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14. ABSTRACT

Prostate cancer is not only heterogeneous among individuals, but tumors are heterogeneous on the molecular level within a given individual. One well-documented phenomenon is the presence of castrate-resistant prostate cancer with neuroendocrine features (CRPC-NE) that evolves over the course of anti-androgen therapy. Our group has discovered that CRPC-NE have a unique cell surface glycan composition enriched with fucose sugars. Therefore, the ability to image glycan fucosylation could be used to predict the emergence of lethal prostate cancer in men. This proposal tests the feasibility of a previously developed PET agent, [^{18}F] fluorofucose (Fuc-PET) as a functional method to quantify PCa glycan fucosylation, and thus, the burden of lethal disease using animal models. Our **hypothesis** is that Fuc-PET can quantify the amount of glycan fucosylation in tumors noninvasively and thus predict aggressive pathology in vivo.Thus far, we have discovered significant advancements in the field. First, we discovered a fucosylated glycan signature that predicts the development of metastatic prostate cancer at the time of prostatectomy. Second, small molecule inhibition of glucose metabolism and fucosylation has a supportive effect on tumor growth because of immune system inhibition. We have overcome that limitation with the ketogenic diet. These findings indicate that dietary modifications could enhance therapeutic efficacy in men with advanced prostate cancer.

15. SUBJECT TERMS
Prostate cancer, CRPC-NE, glycans, fucose

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INTRODUCTION

Prostate cancer is not only heterogeneous among individuals, but tumors are heterogeneous on the molecular level within a given individual. One well-documented phenomenon is the presence of castrate-resistant prostate cancer with neuroendocrine features (CRPC-NE) that evolves over the course of anti-androgen therapy. Our group has discovered that CRPC-NE have a unique cell surface glycan composition enriched with fucose sugars. Moreover, this enriched glycan fucosylation is not only present in CRPC-NE, but also a subset of prostate adenocarcinomas at initial diagnosis and are associated with adverse clinical outcomes. Therefore, the ability to image glycan fucosylation could be used to stratify men and initial diagnosis as well as predict the emergence of lethal prostate cancer in men. This proposal tests the feasibility of a previously developed PET agent, [^{18}F] fluorofucose (Fuc-PET) as a functional method to quantify PCa glycan fucosylation. The degree of fucosylation will be proportional to the burden of lethal disease using animal models. Our hypothesis is that Fuc-PET can quantify the amount of glycan fucosylation in tumors noninvasively and thus predict aggressive pathology in vivo. Aim 1 will correlate Fuc-PET activity with tumor glycan fucosylation. Aim 2 will identify the effects of key fucosyltransferases (FUT's) on tumor glycan synthesis. Aim 3 will assess the effect of pharmacologic inhibition of tumor fucosylation on tumor growth and tumor immunity.

KEYWORDS

Prostate Cancer
Neuroendocrine Prostate Cancer
Castrate Resistant Prostate Cancer
Glycans
Fucose
Positron Emission Tomography
Fucosyltransferases
Fluorofucose
Immunotherapy

ACCOMPLISHMENTS

What were the major goals of the project?

Aim 1. To correlate fucose-PET (Fuc-PET) activity with tumor glycan fucosylation. (95% complete)
1a. To characterize fucosylation patters across prostate cancer models.
1b. To perform Fuc-PET imaging in models.

Aim 2. To identify the effects of key fucosyltransferases (FUT's) on tumor glycan synthesis. (80% complete)
2a. To knock out key FUT in neuroendocrine prostate cancer cell lines.
2b. To identify effects of knockouts with MALDI and PET imaging of mice with tumors.

Aim 3: To assess the effect of pharmacologic inhibition of tumor fucosylation on tumor growth and tumor immunity. (80% complete)
3a. To determine the effect of inhibition of tumor fucosylation on tumor growth.
3b. To determine the effect of co-inhibition of tumor fucosylation in combination with immunotherapy.

What was accomplished under these goals?
We have made substantial progress despite the COVID delays in the past. The details are provided below as part of each Aim.

Aim 1. To correlate fucose-PET (Fuc-PET) activity with tumor glycan fucosylation.

1a. To characterize fucosylation patters across prostate cancer models.

1b. To perform Fuc-PET imaging in models.

As discussed in the last update, fucose PET imaging of mouse models demonstrated relatively weak uptake in tumor compared to other normal organs. Despite this limiation, we have expanded both preclinical and clinical characterization of fucosylated glycans as a biomarker for lethal disease, as will be discussed below.

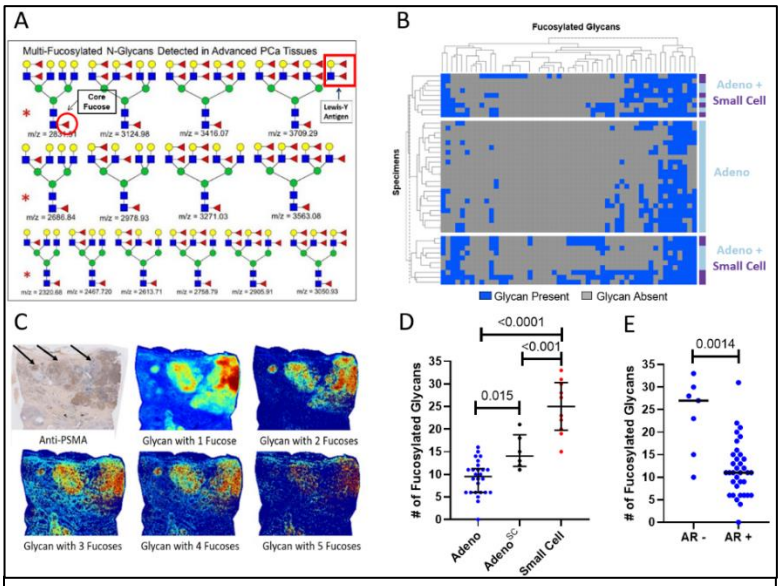

Figure 1. Fucosylated glycans are enriched PCa with neuroendocrine/small cell features. A. Example of glycans with high fucose content (red triangles) enriched in PCa with neuroendocrine/small cell features. **B.** Hierarchical clustering shows a subset of conventional PCa (Adeno) that cluster with neuroendocrine/small cell PCa based on the fucose score (blue=present). **C.** MALDI imaging of PCa expressing glycans with multiple fucoses co-registered with PSMA. **D-E.** The number of fucosylated glycans are highest in neuroendocrine/small cell PCa > conventional PCa adenocarcinomas with neuroendocrine/small cell features (Adeno^{SC}) > conventional PCa adenocarcinomas. Fucosylated glycans are also higher in tumors that are androgen receptor (AR) negative (i.e., castrate-resistant).

N-Glycans enriched in fucose (fucosylated glycans) are present in lethal PCa. Prostate adenocarcinoma is the most common histologic subtype of PCa and originates from a luminal epithelial cell origin [1]. Men undergoing androgen deprivation therapy (ADT)—standard of care for advanced PCa—will eventually develop castrate-resistant disease. However, the incidence of neuroendocrine/small cell features (both histologic and molecular) has been increasing in PCa, especially following ADT. PCa with neuroendocrine/small cell features are linked with uniformly poor outcomes [2-10]. This subtype is resistant to ADT and chemotherapy, rapidly metastasizes, and is associated with survival of less than a year [11]. Our group, led by Dr. Ippolito (PI), has spent many years identifying the metabolic biomarkers present in PCa with neuroendocrine/small cell features in both mouse models and patients that are predictive of outcomes [12-16]. This has led to an active collaboration with Dr. Richard Drake (Subaward PI) where we have used MALDI histologic imaging to identify unique N-glycan species associated with lethal PCa. The MALDI imaging platform allows direct assessment of number, structure and location of glycans in the tumor [17]. In short, we have discovered a panel of N-glycans with an abundance of fucose sugars (i.e., fucosylated glycans) that are enriched in lethal PCa with neuroendocrine/small cell features (**Figure 1A-C**). We discovered that the amount of fucosylated glycans were not only higher in neuroendocrine/small cell PCa, but also a subgroup of conventional histologic adenocarcinoma PCa that clustered with neuroendocrine/small cell PCa based upon their molecular profile (**Figure 1D**). In addition, we discovered that more glycan fucosylation was associated with lower androgen receptor (AR) expression, i.e., resistant to ADT or castrate resistant (**Figure 1E**). This suggested that fucosylated glycans could be used to identify a subgroup of conventional adenocarcinomas associated with recurrence, metastasis, and death.

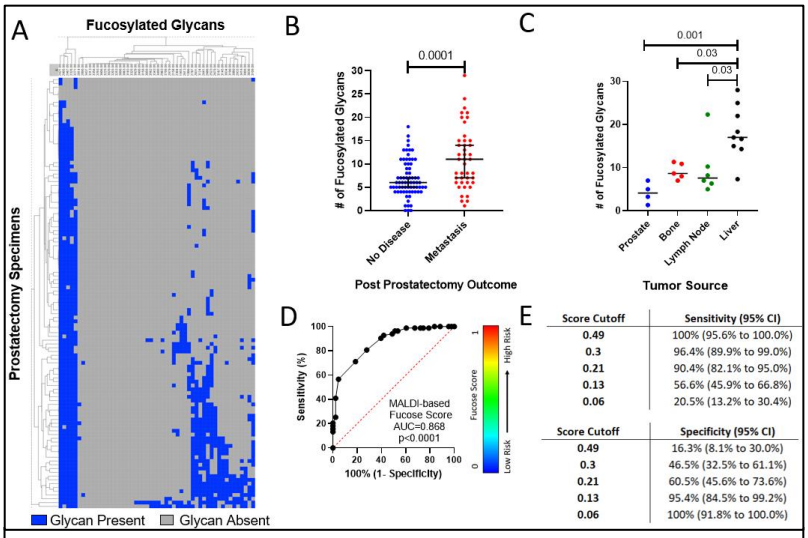

Figure 2. Fucose score is higher in PCa associated with future metastatic disease, particularly liver metastases. A. Heatmap of PCa with detected fucosylated glycans (blue=present). **B.** The amount of fucosylated glycans are higher in tumors that progressed to metastatic disease. **C.** Fucose score is highest in LuCaP PDX models from liver metastases. **D-E.** ROC analysis of a weighted fucose score (range 0→1) based upon expression of fucosylated glycans predicts future metastatic disease with high sensitivity.

Development of a fucose scoring method to identify lethal PCa at initial diagnosis. We analyzed an independent PCa (only conventional adenocarcinomas) tissue microarray (TMA) with longer follow-up. We discovered significantly more fucosylated glycans in patients who developed metastatic disease following initial treatment (**Figure 2A-B**). This was supported by another

independent TMA from LuCaP PDX models [18] where liver metastases had the most fucosylated glycans of the metastatic sites (**Figure 2C**). This is clinically important, as the development of PCa liver metastases signals an extremely poor prognosis with a median survival of less than 6 months [19]. To convert these results into a more clinically relevant and useful format, we developed a weighted "fucose score". The highest weight is given to the expression of 10 glycans unique to recurrent tumors, followed by 14 glycans that are significantly enriched in recurrent vs non-recurrent tumors, followed by 32 glycans that are not significantly different between recurrent and non-recurrent tumors. It ranges from zero to one, (similar to the Decipher® genomic scoring system), where a higher value is associated with a higher risk of future metastatic disease after prostatectomy. Using a receiver operator curve (ROC) analysis, we identified that the fucose score significantly predicted future metastatic disease with a cutoff of 0.49 having a sensitivity of 100% (**Figure 2D-E**). These results suggest to us that the fucose content of PCa microenvironments, when combined with other molecular predictors such as collagen variants (described below as part of our FuCol score), Decipher®, or imaging data such as conventional MRI or DBSI metrics, could result in improved prediction of future metastasis and death in PCa.

Can we do better than the fucose score? Inception of a fucose-collagen (FuCol) score that informs the structure of the tumor extracellular matrix (ECM) and future outcomes. The presence of unique fucosylated-glycans present on the cell surfaces of lethal PCa suggested to us that the ECM of these tumors might also be molecularly distinct from the ECM of less aggressive, indolent PCa. The tumor ECM is critically important to the tumor microenvironment to promote tumor proliferation, protection from apoptosis, and resistance to systemic therapies [20, 21]. Compared with other cancer types, the ECM in neuroendocrine/small cell PCa is particularly extensive, encasing tumor cells in both the primary and metastatic sites. In these cancers, the ECM is composed of many types of fibrillary and non-fibrillary collagens, fibronectin and proteoglycans, further supporting the possibility that fucosylated-glycans may be an important component of ECM modifications [20, 21]. The importance of the ECM in PCa aggressiveness is further highlighted by recent discoveries that type 1 collagen (COL1) content is a marker for a permissive ECM that facilitates PCa aggressiveness in animal models [22]. Using the ECM-targeted MALDI imaging approach developed by Dr. Angel (co-I), several hundred PCa tissues have been analyzed and linked with identification of specific collagen variants in the tumor microenvironment, as well as a database of several thousand collagen peptides including variation in post-translational modifications [23]. One notable modification associated with PCa aggressiveness is increased hydroxyl-proline content of collagen subtypes. An example is shown for a COL1A1 peptide with two proline residues in **Figure 3.** Non-hydroxylated proline peptides result in minimal signal detection, while a single hydroxylated species is localized to normal prostate stoma and two hydroxylated proline residues localize to tumor regions [22], demonstrating the usefulness of MALDI in the characterization of the PCa tumor microenvironment.

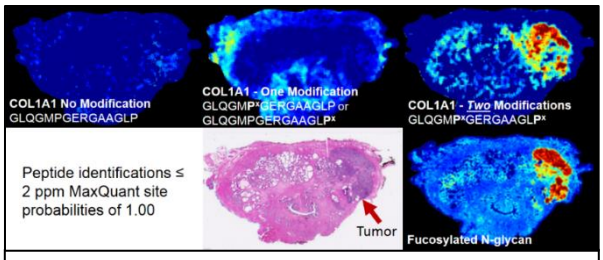

Figure 3. Prostate tumor-specific localization of post-translational collagen modifications with hydroxylated proline. MALDI imaging demonstrates that COL1A1 peptide with two hydroxyl-proline modifications co-localizes with higher levels of fucosylated glycans in PCa.

Together, these data demonstrate the potential utility of developing a prognostic score based upon collagen that compose the ECM. In fact, we propose combining MALDI data from fucosylated glycans and collagen proteins as part of a fucose-collagen (FuCol) score. The objective of the FuCol score is to improve the prediction of future metastatic disease by combining these molecular signatures. To demonstrate the feasibility of FuCol score in predicting progression-free survival, we used transcriptome and survival data from The Cancer Genome Atlas (TCGA). We developed a 12 gene score (range 0→1) equally weighted to six genes involved in fucosylation and six genes encoding collagen proteins. We discovered that patients whose tumors had FuCol scores in the highest quartile had significantly worse progression free survival (**Figure 4**). Together, this forms the justification for MALDI-based FuCol scoring that can be readily performed on FFPE tissues of biopsies and prostatectomy specimens.

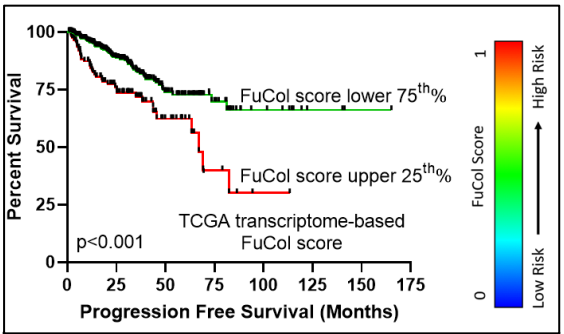

Figure 4. A transcript-based FuCol score predicts outcomes in treatment-naïve PCa. A 12 transcript signature equally weighted toward glycan fucosylation and collagen synthesis was used to develop a FuCol score (0→1) where prostatectomy specimens with a higher score (highest quartile) have significantly worse progression free survival.

The fact that the ECM (defined by differentially expressed glycans and collagen modifications) is different in lethal PCa suggests that

lethal PCa will also appear differently on imaging. In fact, Drs. Ippolito and Kim (MPI) have already published on the presence of significant differences in the tumor / ECM proteomes between “visible” and “invisible” PCa on conventional MRI [24]. *This introduces one of the core objectives of this proposal: the structure of the PCa tumor microenvironment influences the diffusion of water. Thus, the structure of the tumor microenvironment can be measured with advanced diffusion MRI approaches (i.e., DBSI) to identify lethal PCa non-invasively prior to treatment.*

Aim 2. To identify the effects of key fucosyltransferases (FUT’s) on tumor glycan synthesis.
2a. To knock out key FUT in neuroendocrine prostate cancer cell lines.
2b. To identify effects of knockouts with MALDI and PET imaging of mice with tumors.

This Aim has been restructured, as originally proposed. We intended to focus on FUT8 as highlighted above. However, this aim was the most critically reviewed at the initial finding stage. FUT has been investigated in several cell culture models including prostate and been linked to poor outcomes [25-28]. Thus, this may result in diminishing returns. Second, we have uncovered potentially significant data in Aim 1 with regard to liver-specific modulation of tumor fucosylation and Aim 3 with regard to the effects of fucosylation inhibition on immunotherapy. We have uncovered an immediately translatable method for reducing tumor fucosylation through the ketogenic diet as will be described below.

Carbohydrate depletion from the ketogenic diet (KD) reduces fucosylated glycan content. The dependence of aggressive tumors on glucose is well known. Dietary carbohydrate restriction in the form of calorically-limited ketogenic diets (KD) has been investigated as a means to reduce tumor growth and enhance therapeutic efficacy in PCa through reduction in circulating carbohydrates [29-34].

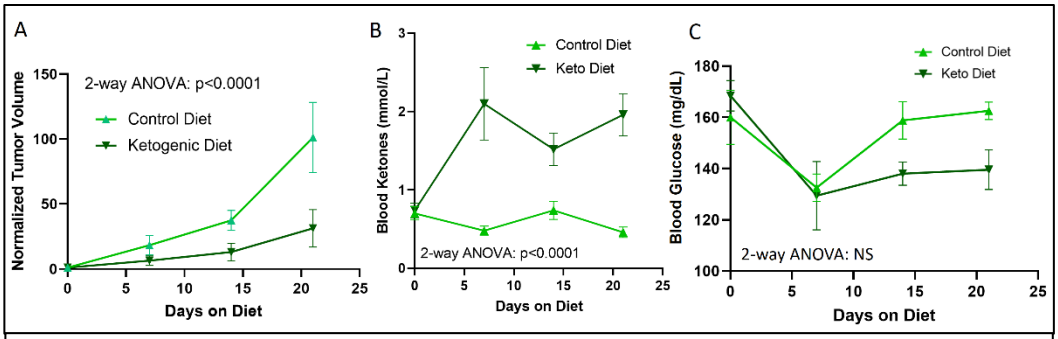

Figure 5. Ketogenic Diet has inhibitory effects on neuroendocrine prostate cancer growth. PNEC xenografts were generated and treated over three weeks. There are significant differences in tumor growth (A), and ketones (B), but not glucose (C).

We placed PNEC xenografted mouse models on a strict KD over the period of a month compared to a calorically matched control diet. We discovered that the mice on the KD had a robust tumor-static response to the KD that occurred rapidly, once placed on the diet (**Figure 5A**). In addition, there were significantly increased blood ketones in the KD versus control diet mice (**Figure 5B**), but not significantly different blood glucose levels (**Figure 5C**). These molecular changes parallel what is known about the KD; ketones, rather than glucose, may have major anti-cancer effects. Thus, using techniques from Drs Drake and Wu, we will be able to perform trials of the ketogenic diet in immunocompetent mice and identify the potential synergy of diet and immunotherapy on prostate cancer viability, with an emphasis on liver metastases.

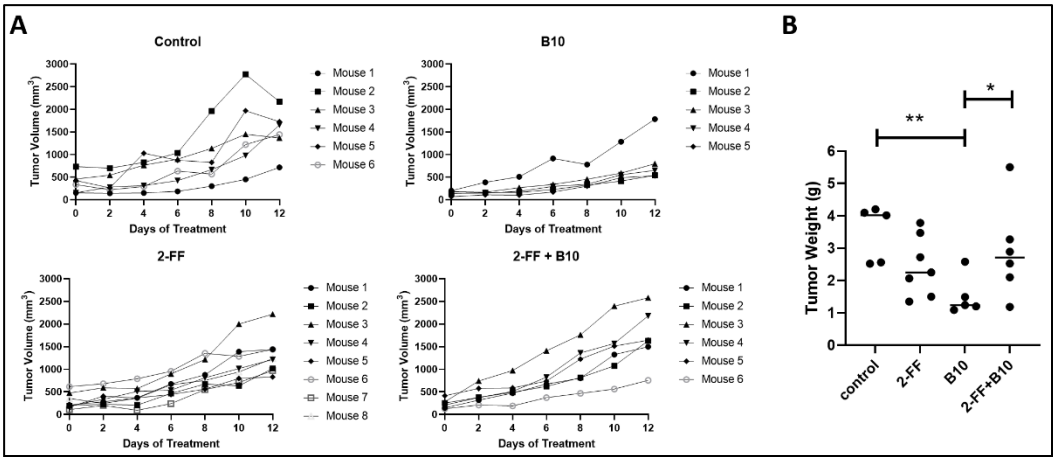

Figure 6. 2-fluorofucose (2-FF) impairs B10 immunotherapy in mice with prostate cancer. A. Tumor volume measurements over 12 days of therapy demonstrate that although B10 antibody therapy has beneficial effects, the addition of 2-FF diminishes those positive effects. B. Tumor weights at the end of the study confirm that 2-FF reduces the effects of B10 immunotherapy. *p<0.05, ** p<0.01.

Aim 3: To assess the effect of pharmacologic inhibition of tumor fucosylation on tumor growth and tumor immunity.

3a. To determine the effect of inhibition of tumor fucosylation on tumor growth.
3b. To determine the effect of co-inhibition of tumor fucosylation in combination with immunotherapy.

To date, we have completed two independent *in vivo* studies to address our tasks in Aim 3a and 3b. In the first experiment, we subcutaneously implanted the sMIC expressing TRAMP-C2 (sMIC-TC2) tumors into the syngeneic MICB transgenic mice. When tumors reached 250-500 mm3 in size, animals were randomized to 4 therapeutic groups: 1) control IgG, 2) 2-FF; 3) anti-sMIC antibody B10 (also B10G5) as previously described in Dr. Wu's publication; 4) a combination of 2-FF and B10 antibody. B10 was given at 6 mg/kg i.p twice weekly. To ensure that 2-FF can act on tumor cells and tumor microenvironment, we injected 2-FF intratumorally at 12.5 uM twice weekly, according to published literature. Tumor volume was monitored twice weekly. As shown in **Figure 6**, single agent therapy with 2-FF presented some, but not significant, inhibition of tumor growth. B10 antibody significantly inhibited tumor growth. However, combination of 2-FF with B10 did not present a significant inhibition of tumor growth. ***Unexpectedly, these observations suggested that 2-FF inhibits the efficacy of immunotherapy.***

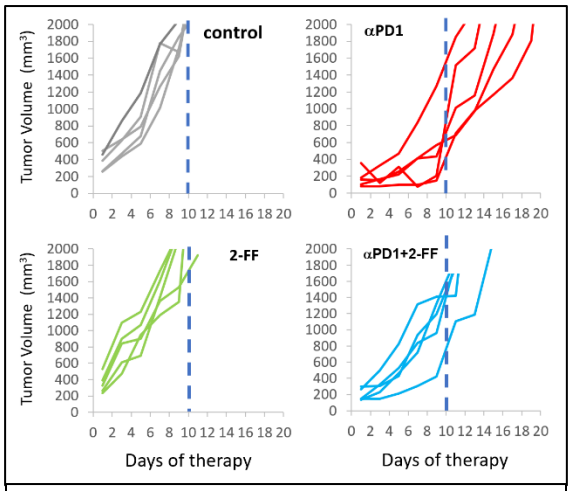

Figure 7. 2-fluorofucose (2-FF) impairs anti-PD1 (αPD1) immunotherapy in mice with prostate cancer. Tumor volume measurements over therapy demonstrate that 2-FF treatment is similar to control and that 2-FF nearly eliminates the advantages of αPD1 immunotherapy. Vertical line indicates the performance of controls as a reference for the treatment groups.

To confirm that 2-FF inhibition of fucosylation inhibits anti-tumor immune responses, we performed similar therapeutic experiments with anti-PD1 antibody in the syngeneic TRAMP-C2 tumor model. As shown in **Figure 7**, only nominal inhibition of TRAMP-C2 tumor growth was achieved by 2-FF. Consistently, the tumor growth inhibition effect with anti-PD1 single agent was abolished by addition of 2-FF. ***Together, these data confirmed the inhibitory effect of 2-FF on immunotherapy***. We are still in the process of analyzing the immune cell function in the tumors in these therapeutic settings, to better understand the impact of 2-FF on tumor immune microenvironment. **This is an especially significant finding, as all the published studies with 2-FF treatment of tumors were conducted in immune-deficient mice, lending even further power and significance to our studies that use immunocompetent mice.**

We performed flow cytometry analyses of tumor infiltrated major anti-tumor effector cells, NK cells and CD8 T cells, and their ability to produce the anti-tumor effector molecule IFNg. As shown in **Figure 8**, although 2-FF treatment did not significantly impact tumor infiltrated NK cells and CD8 T cells overall (**Figure 8A and C**), it negatively impacted the function of both NK and CD8 T cells. Therefore, the overall outcome of 2-FF in

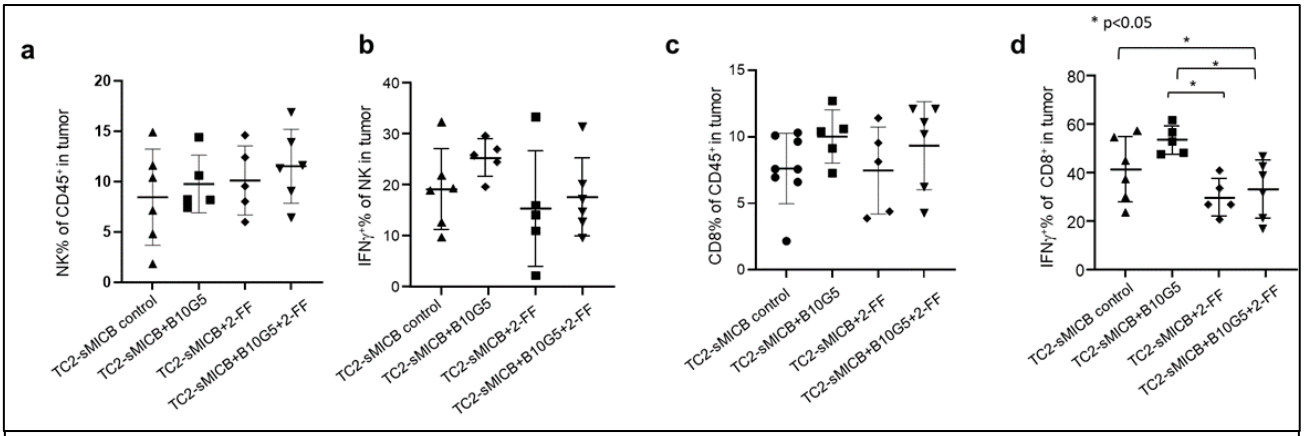

Figure 8. Effects of 2-FF therapy on immune cell populations in treated prostate tumors. A. NK T-cells. **B.** Interferon gamma (IFNg) production by NK cells. C. CD8 T-cells. D. Interferon gamma (IFNg) production by NK cells.

combination with immunotherapy needs take consideration of the dual impact of glycans on tumor cells and immune cells. We are current performing multiplex immunohistochemistry on the tumor section from this study to define whether there is a spatial correlation of NK cell and CD8 T cell function in tumors. We are also in the process of assessing other inflammatory cell types, such as macrophages in these tumor tissues.

Fucosylation plays many roles in normal immune cell function [38, 39]. Our data suggest that tumor fucosylation may play a potentially significant role in tumor-immune cell interactions, whether it be from direct inhibition of immune cells or a way to hide from the immune system itself. During this final year, we will further characterize this interaction in our immunocompetent models and try different clinically relevant metabolic inhibition strategies to selectively deplete tumor fucosylation and enhance immunotherapy.

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Opportunities for Training and Professional Development: Our lab is training two undergraduate students, Ms. Hannah Johnston and Ms. Shreya Ashok. Here, they will learn about tumor glycosylation, PET imaging as well as mouse studies.

How were results disseminated to communities of interest?: COVID has limited us in this respect. However, we are in the process of submitting a manuscript based on Aim 1 and will disseminate this on social media and as a pre- print on Biorxiv. We will present this at the next Prostate Cancer Foundation retreat. We will also circulate this through Dr. Wu and the Northwestern prostate SPORE.

What do you plan to do during the next reporting period to accomplish the goals? Aim 1: Submit the manuscript for Aim 1 that will validate fucose as a novel biomarker for neuroendocrine prostate cancer this spring. Aim 2: Dr. Ippolito's lab will complete the KD experiments this spring and work with Dr. Wu to combine it with immunotherapy. Aim 3: Dr. Wu will complete the experiments for Aim 3 and submit a manuscript by fall.

IMPACT

What was the impact on the development of the principal discipline(s) of the project?
This project not only develops a new PET imaging agent to detect lethal prostate cancer noninvasively, but it characterizes the target molecule, i.e. fucosylated cell surface glycans, on the histopathologic level. Specifically,

our group is correlating expression of fucosylated glycans with important clinical metrics such as grade, stage, and development of castrate-resistant disease. We are developing a molecular scoring system, similar to the Decipher genomics scoring system that predicts future lethal metastatic disease after initial therapy. This has clear implications for the pathology field where both MALDI imaging mass spectrometry and immunohistochemistry could be used to assess these fucose scores on tumors from prostatectomies at initial diagnosis.

We are discovering that the ketogenic diet has the ability to effectively "prune" these fucosylated glycans and convert them to high mannose glycans that are implicated in inflammation and immune activation. Thus, it is possible that we might be able to use diet as a clinically actionable means to enhance tumor killing through immune recognition.

Finally, we are making significant impact in the field of immunotherapy. The majority of mouse models rely on immunocompromised hosts, thus ignoring the importance of the immune system not only for tumorigenic mechanisms, but also for therapeutic strategies. We have discovered that metabolic inhibition through drugs such as 2-fluorofucose (2-FF) may look promising in immunocompromised models through tumor inhibition, but have the opposite effect in models with a competent immune system. Thus, the metabolic mechanisms needed for tumorigenesis may also be shared with immune cells. This opens up the field with new opportunities to develop tumor selective-metabolic inhibitors to kill tumors and enhance immune function.

What was the impact on other disciplines?
This has clear impact on pathology and how specimens could be assessed on the clinical level. This will also have an impact in oncology, especially as new trials advancing immunotherapy become more widespread. We believe that we may be able to use diet as a means to selectively modulate tumor fucosylation, which can readily be deployed in the clinical setting.

What was the impact on technology transfer?
Our clinical data with MALDI and Lewis-y antigen staining are further advancing the potential efficacy of Lewis-y antigen and core glycan fucosylation by FUT8 as biomarkers for lethal, castrate-resistant prostate cancer. As these biomarkers are measurable with MALDI imaging mass spectrometry, this could advance the role of MALDI in histopathologic assessment.

What was the impact on society beyond science and technology? Nothing to report.

CHANGES/PROBLEMS

Changes in approach and reasons for change:
Initially, we had major limitations in year 1 and part of year 2 due to COVID. Despite that, we have ramped back up fast and have made significant advancements in all facets of the project. Although the 2-FF inhibition had the opposite effect on immunotherapy in Aim 3, this is still a significant advancement for the project for several reasons highlighted above and lends further rationale for the impetus to test different metabolic strategies to inhibit tumor fucosylation, such as with the ketogenic diet as will be expanded as part of Aim 2.

Actual or anticipated problems or delays and actions or plans to resolve them:
In year 1, we had several delays with COVID and lab moves. We moved beyond those delays and made significant progress this year. We had some additional limitations with problems in the imaging facility and were unable to image mice for a while. However, we have achieved the goals and will proceed to complete the rest of the project.

Changes that had a significant impact on expenditures:
In year 1, COVID forced lab shutdown and expenses on the project. My technician was kept out of furlough, doing remote data analyses that moved the clinical aspects of the project forward. In year 2, we lost some time ramping back up as well as had to deal with problems with non-functioning scanners in the imaging facility. Those problems have been resolved and we will complete by the end of the proposed NCE period.

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

None

Significant changes in use or care of human subjects:
N/A

Significant changes in use or care of vertebrate animals:
None

Significant changes in use of biohazards and/or select agents:
None

PRODUCTS

Nothing to report

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name	Joseph Ippolito (Washington University)
Project Role	PI
Researcher Identifier	eRA commons: ippolitoj
Nearest Person-month worked	1.2
Contribution to project	Overseeing entire project
Funding support	NA

Name	Richard Drake (MUSC subcontract)
Project Role	Co-PI
Researcher Identifier	eRA commons: RICHARD_R_DRAKE
Nearest Person-month worked	0.6
Contribution to project	Overseeing all MALDI analyses
Funding support	NA

Name	Jennifer Wu (Northwestern subcontract)
Project Role	Co-PI
Researcher Identifier	eRA commons: wumedd
Nearest Person-month worked	0.8
Contribution to project	Overseeing development of TRAMP/MIC model
Funding support	NA

Name	Dong Zhou (Washington University)
Project Role	Co-I
Researcher Identifier	eRA commons: D_ZZZZ
Nearest Person-month worked	1.2
Contribution to project	Synthesis, QI and QA of fluorofucose
Funding support	NA

Name	Elena Nunez (Washington University)
Project Role	technician
Researcher Identifier	NA
Nearest Person-month worked	12
Contribution to project	Cell culture, mouse handling, data analysis
Funding support	NA

Name	Grace Grimsley (MUSC subcontract)

Project Role	Technician
Researcher Identifier	NA
Nearest Person-month worked	1
Contribution to project	MALDI imaging and data analysis, tissue staining
Funding support	NA

Name	Ju Wu (Northwestern subcontract)
Project Role	Staff scientist
Researcher Identifier	NA
Nearest Person-month worked	2.4
Contribution to project	Cell culture, mouse handling, development of TRAMP/MIC
Funding support	NA

SPECIAL REPORTING REQUIREMENTS

N/A

APPENDICES

N/A