AWARD NUMBER: W81XWH-18-1-0523

TITLE: Mesenchymal Stem Cell Control of Metastatic Prostate Cancer Cell Evolution and Therapy Resistance in the Bone Microenvironment

PRINCIPAL INVESTIGATOR: Conor C. Lynch, PhD

CONTRACTING ORGANIZATION: H. Lee Moffitt Cancer Center & Research Institute
Tampa, FL

REPORT DATE: December 2022

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
December 2022	Final	15Aug2018-14Aug2022

4. TITLE AND SUBTITLE

Mesenchymal Stem Cell Control of Metastatic Prostate Cancer Cell Evolution and Therapy Resistance in the Bone Microenvironment

5a. CONTRACT NUMBER
W81XWH-18-1-0523

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Conor C. Lynch, PhD

E-Mail:

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

H. Lee Moffitt Cancer Center
and Research Institute
12902 Magnolia Blvd
Tampa, FL, 33612 USA

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The goal of this proposal is to examine the impact of interleukin-28 in promoting the resistance of prostate cancer cells in bone. In the third year of this award we have made significant progress and have published our work Nature Communications (IF=15). The publication represents completed Aim 1&4. Aim 2&3 are nearing completion.

15. SUBJECT TERMS
Prostate Cancer, Bone Metastasis, Interleukin-28, Apoptosis Resistance, STAT Signaling, Osteoblasts, Mesenchymal Stem Cell, MSC, Osteoblast, Osteoclast.

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	28	**19b. TELEPHONE NUMBER** *(include area code)*

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1. Introduction

This year in the United States alone, prostate cancer will claim the lives of over 26,000 men. The reason for the demise of these patients is that their disease has spread/metastasized from the prostate to secondary sites and has become resistant to therapy. Castrate resistant prostate cancer (CRPC) typically presents as metastatic disease (mCRPC) in the skeleton. Studies have shown that 90% of men that succumb to the disease, have evidence of bone metastasis. In the skeleton, prostate cancer cells manipulate the normal cells of the bone to generate lesions that have areas of extensive bone destruction caused by cells known as osteoclasts and bone formation caused by cells known as osteoblasts. These bony metastases are very painful and greatly impact the patient's quality of life. Clinically, androgen deprivation therapy (enzalutamide, abiraterone), chemotherapy (docetxel, cabazitaxel), and radiation therapy (radium-223/Xofigo) have increased overall survival. Unfortunately, it is only a matter of time before the disease becomes castrate and/or chemoresistant to these therapies and progresses. Given the number of men dealing with bone metastases, understanding how resistance arises and identifying new therapies that extend overall survival are an urgent and unmet clinical need. Our group has been investigating castrate resistant bone metastatic prostate cancer and emerging work has revealed a number of new findings. ***Our preliminary findings:*** Mescenchymal stromal/stem cells (MSCs) reside in the bone marrow and in response to prostate cancer derived factors can become osteoblasts and contribute to bone formation. We observed that reciprocally, MSCs can promote the evolution of mCRPC cell populations that have enhanced resistance to cell death. Furthermore, the MSC educated prostate cancer cells were also significantly more resistant to the chemotherapy, docetaxel. We have found that and MSC secreted factor, interleukin-28 (IL-28) can promote prostate cancer cell death by binding to its receptor IL-28R. The IL-28R receptor typically stimulates the activity of targets known as STAT1 and STAT3. We observed that the MSC educated prostate cancer cells have reduced STAT1 activity and elevated STAT3 activity. STAT3 has been shown to be active in human cases of bone metastatic prostate cancer. Here at Moffitt we have developed a novel inhibitor that blocks STAT3 activity, S3I-201. Our early results show that MSC educated prostate cancer cells are sensitive to this inhibitor *in vitro* and an expected outcome is that these cells will also be sensitive to STAT3 inhibition in pre-clinical mouse models of bone metastatic prostate cancer. We also expect that blocking STAT3 will make the resistant prostate cancer cells more sensitive to docetaxel chemotherapy.

2. Keywords

Prostate Cancer, Bone Metastasis, Interleukin-28, Apoptosis Resistance, STAT Signaling, Osteoblasts, Mesenchymal Stem Cell, MSC, Osteoblast, Osteoclast.

3. Accomplishments

Aim 1. Do MSC-educated prostate cancer cells have a growth advantage or impact bone disease in vivo compared to MSC naïve prostate cancer cells? The intratibial growth of naïve and MSC educated prostate cancer cells (PAIII and DU145) in the presence or absence of mCherry labeled MSCs will be measured via bioluminescence imaging. Relative luminescence units (RLUs) will be used as pre-clinical endpoints to generate survival curves. Bone pathophysiology changes will be analyzed via μCT and histomorphometry. Cancer cell growth, MSC content, and stromal responses will be determined histochemically.

Progress. This Aim has been completed and have identifies that MSC educated prostate cancer cells grow significantly faster than their parental counterparts (**Fig. 1**). The results of our studies were published in *Nature Communications* in 2021

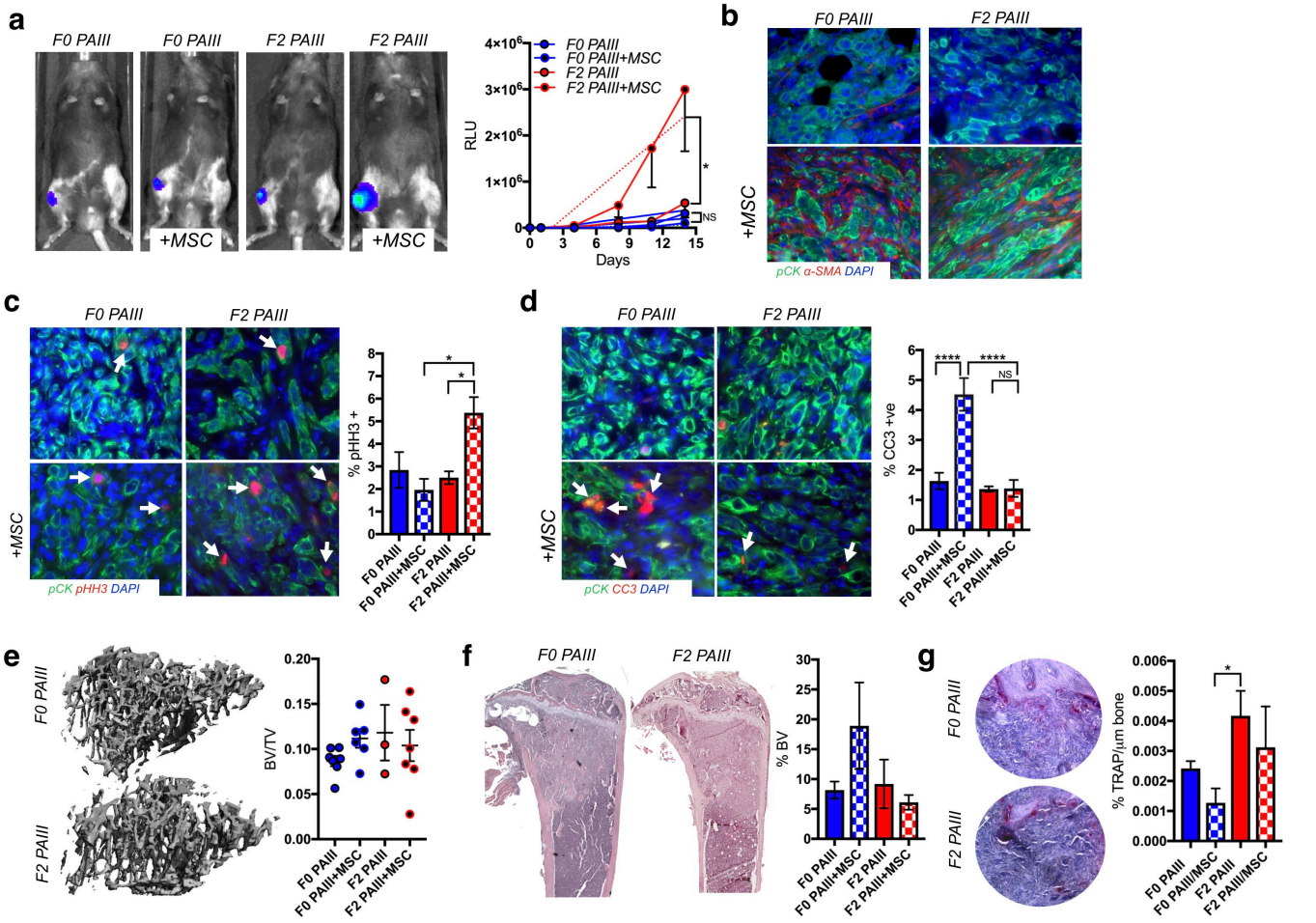


Figure 1. MSC selected prostate cancer cell growth is promoted rather than suppressed by the presence of MSCs. **a,** Parental (F0 PAIII) and MSC selected (F2 PAIII) growth over time in the presence (1:1 ratio) or absence of MSCs (n≥8/group). Representative images of bioluminescence in each group are shown at day 11 time point. Graphs illustrate collected RLUs over time for each group. **b,** Representative images of smooth muscle actin staining (α-SMA; red) in tissues derived from the F0 and F2 groups in the presence or absence of MSCs. Pan-cytokeratin (pCK; green) was used to localize prostate cancer cells. Dashed box in merge represents area of magnification. **c, d,** *Ex vivo* analyses from study endpoint of proliferative and apoptotic indices using phospohistone H3 (pHH3; red arrows; b) and cleaved caspase 3 (CC3; red, arrows, b) respectively. Pan-cytokeratin (green) was used to identify prostate cancer cells. **e,** μCT scan analysis of cancer-induced bone destruction. Representative μCT images of the trabecular bone are shown for the F0 and F2 PAIII group. The trabecular bone volume was calculated as a ratio to total volume analyzed (BV/TV). **f,** Trabecular bone volume (BV) was measured via histomorphometry on non-sequential H&E multiple sections derived from each group and calculated as a percentage of total volume. Representative gross H&E images are illustrated from the F0 and F2 groups. **g,** The number of osteoclasts (TRAcP positive; red, multi-nucleated; arrows) per μm of bone was calculated in non-sequential sections derived from each group. Asterisks denotes statistical significance (*p≤0.05, ****p≤0.0001) while NS denotes not significant.

Aim 2. Is IL-28 the primary mechanism through which MSCs drive apoptotic resistant bone metastatic prostate cancer? Using IL-28Rα null (CRISPR) prostate cancer cell lines, we will identify whether MSC derived IL-28 is the primary molecular mechanism through which MSCs promote apoptosis resistance in prostate cancer cells *in vitro*. The impact of IL-28Rα ablation on the activity of downstream effectors such as STAT1 and STAT3 will also be determined. *In vivo*, we will address whether IL-28Rα impacts the progression of bone metastatic prostate cancer by comparing the growth rates, overall survival and bone pathophysiology of control or IL-28Rα null (PAIII and DU145) cell lines.

Progress. Aim 2 has been completed with the exception of performing the IL-28Rα null PAIII and DU145 cell line studies. CRISPR knockout proved challenging and we reverted to using shRNA and siRNA approaches. Using this approach, we showed that the IL-28 receptor is critical in mediating the MSC induced apoptotic effect (**Fig. 2**). We spent much of our time examining the down stream signaling pathways in the parental and MSC educated cell lines focusing primarily on STAT1 and STAT3. Using immunoblot and STAT activity assays, we show demonstrate preferential STAT3 signaling in the PAIII/DU145 MSC educated cell lines compared to the parental counterparts while conversely STAT1 signaling is higher in the parental PAIII/DU145 cells compared to their MSC educated cell lines.

Aim 3. Can STAT3 inhibitors sensitize bone metastatic prostate cancer to chemotherapy? The efficacy of S3I-201 as single agent or in combination with docetaxel in limiting the viability of MSC naïve and educated prostate cancer cell (PAIII and DU145) growth *in vitro and in vivo* will be assessed. The effect of STAT3 inhibition on overall survival and bone pathophysiology will also be examined.

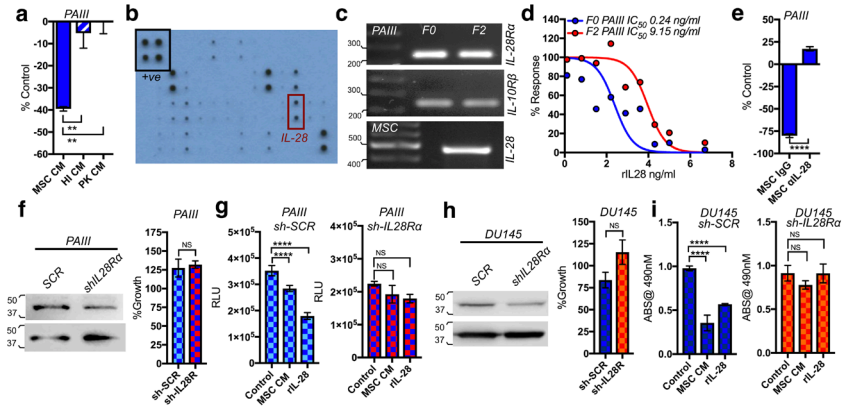


Figure 2. MSC-derived IL-28 directs PCa apoptosis. a, PAIII growth (F0) in response to treatment with MSC CM, heat-inactivated (HI) MSC CM, or proteinase-K (PK) treated MSC CM. b, Cytokine Array of MSC CM. Black box indicates positive control (+ve), red box indicates IL-28. c, RT-PCR analysis of PAIII (F0 and F2) of IL28Rα, IL-10Rβ and IL-28 expression. Molecular weights in base pairs are shown. d, Growth of PAIII (F0) in MSC CM immune-depleted of IL-28 (MSC αIL-28). IgG was used as negative control (MSC IgG). Growth is expressed as a percentage of non-treated cells. e, Treatment of PAIII F0 and F2 cell lines with the indicated concentrations of recombinant IL-28 (rIL-28) for 48 hr. f, Growth of IL-28Rα silenced (sh-IL28R) and scrambled control (sh-SCR) compared to parental PAIII cell lines. g, h, Control (sh-SCR) and IL-28Rα (sh-IL28R) PAIII and DU145 growth in MSC CM or rIL-28 as measured by luminescence assay and relative light unit (RLU) measurement or MTT assay. Asterisks denotes statistical significance (**p≤0.01, ****p≤0.0001)

Progress. We showed that as a single agent, the STAT3 inhibitor, S3I-201 is effective inhibiting the growth of PAIII and DU145 but does not impact cancer induced bone disease. Our next step was examine the impact of combined docetaxel treatment with S3I-201. *In vitro,* we showed synergy between S3I-201 and docetaxel in the MSC educated PAIII cell lines (data not shown) but this did not translate *in vivo* where we observed toxicity in the combination group. We anticipate that newer versions of STAT3 inhibitors will prove less toxic and more synergistic with chemotherapy.

Aim 4. What is the MSC content and pSTAT1/3 status in human bone metastatic cancer? MSC content in specimens and tissue microarrays of bone metastatic prostate cancer will be evaluated using immunofluorescent multispectral techniques (Vectra) to identify MSC CD73/CD90/CD105 markers. We will also examine the status of IL-28Rα and pSTAT1/3 in pan-cytokeratin positive prostate cancer cells.

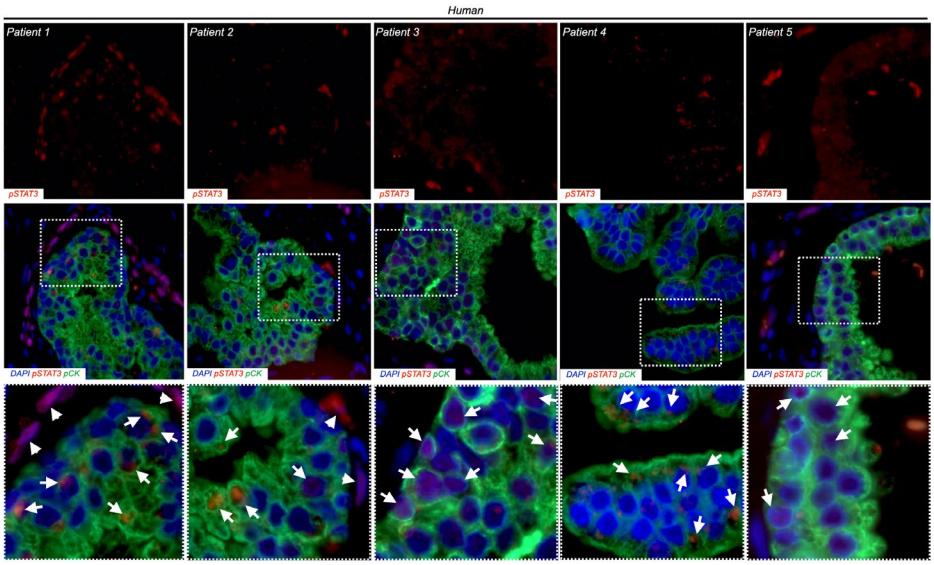


Fig. 3 pSTAT3 localization in human bone metastatic prostate cancer specimens. Representative images of pSTAT3 staining (red) in human samples of bone metastatic prostate cancer (n=10; five representative patients are shown). Pan-cytokeratin (pCK; green) was used to localize prostate cancer cells while DAPI (blue) was used as a nuclear stain. Dashed box in merge represents area of magnification. Arrows used to identify pSTAT3 staining in prostate cancer cells while arrow heads identify positive staining in the supporting bone stromal cells.

Progress. We have completed and published these studies in our *Nature Communications* publication this year. (**Fig. 3** demonstrates the presence of pSTAT3 in human biopsies with clear presence of MSCs and bone lining osteoblasts present around the prostate cancer cells).

4. Impact.

Short-term impact: Studies in this proposal determined how MSCs drive the evolution of more aggressive apoptosis resistant subpopulations of prostate cancer. Our studies shed light on novel molecular mechanisms

that control prostate cancer cell survival namely, IL-28Rα activation and altered downstream STAT1/3 activity. Further, our results demonstrated that MSC educated prostate cancer cells are sensitive to STAT3 inhibition with small molecule inhibitors and provide rationale for targeting this pathway in the context of therapy resistant bone metastatic prostate cancer. In the short term we believe our proposed studies will greatly impact the field's understanding of how cells of the bone microenvironment promote the progression of bone metastatic CRPC.

Long-term impact: Unraveling the mechanisms that contribute to disease resistance in patients with advanced bone metastatic prostate cancer will play a critical role in extending overall survival in this high-risk population. We expect that the results of our pre-clinical studies using STAT3 inhibitors will provide rationale for future clinical trials and/or the design of cancer specific targeted STAT3 inhibitors to offset potential adverse side effects. We are also excited by the prospect that STAT3 inhibition may resensitize chemotherapy resistant disease. The expected results could be of huge potential impact to advanced bone metastatic CRPC patients that have become refractory to chemotherapy.

5. Changes/Problems

We have encountered no difficulties in executing the proposed studies and have made no changes to the experimental approach.

6. Products

Lynch CC. AACR Major Symposia. Bone Marrow Sensing of Distant Tumors: From Early Detection to Possible Therapy. "*MSCs drive the evolution of apoptotic resistant prostate cancer."* AACR, Atlanta, GA April 2, 2019

McGuire JJ, Frieling JS, Lo CH, Li T, Muhammad A, Lawrence HR, Lawrence NJ, Cook LM, **Lynch CC**. Mesenchymal stem cell-derived interleukin-28 drives the selection of apoptosis resistant bone metastatic prostate cancer. Nat Commun. 2021 Feb 1;12(1):723. PMID: 33526787

Also, it should be noted that the primary person working on this project, Jeremy McGuire completed his PhD upon publication of this paper and graduated. He is now a Research Assistant Professor at the University of Rochester.

https://www.urmc.rochester.edu/people/32029437-jeremy-j-mcguire

7. Participants & Other Collaborating Organizations

Name:	*Conor Lynch*
Project Role:	*PD/PI*
Nearest person month worked:	*2*

Name:	*Jasreman Dhillon*
Project Role:	*Co-I*
Nearest person month worked:	*0*

Name:	*Tao Li*

Project Role:	*Res. Project Specialist*
Nearest person month worked:	*12*

Name:	*Marilena Tauro*
Project Role:	*Res Sci III*
Nearest person month worked:	*5*

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, since the last reporting period Dr. Lynch was awarded the below. Please see attached other support in section 9.

CONOR LYNCH
NOW ACTIVE
Title: Developing ULK3 inhibitors for Multiple Myeloma
Major Goals The primary goal of this Team Science application is to further develop novel ULK3 inhibitors and test their in vitro and in vivo efficacy. To this end, there are two specific aims proposed. Aim 1. Design, synthesize, and assess the activity of ULK3 inhibitors using a carefully designed and research operating plan and, Aim 2. Test the efficacy of ULK3 specific compounds on myeloma in vitro and in vivo. We will interrogate the impact of novel ULK3 inhibitors in vitro and on MM progression and overall survival in vivo compared to Momelotinib and the autophagy inhibitor, chloroquine (CQ). we will also determine the role of ULK3 in MM induced bone destruction - a clinically significant aspect of this disease.
Status of Support: Active
Project Number: N/A
MPI: Lynch, C; Lawrence, N
Source of Support: Moffitt Cancer Center/PMRC
Grant Officer: Rae Reuille
Email: Rae.reuille@moffitt.org
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 07/01/2022-06/30/2024
Total Costs for Tissue Core Project:
Calendar Months: 0.24 Calendar Months

8. Special Reporting Requirements
N/A

9. Appendices
Attached.

PHS OTHER SUPPORT
For All Application Types – DO NOT SUBMIT UNLESS REQUESTED

Name of Individual: Lynch, Conor
Commons ID: LYNCHC1

ACTIVE

Title: Defining bone ecosystem effects on metastatic prostate cancer evolution and treatment response usingan integrated mathematical modeling approach
Specific Aims: Aim 1: Develop and calibrate an integrative HCA model of the mPCa-bone ecosystem. Aim 2:Evaluate bone ecosystem impact on mPCa progression in response to standard of care therapy. Aim 3: Optimize mPCa treatment using an eco-evolutionary validated HCA.
Status of Support: Active
Project Number: 5U01CA244101-02
MPI: Lynch, C; Basanta, D
Source of Support: NIH/NCI
Grant officer: Joy Kearse
Email: kearsej@mail.nih.gov
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 06/11/2020 – 05/31/2025
Total Costs:
Calendar Months: 1.8 Calendar months

Year (YYYY)	Person Months (Calendar)
1. 2021	2.04
2. 2022	2.04
3. 2023	1.8
4. 2024	1.8
5. 2025	1.8

Title: Identifying How HDAC Suppression of SLC17A7 Drives Osteosarcoma Progression and Metastasis
Specific Aims: Aim 1. Determine how does SLC17A7 control osteosarcoma cell growth. Aim 2. Interrogate if SLC17A7 is necessary for osteosarcoma progression and metastasis in mice. Aim 3**.** Examine if the administration of low-dose HDAC inhibitors improve the efficacy of single agent chemotherapy.
Status of Support: Recently awarded – pending start date
Project Number: 23L09
Name of PD/PI: Lynch, C.
Source of Support: Florida Biomedical Research Program- Live Like Bella
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Project/Proposal Start and End Date: 04/01/2023 – 02/28/2026
Total Award Amount (including Indirect Costs):
Calendar Months: 1.20 Calendar Months

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

Title: Understanding the influence of bone-metastatic prostate cancer and mesenchymal stromal cells on γδ Tcells, in the bone microenvironment.
Specific Aims: Aim 1: Defining the optimum γδ CAR-T design that will significantly enhance CRPC cytotoxicity.Aim 2: Determining if ZOL can drive γδ CAR-T recruitment and anti-bone metastatic CRPC activity in vivo. Aim3: Dissecting the reciprocal effects of γδ CAR-T on the bone metastatic CRPC microenvironment.
Status of Support: Active
Project Number: 5R01CA241169-03
Name of PD/PI: Abate-Daga, D, Role: Co-Investigator
Role: Source of Support: NIH/NCI
Grant Officer: Salomon, Rachelle
Email: rachelle.salomon@nih.gov
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 03/09/2020-02/28/2025
Total Costs:
Calendar Months: 1.20 Calendar months

Year (YYYY)	Person Months (Calendar)
1. 2021	1.20
2. 2022	1.20
3. 2023	1.20
4. 2024	1.20
5. 2025	1.20

Title: Local and Systemic Control of Multiple Myeloma Colonization and Growth by MMP-13
Major Goals: Aim 1. What are the roles of tumor and osteoblast derived MMP-13 in myeloma progression? Aim2. Does exosomal MMP-13 enhance the skeletal colonization/progression of myeloma? Aim 3. Can selectiveMMP-13 inhibition limit multiple myeloma growth and associated bone disease?
Status of Support: Active
Project Number: 5R01CA239214-03
Name of PD/PI: Lynch, C
Source of Support: NIH/NCI
Grant officer: Joy Kearse
Email: kearsej@mail.nih.gov
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 03/01/2019-02/28/2024
Total Costs:
Calendar Months: 1.8 Calendar months

Year (YYYY)	Person Months (Calendar)
1. 2020	2.22
2. 2021	2.22
3. 2022	2.22
4. 2023	1.8
5. 2024	1.8

Title: Moffitt Cancer Center Support Grant (CCSG)
Major Goals: Moffitt is a free-standing cancer center whose sole mission is "to contribute to the prevention and cure of cancer." By fostering transdisciplinary research, MCC translates unique capabilities in basic, clinical, and population science, as well as training and education, to benefit the patients, caregivers, and professionals through the catchment area, the state of Florida, and beyond. Specific aims are to: 1) Conduct research at the bench, at the bedside, and in the community; 2) Stimulate and foster team science; 3)

Inspire a culture of innovation; 4) Conduct research benefitting the catchment area; 5) Train the next generation of cancer scientists; and 6) Engage in rigorous planning and evaluation activities.
Status of Support: Active
Project Number:
Name of PD/PI: Cleveland, John L.; Role: Scientific Co-Director, TC
Source of Support: NIH/NCI
Grant officer: Joy Kearse
Email: kearsej@mail.nih.gov
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 02/01/2022-01/31/2027
Total Costs for Tissue Core Project:
Calendar Months: 0.60 Calendar Months

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

Title: 2/2 Ponce School of Medicine-Moffitt Cancer Center Partnership
Major Goals: The major goals of this project are to improve cancer outcomes for Hispanic cancer patients in Puerto Rico and Florida who are currently underserved with respect to cancer care, personalized medicine, and participation in clinical research.
Status of Support: Active
Project Number: U54CA163068-10S1
Name of PD/PI: Wright, K./Monteiro, A (MPIs); Role: IAC Member
Source of Support: NIH/NCI
Grant officer: Joy Kearse
Email: kearsej@mail.nih.gov
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 09/25/2017-08/31/2023
Total Costs:
Calendar Months: 0.3 Calendar Months

Year (YYYY)	Person Months (Calendar)
1. 2023	0.24

Title: Developing ULK3 inhibitors for Multiple Myeloma
Major Goals The primary goal of this Team Science application is to further develop novel ULK3 inhibitors and test their in vitro and in vivo efficacy. To this end, there are two specific aims proposed. Aim 1. Design, synthesize, and assess the activity of ULK3 inhibitors using a carefully designed and research operating plan and, Aim 2. Test the efficacy of ULK3 specific compounds on myeloma in vitro and in vivo. We will interrogate the impact of novel ULK3 inhibitors in vitro and on MM progression and overall survival in vivo compared to Momelotinib and the autophagy inhibitor, chloroquine (CQ). we will also determine the role of ULK3 in MM induced bone destruction - a clinically significant aspect of this disease.
Status of Support: Active
Project Number: N/A
MPI: Lynch, C; Lawrence, N
Source of Support: Moffitt Cancer Center/PMRC
Grant Officer: Rae Reuille

Email: Rae.reuille@moffitt.org
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 07/01/2022-06/30/2024
Total Costs for Tissue Core Project:
Calendar Months: 0.24 Calendar Months

Year (YYYY)	Person Months (Calendar)
1. 2023	0.24
2. 2024	0.24

PENDING

Title: Role of ULK3 in Sensitive and Refractory Multiple Myeloma
Specific Aims: Aim 1. Does ULK3 contribute to MM progression and skeletal colonization in vivo? Aim 2. Can the dual ULK3/BRD4 MA9-060 inhibitor compromise MM progression in vivo? Aim 3. Will depleting/targeting ULK3 resensitize refractory MM to proteasome inhibitors?
Status of Support: Pending
Project Number: R01CA269721-A1 (resubmission)
Name of PD/PI: Lynch, C.
Source of Support: NIH/NCI
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Project/Proposal Start and End Date: 09/01/2022 – 08/31/2027
Total Award Amount (including Indirect Costs):
Calendar Months: 1.80 Calendar Months

Year (YYYY)	Person Months (Calendar)
1. 2023	1.80
2. 2024	1.80
3. 2025	1.80
4. 2026	1.80
5. 2027	1.80

Title: ASAH1 Control of Multiple Myeloma Drug Resistance
Specific Aims: Aim 1. Does extracellular vesicle derived ASAH1 contribute to drug resistance in multiple myeloma? Aim 2. What is the role of intrinsic ASAH1 in MM myeloma progression and resistance? Aim 3. Does selective ASAH1 inhibition re-sensitize drug resistant clones to therapies?
Status of Support: Pending
Project Number: R01CA273245 (resubmission)
Name of PD/PI: Lynch, C. and Shain, K. (MPI)
Source of Support: NIH/NCI
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Project/Proposal Start and End Date: 04/01/2023 – 03/31/2028
Total Award Amount (including Indirect Costs):
Calendar Months: 2.40 Calendar Months

Year (YYYY)	Person Months (Calendar)
1. 2023	2.40
2. 2024	2.40
3. 2025	2.40
4. 2026	2.40
5. 2027	2.40

Title: 2/2 Ponce Health Sciences University-Moffitt Cancer Center Partnership
Major Goals: The goal of this project is to reduce cancer disparities in the Hispanic/Latino (H/L) communities and to contribute to the elimination of health disparities in the population at large.
Status of Support: Pending

Project Number: U54 CA163068
Name of PD/PI: Wright, KL/Monteiro, A (MPIs)
Role: Member, Internal Advisory Committee (Planning and Evaluation Core)
Source of Support: NIH/NCI
Primary Place of Performance: Moffitt Cancer Center, Tampa, FL
Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/01/2023 – 08/31/2028 Total Award Amount (including Indirect Costs):
Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (Calendar)
1. 2023-2024	0.24
2. 2024-2025	0.24
3. 2025-2026	0.24
4. 2026-2027	0.24
5. 2027-2028	0.24

Title: An eco-evolutionary mathematical model of multiple myeloma to guide adaptive therapy
Specific Aims: SA1. Mathematically model the interplay between treatment naive and PI-resistant MM populations. SA2. Determine the PI impact on naive and resistant MM evolutionary-ecosystem dynamics. SA3. Optimize standard of care treatments using adaptive therapy approach.
Status of Support: Pending
Project Number: R01CA273342 (resubmission)
Name of PD/PI: Lynch, C. and Basanta, D.
Source of Support: NIH/NCI
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Project/Proposal Start and End Date: 04/01/2023 – 03/31/2028
Total Award Amount (including Indirect Costs):
Calendar Months: 1.80 Calendar Months

Year (YYYY)	Person Months (Calendar)
1. 2023	1.80
2. 2024	1.80
3. 2025	1.80
4. 2026	1.80
5. 2027	1.80

Title: Integrated multiscale modeling of metaphyseal bone injuries and repair
Specific Aims: Aim 1. Develop a mathematical model of bone injury repair and intervention. Aim 2. Scale the ODE bone injury repair model to incorporate aging. Aim 3**.** Identify the optimal intervention strategy to enhance bone injury repair times.
Status of Support: Pending
Project Number: R01
MPI: Lynch, C. and Basanta D (MPI)
Source of Support: NIH/NCI
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Project/Proposal Start and End Date: 07/01/2023 – 06/30/2028
Total Award Amount (including Indirect Costs):
Calendar Months: 1.80 Calendar Months

Year (YYYY)	Person Months (Calendar)
1. 2024	1.80
2. 2025	1.80
3. 2026	1.80
4. 2027	1.80

5. 2028	1.80

Title: Proprietary arginine vasopressin receptor type 1a (AVPR1a) an tagonists for treatment of lethal prostate cancer
Specific Aims: Aim 1. Complete in vivo drug metabolism and pharmacokinetics (DMPK) and selectivity analysis of the novel, AVPR1A-selective balovaptan analogs. Aim 2. Evaluate the lead AVPR1A antagonist in robust CRPC pre-clinical models of established CRPC (including patient-derived xenografts) and invasive disease. Aim 3. Evaluate the lead AVPR1A antagonist in late stage CPRC growth in the bone metastatic niche (including an immunocompetent model) and determine the importance of AVPR1A targeting in the context of autocrine/paracrine actions of AVP
Name of PD/PI: Lynch, C.
Source of Support: US Army
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Project/Proposal Start and End Date: 03/01/2023 – 02/28/2026
Total Award Amount (including Indirect Costs):
Calendar Months: 0.3 Calendar Months

Year (YYYY)	Person Months (Calendar)
1. 2024	0.3
2. 2025	0.3
3. 2026	0.3

COMPLETED WITHIN THE LAST 5 YEARS

Title: Mesenchymal Stem Cell Control of Metastatic Prostate Cancer Cell Evolution and Therapy Resistance in the Bone Microenvironment
Major Goals: The goal of this proposal is to examine the impact of interleukin-28 in promoting the resistance of prostate cancer cells in bone.
Status of Support: Completed
Project Number: W81XWH1810523
MPI: Lynch, C
Source of Support: US Army
Grant Officer: Kimberly Carter
Email: Kimberly.m.carter47.civ@health.mil
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute
Performance Period: 08/15/2018 – 08/14/2022 (NCE)
Total Costs:
Calendar Months: 1.8 Calendar months

5BC-01 (PI: Lynch, C)
Title: *An Integrated computational and biological approach to curing prostate to bone metastases*
Effort: 3.0 Calendar months
Supporting Agency: Bankhead-Coley Cancer Research Program Florida Department of Health
Grants Officer: Jennifer Drake, Government Analyst II
Performance Period: 05/15/2015-05/14/2018
Level of Funding:
Specific Aims: Aim 1. What is the role of TGFβ in bone metastatic prostate cancer? Aim 2: What is the role of cyclical osteoclast influx in prostate cancer growth in bone? Aims 3: What is the contribution of MSC to prostate cancer-induced osteogenesis?
Role: PI

W81XWH1610673 (MPI:Rai/Burnstein)
Title: *Redox Stress-Mediated Inappropriate Androgen Receptor Elevation as a Novel Treatment*

Paradigm for Castration-Resistant Prostate Cancer
Effort: 0.6 Calendar months
Supporting Agency: Department of Defense (PTE: University of Miami)
Grant Officer: Not available
Performance Period: 09/29/2018-09/29/2019
Level of Funding:
Goal: The goal of this project is the development of MMP-13 inhibitors for therapeutic testing and application.
Role: Co-I

Chotiner Pediatric Cancer Research Award (PI: Lynch)
Title: *Evaluating the impact of novel chemotherapies on osteosarcoma progression and metastasis*
Effort: 0.12 Calendar months
Supporting Agency: MCC
Grant Officer: Rae Reuille
Email: Rae.reuille@moffitt.org
Performance Period: 08/01/2015 - 06/30/2018
Level of Funding:
Goal: Our goals in this proposal are straightforward; to test how good this drug combination is in preventing the growth of the osteosarcoma in mouse bones and also in identifying if the drug combination can stop lung metastasis. We expect that our results will be critical for the future design of human clinical trials to treat and impact this deadly pediatric disease.

Chotiner Pediatric Cancer Research Award (PI: Lynch)
Title: *Evaluating the Role of HDAC2 on Osteosarcome Progression and Metastasis*
Effort: 0.12 Calendar months
Supporting Agency: MCC
Grant Officer: Rae Reuille
Email: Rae.reuille@moffitt.org
Performance Period: 10/13/2017 – 10/12/2018
Level of Funding:
Specific Aims: Aim 1. Does genetic ablation of HDAC2 limit OS progression and metastasis in vivo? Aim 2. What is the genetic program being regulated by HDAC2 in OS? We believe our results will be critical for the future design of human clinical trials to treat and impact this deadly pediatric disease.

Team Science Award Pilot Award (PI: Lynch)
Title: *Targeting Drug Resistance in Castration Resistant Prostate Cancer (Pilot projects for PO1)*
Effort: 1.8 Calendar months
Supporting Agency: MCC
Grant Officer: Rae Reuille
Email: Rae.reuille@moffitt.org
Performance Period: 03/15/2018 – 06/30/2018
Level of Funding:
Goal: This proposal is comprised of 4 Pilot projects, which are designed to obtain critical preliminary data for PO1 proposal that was submitted on 25th of May, 2018. Project 1. ACK-1 inhibition for the treatment of bone metastatic castrate resistant prostate cancer (PI: Dr. Conor Lynch)

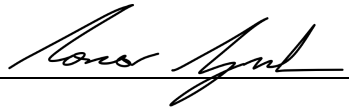
R21CA191981 (PI: Lynch, C)
Title: *Specific Skeletal Targeting of MMP-2 for the Treatment of Multiple Myeloma*
Effort: 2.4 Calendar months

Supporting Agency: NIH
Grants Officer: Renee Carruthers
Performance Period: 07/02/2015-06/30/2018
Level of Funding:
Project Goals: The role of MMP-2 and bone seeking MMP inhibitors will be examined in a novel model of multiple myeloma progression.
Specific Aims: Aim 1. Define the role of tumor and host derived MMP-2 in multiple myeloma progression. Aim 2. Determine the impact of MMP-2 selective BMMPIs as a single therapeutic agent on the progression of multiple myeloma.
Role: PI
Overlap: None

Miles for Moffitt (MPI: Lynch, C/Schonbrunn, E)
Title: *Dual BET Domain/Kinase Inhibitors for the Treatment of Multiple Myeloma*
Effort: 0.60 Calendar months
Supporting Agency: Moffitt Cancer Center
Grant Officer: Rae Reuille
Email: Rae.reuille@moffitt.org
Performance Period: 07/01/2018 - 05/31/2020
Level of Funding:
Goal: The goals of this project are to determine the efficacy of novel dual kinase inhibitors on the progression of multiple myeloma and to dissect the potential mechanisms of action of these reagents
Role: Contact PI
Overlap: None

Gift from the Community Foundation for Brevard (PI: Lynch)
Title: *Prostate Cancer Research*
Supporting Agency: Community Foundation for Brevard
Grant Officer: Dawn Myers
Email: cfbrevard.org
Performance Period: 09/10/2019-09/10/2020
Level of Funding:
Goal: This gift is to solely support the Lynch lab for Prostate Cancer Research
Role: PI
Overlap: None

IN-KIND
None
OVERLAP
None.
ADDITIONAL SUPPORT FROM FOREIGN OR DOMESTIC ENTITIES
None

*Signature: 

Date: March 6th, 2023

*Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Other Support

ACTIVE

***Title: Phase II Clinical Trial of Green Tea Catechin in Men on Active Surveillance**
Major Goals: The goal of the phase II, randomized clinical trial to evaluate the bioavailability, safety, effectiveness and mechanism by which Green tea catechins prevent clinical progression of disease in men on Active Surveillance for prostate cancer.
*Status of Support: Active
Project Number: R01 CA235032-01A1
Name of PD/PI: Kumar (Dhillon, Co-Investigator)
*Source of Support: NIH/NCI
Contracting/Grants Officer: Candace M Cofie, candace.cofie@nih.gov
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 06/01/2019-06/30/2025
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2019-20	0.6 calendar months
2. 2020-21	0.6 calendar months
3. 2021-22	0.6 calendar months
4. 2022-23	0.12 calendar months *effort change 7/1/22
5. 2023-24	0.12 calendar months

Overlap: None

***Title: Characterize the Immune-Oncologic Profile of Lethal Prostate Cancer in African American Men and Develop New Therapeutic Avenues for This Patient Population**
Major Goals: The goal of this project is to characterize immune regulators of lethal PCa in AAM as compared with EAM and to identify novel immune targets for treatment.
Aim 1: Characterize and compare the immuno-oncology mechanisms of PCa in AAM and EAM.
Aim 2: Identify immune-related genes as novel treatment targets for PCa in AAM.
*Status of Support: Active
Project Number: W81XWH1910435
Name of PD/PI: Yamoah/Rounbehler/Park (Dhillon, Co-Investigator)
*Source of Support: Department of Defense
Contracting/Grants Officer: Teresa Parker-Reeser, Teresa.M.ParkerReeser.civ@mail
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 08/15/2019-07/31/2023
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2019-20	0.24 calendar months
2. 2020-21	0.24 calendar months

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Year (YYYY)	Person Months (##.##)
3. 2021-22	0.24 calendar months

Overlap: None.

***Title: Defining bone ecosystem effects on metastatic prostate cancer evolution and treatment response using an integrated mathematical modeling approach**
Major Goals: Overall, this unique integrated approach will elucidate how the bone ecosystem regulates mPCa evolution and resistance and will yield a scalable HCA that can be personalized for use in human clinical trial settings. Aim 1. Develop and calibrate an integrative HCA model of the mPCa-bone ecosystem.
Aim 2. Evaluate bone ecosystem impact on mPCa progression in response to standard of care therapy.
Aim 3. Optimize mPCa treatment using an eco-evolutionary validated HCA.
*Status of Support: Active
Project Number: U01CA244101
Name of PD/PI: Lynch/Basanta (Dhillon, Co-Investigator)
*Source of Support: NIH/NCI
Contracting/Grants Officer: Joy Kearse, Email: kearsej@mail.nih.gov
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 06/11/2020-05/31/2025
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2020-21	0.6 calendar months
2. 2021-22	0.6 calendar months
3. 2022-23	0.6 calendar months
4. 2023-24	0.6 calendar months
5. 2024-25	0.6 calendar months

Overlap: None.

***Title: Disrupting the prostate tumor microenvironment in African American men to promote response to immune-modulatory therapy**
Major Goals: The specific aims are to: 1) To functionally characterize the differential expression pattern of immuno-modulatory genes within the tumor microenvironment in AAM using a computational deconvolution approach. 2) To determine whether the functional and mechanistic differences in tumor and immune microenvironment can be exploited for therapeutic gain in AAM. 3) To evaluate whether AAM with increased TIME will respond better to combined immuno-modulatory therapy.
*Status of Support: Active
Project Number: 1R37CA264518-01A1
Name of PD/PI: Yamoah (Dhillon, Co-Investigator)
*Source of Support: NIH/NCI
Contracting/Grants Officer:
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 09/01/2022-08/31/2027
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Year (YYYY)	Person Months (##.##)
1. 2022-23	0.6 calendar months
2. 2023-24	0.6 calendar months
3. 2024-25	0.6 calendar months
4. 2025-26	0.6 calendar months
5. 2026-27	0.6 calendar months

Overlap: None

***Title: Decoding the Resistance Mechanisms to Oncolytic Virotherapy in Muscle-Invasive Bladder Cancer**
Major Goals: The goal is to leverage samples collected on trial to dissect the potential mechanisms of resistance to oncolytic virotherapy in bladder cancer. Specific Aims: 1) Explore the predictive value of pre-treatment biomarkers for viral infectivity and treatment response, 2) Interrogate the mechanism of anti-tumor immunity induction following oncolytic virus and ICI.
*Status of Support: Active
Project Number: W81XWH2210395
Name of PD/PI: Li,R. (Dhillon, Co-Investigator)
*Source of Support: DoD/CDMRP
Contracting/Grants Officer:
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 09/01/2022-06/30/2025
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022-23	0.24 calendar months
2. 2023-24	0.24 calendar months
3. 2024-25	0.24 calendar months

Overlap: None

***Title: ECOG-ACRIN NCORP Research Base -CT (A Phase II Randomized Double Blinded Study of Green Tea Catechins (GTC) vs. Placebo in Men on Active Surveillance for Prostate Cancer: Modulation of Biological and Clinical Intermediate Biomarkers)**
Major Goals: Positive results obtained from this trial will inform planning and implementation of a well-powered prospective, large, national phase III clinical trial using GTC for preventing progression of PCa in men on AS that can be performed not only at academic but also in non-academic institutions.
*Status of Support: Active
Project Number: UG1 CA189828-08
Name of PD/PI: Kumar (Dhillon, Co-Investigator)
*Source of Support: NIH/NCI PTE: ECOG
Contracting/Grants Officer: Deb Strandberg email: dstrandberg@ecog-acrin.org
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 08/01/2020-07/31/2023 (NCE)*
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Year (YYYY)	Person Months (##.##)
2022-23	0.6 calendar months *effort begin 7/1/22.

PENDING

***Title: Partnership to Assess Viral and Immune Landscape Intersections with ONcology for People Living with HIV (PAVILION)**
Major Goals: The overall goal of PAVILION is to provide the data necessary to inform prevention and therapeutic strategies to reduce the burden of cancers among people living with HIV in sub-Saharan Africa. Aim 1: Establish a multi-national partnership with research infrastructure to conduct collaborative, innovative, and impactful research that advances prevention and treatment of infection-related cancers among PLWH in Sub-Saharan Africa. Aim 2: Understand the fraction of tumors attributable to specific oncogenic viruses, the characterization of the immune microenvironment of tumors unique to the setting of HIV, and a more complete understanding of clinical outcomes for PLWH and cancer in SSA. Aim 3: Build capacity through active mentorship and training programs for early stage and junior faculty at partnership institutions.
*Status of Support: Pending
Project Number: U54CA277834
Name of PD/PI: Giuliano/Coghill/Botha MPI (Dhillon, Co-Investigator)
*Source of Support: NIH/NCI
Contracting/Grants Officer: pending
*Primary Place of Performance: Stellenbosch University, South Africa; University of Zimbabwe, Zimbabwe; H. Lee Moffitt Cancer Center & Research Institute, Inc.; Vanderbilt University Medical Center; German Cancer Research Center (DKFZ); Cornell University Weill College of Medicine
Project/Proposal Start and End Date: 12/01/2022-11/30/2027
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022-23	0.24 calendar months
2. 2023-24	0.24 calendar months
3. 2024-25	0.24 calendar months
4. 2025-26	0.24 calendar months
5. 2026-27	0.24 calendar months

Overlap: None

***Title: Development of a Rare Genitourinary Cancer Biorepository with Multi-omics Profiling and Matched Clinical Data to Enable Therapeutic Target Discovery**
Major Goals: We hypothesize a prospective rare GU cancer biorepository, coupled with multi-omics profiling and matched clinical data, will accelerate tumor classification, novel target discovery and drug repurposing. Further, this public resource will support rare GU tumor community connections to improve knowledge dissemination. The aims of this project are to 1) develop infrastructure to launch and sustain a prospective rare GU tumor biorepository with matched clinical data; 2) perform integrative multi-omics analyses on rare GU tumors for molecular classification and drug target discovery and 3) develop a visualization tool which integrates multi-omics and matched de-identified clinical data for knowledge dissemination and discovery.
*Status of Support: Pending

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Project Number:
Name of PD/PI: Grass (Dhillon, Co-Investigator)
*Source of Support: USArmy, CDMRP
Contracting/Grants Officer: pending
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Inc
Project/Proposal Start and End Date: 09/01/2023-08/31/2026
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2023-24	0.72 calendar months
2. 2024-25	0.72 calendar months
3. 2025-26	0.72 calendar months

Overlap: None

***Title: bpMRI and polygenic risk score for optimizing detection and management of clinically significant prostate cancer in African American Men.**
Major Goals: Aim 1: Define the role of PRS and bpMRI as a screening tool for early detection of clinically significant PCa in AAM. Aim 2: Reduce time to management for screening positive patients (Biopsy positive AAM with clinically significant disease).
*Status of Support: Pending; submitted 10/17/2022
Project Number: TBD
Name of PD/PI: Jong Park, PhD
*Source of Support: American Cancer Society – Research Scholar Grant
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Inc.
Project/Proposal Start and End Date: 07/01/2023 – 06/30/2027
*Total Award Amount (including Indirect Costs):
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

Overlap: None

***Title: Functional roles of HELLPAR macroRNA and associated mRNAs in regulation of prostate cancer aggressiveness in African American men.**
Major Goals: 1) Investigate differential expression of the mcrRNA and mRNA genes as biomarkers for prostate cancer aggressiveness using clinical specimens from AA and CA patients. 2) Investigate HELLPAR and target mRNAs mediated modulation of the downstream effector genes involved in specific signaling pathways as biomarkers for aggressive prostate cancer in AA patients. 3) Investigate the involvement of HELLPAR in tumor growth and treatment response of PCa cells using xenograft models and cell lines from AA and CA origins.
*Status of Support: Pending
Project Number: TBD
Name of PD/PI: MPIs: Ratna Chakrabarti, PhD & Jong Park, PhD
*Source of Support: NIH/NCI (R01)

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Primary Place of Performance: Univ. of Central Florida & Moffitt Cancer Center
Project/Proposal Start and End Date: 07/01/2023 – 06/30/2028
*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

Overlap: None

***Title: An integrative analysis of HELLPAR macroRNA and associated mRNAs involved in cellular functions in African Americans with prostate cancer.**
Major Goals: 1) Investigate differential expression the mcrRNA and mRNA and mRNA genes as biomarkers for prostate cancer aggressiveness using clinical specimens from AA and EA patients. 2) Investigate gene functions involved in specific signaling pathways for aggressive PCa using PCa cell lines from AA and EA men. 3) Examine the function of this mcrRNA and mRNA network in preclinical models upon knock-down of *HELLPAR* in cell lines from AA and EA patients. Additionally, this model will be used for examining treatment response.
*Status of Support: Pending; submitted 08/25/2022
Project Number: TBD
Name of PD/PI: Ratna Chakrabarti, PhD (subcontract site PI: Jong Park, PhD)
*Source of Support: DoD-Prostate Cancer Research Program
Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Inc.
Project/Proposal Start and End Date: 09/30/2023 – 09/29/2026
*Total Award Amount (including Indirect Costs):
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

Overlap: None

PREVIOUS

***Title: Mesenchymal Stem Cell Control of Metastatic Prostate Cancer Cell Evolution and Therapy Resistance in the Bone Microenvironment**
Major Goals: The goal is to understand how mesenchymal stem cells contribute to the generation of apoptosis resistant prostate cancer cells via an IL-28 mechanism.
Aims: 1) Do MSC-educated prostate cancer cells have a growth advantage or impact bone disease in vivo compared to MSC naïve prostate cancer cells? 2) Is IL-28 the primary mechanism through which MSCs drive apoptotic resistant bone metastatic prostate cancer? 3) Can STAT3 inhibitors sensitize bone metastatic prostate cancer to chemotherapy? 4) What is the MSC content and pSTAT1/3 status in human bone metastatic cancer?
*Status of Support: Complete

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Project Number: W81XWH1810523
Name of PD/PI: Lynch (Dhillon, Co-Investigator)
*Source of Support: Department of Defense
Contracting/Grants Officer: Janet P. Kuhns, janet.p.kuhns.civ@mail.mil
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 08/15/2018-08/14/2022(NCE)
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2018-19	0.36 calendar months
2. 2019-20	0.36 calendar months
3. 2020-21	0.36 calendar months
4. 2021-22 (NCE)	0 calendar months

Overlap: None (inactive)

***Title: Characterize the Immune-Oncologic Profile of Lethal Prostate Cancer in African American Men and Develop New Therapeutic Avenues for This Patient Population**
Major Goals: The goal of this project is to characterize immune regulators of lethal PCa in AAM as compared with EAM and to identify novel immune targets for treatment.
Aim 1: Characterize and compare the immuno-oncology mechanisms of PCa in AAM and EAM.
Aim 2: Identify immune-related genes as novel treatment targets for PCa in AAM.
*Status of Support: Complete
Project Number: W81XWH1910435
Name of PD/PI: Yamoah/Rounbehler/Park (Dhillon, Co-Investigator)
*Source of Support: Department of Defense
Contracting/Grants Officer: Teresa Parker-Reeser, Teresa.M.ParkerReeser.civ@mail
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 08/15/2019-07/31/2022
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2019-20	0.24 calendar months
2. 2020-21	0.24 calendar months
3. 2021-22	0.24 calendar months

Overlap: None (inactive)

***Title: 2/2 Ponce Health Sciences University-Moffitt Cancer Center Partnership**
Major Goals: The goal of this grant is to further grow and engage faculty and students in cancer precision medicine research that directly impacts H/L populations in Florida and Puerto Rico.
*Status of Support: Complete
Project Number: U54CA163068
Name of PD/PI: Wright/Monteiro (Dhillon, Co-Investigator)
*Source of Support: NIH/NCI
Contractor/Grants Officer: Sandra San Miguel-Majors, sandra.sanmiguel-majors@nih.gov
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Project/Proposal Start and End Date: 09/25/2017-08/31/2022*
* Total Award Amount (including Indirect Costs):
* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
5. 2021-2022* *Effort begin 3/1/2021	0.12 calendar months

Overlap: None (inactive)

***Title: Multicenter validation of genomic subtyping and whole transcriptome profiling for predicting non-organ confined disease in patients with clinical T1/T2 urothelial carcinoma of the bladder**
Major Goals: The primary study objective is to validate the finding that patients with cT1/T2 urothelial carcinoma of the bladder (UCB) with luminal subtype have lower risk of upstaging to non-organ confined disease (NOC) (pT3/4Nany) than patients with non-luminal subtype. Therefore, the primary endpoint for this study is upstaging of clinical stage to non-organ confined disease (any T3/T4 pathologic stage or N+ disease) detected at radical cystectomy (RC). The secondary endpoint for this study is cancer-specific mortality (CSM) following surgery.
*Status of Support: Active
Project Number: Research Agreement
Name of PD/PI: Li (Dhillon, Co-Investigator)
*Source of Support: Decipher Biosciences
Contractor/Grants Officer: Decipher Biosciences
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 09/31/2021-03/12/2022*
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021-2022* *Effort begin 1/2/2022	0.24 calendar months

Overlap: None (inactive)

***Title: Validating and tailored targeting of identified immune signature in the tumors of African American Prostate cancer patients**
Major Goals: To validate the increased Treg presence and differentially expressed inhibitory and stimulatory receptors in tumor-associated T cells of AA PCa patients relative to their Caucasian counterparts and to determine whether the immunological landscape of African American prostate cancer is preferentially amenable to Treg targeting and immune checkpoint inhibition
*Status of Support: Inactive
Project Number:
Name of PD/PI: Adegbee (Dhillon, Co-Investigator)
*Source of Support: Mike Slive Foundation
Contracting/Grants Officer: inactive
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 01/01/2021 – 12/31/2021
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Year (YYYY)	Person Months (##.##)
1. 2021	0.24 calendar months

Overlap: None (inactive)

***Title: Deciphering the role of EGFR splice variants and tumor-immune microenvironment in renal cell carcinoma**

Major Goals: The goal of our research project is to characterize the clinical associations with patients who have EGFR splice variants and identify immune and molecular associations that predict responses to the 2 most commonly used classes of systemic therapies in mRCC: TTs and ITs. Specific Aims: Aim 1. Evaluate the prevalence and determine the clinical significance of a recently identified novel epidermal growth factor receptor (EGFR) splice variant in the 131 RCC tumors. Aim 2. Identify and characterize the TIM of 131 RCC tumors in the context of their EGFR splice status and the presence and geographic location (i.e. colocalization) of candidate tissue biomarkers for treatment response.
*Status of Support: Inactive
Project Number: W81XWH1910663
Name of PD/PI: Manley (Dhillon, Co-Investigator)
*Source of Support: Dept. of the Army – USAMRAA
Contracting/Grants Officer: (inactive) Raven Conner, raven.n.conner.civ@mail.mil
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 08/15/2019-08/14/2021
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2019-20	0.36 calendar months
2. 2020-21	0.36 calendar months

Overlap: None (inactive)

***Title: Genomic Predictors of Aggressive and Lethal Prostate Cancer in African American Men**

Major Goals: The specific aims of this proposal are to: (1) to identify tumor DNA- and RNA-based biomarkers that are associated with aggressive and lethal PCa in AAM; and (2) assess if ETA-dependent genomic methylation status predicts radiosensitivity in prostate tumors. We will evaluate the performance of our novel tumor DNA- and RNA-based biomarker signatures in predicting aggressive lethal PCa using clinical endpoints, specifically: (1) adverse pathologic outcomes, defined as evidence of pathologic T3 disease (pT3: extraprostatic extension and/or seminal vesicle invasion); (2) 3-year biochemical recurrence rate (BCR); and (3) 5-year rate of metastatic/lethal PCa (distant metastases [DM]).
*Status of Support: Inactive
Project Number: N/A
Name of PD/PI: Park/Yamoah (Dhillon, Co-Investigator)
*Source of Support: V Foundation
Contact: (inactive) Carole Wagner, kowoeye@jimmyv.org
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 10/01/2017-09/30/2020
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Years (YYYY)	Person Months (##.##)
2017-2020	0.24 calendar months

Overlap: None (inactive)

***Title: Multi-Scale Modeling of Bone Environment Responses to Metastatic Prostate Cancer**
Major Goals: Our innovative studies will; 1) generate a robust and dynamic multi-scale computational model of the prostate cancer-bone microenvironment, 2) will define novel roles for monocyte derived cells (osteoclasts/M1/M2 macrophages) in driving prostate cancer growth, 3) will define new roles for MSCs in promoting prostate cancer induced osteogenesis, 4) will predict the key circuits driving bone metastatic prostate cancers and 5) will predict and test curative strategies for eradicating bone metastatic prostate cancer.
Aim 1: An enhanced molecular and cellular multiscale computational model will be developed and the key circuits driving bone metastatic cancer growth will be predicted.
Aim 2: We will predict the role of cyclical osteoclast infiltration and macrophage polarization (M1/M2) in promoting prostate cancer growth.
Aim 3: Will dissect the role of MSC recruitment in prostate cancer induced osteogenesis in silico. Importantly, the predictions generated in each aim will be tested with relevant in vivo rodent models of bone metastatic prostate cancer and validated in human clinical specimens.
*Status of Support: Inactive
Project Number: U01CA202958
Name of PD/PI: Basanta/Lynch (Dhillon, Co-Investigator)
*Source of Support: NIH
Contact: (inactive) Jennifer Couch couchj@ctep.nci.nih.gov
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 06/08/2016-05/31/2022
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Years (YYYY)	Person Months (##.##)
2016-2020	0.12 calendar months

Overlap: None (inactive)

Title: Modeling spatial ecology in clear cell renal cell carcinoma model: A novel tool to support drug sequencing decisions
Major Goals: Our project will seek to identify how unique tumor-stromal architecture can differentiate between those patients who will respond and not respond to the 2 most common drug classes given for the first-line treatment of metastatic ccRCC. The goal is to develop computational models on the basis of spatial ecology in ccRCC that would be used to study larger patient cohorts.
Specific Aims: Aim 1: Characterize the TSM of ccRCC tumors through histological analyses using specific immunohistochemical stromal and proliferative markers, which will capture differences in stromal architecture among patients who responded to or progressed on specific classes of systemic therapies. Aim 2: Develop novel computational tools and in silico models that can be used to better predict tumor evolution by inputting analyses from Aim 1 on stromal architecture and proliferative markers. A scoring system built on spatial-ecology that can be applied to RCC in relationship to specific treatments will be used to estimate the most likely cancer-stromal cell interaction range. This will be tested to augment treatment response and clinical outcomes.
*Status of Support: Inactive
Project Number: W81XWH1910655

Name of Individual: Dhillon, Jasreman
Commons ID: JDHILLON

Name of PD/PI: Manley (Dhillon, Co-Investigator)
*Source of Support: Dept. of the Army – USAMRAA
Contact: (inactive) Raven Conner, Grants Management Specialist; raven.n.conner.civ@mail.mil
*Primary Place of Performance: H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL
Project/Proposal Start and End Date: 08/15/2019 – 08/14/2020
*Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period.

Years (YYYY)	Person Months (##.##)
2019-2020	0.36 calendar months

Overlap: None (inactive)

IN-KIND
*Summary of In-Kind Contribution: NONE

OVERLAP
As noted individually above.

I, PD/PI or other senior/key personnel, certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

*Signature: jasreman dhillon (Mar 7, 2023 11:44 EST)

Date: Mar 7, 2023

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