	1.80 calendar
3. 2026	1.80 calendar

4.	2027	1.80 calendar
5.	2028	1.80 calendar

PENDING

*Title: Clinical Scholars Biomedical Research Training Program
*Major Goals: Physician-scientists functioning at the interface between the laboratories and the clinics, play a critical role in the translation of scientific discoveries into new diagnostics and therapeutics. The Clinical Scholars Biomedical Research Training Program (CSTP) is designed to prepare board eligible/certified physician-scientists to carry out independent laboratory-based research aimed towards clinical translation. These individuals will increase our understanding of the pathogenesis of cancer and lead the development of new cancer treatments.
*Status of Support: Pending
Project Number: 2 T32 CA009512-34A1
Name of PD/PI: Chi, P
Source of Support: National Cancer Institute
Contracting Officer: Adriana Stoica, stoicaa2@mail.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 7/1/2023 - 6/30/2028
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2023	1.20 calendar
2.	2024	1.20 calendar
3.	2025	1.20 calendar
4.	2026	1.20 calendar
5.	2027	1.20 calendar

*Title: Enhancing Immunogenicity and Cytotoxicity in PRC2-inactivated Sarcomas
*Major Goals: Aim 1. Evaluate synthetic dsRNA as a strategy to induce cytotoxicity in PRC2-loss tumors. Aim 2. Evaluate novel therapeutics of activating dsRNA-responses in PRC2-loss murine sarcoma models.
*Status of Support: Pending
Project Number: Sarcoma Research Collector Fund Chi
Name of PD/PI: Chi, P
Source of Support: Sarcoma Research Collector Fund
Contracting Officer: Not Available
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 7/1/2023 – 6/30/2025
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2023	0.60 calendar
2.	2024	0.60 calendar

*Title: Radiotheranostic antibody-targeting of DLK1
*Major Goals: The goals of this project are to further develop and optimize humanized DLK1-specific antibodies for both diagnostic evaluation by radio-imaging and plasma-based ELISA assay, and for therapeutic use by targeting DLK1-positive cancers with radioimmunotherapy.
*Status of Support: Pending
Project Number: Technology Development Fund 2023

Name of PD/PI: Chi, P
Source of Support: Technology Development Fund
Contracting Officer: Not Available
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 10/1/2023 - 9/30/2025
*Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period.
Overlap: None

	Year (YYYY)	Person Months (##.##)
1.	2023	0.60 calendar
2.	2024	0.60 calendar

*Title: Activating neutrophils by a novel immune activating non replicative recombinant modified vaccinia virus Ankara for cancer immunotherapy
*Major Goals: The goals of this study are to (i) assess human immune responses to intratumoral (IT) hMQ710 therapy and identify biomarkers for clinical responses; (ii) elucidate the mechanisms of action of our second generation recombinant MVA expressing IL 12 anchored to the extracellular matrix, MQ833, and to test the hypothesis that IT MQ833 results in remodeling of the TME, and thereby overcoming resistance to ICB, chemotherapy, and engineered T cell therapy.
*Status of Support: Pending
Project Number: R01_PAR 22-085_06/05/23
Name of PD/PI: Deng, L
Source of Support: National Institute of Health
Contracting Officer: Not Available
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2024 - 3/31/2029
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
1.	2024	0.36 calendar
2.	2025	0.36 calendar
3.	2026	0.36 calendar
4.	2027	0.36 calendar
5.	2028	0.36 calendar

*Title: SPORE in Soft Tissue Sarcoma (Project 1: Molecular determinants of gastrointestinal stromal tumor pathogenesis)
*Major Goals: Gastrointestinal stromal tumor (GIST), a common subtype of soft tissue sarcoma, often exhibits aggressive clinical behavior, and is incurable in advanced and metastatic settings. Through genomic and clinical analysis of large cohorts of patients with GIST, we associated *MAX/MGA/MYC* genetic alterations and arm-level deletions of *1p* with metastatic GIST and poor relapse-free survival in resected GIST. Here, we propose comprehensive, collaborative, and multidisciplinary studies to investigate the mechanisms of *MAX/MGA/MYC* perturbation involved in aggressive GIST behavior, identify, and validate molecular biomarkers predictive of recurrence risk, and develop a combinatorial pathologic-genomic nomogram to guide adjuvant imatinib therapy decisions and identify novel strategies to target metastasis in advanced GIST.
*Status of Support: Pending
Project Number: 2 P50 CA217694-06A1
Name of PD/PI: Singer, S / Chi, P
Source of Support: National Institutes of Health

Contracting Officer: Anita Tandle, tandlea@mail.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/1/2024 - 8/31/2029
*Total Award Amount (including Indirect Costs):
Overlap: None

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
1.	2024	1.20 calendar
2.	2025	1.20 calendar
3.	2026	1.20 calendar
4.	2027	1.20 calendar
5.	2028	1.20 calendar

LESLIE, CHRISTINA

PREVIOUS / CURRENT / PENDING SUPPORT

PREVIOUS

*Title: Discovery and validation of tumor suppressor genes in colorectal cancer using a novel cross
*Major Goals: Discovery and validation of tumor suppressor genes in colorectal cancer using a novel cross Screening of candidate CRC TSGs in Drosophila. Using GISTIC2 analysis of the TCGA dataset we have identified a preliminary list of 615 Drosophila orthologs of human genes that show recurrent alteration in CRC. 219 of them are considered high confidence as they are identified in different analyses (see preliminary studies).
Specific Aims:
Aim 1: Screening of candidate CRC TSGs in Drosophila.
Aim 2: Investigating candidate TSGs using ESC-GEMMs of CRC
*Status of Support: Completed
Project Number: I8-A8-030
Name of PD/PI: Lowe, S
Source of Support: Starr Cancer Consortium
Contracting Officer: Eileen Lopez; Email: lopeze2@mskcc.org Phone: (646) 888-3774
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2015 - 12/31/2017
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2015	0.60 calendar
2. 2016	0.60 calendar
3. 2017	0.60 calendar

*Title: Decoding in vivo regulatory programs of CD4+ T lymphocyte populations in inflammation
*Major Goals: This project investigates the genomics of gene regulation of regulatory T cells, specialized immune cells that suppress immune responses and inflammation, in a mouse model of a short-term inflammatory disorder. Our study has implications for diverse aspects of human health, from autoimmunity, injury, and infection, to pregnancy, and cancer.
Specific Aims:
Specific Aim 1: To decode the changes in the enhancer landscape that govern the activation of distinct CD4+ T lymphocyte populations
Specific Aim 2: To model the differential transcriptional output of genes in CD4+ T cells as a function of the sequence and activity of their enhancers.
Specific Aim 3: To model the expression distribution of genes over a population of cells as a function of their enhancer state space.
*Status of Support: Completed
Project Number: 5 U01 HG007893-03
Name of PD/PI: Leslie/Rudensky
Source of Support: NHGRI
Contracting Officer: Susan Toy Email: toys@mail.nih.gov Phone: 301-594-3519 Fax: 301-480-1956
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/5/2015 - 11/30/2018
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.
Year (YYYY) Person Months (##.##)

Year (YYYY)	Person Months (##.##)

1.	2015	2.40 calendar
2.	2016	2.40 calendar
3.	2017	2.40 calendar
4.	2018	2.40 calendar

*Title: Modeling the impact of mutations in ubiquitin ligase genes on transcriptional programs in endometrial cancer
*Major Goals: We develop and apply this approach in endometrial cancer to study the role of a number of frequently altered genes that have not been well studied in this malignancy.
Specific Aims:
Specific Aim 1: To computationally integrate publicly available transcriptomic and proteomic data from three endometrial cancer subtypes with new epigenomic data in appropriate cell line models in order to predict and functionally validate the impact of the frequently mutated ubiquitin pathway genes FBXW7, SPOP, and RNF43 on transcriptional programs and signaling pathways.
Specific Aim 2: To computationally and experimentally examine the potential role of mutant FBXW7 in platinum resistance in uterine serous carcinoma through comparative modeling with high-grade ovarian serous carcinoma and integrative analysis of cancer cell line drug response data.
*Status of Support: Completed
Project Number: 5 R21 CA205819-02
Name of PD/PI: Leslie
Source of Support: NCI
Contracting Officer: Funmi Elesinmogun; Email: elesinmf@mail.nih.gov Phone: (240) 276-6313 Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2016 - 3/31/2019
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2016	0.60 calendar
2. 2017	0.60 calendar
3. 2018	0.60 calendar
4. 2019	0.60 calendar

*Title: Encoding genomic architecture in the encyclopedia: linking DNA elements, chromatin state, and gene expression in 3D
*Major Goals: This project develops advanced computational methods for integrating information on the 3D structure of the human genome with large-scale genomics data sets generated by the ENCODE project to gain insight into cell-type specific chromatin state and gene regulation. These studies have broad relevance for understanding the regulation of gene expression in human cells and the disruption of gene expression programs in disease.
Specific Aim 1: Learn a DNA sequence grammar for regulatory/structural elements and 3D chromatin loops.
Specific Aim 2: Model 3D chromatin state and predict 3D looping from 1D DNA sequence and epigenetic data.
Specific Aim 3: Learn predictive models of gene regulation from DNA sequence, chromatin state, and 3D architecture.
*Status of Support: Completed
Project Number: 3 U01 HG009395-04
Name of PD/PI: Leslie
Source of Support: NGHRI
Contracting Officer: Lisa A. Oken; Email: loken@mail.nih.gov Phone: 301-594-5250
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 8/18/2020 - 1/31/2021

*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2020	2.40 calendar
2. 2021	2.40 calendar
3. 2022	2.40 calendar

*Title: Systems biology of the tumor immune microenvironment
*Major Goals: Overview. Research activities proposed for the extension year will exploit syngeneic murine cancer models established with U54 funding (Projects 1, 3) and recent single cell epigenetic/multiomic and spatial transcriptomic technologies deployed at our Center (Projects 1, 2, Shared Resource Core), enabling experimental and computational modeling of tumor-immune interactions with high fidelity to human tumor biology and at rich single cell and spatial resolution.
*Status of Support: Completed
Project Number: 3U54CA209975-05S1
Name of PD/PI: Leslie, C
Source of Support: National Cancer Institute
Contracting Officer: DUECK, HANNAH RUTH email: hannah.dueck@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 8/1/2021 - 7/31/2022
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022	0.00 calendar

*Title: The CSBC Research Center for Cancer Systems Immunology at MSKCC (A systems biology approach to investigate how the microbiome impacts colorectal cancer)
*Major Goals: Metabolic factors that influence the tumor immune ecosystem and BET bromodomain proteins are critical to understand, as positive co-regulators of cytokine and chemokine gene transcription and production by human T cell subsets that infiltrate breast adipose tissue, as effectors of cytokine signaling, and as critical regulators of T cell tolerance. Improved mechanistic understanding will help clinical decision making in breast cancer patients with obesity and co-morbid metabolic disease.
*Status of Support: Completed
Project Number: 5U54CA209975-05
Name of PD/PI: Leslie, C
Source of Support: National Cancer Institute
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 8/26/2016 - 7/31/2022 NCE
*Total Award Amount (including Indirect Costs):
Contracting Officer: Barbara Hodgkins Email: barb.hodgkins@nih.gov

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2022	0.00 calendar

*Title: The CSBC Research Center for Cancer Systems Immunology at MSKCC (Administrative Core)
*Major Goals: Metabolic factors that influence the tumor immune ecosystem and BET bromodomain proteins are critical to understand, as positive co-regulators of cytokine and chemokine gene transcription and production by human T cell subsets that infiltrate breast adipose tissue, as effectors of cytokine signaling, and as critical regulators of T cell tolerance. Improved mechanistic understanding will help clinical decision making in breast cancer patients with obesity and co-morbid metabolic disease.
*Status of Support: Completed
Project Number: 5U54CA209975-05

Name of PD/PI: Leslie, C / Rudensky, A
Source of Support: National Cancer Institute
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 8/26/2016 - 7/31/2022 NCE
*Total Award Amount (including Indirect Costs):
Contracting Officer: Barbara Hodgkins Email: barb.hodgkins@nih.gov

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2022	1.20 calendar

*Title: The CSBC Research Center for Cancer Systems Immunology at MSKCC (Tumor-specific T cell state dynamics and heterogeneity in early tumorigenesis)
*Major Goals: Metabolic factors that influence the tumor immune ecosystem and BET bromodomain proteins are critical to understand, as positive co-regulators of cytokine and chemokine gene transcription and production by human T cell subsets that infiltrate breast adipose tissue, as effectors of cytokine signaling, and as critical regulators of T cell tolerance. Improved mechanistic understanding will help clinical decision making in breast cancer patients with obesity and co-morbid metabolic disease.
*Status of Support: Completed
Project Number: 5U54CA209975-05
Name of PD/PI: Leslie, C / Schietinger, A
Source of Support: National Cancer Institute
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 8/26/2016 - 7/31/2022 NCE
*Total Award Amount (including Indirect Costs):
Contracting Officer: Barbara Hodgkins Email: barb.hodgkins@nih.gov

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2022	1.20 calendar

*Title: Elucidating SETD2 Loss-Induced Alterations of 3D Chromatin Architecture in Kidney Cancer Metastasis
*Major Goals: Assess the impact of SETD2 loss on 3D chromosome architecture by high-resolution chromosome conformation capture (Hi-C).
*Status of Support: Completed
Project Number: W81XWH-21-1-0814 Log#KC200095
Name of PD/PI: Cheng, E
Source of Support: Congressionally Directed Medical Research Programs
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/30/2021 - 8/31/2022

*Total Award Amount (including Indirect Costs):

Contracting Officer: Joshua McKean, Email: joshua.d.mckean3.civ@mail.mil

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022	0.12 calendar

*Title: Epigenetic and transcriptional regulation in FOXA1 mutant prostate and breast cancer
*Major Goals: The goal of this project is to elucidate the molecular details of how this co-option of pioneering TF activity occurs. We will accomplish this through a comprehensive systems biology analysis of the epigenetic and transcriptional changes induced by mutant FOXA1 alleles, using prostate and breast organoid models developed by our group that allow us to annotate these changes over a carefully controlled time course.
*Status of Support: Completed
Project Number: AWD-GC-260677

Name of PD/PI: Leslie, C
Source of Support: Geoffrey Beene Cancer Research Center
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/1/2020 - 8/30/2022
*Total Award Amount (including Indirect Costs):
Contracting Officer: Scott Lowe email: lowes@mskcc.org

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
2.	2022	0.36 calendar

*Title: Precision Macrophage Targeting to Overcome Treatment Resistance in Renal Cell Carcinoma
*Major Goals: Aim 1: Fully characterize the macrophage compartment in untreated and treated human ccRCC. We hypothesize that specific myeloid populations such as TAMs are associated with resistance to ICB and ICB-VEGF inhibitor combination therapy. To investigate this, we will finely characterize and develop expression signatures for TAMs and other antigen-presenting cells (APCs) in ccRCC from patients with high-risk localized disease in 3 cohorts: treatment-naive, responding to ICB and ICB/VEGF inhibitor combination therapy, and resistant to those therapies. Using single-cell and T cell receptor sequencing, we will complete an atlas of APC diversity and associated T cell phenotypes to discover APC and T cell subsets associated with therapeutic resistance.
Aim 2: Develop and refine novel immunogenomic models of response to systemic therapy in ccRCC. We hypothesize that specific TAM gene expression programs are enriched in tumors resistant to ICB and combination therapy. We will therefore determine the prognostic significance of overexpression of genes in these programs in several large patient cohorts from clinical trials (data in hand). By integrating this data with existing whole exome and clinical data we will develop new predictive models for response of patients with ccRCC to ICB, VEGF inhibition, or combination treatment.
Aim 3: Therapeutically target TAMs to overcome resistance to ICB and VEGF inhibitor therapies. We hypothesize that responses to ICB and VEGF therapy can be improved by targeting the specific TAM populations associated with resistance to the therapy. This aim will use a novel CRISPR-based somatic mosaic model of ccRCC, in which mice spontaneously develop ccRCCs similar to human disease. After defining the specific murine TAM phenotypes associated with resistance to anti-PD1, anti-PDL1, and VEGF inhibitor treatment, we will assess whether inhibitors of specific macrophage subsets can overcome resistance. We will use inhibitors that are already in clinical trials, so this aim may yield treatment strategies that could be rapidly translated to the clinic.
*Status of Support: Completed
Project Number: 2020 Cycle for Survival's Equinox Innovation
Name of PD/PI: Hakimi, A
Source of Support: Cycle for Survival
Contracting Officer: Kathleen Bourke, Project Coordinator; bourkek@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2021 - 12/31/2022
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
2.	2022	0.12 calendar

*Title: Mechanisms of dynamic chromatin reorganization regulating B-cell differentiation and
*Major Goals: Define the epigenetic and functional programs driven by the phosphorylation of histone H3 (H3S28ph and H3.3S31ph) in GC B-cell differentiation.
*Status of Support: Completed
Project Number: I14-0020
Name of PD/PI: Leslie, C
Source of Support: Starr Cancer Consortium
Contracting Officer: Sylvie Le Blancq email: leblancqs@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2021 - 12/31/2022

*Total Award Amount (including Indirect Costs): Person

Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2022	0.60 calendar

*Title: Discovery and Validation of Splicing and Gene Expression Programs in Cancer
*Major Goals: Specific Aim 1. Detection of splicing and gene expression programs downstream of oncogenic signaling in cancer.
Specific Aim 2. Clinical and functional validation of gene expression and splicing alterations mediated by oncogenic PI3K
*Status of Support: Completed
Project Number: 2004981145
Name of PD/PI: Leslie, C
Source of Support: Innovation in Cancer Informatics
Contracting Officer: Not Available
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2021 - 2/1/2023
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2023	0.24 calendar

*Title: Identification of therapeutic targets for leukemia stem cells in AML-iPSC models
*Major Goals: The proposed studies leverage the unique expertise of the Papapetrou lab in iPSC modeling, combined with the expertise of the Kharas lab in studying molecular mechanisms of myeloid malignancy and can generate new insights into LSC biology and identify new therapeutic targets for future drug development.
*Status of Support: Completed
Project Number: (R01-CA225231)
Name of PD/PI: Kharas, M
Source of Support: Mount Sinai / National Cancer Institute
Contracting Officer: Funmi Elesinmogun; Email: elesinmf@mail.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 3/1/2018 - 2/28/2023
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2023	0.60 calendar

*Title: Elucidating the role of the SWI/SNF complex in mediating hormone therapy resistance in breast cancer
*Major Goals: This is a consortium project with JHU (PI: Toska). Most breast cancers are dependent on estrogen for their growth and, whilst endocrine therapies are beneficial, all metastatic breast cancers eventually become resistant to these therapies. To understand what drives resistance to endocrine therapy, we have analyzed the genomes of over 2,000 breast cancers, of which >700 after no further responding to therapy, and conducted parallel laboratory studies utilizing preclinical models.
*Status of Support: Completed
Project Number: R21CA252530
Name of PD/PI: Razavi, P
Source of Support: Johns Hopkins University / National Cancer Institute
Contracting Officer: Shaoxian Jiang; sjiang6@jhmi.edu
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 6/1/2021 - 5/31/2023

*Total Award Amount (including Indirect Costs): Person

Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2023	0.24 calendar

ACTIVE

*Title: Chemical Genetic Dissection of SWI/SNF Chromatin Remodeling Complex Functions in Cerebral Cortex Development
*Major Goals: The proposed study seeks to develop improved model systems and apply new experimental tools to study the function of these proteins during normal brain development.
*Status of Support: Active
Project Number: 1R01 NS126921-01A1
Name of PD/PI: Vierbuchen, T
Source of Support: National Institutes of Health
Contracting Officer: Muskan Pathak, muskan.pathak@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 4/1/2023 - 3/31/2028
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2024	0.30 calendar
2. 2025	0.30 calendar
3. 2026	0.30 calendar
4. 2027	0.30 calendar
5. 2028	0.30 calendar

*Title: Harnessing double stranded-RNA (dsRNA)-response and anti-tumor effect in PRC2-inactivated cancer
*Major Goals: We propose innovative and integrative approaches to dissect the molecular mechanisms and evaluate novel therapeutic strategies (e.g., DNMT1 inhibitors, synthetic dsRNA, second generation of engineered immunogenic viruses) in relevant PRC2-loss cancer models to facilitate future design of biomarker driven clinical trials in PRC2-loss cancers with the goal to improve outcomes in individuals with MPNST and other PRC2-loss cancers.
*Status of Support: Active
Project Number: R01CA280657-01
Name of PD/PI: Chi, P
Source of Support: National Institutes of Health
Contracting Officer: Naydia Rowe, naydia.rowe@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 3/22/2023 – 2/29/2028
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2024	0.60 calendar
2. 2025	0.60 calendar
3. 2026	0.60 calendar
4. 2027	0.60 calendar
5. 2028	0.60 calendar

*Title: Mechanisms of dynamic chromatin reorganization regulating B cell differentiation and Lymphomagenesis
*Major Goals: Germinal center (GC) B cells manifest many hallmarks of cancer cells explaining why a majority of lymphomas arise from B cells transiting the GC reaction1. GC B cells oscillate between two

main phenotypic states: i) proliferative and mutagenic centroblasts, and ii) quiescent centrocytes, which exit the GC reaction to undergo subsequent terminal differentiation. These distinct phenotypic states are encoded through opposing epigenetic mechanisms (Figure 2B). The transition from centroblast to centrocyte is determined by signaling through the "immune synapse"2. It is not known how the immune synapse reprograms chromatin to enable the switch between these opposing epigenetic forces. Our preliminary data indicate molecular mechanisms by which histone H3 phosphorylation, downstream of immune synapse signaling, can potently disrupt and reshape chromatin states. Thus, we hypothesize that immune synapse mediated H3 phosphorylation controls this critical GC epigenetic switch (Figure 2B). Activated B cell like diffuse large B cell lymphoma (ABC DLBCLs) are aggressive lymphomas that reflect post GC B cells (Figure 2B, right), and harbor mutations that induce strong immune synapse signaling1. Targeting of proximal signaling factors (e.g. ibrutinib) is only modestly effective in these tumors3,4, and more effective therapy remains a critical unmet need. We predict that ABC DLBCLs are addicted to H3 phosphorylation and its corresponding epigenetic effects, mediated by the kinase MSK, and will be selectively killed by its inhibition, since it represents the convergence of many branches of immune synapse signaling5. This team is uniquely suited to address these conceptual and cancer treatment directed questions with expertise in lymphoma biology, epigenetics, histone biochemistry, biophysics, and computational epigenomics.
*Status of Support: Active
Project Number: I16-0068
Name of PD/PI: Leslie, C
Source of Support: Starr Cancer Consortium
Contracting Officer: Sylvie Le Blancq email: leblancqs@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2023 - 12/31/2023

*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
1.	2023	0.60 calendar

*Title: The Center for Tumor-Immune Systems Biology at MSKCC **(Admin-Core)**
*Major Goals: Cancer immunotherapies are designed to harness the human immune system to attack cancer cells and eliminate tumors. Breakthroughs in cancer immunotherapy such as checkpoint blockade agents have revolutionized cancer care, but only a fraction of patients with specific tumor types respond to these new treatments. Our proposed Research Center will deploy tools from systems biology to improve our fundamental understanding of tumor-immune interactions in contexts where current immunotherapies fail and to develop novel strategies for enhancing responses in contexts where they have only partial success.
*Status of Support: Pending
Project Number: 1U54CA274492-01
Name of PD/PI: Leslie, C / Leslie, C
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk; michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/16/2022 - 8/31/2027
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
1.	2023	0.60 calendar
2.	2024	0.60 calendar
3.	2025	0.60 calendar
4.	2026	0.60 calendar
5.	2027	0.60 calendar

*Title: The Center for Tumor-Immune Systems Biology at MSKCC (**Project-002: Immune regulatory circuits in primary colon cancer and lymph node and liver metastases)**
*Major Goals: Cancer immunotherapies are designed to harness the human immune system to attack

cancer cells and eliminate tumors. Breakthroughs in cancer immunotherapy such as checkpoint blockade agents have revolutionized cancer care, but only a fraction of patients with specific tumor types respond to these new treatments. Our proposed Research Center will deploy tools from systems biology to improve our fundamental understanding of tumor-immune interactions in contexts where current immunotherapies fail and to develop novel strategies for enhancing responses in contexts where they have only partial success.
*Status of Support: Active
Project Number: 1U54CA274492-01
Name of PD/PI: Leslie, C / Rudensky, A
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk; michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/16/2022 - 8/31/2027
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2023	1.00 calendar
2.	2024	1.00 calendar
3.	2025	1.00 calendar
4.	2026	1.00 calendar
5.	2027	1.00 calendar

*Title: The Center for Tumor-Immune Systems Biology at MSKCC (**Project-003: Engineering immunogenic cell death in melanoma and renal cell carcinoma)**
*Major Goals: Cancer immunotherapies are designed to harness the human immune system to attack cancer cells and eliminate tumors. Breakthroughs in cancer immunotherapy such as checkpoint blockade agents have revolutionized cancer care, but only a fraction of patients with specific tumor types respond to these new treatments. Our proposed Research Center will deploy tools from systems biology to improve our fundamental understanding of tumor-immune interactions in contexts where current immunotherapies fail and to develop novel strategies for enhancing responses in contexts where they have only partial success.
*Status of Support: Active
Project Number: 1U54CA274492-01
Name of PD/PI: Leslie, C / Cheng, E
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk; michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/16/2022 - 8/31/2027
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2023	0.80 calendar
2.	2024	0.80 calendar
3.	2025	0.80 calendar
4.	2026	0.80 calendar
5.	2027	0.80 calendar

*Title: Phase II Study of ASTX727 in Patients with PRC2 loss Malignant Peripheral Nerve Sheath Tumor (MPNST)
*Major Goals: Aim 1: Conduct a proof-of-concept investigator-initiated phase II trial (IIT) to evaluate the efficacy of ASTX727 (combination of decitabine and cedazuridine) in patients with PRC2-loss MPNST (IRB#21-048, clinicaltrials.gov NCT04872543). Aim 2: Investigate the molecular mechanisms that regulate the sensitivity and resistance to DNMT inhibitors in PRC2-loss MPNST using pre-, on-treatment and at progression biopsy samples and treatment responses from the prospective clinical trial.

*Status of Support: Pending
Project Number: 1 R01 FD007544-01
Name of PD/PI: Chi, P
Source of Support: Food and Drug Administration
Contracting Officer: Shashi Malhotra; shashi.malhotra@fda.hhs.gov Primary
Place of Performance: Sloan Kettering Institute For Cancer Research Project/
Proposal Start and End Date (MM/YYYY): 9/15/2022 - 8/31/2026
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2023	0.12 calendar
2.	2024	0.12 calendar
3.	2025	0.12 calendar
4.	2026	0.12 calendar

*Title: Therapeutic Activation of Immunogenic Cell Death to Improve Immunotherapy for Kidney Cancer
*Major Goals: Aim 1. Complete the validation of HTS to identify additional activators of BAX/BAK dependent immunogenic cell death and evaluate the anti tumor efficacy of promising agents in PDX models. Aim 2. Interrogate the impact of BAX/BAK dependent immunogenic cancer cell death on tumor immune crosstalk and anti tumor immunity in GEMMs. Aim 3. Determine whether activation of BAX/BAK dependent immunogenic cell death in cancer cells sensitizes kidney cancer to immune checkpoint blockade in GEMMs. Aim 4. Determine whether and how activation of BAX/BAK dependent immunogenic cell death in tumor microenvironment sensitizes kidney cancer to immune checkpoint blockade in GEMMs.
*Status of Support: Active
Project Number: W81XWH22-1-0835 (KC210165)
Name of PD/PI: Cheng, E
Source of Support: Congressionally Directed Medical Research Programs
Contracting Officer: Elfreda Nymn Tel: (301) 619-7150 Email: elfreda.r.nymn.civ@health.mil
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/1/2022 - 8/31/2025
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
2.	2023	0.12 calendar
2.	2024	0.12 calendar
3.	2025	0.12 calendar

*Title: Mechanisms and therapeutic implications of human clonal hematopoiesis (CH) mutations
*Major Goals: Dr. Leslie is a Member of the Computational and Systems Biology Program at the Sloan Kettering Institute for Cancer Research. She is a computational biologist with extensive expertise in transcriptomics and epigenomics. Her group develops statistical and machine learning methods to model gene regulatory mechanisms, epigenetic programs governing cell fate decisions in differentiation, and the dysregulation of gene expression programs in cancer. Dr. Leslie will be responsible for supervising computational analyses for Dr. Papapetrou's R01 project, including integrative analyses of all high-throughput bulk epigenomic and transcriptomic data and scRNA-seq analyses.
*Status of Support: Pending
Project Number: 5R01 CA271331-02
Name of PD/PI: Papapetrou, E
Source of Support: Mt. Sinai School of Medicine / National Cancer Institute
Contracting Officer: Jessica Moise; contracts@mssm.edu
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 6/15/2022 – 05/31/2027

*Total Award Amount (including Indirect Costs): Person Months

(Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
1.	2023	0.45 calendar
2.	2024	0.45 calendar
3.	2025	0.45 calendar
4.	2026	0.45 calendar
5.	2027	0.45 calendar

*Title: Reprogram cancer cell and cancer microenvironment for anti-tumor immunity in NF1-associated MPNST
*Major Goals: Aim 1: Characterize the transcriptional plasticity and tumor heterogeneity and tumor evolution of NF1-associated MPNST under the selective pressure of TME in genetically defined in vitro and in vivo MPNST models. Aim 2: Evaluate the impact of epigenomic reprograming of cancer cells by DNMT1 and bromodomain CBP/P300 inhibitors to elicit antigen presentation and immune-response signature and to capitalize on cytotoxic T lymphocyte-mediated cancer cell immunotherapy in MPNST.
*Status of Support: Active
Project Number: W81XWH22-1-0326
Name of PD/PI: Chi, P
Source of Support: Congressionally Directed Medical Research Programs
Contracting Officer: JoAnn Martin email: joann.l.martin2.civ@mail.mil
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 5/15/2022 - 5/14/2025

*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
2.	2024	1.20 calendar
3.	2025	1.20 calendar

*Title: Impact of mutational order on molecular mechanisms of oncogenesis
*Major Goals: Dr. Leslie is a Member of the Computational and Systems Biology Program at the Sloan Kettering Institute for Cancer Research. She is a computational biologist with extensive expertise in transcriptomics and epigenomics. Her group develops statistical and machine learning methods to model gene regulatory mechanisms, epigenetic programs governing cell fate decisions in differentiation, and the dysregulation of gene expression programs in cancer. Dr. Leslie will be responsible for supervising computational analyses for Dr. Papapetrou's R01 project, including integrative analyses of all high-throughput bulk epigenomic and transcriptomic data and scRNA-seq analyses.
*Status of Support: Active
Project Number: 5R01CA260711-02
Name of PD/PI: Papapetrou, E
Source of Support: Mt. Sinai School of Medicine / National Cancer Institute
Contracting Officer: Jessica Moise; contracts@mssm.edu
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 5/10/2022 - 2/28/2027
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)		Person Months (##.##)
2.	2024	0.60 calendar
3.	2025	0.60 calendar
4.	2026	0.60 calendar
5.	2027	0.60 calendar

*Title: Ferroptosis and Cancer Cell Signaling

*Major Goals: Success of the proposed research will unveil in-depth mechanisms of ferroptosis, as well as its functional communication with various cancer-relevant intercellular and intracellular molecular events. The proposed research will also lead to the identification of biomarkers that predict cancer responsiveness to future ferroptosis inducing cancer therapy.
*Status of Support: Active
Project Number: 5R01CA258622-02
Name of PD/PI: Jiang, X
Source of Support: National Institutes of Health
Contracting Officer: Jennifer Meininger Email: Jennifer.meininger@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 2/1/2022 - 1/31/2027
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2024	0.10 calendar
3. 2025	0.10 calendar
4. 2026	0.10 calendar
5. 2027	0.10 calendar

*Title: Investigating the Immunologic Basis of the Obesity Paradox in Renal Cell Carcinoma
*Major Goals: Aim 1: Compare obese and nonobese patients with advanced ccRCC in terms of the tumor immune microenvironment and the spatial arrangement of immune cells. Aim 2: Model the effect of obesity on tumor development and progression in novel immunocompetent ccRCC murine models.
*Status of Support: Active
Project Number: Hakimi AICR Award
Name of PD/PI: Hakimi, A
Source of Support: American Institute for Cancer Research
Contracting Officer: Nigel Brockton email: n.brockton@aicr.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2022 - 12/31/2023
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2023	0.30 calendar

*Title: The role of TREM2-expressing macrophages in the obesity paradox in clear cell renal cell carcinoma
*Major Goals: Interrogate the spatial arrangement of immune and other cells at the tumor/fat interface in obese and normal weight patients.
*Status of Support: Active
Project Number: W81XWH-21-1-0941-KC200216
Name of PD/PI: Hakimi, A
Source of Support: Congressionally Directed Medical Research Programs
Contracting Officer: Joshua McKean, Email: joshua.d.mckean3.civ@mail.mil
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/30/2021 - 9/29/2024
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2023	0.36 calendar
3. 2024	0.36 calendar

*Title: Developing Mechanism-Based Therapeutic Strategies for Aggressive Rare Kidney Cancer

*Major Goals: Characterize immune cell infiltrates in genetically defined human uRCC tumors using multiplex immunofluorescent (MxIF).
*Status of Support: Active
Project Number: W81XWH-21-1-0897 Log#KC200289
Name of PD/PI: Cheng, E
Source of Support: Congressionally Directed Medical Research Programs
Contracting Officer: Joshua McKean, Email: joshua.d.mckean3.civ@mail.mil
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/30/2021 - 9/29/2024
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2023	0.12 calendar
3. 2024	0.12 calendar

*Title: Deciphering the Genomics of Gene Network Regulation of T Cell and Fibroblast States in Autoimmune Inflammation
*Major Goals: We will develop advanced machine learning approaches to combine single-cell multiomic and bulk 3D interactome data to model the impact of genetic variation on gene regulation, using rheumatoid arthritis (RA) as a disease model. Our gene regulatory models and experimental analyses will focus on two cell types that drive RA tissue pathology—T cells and synovial fibroblasts—and will serve as a case study for examining the genetics of polygenic human diseases that dysregulate multiple interacting cell types within affected tissues.
*Status of Support: Active
Project Number: 5U01HG012103-02
Name of PD/PI: Leslie, C / Rudensky, A
Source of Support: National Institutes of Health
Contracting Officer: Zephaun Harvey email: harveyz@mail.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 8/20/2021 - 5/31/2026
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2023	2.40 calendar
3. 2024	2.40 calendar
4. 2025	2.40 calendar
5. 2026	2.40 calendar

*Title: Role of ETS factors in specifying prostate luminal cell identity and androgen receptor dependence
*Major Goals: A mechanism by which AR misregulation is thought to occur is through acquisition of new binding sites throughout the genome that shift the transcriptional program from differentiation to proliferation. In this proposal, we investigate how mutations in ETS factors, clinically important oncogenic drivers of prostate cancer, promote luminal cell identity and regulate chromatin architecture of cancerous prostate tissues, including by co-option of AR function.
*Status of Support: Active
Project Number: 5R01CA193837-07
Name of PD/PI: Sawyers, C
Source of Support: National Cancer Institute
Contracting Officer: Olivia Paolucci email: Olivia.paolucci@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 2/9/2021 - 8/31/2025
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
8. 2024	0.36 calendar
9. 2025	0.36 calendar

*Title: Characterizing and Targeting Tumor-immune Interaction in Aggressive Rare Kidney Cancer
*Major Goals: Aim 1. Establish a novel Nf2-/-Setd2-/- mouse kidney cancer model and investigate the underlying tumor suppressor and immune regulatory mechanisms.
Aim 2. Assess the in vivo therapeutic effects of mechanism-based targeted therapies in combination with immunotherapy using the mouse Nf2-/-Setd2-/- uRCC model.
Aim 3. Characterize immune cell infiltrates and tumor-immune crosstalk in human NF2-loss uRCC tumors using single nucleus RNA-seq.
*Status of Support: Active
Project Number: 2020 Cycle for Survival's Equinox Innovation Award in Rare Cancers
Name of PD/PI: Chen, Y
Source of Support: Cycle for Survival
Contracting Officer: Kathleen Bourke, Project Coordinator; bourkek@mskcc.org
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2021 - 12/31/2023 NCE
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
2. 2022	0.00 calendar*

**No specified effort required for remainder of project period*

*Title: Defining Transcription Factor Networks Governing Androgen Receptor-Null Prostate Cancer
*Major Goals: Aim 1. Determine gene expression and chromatin landscape changes associated with potent AR inhibition Aim 2. Identify vulnerabilities responsible for maintenance of the AR-low/null state Aim 3. Characterize the AR-low/null state in CRPC patients using single cell and organoid technologies
*Status of Support: Active
Project Number: W81XWH-20-1-0289
Name of PD/PI: Sawyers, C
Source of Support: Congressionally Directed Medical Research Programs
Contracting Officer: Joshua McKean, Email:joshua.d.mckean3.civ@mail.mil
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/30/2020 - 9/30/2023
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
3. 2023	0.12 calendar

*Title: Discovery of diabetes-relevant β cell enhancers through 4D enhancer mapping, integrative analysis, and large-scale CRISPRi perturbation screens
*Major Goals: This project will take an integrative approach involving generating a 4D atlas of regulatory interactions during both development and disease progressions, computationally nominating diabetes-relevant β cell enhancers through integrative analysis and discovering functional enhancers through large-scale perturbation screens.
*Status of Support: Active
Project Number: 5 U01 DK128852-03
Name of PD/PI: Huangfu, D / Leslie, C / Apostolou, E
Source of Support: National Institute of Diabetes & Digestive & Kidney Diseases
Contracting Officer: Lesley Whipp; whipplc2@niddk.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/15/2020 - 6/30/2025
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
3.	2023	0.91 calendar
4.	2024	0.91 calendar
5.	2025	0.91 calendar

*Title: Understanding human pancreas development for diabetes cell-replacement therapy
*Major Goals: This project aims to combine sophisticated genetic manipulation, state-of-art single-cell technology, and human pluripotent stem cell (hPSC) directed differentiation to uncover mechanisms that control pancreatic β cell differentiation and function. Our human-cell based system will provide unique mechanistic understanding of neonatal and adult-onset diabetes not evident in mouse models, and facilitate the development of improved hPSC directed differentiation protocols.
*Status of Support: Active
Project Number: 5 R01 DK096239-09
Name of PD/PI: Huangfu, D
Source of Support: National Institute of Diabetes & Digestive & Kidney Diseases
Contracting Officer: Craig Bagdon Email: bagdonc@niddk.nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/20/2018 - 7/31/2023 NCE
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
9.	2023	0.00 calendar*

**No specified effort required for remainder of project period*

*Title: Genetic Loss-of-Function Studies of SETD2 in Kidney Tumorigenesis
*Major Goals: Our goals are to establish physiological preclinical models of ccRCC based on human cancer genomics, to provide mechanistic understanding of how dysregulated epigenetics conferred by SETD2 loss promotes tumor initiation and metastasis, and to discover novel therapeutic vulnerabilities associated with loss of SETD2.
*Status of Support: Active
Project Number: 5 R01 CA223231-05
Name of PD/PI: Cheng, E
Source of Support: National Cancer Institute
Contracting Officer: Jennifer Meininger Email: Jennifer.meininger@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 5/7/2018 - 4/30/2024 NCE
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
5.	2024	0.36 calendar

*Title: Understanding Resistance to Next Generation Antiandrogens
*Major Goals: In summary, this application will generate novel mechanistic insight into lineage plasticity In prostate cancer, with obvious implications for the clinical challenge of drug resistance. The findings are also likely to have relevance for other epithelial tumor types such as lung cancer, breast cancer and melanoma where evidence implicating lineage plasticity as a cause of drug resistance has also emerged.
*Status of Support: Active
Project Number: 5 R01 CA155169-10
Name of PD/PI: Sawyers, C
Source of Support: National Cancer Institute
Contracting Officer: Rogers Gross, Email: rogers.gross@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 1/1/2018 - 12/31/2023 NCE

*Total Award Amount (including Indirect Costs): Person

Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
10. 2023	0.00 calendar*

**No specified effort required for remainder of project period*

*Title: The MSKCC-UW/Fred Hutch Prostate Cancer Drug Resistance and Sensitivity Center (Project 1: Resistance caused by AR pathway reactivation)
*Major Goals: The overarching goal of this DRSC proposal is to evaluate these translational opportunities across a unique set of preclinical organoid and PDX models (again, discovered and developed by our DRSC team members) and to catalyze the initiation of clinical studies in patients most likely to benefit based on appropriate biomarker profiles.
*Status of Support: Active
Project Number: 5U54CA224079-04
Name of PD/PI: Sawyers, C / Sawyers, C
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk; Michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/30/2017 - 8/31/2023 NCE
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2022	0.00 calendar

*Title: The MSKCC-UW/Fred Hutch Prostate Cancer Drug Resistance and Sensitivity Center (Project 2: Reversing resistance caused by lineage plasticity through epigenetic therapy)
*Major Goals: The overarching goal of this DRSC proposal is to evaluate these translational opportunities across a unique set of preclinical organoid and PDX models (again, discovered and developed by our DRSC team members) and to catalyze the initiation of clinical studies in patients most likely to benefit based on appropriate biomarker profiles.
*Status of Support: Active
Project Number: 5U54CA224079-04
Name of PD/PI: Sawyers, C / Sawyers, C
Source of Support: National Cancer Institute
Contracting Officer: Michael Kluk; Michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/30/2017 - 8/31/2023 NCE
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2022	0.00 calendar

*Title: The MSKCC-UW/Fred Hutch Prostate Cancer Drug Resistance and Sensitivity Center (Project 3: Defining the appropriate context for targeting kinase signaling in combination with androgen receptor blockade to enhance therapeutic response in metastatic prostate cancer)
*Major Goals: The overarching goal of this DRSC proposal is to evaluate these translational opportunities across a unique set of preclinical organoid and PDX models (again, discovered and developed by our DRSC team members) and to catalyze the initiation of clinical studies in patients most likely to benefit based on appropriate biomarker profiles.
*Status of Support: Active
Project Number: 5U54CA224079-04
Name of PD/PI: Sawyers, C / Sawyers, C
Source of Support: National Cancer Institute

Contracting Officer: Michael Kluk; Michael.kluk@nih.gov
Primary Place of Performance: Sloan Kettering Institute For Cancer Research
Project/Proposal Start and End Date (MM/YYYY): 9/30/2017 - 8/31/2023 NCE
*Total Award Amount (including Indirect Costs):

Person Months (Calendar/Academic/Summer) per budget period.

	Year (YYYY)	Person Months (##.##)
5.	2022	0.00 calendar

PENDING: None

OVERLAP:
None