AWARD NUMBER: W81XWH-21-1-0763

TITLE: Identifying Different Metabolic Subtypes of Prostate Cancer for Early Therapeutic Assessment

PRINCIPAL INVESTIGATOR: Pratip Bhattacharya, Ph.D.

CONTRACTING ORGANIZATION: The University of Texas MD Anderson Cancer Center Houston, TX

REPORT DATE: October 2023

TYPE OF REPORT: Annual

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
October 2023	Annual	01Sep2022-31Aug2023

4. TITLE AND SUBTITLE

Identifying Different Metabolic Subtypes of Prostate Cancer for Early Therapeutic Assessment

5a. CONTRACT NUMBER
W81XWH-21-1-0763

5b. GRANT NUMBER
PC200641

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Pratip Bhattacharya, Ph.D.

E-Mail: pkbhattacharya@mdanderson.org

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

The University of Texas MD Anderson Cancer Center
1515 Holcombe Blvd
Houston, Texas 77030-4009

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

In the second reporting project, we have made substantial progress on Specific Aim I and II and we have started working on the most impactful aim of the project, Specific Aim III on imaging to overcome Enzalutamide resistance by targeting Monocarboxylate Transporter (MCT) pathway. Our preliminary HP-MR data on one of the AR positive Enzalutamide resistant PDX models (274-4) shows that MCT inhibition with the clinical drug, Syrosingopine can overcome resistance to Enzalutamide. Two manuscripts are currently under review and a conference abstract that has resulted in an invite for oral presentation at the 25th International Symposium on Radiopharmaceutical Sciences (iSRS) in May 22-26, 2023. The results from the metabolic imaging and other "omics" data from this project is also laying the foundation of an Artificial Intelligence driven project on classifying the different sub-types of prostate cancer at the time of initial diagnosis.

15. SUBJECT TERMS
None listed.

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	59	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. INTRODUCTION:

Patients with advanced prostate cancer (PCa) receive anti-androgens (Enzalutamide) as the first line of treatment. Unfortunately, many patients develop resistance, and the disease relapses with aggressive histology and metastatic castrate-resistant (mCRPC) phenotype. Treatment options for mCRPC patients are limited and continue to pose a significant oncological challenge. There is growing recognition that alterations in cell metabolism and reprogramming of metabolic pathways are key drivers of PCa aggressiveness, progression and eventual resistant to therapy. The overarching goal of this project is to develop metabolic imaging to target treatment strategies of different metabolic sub-types of PCa. Recent studies from our group have demonstrated that the tumor's metabolic profile that impacts anti-androgens response can be identified early on by usinghyperpolarized Magnetic Resonance Imaging (HP-MRI). We also discovered that MonocarboxylateTransporter (MCT) is dysfunctional in mCRPC and may be a viable target for therapeutic intervention. In this research, we will employ HP-MRI and Positron Emission Tomography (PET) to interrogate both glycolysis and carnitine metabolism that is closely linked with fatty acid metabolism in PCa. We will evaluate the treatment response of Enzalutamide in clinically relevant patient derived mouse models of PCa. We will correlate imaging data with metabolomics, immunohistochemistry and transcriptome profile analysis of the *ex vivo* tissue samples to elucidate the metabolic drivers of resistance. In two of the resistant models, we will attempt to restore drug sensitivity by targeting Monocarboxylate Transporter (MCT) pathway and image this transformation from resistance to sensitization by performing HP-MRI and PET. If successful, this research will provide mechanistic insights to advance our knowledge about mCRPC tumors and validate the efficacy of targeting MCT protein for therapeutic benefit.

2. KEYWORDS:

prostate cancer, treatment resistance, hyperpolarization, ^{13}C MR, ^{18}F-FPIA, PET, MRI, mCRPC, PDX, PCa, MCT, ENO2, metabolic imaging

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Specific Aim I: To perform HP-^{13}C Pyruvate MRI, [^{18}F]FPIA -PET imaging in parallel in four well characterized patient derived xenograft (PDX) murine models of prostate cancer *in vivo* before and after the antiandrogen therapy with Enzalutamide to image both alteration in glycolytic and fatty acid oxidation pathways after treatment response. (1-15 Months).
Under Specific Aim I, there are four tasks:
Task 1: Generation of PDX models: 100% completed
Task 2: Synthesize ^{18}F-Fluoropivalate ([^{18}F]FPIA). 100% completed
Task 3: ^{13}C Pyruvate HP-MRI and [^{18}F]FPIA PET to interrogate both glycolysis and fatty metabolism at the preclinical PET-MRI scanner at the before treatment and three other time points on the 7 day, 14th day of treatment and upon resistance. 75% completed

Task 4: Harvesting of tumors and storing for NMR spectroscopy, Mass spectrometry, immunohistochemistry and RNA sequencing studies at different time points. 100% completed

Specific Aim II: To elucidate the metabolic drivers of ADT resistance. (9-24 months)
Under Specific Aim II, there are four tasks.
Task 5: NMR spectroscopy based metabolomics of flash frozen tissues (four PDX lines; from task 4). 75% completed
Task 6: Mass Spectrometry based metabolomics (four PDX lines; from task 4). 50% completed
Task 7: Transcriptome analysis of Tumors (four PDX lines; from task 4). 25% completed
Task 8: Immunohistochemistry analysis of Tumors (four PDX lines; from task 4). 25% completed

Specific Aim III: To image overcoming the ADT resistance by targeting Monocarboxylate Transporter (MCT) pathway by performing HP-13C Pyruvate MRI in two well characterized patient derived xenograft (PDX) murine models of prostate cancer *in vivo.* [18F]FPIA -PET imaging, performed in parallel, will inform on correlation of the modulation of glycolysis (via MCT inhibition with the clinical drug, Syrosingopine) with modulation of fatty acid oxidation. (15-36 months)
Task 9: Two of the Enzalutamide resistant PDX models. 274-4 and 133 will be employed for imaging experiments. When the SC tumors are about 0.5 cm, the tumor bearing mice will be randomized into two treatment groups (N=20 per PDX sub-type). Mice in Group 1 will receive 10mg/kg body wt Enzalutamide by oral gavage while Group 2 mice will receive Enzalutamide and intraperitoneal injection of Syrosingopine, MCT4 inhibitor (7.5mg/kg body weight). 25% completed
Task 10: Synthesize ^{18}F-Fluoropivalate ([^{18}F]FPIA). 100% completed
Task 11: Simultaneous ^{13}C Pyruvate HP-MRI and [^{18}F]FPIA PET to interrogate both glycolysis and fatty acid oxidation pathways at the preclinical PET-MRI scanner at two time points on the 14th and 21st day. 25% completed
Task 12: Harvesting of tumors and storing for NMR spectroscopy, Mass spectrometry, immunohistochemistry and RNA sequencing studies at different time points. 20% completed
Task 13: NMR spectroscopy based metabolomics of flash frozen tissues (two PDX lines; from task 12). 20% completed
Task 14: Mass Spectrometry based metabolomics (two PDX lines; from task 12). Not started
Task 15: Transcriptome analysis of Tumors (two PDX lines; from task 12). Not started
Task 16: Validation of nominated genes. Not started
Task 17: Immunohistochemistry analysis of Tumors (two PDX lines; from task 12). Not started

What was accomplished under these goals?

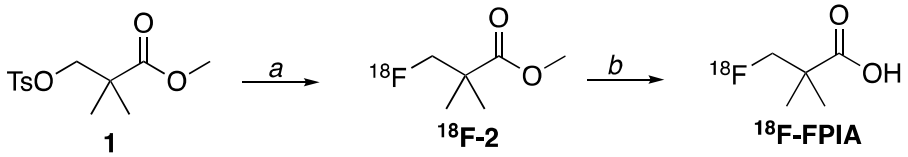
A. Major Activities:

Aim I, Task 1: Generation of PDX models:
In the proposal, **we suggested these following four PDX models for study**
274-4 (AR+, Enzalutamide resistant)
133-3 (AR+, Enzalutamide resistant)
183-A (AR+, Enzalutamide sensitive)
170-1 (AR+, Enzalutamide sensitive)
However, we ran into some logistical challenges to generate all PDX models we originally proposed from our PDX core facility as the core ran into several issues in one past one year. Therefore, we have kept performing experiments on the models that are available and fit the overall goals of the project.

PDX models employed so far in the study

PDX	HP-MR	FPIA-PET	NMR met	MS met	AR	Enzalutamide	phenotype
144	x	x	x	x	negative		
118	x	x	x		negative		
232	x	x	x	x	negative		Adenocarcinoma
337	x	x	x		negative		Neuroendocrine carcinoma
183	x	x	x	x	positive	sensitive	
274	x	x	x	x	positive	resistant	
177	x	x	x		negative		
180	x		x	x	positive	sensitive	
477	x	x	x		positive	resistant	

Aim I, Task 2: Radiosynthesis of ^{18}F-Fluoropivalate ([^{18}F]FPIA) has been streamlined in the last report and the automated radiosynthesis of ^{18}F-FPIA using the GE TracerLab FX FN™ platform is now routinely performed at MD Anderson Cancer Center. The details wre reported in the report last year. I have included a slightly optimized versions in this report as well.
Radiosynthesis of ^{18}F-Fluoropivalate (^{18}F-FPIA).



Scheme 1 Synthesis of ^{18}F-FPIA. *Reaction conditions: a)* ^{18}F-fluoride, K_{222}, $KHCO_3$, DMSO, 105 °C, 10 min; *b)* NaOH, then phosphate buffer.

Synthesis of precursor methyl 2,2-dimethyl-3-[(4-methylbenzenesulfonyl)oxy]propanoate (1)
Precursor methyl 2,2-dimethyl-3-[(4-methylbenzenesulfonyl)oxy]propanoate (**1**) was synthesized accordingly with the published procedure (Pisaneschi et al, *Med. Chem. Commun.*, **2013**, ***4***, 1350-

1353) and purified with a Biotage® Selekt system using a 25 g column and 7% to 60% ethyl acetate/hexane eluent over 10 min. Precursor **1** was obtained in 70% yield, as a white solid, and spectroscopically characterized to match the published material.

Automated radiosynthesis of ^{18}F-FPIA using the GE TracerLab FX FN™ platform.

An aqueous solution of ^{18}F-fluoride in oxygen-18 enriched water (2 mL) was transferred from the cyclotron target to the warm-cell containing the TracerLab FX FN module (General Electric Healthcare, Münster, Germany). The ^{18}F-fluoride was trapped on an ion exchange cartridge (pre-conditioned Sep-PAK® Light QMA Cartridge, ABX GmbH, Radeberg, Germany) and eluted into the reactor with a potassium bicarbonate and Kryptofix$_{222}$ water/CH_3CN solution (1 mL; stock solution: 40 mg of $KHCO_3$, 240 mg of K_{222}, 4 mL of water, 16 mL of CH_3CN). The solution was dried under vacuum and nitrogen flow at 60 °C for 2 min. Dry CH_3CN (500 µL) was added and the mixture was azeotropically dried at 120 °C for an additional 3 min. To the reactor containing dry ^{18}F-fluoride was added precursor **1** (8 mg) in anhydrous DMSO (500 µL) and water (1 µL) and heated at 105 °C for 10 min to produce **^{18}F-2**. After cooling to 60 °C, a solution of NaOH (1 mL, 1M) was added to the reactor and heated to 60 °C for 10 min to produce ^{18}F-FPIA. The reactor was cooled at 40 °C and NaH_2PO_4 (2.5 mL, 0.5 M) was added. The crude reaction mixture was filtered and transferred to the TracerLab HPLC loading vial. The HPLC injection loop (5 mL) was filled and ^{18}F-FPIA was purified by semi preparative HPLC (Luna 5 µm C18(2) column, 100 Å, 250 x 10 mm) column with a mobile phase of NaH_2PO_4 (10 mM) containing 1% EtOH at a flow rate of 4 mL/min. A radioactive peak corresponding to ^{18}F-FPIA eluted at ca. 6.5 min, which was cut for 30-40 sec via a sterile filter (PALL Acrodisc 0.2 µm) into a sterile vial. Quality control was carried out by analytical radio-HPLC (Agilent 1100, Santa Clara, CA, USA) using an Alltech Econosil C18 column (3.5 µm, 4.6x250 mm) with a 30% to 95% CH_3CN/water over 19 min gradient. The identity of the radiolabeled compound was confirmed by co-elution with commercially available fluoropivalate (Thermo Fisher Scientific, Waltham, MA).

^{18}F-FPIA was obtained in 25.4±3.8 (n=9) activity yield (non-decay corrected), >99% radiochemical purity and high UV purity

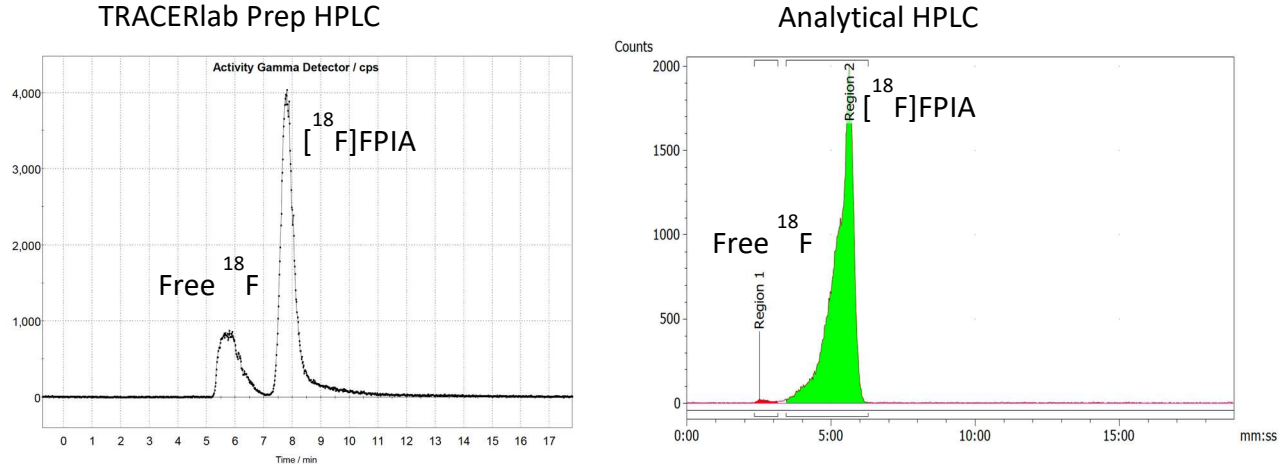


Figure 1: HPLC traces of ^{18}F-FPIA production in Tracerlab Prep HPLC and analytical HPLC. Analytical HPLC indicated production of ^{18}F-FPIA > 99% radiochemical purity.

Aim I, Task 3: Imaging experiments.

Mice were housed in pathogen-free conditions and cared for in accordance with guidelines set by the AALAC and were supervised by the IACUC at MD Anderson Cancer Center. All procedures are performed using 1.5% isoflurane as the anesthetic. Standard MR sequences will be employed.

[1-^{13}C] Pyruvate HP-MRI*: In vivo* imaging were performed on a 7T MRI animal scanner situated adjacent to DNP HyperSense polarizer. A solution of 25 µL [1-^{13}C] pyruvic acid (Isotec, Sigma-Aldrich, St. Louis, MO), 15 mM OX63 trityl radical (GE Healthcare) and 1.5 mM of the gadolinium chelate (ProHance) was polarized at 3.35 T and 1.4 K in the DNP polarizer (HyperSense, Oxford Instruments, UK) for one hour. HP pyruvate was rapidly dissolved in 4 mL superheated alkaline buffer containing 100 mg/L ethylenediaminetetraacetate (EDTA), 40 mM NaOH, 40 mM TRIS buffer, and 30 mM NaCl. The final concentration of injected pyruvate was 80 mM with physiologic pH ~ 7.4. 250 µL of HP pyruvate was injected intravenously over a period of 8-10 seconds using a tail vein catheter.

T_2-Weighted Proton MRI: Conventional anatomic MRI images were acquired using a multi-slice T_2-weighted RARE (Rapid Acquisition with Relaxation Enhancement) sequence. Images of different view/planes including axial, coronal, and sagittal were acquired to identify the location of the tumors or region of interest on the flank of the mouse. The imaging parameters of the T_2-weighted scans were: echo time T_E = 17 ms, repetition time T_R = 2.5 s, 4 cm field of view, 256 µm x 256 µm in-plane resolution, ten to fifteen 1 - 1.5 mm slices, and 4 image averages. Three-dimensional (3D) tumor volumes were estimated from these MR images.

***In Vivo* ^{13}C MR Spectroscopy:** A series of slab-selective ^{13}C spectra from the slab thickness 6 - 8 mm were acquired right after injection of HP pyruvate using spFLASH sequence. The subcutaneous tumor location and similar size of the tumors employed in this study aided more precise slab placement through most of the cancer tissue and limited the contribution of non-malignant signal and/or keep the minimal contribution consistent throughout the experiments. A total of 90 transients were acquired using a delay time between each transient being 2 s (total time 3 min). Each transient utilized a 15^o flip angle excitation Gauss pulse and 2048 data points. A small 8M ^{13}C-urea phantom doped with Gadolinium-DPTA was placed in each mouse experiment for chemical shift referencing. Experimental data were processed in MATLAB (MathWorks Inc., Natick, MA) and TopSpin (Bruker BioSpin GmbH, Ettingen, Germany) platforms. The phase correction and 10 to 15 Hz line-broadening were introduced to the individual spectrum. The area under the spectral peaks for pyruvate and lactate were integrated over the entire array. The lactate-to-pyruvate metabolic flux ratios (Lac/Pyr) were estimated by taking the ratio over the integration of lactate and pyruvate signals.

[^{18}F]FPIA-PET Imaging: Mice are anesthetized and then injected intravenously with ~100 µCi [^{18}F]FPIA in 150 µL maximum total volume of phosphate buffer. Each mouse was allowed to recover for 60 min prior to imaging. The imaging protocol consisted of a 10 min PET followed by a 3 min CT scan CT (400 uA, 45 kV, 120 projections) on a Bruker Albira PET/SPECT/CT scanner (Bruker Biospin Corp., Billerica, MA, USA). The images were reconstructed using the Maximum Likelihood Expectation Maximization (MLEM) method with 12 iterations. Scatter, random decay, and attenuation corrections were applied. Analysis was done with Pmod (PMOD Technologies Ltd., Zürich, Switzerland). The mean % injected dose per millimeter cube (%ID/cc) of the tumor and normal tissue were measured. Data are reported as %ID/cc, or as ratio of the tumor to muscle (T/M).

Aim I, Task 4: Harvesting and storage of tissue samples

Prostate cancer PDX tumors were collected 24 to 48 hours after PET and HP-MR imaging. Tissue harvested for mass spectrometry analysis was flash frozen in liquid nitrogen and stored at -80˚C for later workup. A 15 mg piece of PDX tissue were analyzed using mass spectroscopy to quantify

pyruvate and lactate levels for tumor lactate-to-pyruvate ratio measurements as described by Zacharias N, et al. (Zacharias N, Lee J, et al. *Mol Imaging Biol.* **2019** *21*, 86-94. doi: 10.1007/s11307-018-1199-6). To determine aberrant lipid PDX metabolism as described by Whitney TH, et al. (Witney TH, Pisaneschi F, et al *J Nucl Med.* **2014**, *55*, 1506. doi: 10.2967/jnumed.114.140343) we plan to use ESI-LC-MS to quantify acetyl-carnitine, butyryl-carnitine, propionyl-carnitine, and palmitoyl-carnitine molecules using selected ion monitoring (SIM) and multiple reaction monitoring (MRM) mass spectrometry (A and B).

Aim II, Task 5: NMR spectroscopy-based metabolomics of flash frozen tissues

***Ex Vivo* ^{1}H NMR Spectroscopy:** *Ex Vivo* ^{1}H NMR spectroscopic measurements were conducted using a protocol that has been established recently in our laboratory (Zacharias N, Lee J, et al. *Mol Imaging Biol.* **2019** *21*, 86-94. doi: 10.1007/s11307-018-1199-6). Briefly, flash-freezing tumor sample was weighed, crushed, and immersed in 3 mL of methanol-to-water mixture of 2:1 ratio in presence of polymer vortex beads. A process of mechanical homogenization was followed to separate the water-soluble metabolites. For NMR experiments the metabolites were dissolved in a solution containing 600 µL of D_2O, 36 µL of phosphate buffer, and 4 µL of 80 mM DSS (4,4-dimethyl-4-silapentane-1-sulfonic acid). Phosphate buffer was used to stabilize the pH value. The DSS was used as reference standard for normalizing the spectral signal of each metabolite.

NMR Spectra were obtained using a Bruker AVANCE III HD® NMR scanner (Bruker BioSpin Corporation) at a temperature of 298 K that has coupled with cryogenic temperature probe along a Z-axis shielded gradient. The operating frequency was 500 MHz for proton (^{1}H) resonance. Water suppression technique was implemented. Spectra were acquired with a 90º pulse width, a 6.0 s scan delay time, 1024 Hz spectral width, and an acquisition time of 1.09 s (16,000 complex points). Spectroscopic data were processed by applying a number of techniques for cross verification and to test the reproducibility. Chenomx NMR Suite 8.1 software (Chenomx Inc., Edmonton, Canada) was applied for detail metabolic profiling. MestReNova software (Mestrelab Research, A Coruña, Spain) were used for quantitative analysis of metabolic peaks and associate area under the curve. The integral value of each peak was normalized by the value of the integral of the DSS reference peak.

Aim II, Task 6: Mass Spectrometry-based metabolomics

A 15mg piece of PDX tissue are analyzed using mass spectroscopy to quantify pyruvate and lactate levels for tumor lactate-to-pyruvate ratio measurements as described by Zacharias N, et al. (Zacharias N, Lee J, et al. *Mol Imaging Biol.* **2019** *21*, 86-94. doi: 10.1007/s11307-018-1199-6). To determine aberrant lipid PDX metabolism as described by Whitney TH, et al. (Witney TH, Pisaneschi F, et al *J Nucl Med.* **2014**, *55*, 1506. doi: 10.2967/jnumed.114.140343) we have used ESI-LC-MS to quantify acetyl-carnitine, butyryl-carnitine, propionyl-carnitine, and palmitoyl-carnitine molecules using selected ion monitoring (SIM) and multiple reaction monitoring (MRM) mass spectrometry (A and B).

Aim II, Task 7: Transcriptome analysis of Tumors (four PDX lines; from task 4).

Total RNA was prepared using TRIZOL reagent (Invitrogen, USA) and processed at final step using RNEasy-kit (Qiagen, USA). RNA with high RIN values (>1.8) was processed for library and sequencing at the Genomics Core Facility at MD Anderson Cancer Center and paired-end sequencing was performed on an Illumina HiSeq platform (PE 2x100bp, 2 samples per lane) to provide a good coverage of >100X (after clonal read collapse). All post-sequencing analysis was also done at the core facility.

Aim II, Task 8: Immunohistochemistry analysis of Tumors (four PDX lines; from task 4). The tissue cross sections were stained for examining LDH-A, MCT1, MCT4 and Fatty Acid Synthase and Carnitine Acetyltransferase expression levels.

Aim III, Task 9: We have taken the Enzalutamide resistant PDX model, 274-4 for this specific aim. When the tumors are about 0.5 cm, the tumor bearing mice are randomized into two treatment groups. Mice in Group received receive 10mg/kg body wt Enzalutamide by oral gavage while Group 2 mice will receive Enzalutamide and intraperitoneal injection of Syrosingopine, MCT4 inhibitor (7.5mg/kg body weight).

Aim III, Task 10: Synthesize ^{18}F-Fluoropivalate ([^{18}F]FPIA). Described before.

Aim III, Task 11: Imaging experiments.
Simultaneous ^{13}C Pyruvate HP-MRI and [^{18}F]FPIA PET to interrogate both glycolysis and fatty acid oxidation pathways at the preclinical PET-MRI scanner at two time points. Methods described before.

Aim III, Task 12: Harvesting of tumors and storing for NMR spectroscopy, Mass spectrometry, immunohistochemistry and RNA sequencing studies at different time points.

Aim IV, Task 13: NMR spectroscopy based metabolomics of flash frozen tissues.

B. Specific Objectives:

For the first reporting period, we are close to achieve the Milestone 1 as outlined in the Statement of Work. HP-MR imaging will inform us about the pyruvate-to-lactate transition in these PDX models as they respond to Enzalutamide and transition from castration sensitive prostate cancer (mCSPC) to mCRPC. [^{18}F]FPIA PET imaging is expected to capture progressive modulation in activity as the transition from mCSPC to mCRPC unfolds.

C. Key Outcomes:

1. **Potential of metabolic sub-typing of AR positive and negative prostate cancer PDX models by hyperpolarized metabolic imaging and metabolomics.**
   This is now developed into a much larger project involving clinical data and Artificial Intelligence (AI) and we are now seeking extramural support from Department of Defense data Science Program, CPRIT and NCI on the data science application of metabolic classification of prostate cancer.

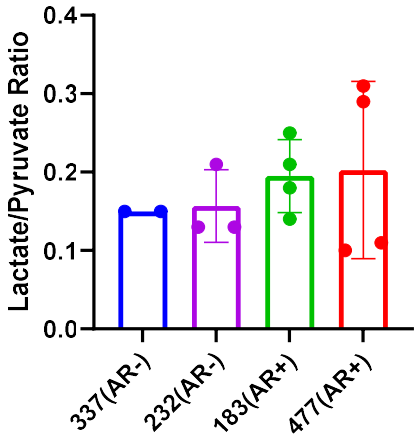
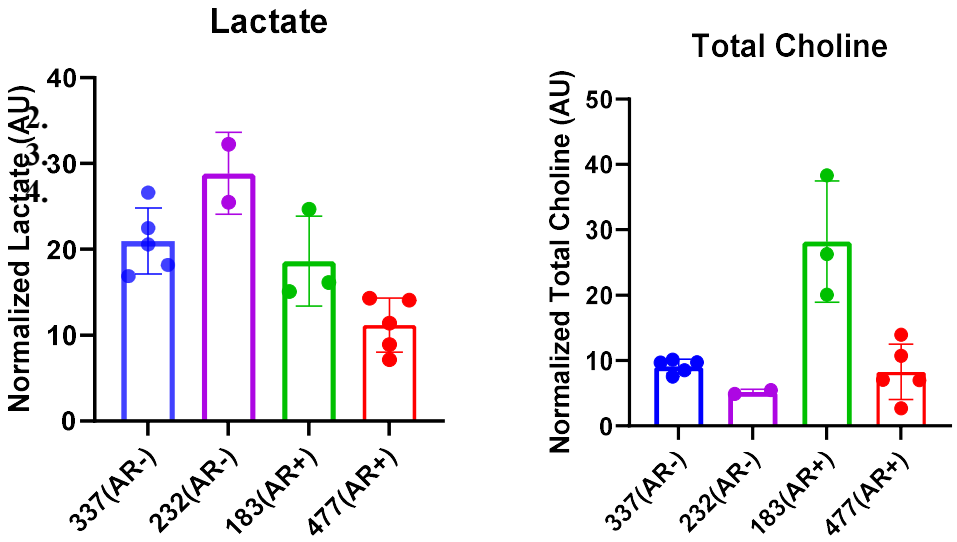


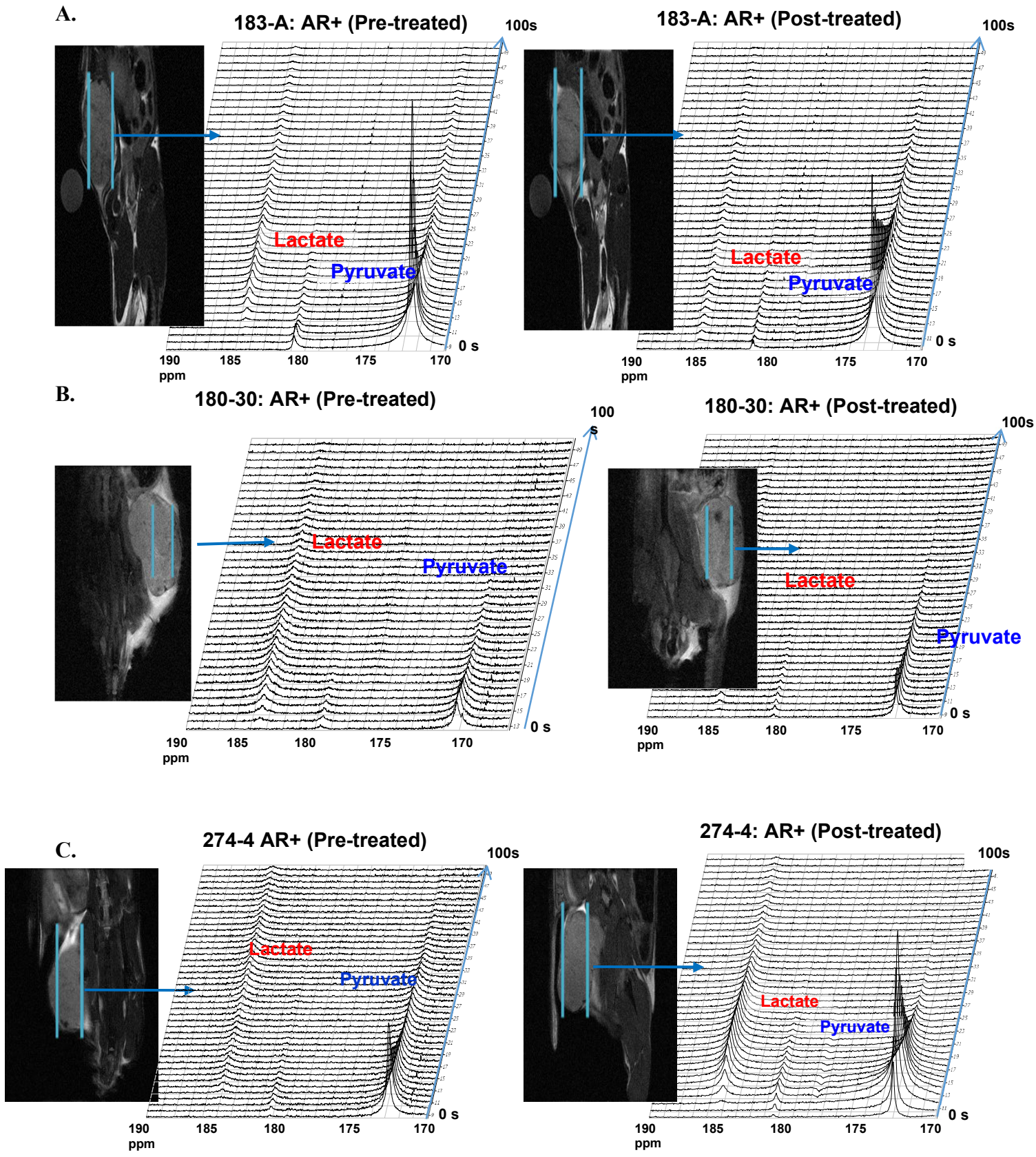
Figure 2. Hyperpolarized lactate-to-pyruvate ratio in patient derived xenografts (PDX) of prostate cancer with AR positive and negative status *in vivo*.

Figure 3. The normalized lactate and choline metabolites were quantified using nuclear magnetic resonance (NMR) metabolomics of *ex vivo* tumor samples for different prostate cancer PDXs with AR+ and AR- status.



2. **Hyperpolarized metabolic imaging of Lactate-to-Pyruvate conversion can be employed to determine Enzalutamide sensitivity or resistance in PDX models of prostate cancer. This was discussed in last year's progress report.**

Figure 4: Representative hyperpolarized metabolic imaging data. In three Androgen Receptor positive (AR+) PDX models of prostate cancer, of which PDXs 183-A and 180-30 are Enzalutamide sensitive and PDX 274-4 is Enzalutamide resistant, hyperpolarized [1-^{13}C] pyruvate metabolic imaging is employed to measure the real-time lactate flux generation before treatment and after 7 days of Enzalutamide treatment (Panels **A-C**). Panel D demonstrates that lactate-to-pyruvate is significantly reduced in Enzalutamide sensitive tumor while, lactate-to-pyruvate is significantly increased in Enzalutamide resistant tumor. This work has resulted in a manuscript under review at *Cancer Research*.


A.
183-A: AR+ (Pre-treated)
100s
Lactate
Pyruvate
0 s
190
185
180
175
170
ppm
183-A: AR+ (Post-treated)
100s
Lactate
Pyruvate
0 s
190
185
180
175
170
ppm
B.
180-30: AR+ (Pre-treated)
100
s
Lactate
Pyruvate
0 s
190
185
180
175
170
ppm
180-30: AR+ (Post-treated)
100s
Lactate
Pyruvate
0 s
190
185
180
175
170
ppm
C.
274-4 AR+ (Pre-treated)
100s
Lactate
Pyruvate
0 s
190
185
180
175
170
ppm
274-4: AR+ (Post-treated)
100s
Lactate
Pyruvate
0 s
190
185
180
175
170
ppm

D.

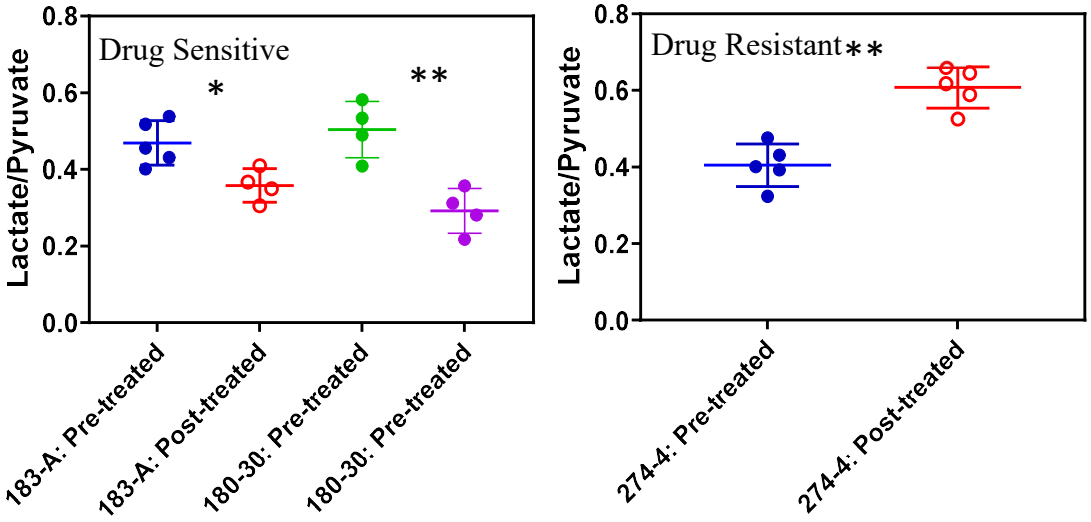
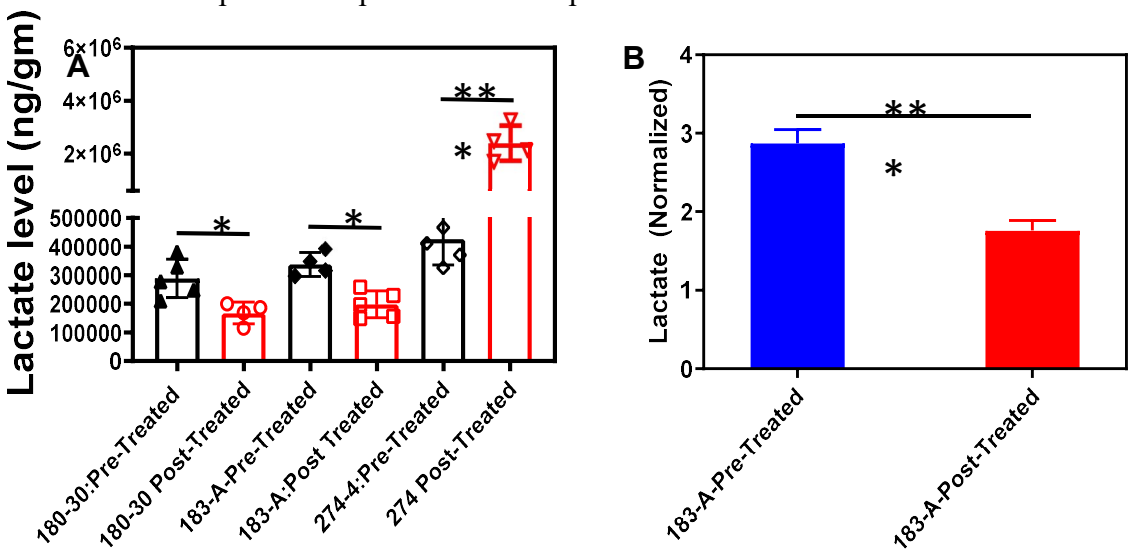


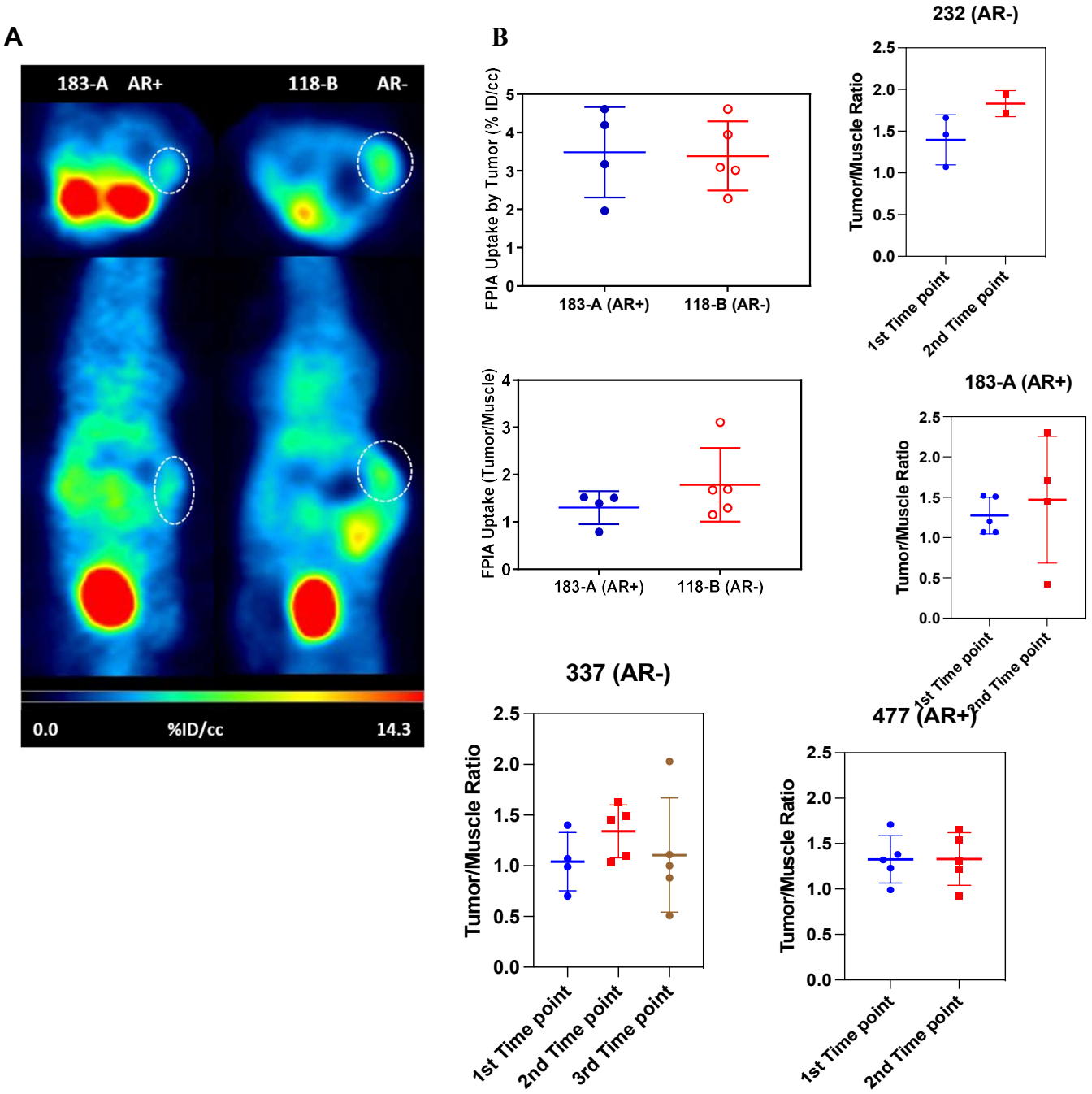
Figure 5. Representative metabolomics data. Both Mass Spectrometry (Panel **A**) and NMR spectroscopy-based (Panel **B**) metabolomics of *ex vivo* flash frozen tumor samples support the *in vivo* data from hyperpolarized metabolic imaging (**Figure 4**). In panel **A**, the *ex vivo* lactate pool size is higher in post treated samples in Enzalutamide resistant, PDX 274-4, whereas the *ex vivo* lactate pool is lower in post-treated samples in Enzalutamide sensitive PDX 180-30. Similar lower *ex vivo* lactate pool is observed in panel **B** in post-treated samples in Enzalutamide sensitive PDX 183-A.



3. [^{18}F]FPIA-PET imaging shows ^{18}F-Fluoropivalate (FPIA) uptake in PDX tumors.

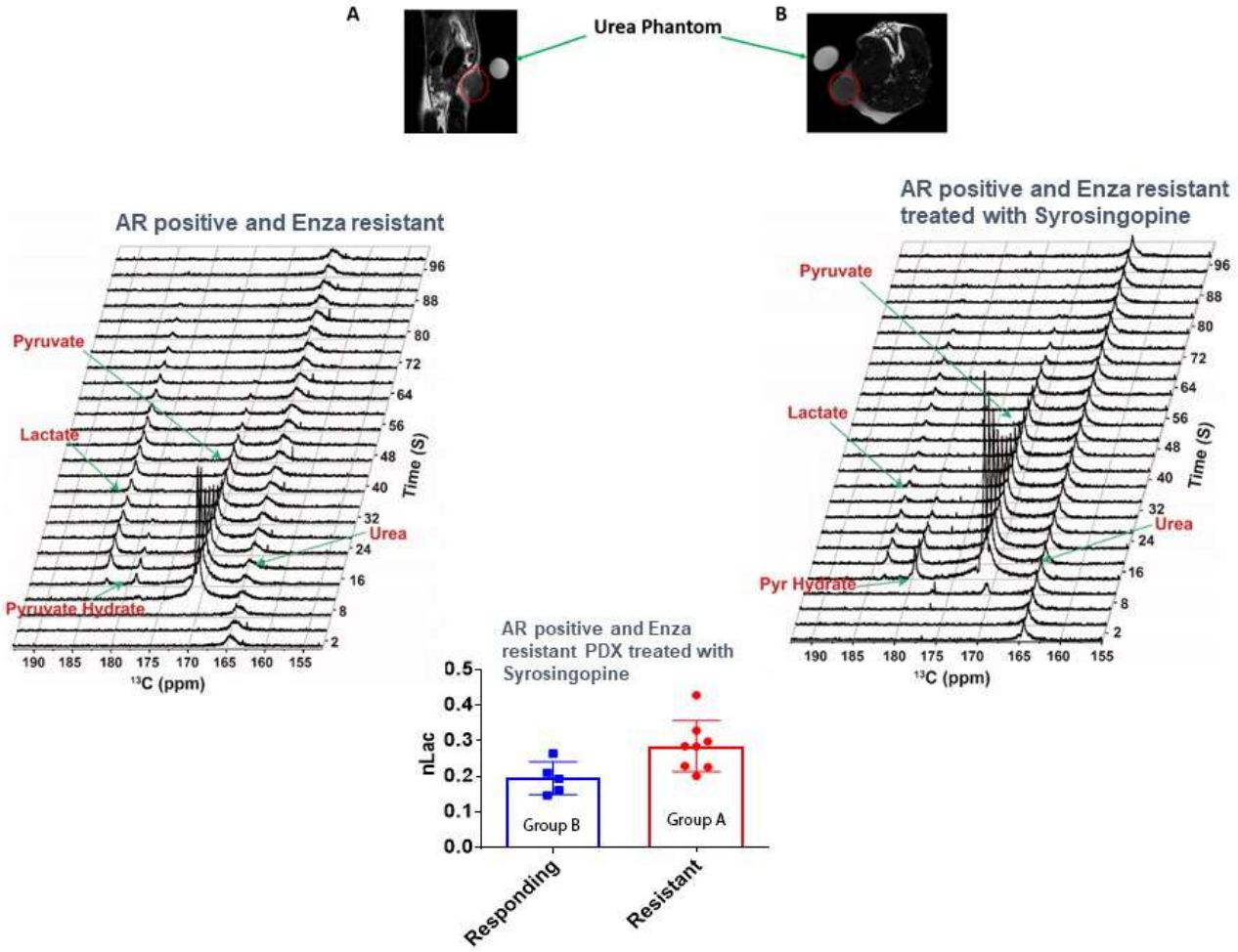
Figure 6. Representative [^{18}F]FPIA–PET imaging data. We imaged several AR positive and negative PDX models. In all models, we observe FPIA uptake, with an average of about 3.5 % ID/cc. A representative image is shown in Panel **A**. Representative FPIA uptake plots are shown in Panel **B**. When data are analyzed as tumor to muscle (T/M), we observe a slightly higher uptake in the AR-PDX, although the difference is not statistically significant (Panel **B**). Our data shows the potential of

FPIA-PET to visualize prostate cancer, and we hope to employ FPIA-PET to pinpoint differences in metabolic reprograming following enzalutamide therapy.



4. **Preliminary HP-MR data in one AR resistant PDX model (274-4) shows that MCT inhibition with the clinical drug, Syrosingopine can overcome resistance to Enzalutamide (Enza). More work is on going to validate this result and imaging work is currently in progress with ^{13}C Pyruvate HP-MRI and [^{18}F]FPIA PET.**

Figure 7: Preliminary HP-MR data showing dynamic metabolic flux differences the 274-4 AR+, mice treated with Enzalutamide by oral gavage (Group A) and 274-4 AR+, mice treated with Enzalutamide and intraperitoneal injection of MCT4 inhibitor, Syrosingopine (Group B). nLac (lactate-to-pyruvate ratio) shows the reduced metabolic flux of lactate in the Group B treated with MCT4 inhibitor, Syrosingopine.



What opportunities for training and professional development has the project provided?

Dr. Prasanta Dutta who is supported by this project has given an oral presentation on the work he has accomplished in past two years at the 25th International Symposium on Radiopharmaceutical Sciences (iSRS) in May 22-26, 2023. His abstract was selected through a rigorous competitive process for an oral presentation.

How were the results disseminated to communities of interest?

There are two manuscripts currently under review based on the work accomplished in this project. One is under peer review at *Cancer Research* and the other one is at the *Journal of Labelled Compounds and Radiopharmaceuticals*. An oral presentation on "*Combining PET and HP-MR to Interrogate Prostate Cancer Metabolism***"** at the 25th International Symposium on Radiopharmaceutical Sciences (iSRS) on May 25, 2023. This is biggest professional gathering of molecular imaging scientists dedicated to the understanding of biology and medicine through multimodal *in vivo* imaging of cellular and molecular events involved in normal and pathologic processes and utilization of quantitative molecular imaging in patient care.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

In the second reporting period of the project, we have made substantial progress on Specific Aim I and II and we have started working on the most impactful aim of the project, Specific Aim III on imaging to overcoming the ADT resistance by targeting Monocarboxylate Transporter (MCT) pathway. Our preliminary HP-MR data on only one of the AR positive Enzalutamide resistant PDX model (274-4) shows that MCT inhibition with the clinical drug, Syrosingopine can overcome resistance to Enzalutamide. The main task of the next reporting period will be to validate this result with multiomics correlative work and imaging is currently ongoing with ^{13}C Pyruvate HP-MRI and [^{18}F]FPIA PET.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Patients with advanced prostate cancer receive anti-androgen drug, Enzalutamide as the first line of treatment. Unfortunately, many patients develop resistance to treatment, and the disease relapses with aggressive histology and metastatic phenotype. we have employed a non-invasive magnetic resonance imaging (MRI) based technique (hyperpolarized metabolic imaging) to image Enzalutamide sensitivity or resistance in prostate cancer. This has been validated by *ex vivo* metabolomics data. Furthermore, we have employed a novel, Positron Emission Tomography (PET) agent, ^{18}F-FPIA, to image the linked fatty acid oxidation pathway in prostate cancer. We have attempted to restore Enzalutamide sensitivity in a resistant model by targeting the monocarboxylate transporter (MCT) pathway using an MCT inhibitor, Syrosingopine and we have successfully interrogate this transition from Enzalutamide resistance to sensitivity by hyperpolarized metabolic imaging. We believe, we can employ this multi-modal approach to identify the drug resistant patients at an earlier time point. We intend to develop personalized metabolic imaging modality to target treatment strategies of different sub-types of lethal prostate cancer.

What was the impact on other disciplines?

Nothing to report as of now

What was the impact on technology transfer?

Nothing to report as of now

Nothing to report as of now

5. CHANGES/PROBLEMS:

Nothing to report as of now

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

Nothing major to report, In the proposal, **we suggested these following four PDX models for study**
274-4 (AR+, Enzalutamide resistant)
133-3 (AR+, Enzalutamide resistant)
183-A (AR+, Enzalutamide sensitive)
170-1 (AR+, Enzalutamide sensitive)
However, we ran into some logistical challenges to generate all PDX models we originally proposed from our PDX core facility as the core ran into several issues in one past one year. Therefore, we have kept performing experiments on the models that are available and fit the goals of the project.

PDX models employed so far in the study

PDX	HP-MR	FPIA-PET	NMR met	MS met	AR	Enzalutamide
144	x	x	x	x	negative	
118	x	x	x		negative	
232	x	x	x	x	negative	
337	x	x	x		negative	
183	x	x	x	x	positive	sensitive
274	x	x	x	x	positive	resistant
177	x	x	x		negative	
180	x		x	x	positive	sensitive
477	x	x	x		positive	resistant

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

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS:

- **Publications, conference papers, and presentations**
  Journal publications.

No published manuscript to report.

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers and presentations.

Accepted conference abstract for oral presentation at the World Molecular Imaging Congress (WMIC), 2022, Miami.

Dutta P, Enriquez JS, Armijo R, Wang M, Han J, Shepherd P, Frigo DE, Titus MA, Pisaneschi P, Bhattacharya PK. *Combining PET Imaging and HP-MR to Interrogate Prostate Cancer Metabolism.*

- **Website(s) or other Internet site(s)**

Nothing to report

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report

- **Other Products**

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Pratip Bhattacharya, Ph.D.
Project Role: PD/PI
Researcher Identifier (e.g. ORCID ID): 0000-0002-0625-252X
Nearest person month worked: 1.92
Contribution to Project: Oversight and coordination of all research activities.
Funding Support: Please see attached Other Support Document.

Name: Federica Pisaneschi, Ph.D.
Project Role: Co-I
Researcher Identifier (e.g. ORCID ID): 0000-0002-1989-4417
Nearest person month worked: 1.44
Contribution to Project: Radiochemistry
Funding Support: Please see attached Other Support Document

Name: Prasanta Dutta, Ph.D.
Project Role: Research Scientist
Researcher Identifier (e.g. ORCID ID): 0000-0002-9887-6507
Nearest person month worked: 6.00
Contribution to Project: Assistance for Drs. Bhattacharya & Pisaneschi on HP-MR, PET and metabolomics

Name: Peter Shepherd
Project Role: Coordinator, Research Laboratory
Nearest person month worked: 1.32
Contribution to Project: Generating and maintaining the patient derived (PDX) prostate cancer animal Models and transcriptomics

Name: Abishai Dominic, Ph.D.
Project Role: PostDoc Fellow
Nearest person month worked: 1.00
Contribution to Project: Assistance for Drs. Bhattacharya & Pisaneschi on IHC and cyTOF

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

As mentioned in the last year's progress report, Dr. Mark Titus, Associate Professor, Department of Genitourinary Medical Oncology, MD Anderson Cancer Center, who was a co-investigator in this proposal has retired from MD Anderson Cancer Center on last Feb 28, 2023. We have replaced his effort with Peter Shepherd. Peter is a research laboratory coordinator at the Department of Genitourinary Medical Oncology, MD Anderson. Peter is responsible for generating and maintaining the patient derived (PDX) prostate cancer animal models in the research plan as week as administering therapy to these animal models. He is also assisting with transcriptomics data acquisition.

What other organizations were involved as partners?

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *F*

QUAD CHARTS: *I*

9. APPENDICES:

Previous/Current/Pending Support for DOD
Bhattacharya, Pratip

PREVIOUS:

Title:	Circulating Biomarkers and Imaging for Early Detection of Pancreatic Cancer (U01CA214263 – Sen, Killary)
Effort:	0.60 CM, 5% effort
Supporting Agency:	National Institutes of Health / National Cancer Institute
Grants Officer:	Ghosh-Janjigian Sharmistha National Cancer Institute 9609 Medical Center Drive Bethesda, MD 20892 ghoshjanjigias@mail.nih.gov
Performance Period:	08/07/2018 – 07/31/2023
Level of Funding:	
Project Goals	To validate integrated blood-based biomarker signature for detection of early stage PDAC and secondly for biomarker panels in concert with novel imaging for the early detection of PDAC at a precursor stage when the disease remains curative.
Specific Aims	Aim 1: Validation of pathway-associated biomarker signatures of early stage resectable tumors and precision imaging for early detection of asymptomatic PDAC utilizing early stage cohorts. Aim 2: Validation of PDAC early precursor lesion associated biomarker signatures and precision imaging developed with precursor lesions harboring genetically engineered mouse models and well characterized large longitudinal cohorts. Aim 3: Blinded validation of early detection biomarker signatures in retrospective pre-diagnostic samples. Aim 4: Prospective screening of integrated biomarkers and imaging using risk scores in pre-diagnostic high risk PDAC cohorts and Pancreatic Cancer High Risk Clinic (PCHRC) patients.
Overlap:	None

Title:	Imaging Biomarkers for Immunotherapy Resistance in Melanoma In Vivo (85152 – Bhattacharya)
Effort:	0.60 CM, 5% effort
Supporting Agency:	Melanoma Research Alliance – Pilot Award
Grants Officer:	Rachel Fischer 730 15th Street, NW Washington, DC 20005

	rfischer@curemelanoma.org
Performance Period:	06/01/2021 – 05/31/2023
Level of Funding:	
Project Goals	To develop biomarkers to image immunotherapy resistance in vivo and to improve its success rate.
Specific Aims	Aim 1: To monitor changes in tumor pHe and HP lactate-to-pyruvate metabolic flux in B16/B16 melanoma clones that acquired resistance to checkpoint blockade immunotherapy through serial in vivo passage using acidoCEST and HP-MRI. Aim 2: To pH-sensitize immunotherapy with MCT1 inhibition treatment, as evaluated with acidoCEST and HP-MRI.
Overlap:	None

Title:	Hyperpolarized Silicon Nanoparticle "Spin Batteries" For Imaging Biochemical Reactions in Vivo
Effort:	0.60 CM, 5% effort
Supporting Agency:	The University of Texas MD Anderson Cancer Center – Institutional Research Grant
Grants Officer:	Nyma Shah, Director, Research Funding Programs The University of Texas MD Anderson Cancer Center – Research Administration Office 1515 Holcombe Blvd., Unit 1436 Houston, TX 77030
Performance Period:	09/01/2018 – 08/31/2022 (NCE)
Level of Funding:	
Project Goals	To address the sensitivity and specificity of hyperpolarized metabolic MR technique in multiple animal models of pancreatic premalignancy.
Specific Aims	Aim 1: Validate through-bond transfer of polarization from hyperpolarized silicon-29 nuclei. Aim 2: Validate though-space transfer of polarization from silicon nucleus to 13C carbonyl using the Nuclear Overhauser Effect (NOE). Aim 3: Test and validate transfer of 29Si hyperpolarization to 13C as a method of sensing proteolytic enzymes, Granzyme B, and oxidative enzymes, e.g., myeloperoxidase.
Overlap:	None

Title:	Translational Applications in an Animal Model of Pancreatic Cystic Neoplasm and Cancer (1 R01 CA218004-01A1 – Maitra)

Effort:	1.20 CM, 10% effort
Supporting Agency:	National Institutes of Health
Grants Officer:	Richard V. Mazurchuk Program Director National Cancer Institute BG 9609 MSC 9760 9609 Medical Center Drive Bethesda, MD 20892-9760
Performance Period:	04/04/2018 – 03/31/2022
Level of Funding:	
Project Goals	To enhance the translational applicability of this model by using it as a controlled platform to address key unmet needs in the management of IPMNs in two areas: imaging correlates and circulating biomarkers.
Specific Aims	Aim 1: Utilizing the Kras;Gnas model of cystic neoplasia for identification of imaging correlates of progression to invasive PDAC, with cross-validation of imaging studies in IPMN patients. Aim 2: Utilizing the Kras;Gnas model of cystic neoplasia for identification of circulating biomarkers of progression to invasive PDAC, with cross-validation in human IPMN-derived biospecimens.
Overlap:	None

Title:	Overcoming ADT Resistance in Metastatic Castration Resistance Prostate Cancer (mCRPC) By Targeting Monocarboxylate Transporter (MCT) Pathway
Effort:	0.60 CM, 5% effort
Supporting Agency:	Mike Slive Foundation
Grants Officer:	Emily Capilouto P.O. Box 530748 Birmingham, AL 35253 emily@mikeslivefoundation.org
Performance Period:	01/01/2021 – 12/31/2021
Level of Funding:	
Project Goals	To develop personalized metabolic imaging modality to target treatment strategies of different sub-types of PCa and to interrogate different metabolic factors by imaging that are associated with a particular sub-type.
Specific Aims	Aim 1: To perform HP-13C Pyruvate MRI in four well characterized PDX murine models of prostate cancer in vivo before and after the antiandrogen therapy with Enzalutamide to image alteration in glycolytic pathway after treatment response. We will further analyze ADT sensitive and ADT resistant PDX utilizing NMR-spectroscopy combined with mass spectrometry-based metabolomics, immunohistochemistry and

	transcriptome profiling. Using this approach, we expect to delineate pathways of ADT resistance. Aim 2: To image overcoming the ADT resistance by targeting Monocarboxylate Transporter (MCT) pathway (via MCT inhibition with the clinical drug, Syrosingopine) by performing HP-13C Pyruvate MRI in two well characterized PDX murine models of prostate cancer in vivo. We will further analyze the overcoming of ADT resistance utilizing NMR-spectroscopy combined with mass spectrometry-based metabolomics, immunohistochemistry and transcriptome profiling
Overlap:	None

Title:	MD Anderson Cancer Center SPORE in Gastrointestinal Cancer (1 P50 CA221707-01 – Kopetz, Maitra)
Effort:	1.20 CM, 10% effort
Supporting Agency:	National Institutes of Health / National Cancer Institute
Grants Officer:	Shane Woodward 9609 Medical Center Drive Bethesda, MD 20892 woodwars@mail.nih.gov
Performance Period:	08/20/2019 – 05/31/2024 (Dr. Bhattacharya's effort ended 11/30/2021)
Level of Funding:	
Project Goals	To reduce mortality and morbidity rates from colorectal cancer (CRC) and pancreatic ductal adenocarcinoma (PDAC), and to improve the quality of life of patients afflicted by these diseases.
Specific Aims	Aim 1: To evaluate clinical activity of an optimized combination of immune checkpoint inhibitors with a personalized, neo-antigen peptide vaccine. Aim 2: To determine the contribution of STAT3 signaling to CRC development in high-risk patients with familial syndromes or inflammatory bowel disease. Aim 3: To evaluate oxidative phosphorylation as a therapeutic vulnerability in pancreatic cancer. Aim 4: Empower GI SPORE research and collaborations through research Cores and Programs. Aim 5: Strategic integration with the translational GI research community.
Overlap:	None

Title:	Early Detection of PanIN by Hyperpolarized Metabolic MR Imaging (16-65-BHAT)
Effort:	0.90 CM, 8% effort
Supporting Agency:	Pancreatic Cancer Action Network
Grants Officer:	Maya Bader 1500 Rosecrans Avenue, Suite 200 Manhattan Beach, CA 90266 mbader@pancan.org
Performance Period:	07/01/2016 – 12/31/2018 (NCE)
Level of Funding:	
Project Goals	To develop the capability of non-invasively detecting advanced pancreatic intraepithelial neoplasia (PanIN) precursor lesions in pancreas prior to invasive disease using metabolic imaging modality.
Specific Aims	Aim 1: Employ metabolic imaging with hyperpolarized 13C pyruvate to detect and monitor the progression of PanIN precursor lesions to pancreatic cancer. Aim 2: Establish the in vivo metabolic flux ratios of alanine-to-lactate (Ala/Lac) and lactate-topyruvate (Lac/Pyr) as predictive biomarkers of neoplastic progression of advanced PanIN to aggressive pancreatic cancer. Aim 3: Employ high resolution Nuclear Magnetic Resonance (NMR) Spectroscopy in ex vivo tumor samples and correlate NMR metabolomics data with real-time in vivo dynamic metabolic flux data in Aim 1 and 2 and immunohistochemistry data for independent validation of the metabolic biomarkers for clinical translation.
Overlap:	None

Title:	TMC-GCC Collaborative Symposium: Metabolism in Cancer
Effort:	0.12 CM, 1% effort
Supporting Agency:	Gulf Coast Consortium - 2016 John S. Dunn Collaborative Research Award Program
Grants Officer:	Suzanne Tomlinson PO Box 1892, MS141 Houston, TX 77251-1892
Performance Period:	04/01/2017 – 03/31/2019
Level of Funding:	
Project Goals	To secure contribution of funds from participating GCC institutions to fund the annual Metabolism in Cancer Symposium for at least two years.
Specific Aims	Aim 1: Learn how metabolism research could benefit cancer patients.

	Aim 2: Bring attention to local investigators working on research projects in metabolism in cancer. Aim 3: Identify possible areas within this broad domain where investigators in the TMC and greater Houston area can collaborate. Aim 4: Assemble investigators into cross-institutional teams and promote their interactions with newly launched TMC initiatives.
Overlap:	None

Title:	Targeted Molecular Imaging of Cell Death in Ovarian Cancer (1R21CA181994-01A1 - Millward, Lu)
Effort:	0.24 CM, 2% effort
Supporting Agency:	NCI Exploratory/Developmental Research Grant Award
Grants Officer:	Anne Menkens 9609 Medical Center Drive Rockville, MD 20850 menkensa@mail.nih.gov
Performance Period:	02/03/2016 – 01/31/2019 (NCE)
Level of Funding:	
Project Goals	Develop targeted molecular imaging agents to visualize apoptosis and autophagy in vivo by PET and MRI.
Specific Aims	Aim 1: Molecular imaging of apoptosis and autophagy can provide an immediate pharmacodynamic readout of chemotherapy and radiation therapy efficacy, allowing clinicians to identify the optimal therapeutic regime in days rather than weeks or months. Aim 2: Non-tumor cell death can be assessed in parallel with tumor destruction, providing insight into potential side effects before clinical presentation. Aim 3: Cell death imaging can be integrated into early phase clinical trials (Phase 0/I) of targeted apoptosis- and autophagy-modulating therapies to predict response and resistance, accelerating the stratification of patients most likely to respond to therapy.
Overlap:	None

Title:	Early Detection of Pancreatic Cancer by Targeted Molecular Imaging of Hyperpolarized Silicon Nanoparticles (RP170593 - Pudakalakatti)
Effort:	0.12 CM, 1% effort
Supporting Agency:	Gulf Coast Consortia – Computational Cancer Biology Training Grant

Grants Officer:	Melissa Glueck, Keck Center Director Gulf Coast Consortia – BioScience Research Collaborative (BRC) Suite 160, 6500 Main St. Houston, TX 77030
Performance Period:	04/01/2017 – 03/31/2019
Level of Funding:	
Project Goals	To improve early detection of pancreatic cancer by Magnetic Resonance Imaging (MRI) using a highly sensitive and specific biomarker of this virtually incurable disease.
Specific Aims	Aim 1: Optimize the levels of hyperpolarization achievable by radical-free ^{29}Si DNP on lactose-functionalized and MUC1-modified hydrogels encapsulated SiNPs as a function of nanoparticle size and *in vitro* targeting efficacy. Aim 2: Demonstrate targeted real-time hyperpolarized MRI with lactose functionalized and MUC1-hydrogel encapsulated SiNPs in two distinct animal models of pancreatic cancer.
Overlap:	None

Title:	Virtual Colonoscopy for Early Detection of Colorectal Cancer
Effort:	0.12 CM, 1% effort
Supporting Agency:	Colon Cancer Coalition
Grants Officer:	Anne Carlson, Executive Director Colon Cancer Coalition 5666 Lincoln Drive, Suite 270 Edina, MN 55436 anne@coloncancercoalition.org
Performance Period:	06/28/2018 – 08/31/2019 (NCE)
Level of Funding:	
Project Goals	To employ hyperpolarized silicon nanoparticles that target highly accessible transmembrane mucin glycoproteins (MUC1) that are overexpressed in colon cancer, as viable MRI based molecular imaging agents for novel, early diagnosis of colorectal abnormalities and cancer.
Specific Aims	Aim 1: Establish and validate real-time targeted molecular imaging of CRC using MUC1 functionalized SiNPs. Aim 2: Apply real-time targeted molecular imaging technique to well annotated CRC mouse models to validate early detection by MUC1 functionalized HP SiNPs.
Overlap:	None

Title:	Elimination of hypoxia sensitizes resistant solid tumors to Immunotherapy (RP170399 - Curran)

Effort:	0.12 CM, 1% effort
Supporting Agency:	Cancer Prevention and Research Institute of Texas – Individual Investigator Research Award
Grants Officer:	Wayne Roberts Cancer Prevention and Research Institute of Texas PO Box 12097 Austin, TX 78711
Performance Period:	12/01/2016 – 11/30/2019
Level of Funding:	
Project Goals	Determine whether disruption of hypoxic zones will compromise the integrity of the suppressive myeloid and myofibroblast network thereby sensitizing solid tumors to T cell co-stimulatory immunotherapy.
Specific Aims	Aim 1: Determine how targeted ablation of tumor hypoxia affects T cell infiltration and function, as well as sensitivity to T cell immunotherapy, in murine models of prostate cancer. Aim 2: Assay the effects of hypoxia ablation and immunotherapy on the immune composition and functional capacity of suppressive myeloid cells in the prostate cancer tumor microenvironment. Aim 3: Assess the impact of hypoxia ablation on the viability, distribution, and immunosuppressive function of myofibroblasts in prostate cancer.
Overlap:	None

Title:	Development of Platelet-based Metabolic Biomarkers for Ovarian Cancer
Effort:	1.20 CM, 10% effort
Supporting Agency:	Rivkin Center for Ovarian Cancer
Grants Officer:	Kiran Dhillon, PhD Director of Scientific Programs Rivkin Center for Ovarian Cancer 801 Broadway, Suite 701 Seattle, WA 98122
Performance Period:	04/01/2019 – 03/31/2020
Level of Funding:	
Project Goals	We hypothesize that tumor educated platelets from blood of ovarian cancer patients would exhibit altered metabolism compared to platelets from healthy volunteers.
Specific Aims	Aim 1: Determine metabolic profiles of human platelets (resting) and human platelets (activated with thrombin or/and collagen) and compare that with the metabolic profiles of human ovarian cancer cell lines with platelets and human ovarian cancer cell lines without platelets.

	Aim 2: Determine metabolic profiles from platelets isolated from healthy donors and ovarian cancer patient donors.
Overlap:	None

Title:	Interdisciplinary Translational Pre/Postdoctoral Program in Cancer Nanotechnology (1T32CA196561-01 - Sokolov)
Effort:	0.12 CM, 1% effort
Supporting Agency:	National Institutes of Health
Grants Officer:	Susan E Lim National Institutes of Health 31 Center Drive MSC 2510 Bethesda, MD 20892-2510
Performance Period:	09/01/2015 – 08/31/2020
Level of Funding:	
Project Goals	The goal of this program is to train scientists who will transfer the great promise of nanotechnology into clinical reality. We have designed a novel training program to educate future leaders in the broad field of nanotechnology with specific interests in cancer-related applications, who are keenly aware of the needs and demands of clinical environment as well as of major challenges of translational research.
Specific Aims	Aim 1: All trainees will work with at least two program faculty mentors (one from Rice and one from MD Anderson) to define and carry out an independent research problem. Aim 2: Incoming trainees will participate in a unique 2-week-long boot camp in "Cancer Management and Nanotechnology" that provides an overview of current opportunities and barriers in the field. Aim 3: Trainees will develop foundational background in the field by taking four courses related to translational cancer or nanotechnology topics. Aim 4: Trainees will gain important lab management skills by participating in a short hands-on course providing an introduction to laboratory and project management.
Overlap:	None

Title:	Metabolic Imaging of Therapeutic Efficacy in Glioblastoma by Hyperpolarized Magnetic Resonance (P50CA127001 – Lang)
Effort:	0.12 SM, 1% effort
Supporting Agency:	The University of Texas MD Anderson Cancer Center – Brain SPORE DRP

Grants Officer:	Biny Joseph, Program Director The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd., Unit 0431 Houston, TX 77030
Performance Period:	09/01/2019 – 08/31/2020
Level of Funding:	
Project Goals	Continue to develop a real-time metabolic imaging platform for early efficacy of therapy in mouse models of brain cancer with the goal of translating this technique in the GBM patients.
Specific Aims	Aim 1: To evaluate the response of individual tumors in three cohorts of patient-derived glioma stem cell intracranial xenografts (GSC) mouse model to 1) radiation therapy, 2) one anti-angiogenic drug (Avastin) and 3) OXPHOS inhibitor IACS-10759 applied *in vivo*, using HP ^{13}C pyruvate MR imaging and spectroscopy. Establish the real-time metabolic flux ratio (nLac) as therapeutic response marker. Aim 2: To perform steady-state high-resolution NMR (Nuclear Magnetic Resonance spectroscopy) metabolomics of *ex vivo* tissues collected from these tumors before and after therapy for metabolic fingerprinting and correlate that *in vivo* HP MR data from Aim 1.
Overlap:	None

Title:	Molecular Targeted Magnetic Resonance Reporter for Cancer Detection (RP180164 – Bhattacharya, Carson)
Effort:	0.60 CM, 5% effort
Supporting Agency:	Cancer Prevention & Research Institute of Texas – High-Impact/High-Risk Research Award
Grants Officer:	Wayne Roberts Cancer Prevention and Research Institute of Texas PO Box 12097 Austin, TX 78711
Performance Period:	08/31/2018 – 02/28/2021 (NCE)
Level of Funding:	
Project Goals	To create a new construct, combining the molecular affinity of antibodies with the sensitivity of hyperpolarized magnetic resonance, in order to create an early detection technology for colorectal cancer.
Specific Aims	Aim 1: Optimize the affinity to MUC1 and the urease activity our MR Reporters. Aim 2: Analyze the ability of the optimized MUC1 targeted MR Reporter to detect CRC using in vivo imaging in a human MUC1 expressing CRC animal model.

	Aim 3: Combine our MR Reporter with gold nanoparticles and optimize our constructs to determine if a theranostic particle can be generated. Aim 4: Test the in vivo diagnostic ability of our gold nanoparticle MR Reporter in our CRC animal models.
Overlap:	None

Title:	Metabolic Imaging of Patients with Prostate Cancer Using Hyperpolarized Pyruvate (Logothetis)
Effort:	1.20 CM, 10% effort
Supporting Agency:	Koch Functional Imaging and Prostate Cancer Project
Grants Officer:	Claudia Delgado, Executive Director The University of Texas MD Anderson Cancer Center Grants and Contracts P.O. Box 301407, Unit 1644 Houston, TX 77030
Performance Period:	12/21/2015 – 07/21/2021 (NCE)
Level of Funding:	
Project Goals	To evaluate sensitivity and specificity of an HP compound for detecting, staging and surveillance of prostate cancer and determining the efficacy of a therapeutic approach.
Specific Aims	Aim 1: Characterize metabolic adaptive response of PDX models in vivo to finasteride using HP pyruvate, fumarate, N-acetyl-aspartylglutamate (NAAG) and Chemical Reaction-Induced Multimolecular Polarization (CRIMP) with histological and in vitro metabolomics correlations. These compounds will interrogate glycolysis, the TCA cycle, PSMA pathway metabolic components respectively that are linked to AR signaling. CRIMP will be employed for real-time pH mapping in vivo. Aim 2: Optimize dynamic MR spectroscopic imaging sequences tailored to the unique spectral and spatiotemporal characteristics of HP substrates on preclinical and clinical imaging systems. Aim 3: Develop and validate GMP production protocol of HP imaging agents.
Overlap:	None

Title:	Mark-III 129Xe Gas Polarizer System (1S10OD027038-01A1 – Bankson)
Effort:	0.00 CM, 0% effort
Supporting Agency:	National Institutes of Health
Grants Officer:	Malgorzata Klosek 9609 Medical Center Drive

	Bethesda, MD 20892 klosekm@csr.nih.gov
Performance Period:	02/01/2020 – 01/31/2021
Level of Funding:	
Project Goals	This Shared Instrumentation Grant for a 129Xe gas polarizer would bring new capabilities for imaging lung function to MD Anderson and the Texas Medical Center.
Specific Aims	N/A
Overlap:	None

CURRENT:

Title:	Hyperpolarized MRI and Artificial Intelligence (AI) to Inform Metabolic Evolution of Glioblastoma Throughout Tumor Progression (Bhattacharya)
Effort:	0.00 CM, 0% effort
Supporting Agency:	The University of Texas MD Anderson Cancer Center SPORE in Brain
Grants Officer:	Biny Joseph, Program Director The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd., Unit 0431 Houston, TX 77030
Performance Period:	09/01/2022 – 04/30/2024 (NCE)
Level of Funding:	
Project Goals	The overarching goal of this proposal is to develop AI driven HP metabolic MRI-based technique to reduce the time necessary to detect brain tumor evolution in three key areas of tumor progression: initial development of the tumor, its regression following therapy, and the eventual recurrence of the tumor.
Specific Aims	Aim 1: To correlate glycolytic metabolic competency in two cohorts of GSC xenografts with graded aggressiveness profiles from medium, to low by employing MRI, HP metabolic imaging and DL for early detection. Aim 2: To evaluate the response of individual tumors in the same two cohorts of GSC xenografts to radiation therapy using MRI, HP metabolic imaging and DL for interrogating early efficacy of therapy and early relapse.
Overlap:	None

Title:	Real Time Metabolic Imaging to Interrogate Early Detection and Prevention of Pancreatic Cancer (PA220132 – Bhattacharya)
Effort:	1.20 CM, 10% effort
Supporting Agency:	Department of Defense PCARP TRPA
Grants Officer:	TBA
Performance Period:	10/01/2023 – 09/30/2026
Level of Funding:	
Project Goals	To develop the capability of non-invasively detecting and imaging the regression of premalignant pancreatic lesions and early stage disease following immunoprevention in preclinical and clinical cohorts using hyperpolarized metabolic imaging (HP-MRI).
Specific Aims	Aim 1: To determine the utility of preclinical imaging with [1-13C] pyruvate hyperpolarized MRI to track the efficacy of an immunopreventive intervention. Aim 2: To demonstrate the feasibility and utility of pancreatic premalignant metabolic imaging with HP [1-13C] pyruvate MRI in a pilot imaging study.
Overlap:	None

Title:	Real Time Metabolic Imaging to Interrogate Early Detection and Prevention of Pancreatic Cancer (Enriquez)
Effort:	0.0 CM, 0% effort (Mentor)
Supporting Agency:	National Institutes of Health
Grants Officer:	Mariam Eljanne Program Representative NATIONAL CANCER INSTITUTE eljannem@mail.nih.gov
Performance Period:	09/01/2023 – 08/31/2025
Level of Funding:	
Project Goals	To develop, demonstrate and validate novel imaging approaches (HP MR and acidoCEST MRI) to detect the early stages of pancreatic cancer prior to invasive disease.
Specific Aims	Specific Aim 1: To demonstrate and validate the sensitivity and specificity of dynamic hyperpolarized metabolic imaging (Dissertation Research Project; F99 phase). Specific Aim 2: To demonstrate detection of premalignant pancreatic lesions with a combination of HP and acidoCEST MR and to determine the efficacy of immunoprevention on premalignant models (Postdoctoral Research Direction; K00 phase).
Overlap:	There is some conceptual overlap with the trainee grant in applying hyperpolarized metabolic imaging for early detection

	of pancreatic cancer with Department of Defense PCARP TRPA and PREVENT. There is no budgetary overlap.

Title:	Employing AI to Predict Clinical Outcomes in Ovarian Cancer (Shams)
Effort:	0.60 CM, 5% effort
Supporting Agency:	San Jose State University/OCRA
Grants Officer:	N/A
Performance Period:	01/01/2023 – 12/31/2025
Level of Funding:	
Project Goals	In this proposal, we will apply artificial intelligence (AI) in this context of morphologic and mutli-platform omics differences observed in HGSOC.
Specific Aims	Aim 1: To detect distinct morphologic patterns in HGSOC by AI at the time of laparoscopy and to correlate these patterns with clinical outcomes. Aim 2: To integrate clinical and laboratory variables with multi-platform omics data obtained from tissue samples at the time of laparoscopic assessment of disease burden to detect distinct biologic patterns in HGSOC by AI. Aim 3: To employ the observed morphologic, clinical, and omics patterns identified above in the development of a hybrid biomarker optimized to predict clinical outcomes for patients with advanced HGSOC.
Overlap:	None

Title:	Interdisciplinary Translational Pre/Postdoctoral Program in Cancer Nanotechnology (T32CA196561 – Sokolov)
Effort:	0.00 CM, 0% effort
Supporting Agency:	National Institutes of Health / National Cancer Institute
Grants Officer:	N/A
Performance Period:	04/01/2022 – 03/31/2027
Level of Funding:	2,659,935
Project Goals	The overall goal of this project is to develop a novel training program to prepare Ph.D. scientists who will transfer the many promises of cancer nanotechnology into clinical reality of the future
Specific Aims	N/A
Overlap:	None

Title:	Evaluation of Real-time Metabolic Imaging Biomarkers for Detection of Pancreatic Premalignant Lesions (75N91019D00021 – Bhattacharya / McAllister / Brown)
Effort:	1.20 CM, 10% effort
Supporting Agency:	National Institutes of Health / National Cancer Institute

	PREVENT
Grants Officer:	Christy L. Hunter 2115 E. Jefferson St. MSC 8500 Suite 4B 432 Bethesda, MD 20892 Christy.hunter@nih.gov 301-624-8788
Performance Period:	09/16/2021 – 12/15/2023
Level of Funding:	
Project Goals	To determine the sensitivity and specificity of a novel metabolism-based imaging technique for early detection of PDAC in the gold standard murine models as well as define correlative biomarkers which could serve to validate findings in humans within pancreatic cancer high risk individuals in the future who undergo yearly screening.
Specific Aims	NA
Overlap:	None

Title:	Developing Imaging Biomarkers for Immunotherapy Resistance In Vivo (RP220270 – Bhattacharya)
Effort:	2.40 CM, 20% effort
Supporting Agency:	Cancer Prevention & Research Institute of Texas (CPRIT) – Individual Investigator Research Awards
Grants Officer:	Cancer Prevention & Research Institute of Texas (CPRIT) 1701 North Congress Avenue, Suite 6-127 Austin, TX 78701 cprit@cprit.state.tx.us
Performance Period:	03/01/2022 – 02/28/2025
Level of Funding:	
Project Goals	To develop biomarkers to image immunotherapy resistance in vivo and to improve the success rate of immunotherapy for patients with cancer.
Specific Aims	Aim 1 To monitor changes in tumor pHe and HP lactate-to-pyruvate metabolic flux in B16/BL6 melanoma clones that acquired resistance to checkpoint blockade immunotherapy through serial in vivo passage using acidoCEST MRI and HP MRS. Aim 2 To identify the best pH-sensitizer with acidoCEST MRI and HP MRS in melanoma model of progressive immunotherapy resistance. Aim 3 To improve the response to immunotherapy in a melanoma model of progressive immunotherapy resistance by

	first applying a pH-sensitizer while monitoring with acidoCEST MRI and HP MRS.
Overlap:	None

Title:	Institutional Startup Research Funding
Effort:	0.12 CM, 1% effort
Supporting Agency:	The University of Texas MD Anderson Cancer Center
Grants Officer:	Nyma Shah, Director, Research Funding Programs The University of Texas MD Anderson Cancer Center – Research Administration Office 1515 Holcombe Blvd., Unit 1436 Houston, TX 77030
Performance Period:	04/01/2012 – 08/31/2024 (NCE)
Level of Funding:	
Project Goals	To develop a real-time molecular and metabolic imaging program at the University of Texas, MD Anderson Cancer Center employing different modalities of hyperpolarization.
Specific Aims	No specific aims, as funding is geared toward investigator's overall research program.
Overlap:	None

Title:	WS #28 – Metabolic Imaging of Prostate Cancer Patients for Monitoring Therapeutic Efficacy (Bhattacharya / Bankson / Kundra)
Effort:	0.60 CM, 5% effort
Supporting Agency:	General Electric Healthcare/Center for Biomedical Imaging
Grants Officer:	Leslie Billings, Administrator The Center for Advanced Biomedical Imaging 1881 East Rd., Unit 1905 Houston, TX 77054
Performance Period:	08/26/2016 – 02/29/24 (NCE)
Level of Funding:	
Project Goals	To employ hyperpolarized pyruvate for prostate cancer risk stratification in preclinical mouse models of prostate cancer and prepare for clinical trial in prostate cancer patients at MD Anderson Cancer Center.
Specific Aims	Aim 1: Infrastructure development for applying MR hyperpolarization imaging on clinical prostate cancer patients at MDACC.

	Aim 2: Optimize dynamic MR spectroscopic imaging sequences tailored to the unique spectral and spatiotemporal characteristics of HP substrates on a 3T clinical scanner. Aim 3: Determine the sensitivity and specificity of MR hyperpolarization with $^{13}C(1)$-pyruvate to predict clinical response in high grade prostate cancer patients enrolled in an on-going abiraterone therapeutic clinical trial.
Overlap:	None

Title:	Real-time Metabolic Imaging Biomarkers for Detection of Pancreatic Premalignant Lesions (Bhattacharya)
Effort:	0.12 CM, 1% effort
Supporting Agency:	The University of Texas MD Anderson Cancer Center /Duncan Family Institute for Cancer Prevention and Risk Assessment Seed-funding Research Program
Grants Officer:	Lori Armstrong 1515 Holcombe Blvd. Houston, TX 77030-4009 laarmstrong@mdanderson.org
Performance Period:	06/01/2021 – 05/31/2024 (NCE)
Level of Funding:	
Project Goals	The overarching goal of this seed proposal is to develop the capability of non-invasively detecting advanced pancreatic intraepithelial neoplasia (PanIN) precursor lesions in pancreas prior to invasive disease in by employing hyperpolarized metabolic imaging.
Specific Aims	Aim 1: To demonstrate the sensitivity of dynamic hyperpolarized metabolic biomarkers to detect and monitor the progression of pancreatic premalignant lesions to pancreatic cancer in inducible GEM models at multiple time points in vivo. Aim 2: The overarching goal of this seed proposal is to develop the capability of non-invasively detecting advanced pancreatic intraepithelial neoplasia (PanIN) precursor lesions in pancreas prior to invasive disease in by employing hyperpolarized metabolic imaging.
Overlap:	None

Title:	Identifying Different Metabolic Sub-types of Prostate Cancer for Early Therapeutic Assessment (W81XWH-21-1-0763 – Bhattacharya)
Effort:	2.40 CM, 20% effort
Supporting Agency:	Department of Defense – Prostate Cancer Research Program – Idea Development Award
Grants Officer:	Joshua McKean 820 Chandler St.

	Fort Detrick, MD 21702 joshua.d.mckean3.civ@mail.mil
Performance Period:	09/01/2021 – 08/31/2024
Level of Funding:	
Project Goals	To develop personalized metabolic imaging modality to target treatment strategies of different sub-types of PCa and to interrogate different metabolic factors by imaging that are associated with a particular sub-type.
Specific Aims	Aim 1: To perform HP-13C Pyruvate MRI, [18F]FPIA -PET imaging in four well characterized patient derived xenograft (PDX) murine models of prostate cancer in vivo before and after the antiandrogen therapy with Enzalutamide to image both alteration in glycolytic and fatty acid oxidation pathways after treatment response. Aim 2: To elucidate the metabolic drivers of ADT resistance. We will analyze ADT sensitive and ADT resistant PDX utilizing NMR-spectroscopy combined with mass spectrometry-based metabolomics, immunohistochemistry and transcriptome profiling. Using this approach, we expect to delineate pathways of ADT resistance. Aim 3: To image overcoming the ADT resistance by targeting Monocarboxylate Transporter (MCT)pathway (via MCT inhibition with the clinical drug, Syrosingopine) by performing HP-13C Pyruvate MRI in two well characterized patient derived xenograft (PDX) murine models of prostate cancer in vivo. [18F]FPIA -PET
Overlap:	This grant has some overlap with the CPRIT Individual Investigator Research Award (IIRA) -RP220313 where co-investigator, Dr. Federica Pisaneschi serves as PI. Conceptually both grants are similar. The scope of the CPRIT grant is however much broader than the DoD Idea Grant in terms of 1) larger numbers and types of PDX mouse models employed, 2) a different hyperpolarized metabolic reagent, 15N-L-Carnitine-d6 employed to track the carnitine pathway, and 3) finally, Enolase 2 (ENO2) (via ENO2 inhibition with natural phosphonate antibiotic, SF2312) inhibition has been employed as a strategy to overcome ADT resistance. CPRIT grant essentially builds up on the DoD grant and is essentially on parallel track with little direct overlap.

Title:	Imaging Metabolic Reprogramming in Prostate Cancer (RP220313 – Pisaneschi)
Effort:	1.20 CM, 10% effort
Supporting Agency:	Cancer Prevention and Research Institute of Texas

Grants Officer:	Patty Moore Cancer Prevention and Research Institute of Texas 1701 North Congress Avenue, Suite 6-127 Austin, TX 78701 pmoore@cprit.texas.gov
Performance Period:	03/01/2022 – 02/28/2025
Level of Funding:	
Project Goals	This proposal will build up on these findings, investigating by PET and HP-MRI how carnitine metabolism is modulated in these PDXs before and after Enzalutamide-treatment. Furthermore, we will attempt to overcome Enzalutamide resistance by targeting MCT and ENO2 proteins with inhibitors, Syrosingopine and SF2312 respectively, and image this transformation from resistance to sensitization by HP-MRI and PET.
Specific Aims	Aim 1: HP MRI and PET imaging. To perform 13C-Pyruvate, 15N-L-Carnitine-d6 HP-MRI and [18F]FPIA-PET imaging in six well characterized patient derived xenograft (PDX) murine models of prostate cancer in vivo before and after the antiandrogen therapy with Enzalutamide to image both alteration in glycolytic and fatty acid oxidation pathways after treatment response. Aim 2: Ex vivo analyses. To understand the mechanistic basis of the success and/failure of HP-MRI and FPIA-PET in imaging specific PDX sub-types of PCa xenografts through metabolic and transcriptome profiling and analyses of key protein expressions in the metabolic pathways. Aim 3: Overcoming resistance. To image overcoming the Enzalutamide resistance by targeting Monocarboxylate Transporter (MCT) (via MCT inhibition with the clinical drug, Syrosingopine) and Enolase 2 (ENO2) (via ENO2 inhibition with natural phosphonate antibiotic, SF2312) and define whether MCT and/or ENOs are viable targets for potential combination therapy with anti-androgens.
Overlap:	This grant has some overlap with DoD PCRP grant (W81XWH-21-1-0763 – Bhattacharya) where co-investigator, Dr. Federica Pisaneschi serves as PI. Conceptually both grants are similar. The scope of the CPRIT grant is however much broader than the DoD Idea Grant in terms of 1) larger numbers and types of PDX mouse models employed, 2) a different hyperpolarized metabolic reagent, 15N-L-Carnitine-d6 employed to track the carnitine pathway, and 3) finally, Enolase 2 (ENO2) (via ENO2 inhibition with natural phosphonate antibiotic, SF2312) inhibition has been employed as a strategy to overcome ADT resistance. CPRIT grant essentially builds up on the DoD grant and is essentially on parallel track with little direct overlap. Dr.

	Pisaneschi has declared the overlap to CPRIT before accepting the award.

Title:	Targeted Hyperpolarized Molecular Beacons for Colorectal Cancer Detection (R21EB031217 – Bhattacharya)
Effort:	1.20 CM, 10% effort
Supporting Agency:	National Institutes of Health / National Institute of Biomedical Imaging and Bioengineering
Grants Officer:	Joseph Peterson 9609 Medical Center Drive Bethesda, MD 20892 petersonjt@mail.nih.gov
Performance Period:	09/30/2021 – 07/31/2024
Level of Funding:	
Project Goals	To combine the versatile molecular affinity of antibodies with the sensitivity of hyperpolarized magnetic resonance (HP MR) to develop "hyperpolarized (HP) molecular beacons" for deep tissue imaging for CRC detection.
Specific Aims	Aim 1: To develop binding and activity assays for MUC1 targeted HP molecular beacons and to optimize construct (0-12 months). Aim 2: To perform non-invasive in vivo MR imaging with optimized MUC1 targeted HP molecular beacon (8-24 months). Aim 3: To generate and optimize binding of gold nanoparticle coupled MUC1 HP molecular beacon construct (18-36 months).
Overlap:	There is scientific overlap of this grant with the CPRTP postdoctoral fellowship given below but there is no budgetary overlap for these projects.

Title:	Hyperpolarized molecular beacons for early detection of colorectal cancer (Dominic)
Effort:	0.0 CM, 0% effort (Mentor)
Supporting Agency:	CPRTP Janice Davis Gordon Memorial in Colorectal Cancer Prevention
Grants Officer:	N/A
Performance Period:	09/01/2023 – 08/31/2025
Level of Funding:	
Project Goals	To significantly increase the ability of detecting cancer by utilizing several amplification steps and combining the versatile binding affinity and specificity of antibodies with the sensitivity of hyperpolarized Magnetic Resonance (HP MR).

Specific Aims	Specific Aim 1: To develop binding and activity assays for MUC1-targeted HP molecular beacons and optimize constructs. Specific Aim 2: To perform non-invasive in vivo MR imaging with optimized MUC1-targeted HP molecular beacons. Specific Aim 3: To expand the repertoire of HP molecular beacons to other cell surface markers in CRC that can be combined to target key biomarkers of CRC.
Overlap:	There is scientific overlap of this trainee grant with the R21EB031217 grant from NIBIB but there is no budgetary overlap for these projects. This fellowship only pays portion of the postdoctoral fellow's salary.

PENDING

Title:	Targeting of metabolic crosstalk between leukemia and macrophages as a therapeutic strategy for disease eradication and restoration of innate immune system (Baran)
Effort:	0.36 CM, 3% effort
Supporting Agency:	Cancer Prevention Research Institute of Texas (CPRIT)
Grants Officer:	TBD
Performance Period:	03/01/2024 – 02/28/2027
Level of Funding:	
Project Goals	To incorporate the concept of OXPHOS/Lactate blockade into anti-leukemia therapy.
Specific Aims	Specific Aim 1: Determine the anti-leukemia efficacy of MCT1/MCT4 blockade on OXPHOS activity and the impact of dual inhibition of MCT1/MCT4 and OXPHOS on AML cells, macrophages, and AML/macrophage co-culture, and characterize the molecular mechanisms of action. Specific Aim 2: To determine the anti-leukemia efficacy of OXPHOS/MCT1/MCT4 blockade in AML models with or without macrophages infusion as a consolidation therapy in vivo. Specific Aim 3: To characterize transcriptomic and metabolic signatures of AML cells and macrophages vulnerable to OXPHOS/MCT1/MCT4 inhibition, and spatial signature of AML-macrophage cross talk upon MCT1/MCT4/OXPHOS inhibition in vivo.
Overlap:	None

Title:	Cancer Prevention Education: Student Research Experiences (Chang)
Effort:	0.0 CM, 0% effort (Mentor)
Supporting Agency:	National Institutes of Health
Grants Officer:	TBA
Performance Period:	12/01/2023 – 11/30/2028
Level of Funding:	
Project Goals	To complement and/or enhance the training of a workforce to meet the nation's biomedical, behavioral and clinical research needs;
Specific Aims	Specific Aim 1: Recruit, select, and train high-performing students for 25 10-week positions annually, using innovative and effective strategies to attract a demographically diverse student population. Specific Aim 2: Cultivate and support the pool of participating faculty mentors. Specific Aim 3: Provide a superlative mentored research training experience in a variety of cancer prevention disciplines Specific Aim 4: Provide highly relevant didactic, career and professional skills development, and research ethics curricula in cancer prevention research and cancer prevention careers. Specific Aim 5: Contribute to broadening participation of groups underrepresented in research careers through development of students' identity as scientists, particularly in cancer research.
Overlap:	None

Title:	Artificial Intelligence for early identification of androgen-indifferent, lethal prostate cancer and therapy selection (Merenyi, Bhattacharya, Pilie)
Effort:	1.20 CM, 10% effort
Supporting Agency:	Rice University/Cancer Prevention Research Institute of Texas (CPRIT)
Grants Officer:	TBA
Performance Period:	03/01/2023 – 02/28/2027
Level of Funding:	
Project Goals	To develop strategies to define the biology of lethal prostate cancer, to develop effective treatments, and address mechanisms of resistance for men with mCRPC.
Specific Aims	Specific Aim 1: Evaluate prediction accuracy of neural map-based AI models using ex vivo and laboratory measurements complemented by in vivo HP-MRI/CSI before and after treatment at multiple time points.

	Specific Aim 2: Evaluate prediction accuracy of AI models using laboratory measurements and in vivo HP-MRI/CSI before and after treatment at multiple time points.
Overlap:	None

Title:	Development of Silicon Nanoparticles as Molecular Beacons for Targeted Molecular Imaging (Bhattacharya)
Effort:	1.20 CM, 10 % effort
Supporting Agency:	National Institutes of Health
Grants Officer:	TBA
Performance Period:	12/01/2023 – 11/30/2025
Level of Funding:	
Project Goals	To develop a suite of molecular beacons of functionalized hyperpolarized SiNPs for real-time MRI detection of all/most polyp subtypes along with a new platform technology for real-time, non-invasive molecular imaging of early-stage CRC using MRI employing targeted imaging, formerly only in the realm of positron emission tomography (PET) and single-photon emission computed tomography (SPECT).
Specific Aims	Specific Aim 1: Establish targeted molecular imaging by MUC1 functionalized HP SiNPs in a well annotated CRC humanized mouse model. Specific Aim 2: Create a library of functionalized SiNPs that recognize and identify most/all polyp subtypes, including flat lesions, without binding to normal tissue. A) Expand the repertoire of receptor targeting moieties to other cell surface markers in CRC that can be targeted with functionalized SiNPs using bioengineered polyp avatars. Specific Aim 3: Measure the ability of the multifunctional SiNP formulation library to recognize the spectrum of pathologically different subtypes of freshly collected human polyp tissue.
Overlap:	None

CERTIFICATION

I, PD/PI, Partnering PI, or other senior/key personnel, certify that the statements herein are current, accurate, and complete to the best of my knowledge; I agree to update such disclosure at the request of the agency prior to the award of support and at any subsequent time the agency determines appropriate during the term of the award; and I have been made aware of the requirements under Section 223(a)(1) of the William M. (Mac) Thornberry National Defense Authorization Act for Fiscal Year 2021. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties (U.S. Code, Title 218, Section 1001).

*Signature: DocuSigned by: Pratip Bhattacharya F20E137D35F349F...

Date: 9/20/2023 | 8:54 AM CDT

Previous/Current/Pending Support for DOD

Pisaneschi, Federica

PREVIOUS:

Title:	Evaluating the Predictive Power of Novel PET Imaging Agents at the intersection of NASH and ICT response
Effort:	Year (YYYY) / Person Months (##.##) 1. 2022 / 0.12 Calendar 2. 2023 / 0.12 Calendar
Supporting Agency:	The University of Texas MD Anderson Cancer Center – QIAC Partnership in Research Grant
Grants Officer:	Lori Armstrong The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd. Houston, TX 77030-4009
Performance Period:	05/01/2021 – 04/30/2023
Level of Funding:	
Project Goals	PET imaging of inflammation and apoptosis, supported by a panel of serum biomarkers, can be used to construct an integrated robust diagnostic model that predicts ICT induced liver damage in the context of NASH and melanoma
Specific Aims	Aim 1: Utilize ^{18}F-TBD in combination with serum biomarkers to discriminate progression to HCC from NASH, NAFLD, and normal murine livers. Aim 2: Utilize [^{18}F]-FN PET in combination with serum biomarkers to discriminate progression to HCC from NASH, NAFLD, and normal murine livers.
Overlap:	None

Title:	PET Imaging of Apoptosis and Inflammation for the Prevention of Hepatocellular Carcinoma (HCC)
Effort:	Year (YYYY) / Person Months (##.##) 1. 2021 / 0.60 Calendar 2. 2022 / 0.60 Calendar
Supporting Agency:	The University of Texas MD Anderson Cancer Center – CABI Pilot Project Program
Grants Officer:	Lori Armstrong The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd. Houston, TX 77030-4009
Performance Period:	07/01/2020 – 03/31/2022
Level of Funding:	
Project Goals	To change the clinical practice of HCC diagnosis, and prevention through non-invasive imaging technologies to identify NASH and monitor its treatment.

Specific Aims	Aim 1: Utilize [^{18}F]-TBD PET to distinguish NASH from NAFLD and measure its value as a predictive imaging biomarker for dietary and pharmacological intervention with Emricasan. Utilize [^{18}F]-TBD PET to distinguish NASH from NAFLD and measure its value as a predictive imaging biomarker for dietary and pharmacological intervention with Emricasan. Aim 2: Utilize [^{18}F]4FN PET to distinguish NASH from NAFLD and measure its value as a predictive imaging biomarker for dietary and pharmacological intervention with Atorvastatin
Overlap:	None

Title:	SUPR Peptides for Immune Checkpoint Blockade Imaging	
Effort:	Year (YYYY)	Person Months (##.##)
	2. 2018	1.20 Calendar
	3. 2019	1.20 Calendar
	4. 2020	1.20 Calendar
	5. 2021	1.20 Calendar
	6. 2022	1.20 Calendar
Supporting Agency:	CABI/G.E. In-Kind Research Award	
Grants Officer:	Praveena Gangakhedkar Academic Research Program Manager Praveena.gangakhedkar@ge.com (281) 536-0503	
Performance Period:	07/01/2016 – 06/30/2021	
Level of Funding:		
Project Goals	To develop a SUPR peptide-based PET tracer for PD-L1 imaging and prediction of response to PD-1/PD-L1 therapies.	
Specific Aims	Aim 1: Generate and Characterize SUPR Peptides Against PD-L1. Aim 2: In vivo Optical Imaging of PD-L1 with Cy5-labeled SUPR Peptides. Aim 3: PET/CT Imaging of PD-L1 using ^{18}F-SUPR Peptides	
Overlap:	None	

Title:	Measuring Tumor Acidosis with PET/MRI Contrast Agents	
Effort:	Year (YYYY)	Person Months (##.##)
	1. 2019	0.6 Calendar
	2. 2020	0.6 Calendar
Supporting Agency:	NIH	
Grants Officer:	Tatjana Atanasijevic 9900 Rockville Pike Bethesda, MD 20892 301-451-6873	
Performance Period: **Level of Funding:**	03/01/2019 – 12/31/2020	

Project Goals	To quantitatively measure extracellular pH (pHe) in the tumor microenvironment to assess tumor acidosis.
Specific Aims	Aim 1: To develop and apply PET/MRI contrast agents that measure in vivo tumor pHe.
Overlap:	None

Title:	Glutamine Imaging for the Detection of Renal Cell Carcinoma Lung Metastases	
Effort:	Year (YYYY)	Person Months (##.##)
	1. 2020	0.84 Calendar
	2. 2021	0.84 Calendar
Supporting Agency:	The University of Texas MD Anderson Cancer Center – CABI Pilot Project Program	
Grants Officer:	Lori Armstrong The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd. Houston, TX 77030-4009	
Performance Period:	04/01/2019 – 01/31/2021	
Level of Funding:		
Project Goals	To determine if radioactive glutamine can discern ccRCC lung metastases versus inflammation in pre-clinical mouse models.	
Specific Aims	Aim 1: In vitro studies: Compare the sensitivity and specificity of uptake of [^{11}C]Gln and [^{18}F]FGln versus [^{18}F]FDG in parental and lung metastases ccRCC cell lines, normal kidney cells (HEK293) and normal lung cells (BEAS-2B).	
Overlap:	None	

Title:	In Vivo Imaging of Over-expressed Micro-RNAs for Lung Cancer Diagnosis and Prognosis	
Effort:	Year (YYYY)	Person Months (##.##)
	1. 2019	0.12 Calendar
	2. 2020	0.12 Calendar
	3. 2021	0.12 Calendar
Supporting Agency:	IRCCS-AUSL Reggio Emilia (Italy)	
Grants Officer:	Dott.ssa Sara Li Dooni Infrastruttura Ricerca-Statistica, Direzione Scientifica Sara.lidonni@ausl.re.it	
Performance Period:	01/01/2019 – 12/31/2021	
Level of Funding:		
Project Goals	To synthesize and radiolabel PNA based probes against miRNA-146a, -21, and -155; to validate the selectivity of anti-miRNA-probes in vitro by using tumor cell lines over-expressing the miRNAs target; to exploit the most promising anti-miRNA-probes for molecular imaging of cancer by means of PET in murine models; and to develop relationship between the two institutions in the field of research, mobility	

	of personnel, and activities for students.
Specific Aims	Aim 1: To validate the selectivity of anti-miRNA-probes in vitro by using tumor cell lines over-expressing the miRNAs target. Aim 2: To exploit the most promising anti-miRNA-probes for molecular imaging of cancer by means of PET in murine models; Aim 3: To develop relationship between the two institutions in the field of research, mobility of personnel, and activities for students.
Overlap:	None

Title:	Evaluating the Predictive Power of Novel PET Imaging Agents in the Transition from NAFLD through NASH to HCC
Effort:	Year (YYYY) / Person Months (##.##) 1. / 0.6 Calendar 2. / 0.6 Calendar 3. / 0.6 Calendar 4. / 0.6 Calendar 5. / 0.6 Calendar
Supporting Agency:	National Institutes of Health / The University of Texas MD Anderson Cancer Center – HCC SPORE DRP
Grants Officer:	Lori Armstrong The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd. Houston, TX 77030-4009
Performance Period:	09/01/2020 – 08/31/2021
Level of Funding:	
Project Goals	To test the hypothesis that PET imaging of inflammation and apoptosis, supported by a panel of serum biomarkers, can be used to construct an integrated, robust diagnostic model that discriminates HCC progression from the following confounders: normal liver, NAFLD, and NASH livers with an AUROC of ≥0.85.
Specific Aims	To test the hypothesis that PET imaging of inflammation and apoptosis, supported by a panel of serum biomarkers, can be used to construct an integrated, robust diagnostic model that discriminates HCC progression from the following confounders: normal liver, NAFLD, and NASH livers with an AUROC of ≥0.85
Overlap:	None

Title:	PET Imaging of Neuroinflammation with 4-[^{18}F]fluoronaphthol
Effort:	Year (YYYY) / Person Months (##.##) 1. 2022 / 0.60 Calendar

	2. 2023	0.60 Calendar
Supporting Agency:	QIAC Partnership in Research Grant	
Grants Officer:	Lori Armstrong 1515 Holcombe Blvd. Houston, TX 77030-4009 laarmstrong@mdanderson.org	
Performance Period:	05/01/2021 – 04/30/2023	
Level of Funding:		
Project Goals	Due to the high production of ROS and upregulation of NOX activity in microglia as a consequence of brain injuries, we hypothesize that [^{18}F]4FN-PET will be able to detect neuroinflammation in mouse models of radiation-induced inflammation and neurodegenerative diseases.	
Specific Aims	Aim 1: [^{18}F]4FN-PET in LPS models of neuroinflammation – a proof of concept experiment. Aim 2: [^{18}F]4FN-PET in a clinically relevant model of neuroinflammation due to Cranial Radiotherapy Aim 3: Intervention. Test the use of [^{18}F]4FN-PET as a marker for drug response using NBD-peptide treatment of CRT- induced brain inflammation.	
Overlap:	None	

Title:	[^{18}F]4FN PET Imaging of Innate Immunity Activation During Immunotherapy-Induced Adverse Events	
Effort:	Year (YYYY)	Person Months (##.##)
	1. 2022	3.00 Calendar
	2. 2023	3.00 Calendar
Supporting Agency:	National Institutes of Health / National Cancer Institute	
Grants Officer:	Lin, Charles linp@mail.nih.gov	
Performance Period:	09/01/2022 – 08/31/2027	
Level of Funding:		
Project Goals	To test the that imaging high redox potential RONS from activation of key innate immune cells will provide selective diagnostic utility by integrating multiple divergent biochemical inputs that converge to produce the majority of irAEs.	
Specific Aims	Aim 1: Characterize an Established Advanced Pre-clinical Model of irAE on a Background of Auto-immunity by [^{18}F]4FN PET Imaging. Aim 2: Determine the effect of Diet-Induced Metabolic Syndrome on a Novel Pre-clinical Model of irAE by [^{18}F]4FN PET Imaging. Aim 3: Quantify immune effector cell-associated neurotoxicity syndrome (ICANS) by [^{18}F]4FN PET Imaging compared to serum markers in a model of CAR T-cell therapy.	
Overlap:	None, Relinquished my portion to PI when I moved to UTHealth-Houston	

Title:	Acquired Resistance to Therapy and Iron (ARTI) Center
Effort:	Year (YYYY) / Person Months (##.##) 1. 2022 / 1.2 Calendar 2. 2023 / 1.2 Calendar
Supporting Agency:	National Institutes of Health / National Cancer Institute
Grants Officer:	Michael Espey 240-276-6230 SP@NIH.GOV
Performance Period:	09/20/2022 – 08/31/2027
Level of Funding:	
Project Goals	The overall goal of the MIC is to implement and manage the precise imaging support infrastructure (personnel, reagents, animals, software, and customized hardware resources) needed to support each project in the ARTI Center.
Specific Aims	Aim 1: Collaborate with the ARTI Center and individual investigators in developing imaging protocols and analyses with appropriate biological and biochemical controls, robust test-retest analysis, and imaging statistical support when appropriate. Aim 2: Provide timely access to unique plasmid-based reporters, reporter animals, PET reagents, and fluorescent biosensors, while leveraging internal core and MD Anderson core expertise to modify reagents when appropriate to meet ARTI Center needs. Aim 3: Provide timely service, training, access to customized macro- and microscopic imaging systems, premium image analytics, and custom imaging analysis.
Overlap:	None, Relinquished my portion to PI when I moved to UTHealth-Houston

Title:	Membrane Permeant Peptides for Imaging Cell Function
Effort:	Year (YYYY) / Person Months (##.##) 1. 2019 / 1.2 Calendar 2. 2020 / 1.2 Calendar 3. 2021 / 1.2 Calendar 4. 2022 / 1.2 Calendar 5. 2023 / 1.2 Calendar
Supporting Agency:	National Institutes of Health / National Eye Institute
Grants Officer:	Hemin R. Chin 31 Center Drive MSC 2510 Bethesda, MD 20892-2510
Performance Period:	09/30/2018 – 08/31/2023
Level of Funding:	
Project Goals	To conduct quantitative pre-clinical testing in advanced glaucoma models to monitor disease progression and quantify dietary (niacin) and gene therapy (Nmnat1) interventions, as well as toxicology analysis, and metabolite profiling. We will advance a lead peptide toward the clinic through a statistically-robust non-human primate model of

	glaucoma.
Specific Aims	Aim 1: Test the hypothesis that our caspase-3-activated cell-penetrating peptides can quantify apoptosis in pre-clinical rodent models of RGC degeneration and treatment interventions. Aim 2: Rigorously test the hypothesis that our lead caspase-3- activated cell-penetrating peptide can quantify apoptosis in an advanced non-human primate model of glaucoma. Aim 3: Perform advanced pre-clinical characterization of a lead activatable cell-penetrating peptide in preparation for eIND filing
Overlap:	None, Relinquished my portion to PI when I moved to UTHealth-Houston

CURRENT:

Title:	Identifying Different Metabolic Sub-types of Prostate Cancer for Early Therapeutic Assessment
Effort:	Year (YYYY) / Person Months (##.##) 1. 2022 / 2.4 Calendar 2. 2023 / 1.2* Calendar 3. 2024 / 1.2* Calendar *Pending new sub contract Notice
Supporting Agency:	DoD
Grants Officer:	Joshua McKean 820 Chandler St. Fort Detrick, MD 21702 joshua.d.mckean3.civ@mail.mil
Performance Period:	09/2021-08/2024
Level of Funding:	
Project Goals	To develop personalized metabolic imaging modality to target treatment strategies of different sub-types of PCa and to interrogate different metabolic factors by imaging that are associated with a particular sub-type.
Specific Aims	Aim 1: To perform HP-^{13}C Pyruvate MRI, [^{18}F]FPIA -PET imaging in four well characterized patient derived xenograft (PDX) murine models of prostate cancer in vivo before and after the antiandrogen therapy with Enzalutamide to image both alteration in glycolytic and fatty acid oxidation pathways after treatment response. Aim 2: To elucidate the metabolic drivers of ADT resistance. We will analyze ADT sensitive and ADT resistant PDX utilizing NMR-spectroscopy combined with mass spectrometry-based metabolomics, immunohistochemistry and transcriptome profiling. Using this approach, we expect to delineate pathways of ADT resistance. Aim 3: To image overcoming the ADT resistance by targeting Monocarboxylate Transporter (MCT)pathway (via MCT inhibition with the clinical drug, Syrosingopine) by

	performing HP-^{13}C Pyruvate MRI in two well characterized patient derived xenograft (PDX) murine models of prostate cancer in vivo. [^{18}F]FPIA -PET
Overlap:	None

Title:	Imaging Metabolic Reprogramming in Prostate Cancer
Effort:	Year (YYYY) / Person Months (##.##) 1. 2023 / 2.4 Calendar 2. 2024 / 2.4 Calendar 3. 2025 / 2.4 Calendar
Supporting Agency:	Cancer Prevention and Research Institute of Texas
Grants Officer:	Patricia Moore, Program Manager for Research, CPRIT (www.cprit.state.tx.us)
Performance Period:	03/2022-02/2025
Level of Funding:	
Project Goals	This proposal will build up on these findings, investigating by PET and HP-MRI how carnitine metabolism is modulated in these PDXs before and after Enzalutamide-treatment. Furthermore, we will attempt to overcome Enzalutamide resistance by targeting MCT and ENO2 proteins with inhibitors, Syrosingopine and SF2312 respectively, and image this transformation from resistance to sensitization by HP-MRI and PET.
Specific Aims	Aim 1: HP MRI and PET imaging. To perform ^{13}C-Pyruvate, 15N-L-Carnitine-d6 HP-MRI and [^{18}F]FPIA-PET imaging in six well characterized patient derived xenograft (PDX) murine models of prostate cancer in vivo before and after the antiandrogen therapy with Enzalutamide to image both alteration in glycolytic and fatty acid oxidation pathways after treatment response. Aim 2: Ex vivo analyses. To understand the mechanistic basis of the success and/failure of HP-MRI and FPIA-PET in imaging specific PDX sub-types of PCa xenografts through metabolic and transcriptome profiling and analyses of key protein expressions in the metabolic pathways. Aim 3: Overcoming resistance. To image overcoming the Enzalutamide resistance by targeting Monocarboxylate Transporter (MCT) (via MCT inhibition with the clinical drug, Syrosingopine) and Enolase 2 (ENO2) (via ENO2 inhibition with natural phosphonate antibiotic, SF2312) and define whether MCT and/or ENOs are viable targets for potential combination therapy with anti-androgens.
Overlap:	None

PENDING

Title:	Imaging of cranial radiotherapy neuroinflammatory sequelae by Positron Emission Tomography
Effort:	Year (YYYY) / Person Months (##.##) 1. 2024 / 2.4 Calendar 2. 2025 / 2.4 Calendar 3. 2026 / 2.4 Calendar 4. 2027 / 2.4 Calendar
Supporting Agency:	Cancer Prevention and Research Institute of Texas
Grants Officer:	Patricia Moore, Program Manager for Research, CPRIT (www.cprit.state.tx.us)
Performance Period:	03/01/2023 – 0/28/2027
Level of Funding:	
Project Goals	To detect cranial radiotherapy induced neuroinflammation early and assess cognitive impairment by Positron Emission Tomography.
Specific Aims	Aim 1: To evaluate [^{18}F]4FN-PET in clinically relevant, whole brain and focal preclinical models of neuroinflammation due to CRT and to compare [^{18}F]4FN with ^{18}F-PBR06. Neuroinflammation as detected by PET will be correlated to cognitive impairment. Aim 2: To develop ^{18}F-COG, a new radiopharmaceutical that targets TREM2, and to test it for TREM2-mediated uptake in cellular and animal models. ^{18}F-COG will then be tested in CRT-induced neuroinflammation models. Aim 3: To use PET to monitor the amelioration of neuroinflammation via treatment with TAD-NBD-peptides, and consequent reduction of cognitive impairment
Overlap:	None

Title:	Targeting the androgen receptor with radiation: an alternative approach to treat prostate cancer
Effort:	Year (YYYY) / Person Months (##.##) 1. 2025 / 0.6 Calendar 2. 2026 / 0.6 Calendar
Supporting Agency:	DoD
Grants Officer:	Not Available
Performance Period:	05/01/2024 – 04/30/2026
Level of Funding:	
Project Goals	This study will create radiolabeled small molecule ligands that have the chemical feature of bearing a stable ^{77}Br-label that can be translocated by AR into the nucleus and to the DNA, where Auger emissions will damage DNA and subsequently induce cell death
Specific Aims	Aim1. To synthesize and test [^{77}Br]BrLGD-3303. Aim2. To synthesize and test [^{77}Br]BrJQ1
Overlap:	None

Title:	Radiolabeling compound libraries for high-throughput screening of novel radiopharmaceuticals
Effort:	Year (YYYY) / Person Months (##.##) 1. 2024 / 0.24 Calendar
Supporting Agency:	DropletPharm Inc / NIH
Grants Officer:	Not Available
Performance Period:	04/01/2024 – 03/31/2025
Level of Funding:	
Project Goals	The proposal is focused on further developing a high-throughput radiochemistry that my lab developed and the company is planning to commercialize.
Specific Aims	No aims assigned to UTHealth
Overlap:	None

Title:	Targeted Cell Death Imaging in Heart Transplantation
Effort:	Year (YYYY) / Person Months (##.##) 1. 2025 / 1.2 Calendar 2. 2026 / 1.2 Calendar 3. 2027 / 1.2 Calendar
Supporting Agency:	Rubicon Biotechnology LLC / NIH
Grants Officer:	Not Available
Performance Period:	04/01/2024 – 03/31/2027
Level of Funding:	
Project Goals	Perform radiolabeling of the fragment with 18Faluminium fluoride and will provide radiochemical characterization of the new probe (i.e. radiochemical purity, chemical purity, molar/specific activity, shelf stability). Once the radiochemistry is optimized, the probe will be radiosynthesized for animal studies.
Specific Aims	Perform radiolabeling of the fragment with 18Faluminium fluoride and will provide radiochemical characterization of the new probe (i.e. radiochemical purity, chemical purity, molar/specific activity, shelf stability). Once the radiochemistry is optimized, the probe will be radiosynthesized for animal studies.
Overlap:	None

I, PD/PI or other senior/key personnel confirm that I:

• Certify that the current and pending support provided on the application is current, accurate and complete;

• Agree to update such disclosure at the request of the agency prior to the award of support and at any subsequent time the agency determines appropriate during the term of the award; and

• Have been made aware of the requirements under Section 223(a)(1) of this Act.10 DOD General Application Instructions 18

False, fictitious, or fraudulent statements or claims may result in criminal, civil, or administrative penalties (U.S. Code, Title 18, Section 1001)

Signature: fpisaneschi Digitally signed by fpisaneschi
Date: 2023.09.21 08:50:05 -05'00'

Date: _____