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| 14. ABSTRACT Prostate cancer disproportionately afflicts African-American men. As such, we feel that it is critically important to recruit researchers from this population if we are to conquer this disease. Numerous programs have attempted to recruit minorities to biomedical research and prostate cancer in particular. Often this involves a short period of research immersion during a summer semester. However, it has been shown that many of these trainees do not persevere in the selected area due to the singular nature of the experience. Our goal is to formalize a program to broaden the scope of and enlarge Tuskegee University's prostate cancer research, which will be accomplished through targeting interested undergraduate students early during their science studies at Tuskegee University and enabling them to participate in summer research and education training periods at the University of Pittsburgh and the University of Pittsburgh Cancer Institute as part of their overall prostate cancer education. | | | | | |
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PITTSBURGH TUSKEGEE PROSTATE TRAINING PROGRAM

Alan Wells (Pittsburgh), Timothy Turner (Tuskegee)

INTRODUCTION

We proposed an extended training program for college undergraduates that aims to build a cadre of young investigators of color in prostate cancer. Prostate cancer disproportionately afflicts African-American men; this increased incidence is compounded by issues of access to and utilization of healthcare resources. As such, we feel that it is critically important to recruit researchers from this population if we are to conquer this disease. Numerous programs have attempted to recruit minorities to biomedical research and prostate cancer in particular. Often this involves a short period of research immersion during a summer semester. However, it has been shown that many of these trainees do not persevere in the selected area due to the singular nature of the experience. *We hypothesized that this combination of intensive summer immersions with ongoing academic year project extension will truly develop dedicated biomedical researchers in the area of prostate cancer.*

We proposed to test this hypothesis by designing an undergraduate research training program in prostate cancer that starts in the home college at Tuskegee University, immerses the students for 10 weeks in a specific research project with mentors at the University of Pittsburgh, and then continues the research after returning to Tuskegee under the aegis of a collaborating mentor. Thus, the student is to undertake the research over a one- to two-year period allowing the student to partake meaningfully in the full cycle of research – thesis generation, experimental planning, experimentation, presentation, and writing and publication. Thus, students will be recruited and selected at the beginning of the year, develop a project that involves collaboration between mentors at Pittsburgh and Tuskegee, take course that contribute to the project prior to the summer, initiate that project in depth at Pittsburgh, and then return to Tuskegee to continue the work as independent study, and communicate the findings at national meetings and in the literature. This extended involvement not only benefits the trainee but also forges collaborations between individual faculty members at the two different institutions. This should provide for further avenues that facilitate mainstreaming and integration of training and research for other undergraduate, graduate and post-doctoral trainees.

BODY

The accepted Statement of Work (attached) described a series of tasks to accomplish the Goals of this training program. However, given the later funding date of May, the timeline for the tasks is changed so that we are partly into Year 2 of the program. We will state the SOW Task and then comment on the work accomplished. In sum, all Tasks for year 1 were accomplished successfully.

Year 1 (2012)

December 2011 – February 2012, Tuskegee University sophomore trainees will be selected as “Prostate Cancer Scholars” for summer internship at the University of Pittsburgh.

Three trainees were selected as a culmination of a new process at Tuskegee University. This involved coordinating the selection process for the PTPTP with other summer opportunities available to students at Tuskegee. This allows for a smoother selection and better matching as students can select based on subject matter and fit, and not on timing of selection. All summer programs are now selected together in March.

February – April 2012, Trainees will be selectively paired with University of Pittsburgh Faculty mentors according to their research interests.

The three students were paired with their mentors at the University of Pittsburgh, in two separate Departments (Table 1).

May 2012 – August 2012, Trainees will travel to the University of Pittsburgh to begin their 10-week prostate cancer research experience.

The three students attended the 10 week onsite program as trainees in the Summer Undergraduate Research Program (SURP) of the Cellular and Molecular Pathology Graduate Program as described in the original proposal. This dual assignment of PTTP and CMP-SURP allows for efficient use of established non-laboratory training activities, including journal clubs, presentation training, resume and application writing, and academic survival skills training. This culminated in their presenting their summer research at the combined program research retreat.

August 2012 - May 2013 Trainees will return from University of Pittsburgh, and continue their research training for the upcoming academic year under guidance of Tuskegee University Faculty Mentors.

These *Prostate Cancer Scholars* will prepare and present communications at national meetings.

The three trainees returned to Tuskegee. Under the guidance of the Tuskegee mentors, they prepared, submitted and presented their work at a national meeting at Tuskegee and a second national meeting in Wisconsin this spring (Table 2).

Year 2 (2013)

December 2012 – March 2013, The second group of Tuskegee University sophomore trainees will be selected as "*Prostate Cancer Scholars*" for summer internship at the University of Pittsburgh.

This is being reported on as the second group of trainees has been selected. All three year 4, Class of 2012 Scholars will be returning, and they will be accompanied by 4 new Scholars.

KEY ACCOMPLISHMENTS

- Three student trainees participated in the summer program
- All completed the summer training successfully
- The new trainees established/continued ongoing research activities at Tuskegee
- All three trainees presented posters or talks at a national meeting

REPORTABLE OUTCOMES

Abstracts – see Table 2.

CONCLUSIONS

This first year of this renewed training award has successfully reached defined milestones. The systems are firmly in place to implement the following years' cadre of trainees.

Importance/Implications: The Key Accomplishments above firmly demonstrate the ability to maintain a summer training program that has continuity with the home HBCU and the summer program itself. The outcomes over time will test whether this produces trainees more committed to research and/or prostate cancer than the usual one summer session disconnected from the home institution.

Recommended changes: The feedback from the trainees and mentors is that there is a learning curve during the first half of the summer program. Thus, the momentum gained during the last month of summer training needs to be seamlessly transferred to the promise of to return the second summer, but of leading to a publication. We have decided to emphasize the continuity of the program to attain lasting outcomes.

Table 1. Class of 2012 student trainees and mentors.

| Student | Project Title | Pitt Mentor |
|------------------|---|--------------------|
| Datiri, Yeipyeng | Exploring the Role of PSMA and Folate in Prostate Cancer and the Novel Localization of PSMA to the Mitochondria | Denise O'Keefe |
| Myers, Kimberly | ERK MAPK Activity Coincides With Prostate Cancer Cell PC3 Mesenchymal to Epithelial Transition | Alan Wells |
| Smith, LeeKira | Effects of ELL2 Loss in Murine Prostate on Vascularity | Laura Pascal |

Table 2. List of student abstracts presented at meetings during the fourth year of the program.

| Student | Abstract | Meeting |
|-------------------------|---|--|
| Datiri, Yeipyeng (2012) | Exploring the Role of PSMA and Folate in Prostate Cancer and the Novel Localization of PSMA to the Mitochondria | Tuskegee University Fourth Joint Annual Research Symposium (JARS), March 14-15, 2013, Kellogg Hotel & Conference Center, Tuskegee, AL |
| Datiri, Yeipyeng (2012) | Exploring the Role of PSMA and Folate in Prostate Cancer and the Novel Localization of PSMA to the Mitochondria | The National Conference on Undergraduate Research (NCUR), April 10-13, 2013, University of Wisconsin, La Crosse, WI |
| Myers, Kimberly (2012) | ERK MAPK Activity Coincides With Prostate Cancer Cell PC3 Mesenchymal to Epithelial Transition | Tuskegee University Fourth Joint Annual Research Symposium (JARS), March 14-15, 2013, Kellogg Hotel & Conference Center, Tuskegee, AL (Poster Award Winner) |
| Myers, Kimberly (2012) | ERK MAPK Activity Coincides With Prostate Cancer Cell PC3 Mesenchymal to Epithelial Transition | The National Conference on Undergraduate Research (NCUR), April 10-13, 2013, University of Wisconsin, La Crosse, WI |
| Smith, LeeKira (2012) | The Effects of ELL2 Loss in Murine Prostate on Vascularity or Angiogenesis Epithelial Defect | The National Conference on Undergraduate Research (NCUR), April 10-13, 2013, University of Wisconsin, La Crosse, WI |
| | | |

Statement of Work (SOW)

Year 1 (2012)

December 2011 – February 2012, Tuskegee University sophomore trainees will be selected as “*Prostate Cancer Scholars*” for summer internship at the University of Pittsburgh.

February – April 2012, Trainees will be selectively paired with University of Pittsburgh Faculty mentors according to their research interests. Student-paired mentors from the University of Pittsburgh will be paired with Tuskegee University Faculty who are in similar areas of research or with similar research interests to facilitate the seamless continuation of summer research projects at Tuskegee University.

May 2012 – August 2012, Trainees will travel to the University of Pittsburgh to begin their 10-week prostate cancer research experience.

August 2012 - May 2013 Trainees will return from University of Pittsburgh, and continue their research training for the upcoming academic year under guidance of Tuskegee University Faculty Mentors. These *Prostate Cancer Scholars* will prepare and present communications at national meetings.

Year 2 (2013)

December 2012 – February 2013, The second group of Tuskegee University sophomore trainees will be selected as “*Prostate Cancer Scholars*” for summer internship at the University of Pittsburgh.

February – April 2013, Second-year Trainees will be selectively paired with University of Pittsburgh Faculty mentors according to their research interests. Student-paired mentors from the University of Pittsburgh will be paired with Tuskegee University Faculty who are in similar areas of research or with similar research interests to facilitate the seamless continuation of summer research projects at Tuskegee University.

May 2013 – August 2013, Second-year Trainees will travel to the University of Pittsburgh to begin their 10-week prostate cancer research experience. First-year Trainees (**Class of 2012**) will be invited to return to the University of Pittsburgh to continue their prostate cancer research projects through one of its existing summer programs for undergraduates.

August 2013 - May 2014, Second-year Trainees will return from University of Pittsburgh, and continue their research training for the upcoming academic year under guidance of Tuskegee University Faculty Mentors. First-year Trainees (Class of 2012) will have completed two years of intensive prostate cancer training and their data will be put into manuscript form and submitted to a peer-reviewed journal for publication. Both Tuskegee University and University of Pittsburgh Faculty Mentors will monitor the publication process and advise Trainees in the application process to graduate programs. These *Prostate Cancer Scholars* and the ones from the prior class (Class of 2012) will prepare and present communications at national meetings.

Year 3 (2014)

December 2013 – February 2014, The third group of Tuskegee University sophomore trainees will be selected as “*Prostate Cancer Scholars*” for summer internship at the University of Pittsburgh.

February – April 2014, Third-year Trainees will be selectively paired with University of Pittsburgh Faculty mentors according to their research interests. Student-paired mentors from the

University of Pittsburgh will be paired with Tuskegee University Faculty who are in similar areas of research or with similar research interests to facilitate the seamless continuation of summer research projects at Tuskegee University.

May – August 2014, Third-year Trainees will travel to the University of Pittsburgh to begin their 10-week prostate cancer research experience. Second-year Trainees (**Class of 2013**) will be invited to return to the University of Pittsburgh to continue their prostate cancer research projects through one of its existing summer programs for undergraduates.

August 2014 - May 2015, Third-year Trainees will return from University of Pittsburgh, and continue their research training for the upcoming academic year under guidance of Tuskegee University Faculty Mentors. Second-year Trainees (Class of 2013) will have completed two years of intensive prostate cancer training and their data will be put into manuscript form and submitted to a peer-reviewed journal for publication. Both Tuskegee University and University of Pittsburgh Faculty Mentors will monitor the publication process and help Trainees in the application process to graduate programs. These *Prostate Cancer Scholars* and the ones from the prior class (Class of 2013) will prepare and present communications at national meetings.

Exploring the Role of PSMA and Folate in Prostate Cancer and the Novel Localization of PSMA to the Mitochondria

Yeipyeng Datiri¹, Jessica Cummings², and Denise O'Keefe²

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Prostate cancer is the second most common cancer in men worldwide. Findings of prostate cancer have had an increased incidence as a result of the widespread availability of serum prostate specific antigen (PSA) test. PSMA (Prostate-Specific Membrane Antigen) is highly expressed in men and is an independent marker of prostate cancer aggressiveness. From previous experiments, it is known that there is a correlation between cancer cell growth and folate levels. Furthermore, expression of PSMA increases folic acid uptake, and causes prostate cancer in a mouse model. The goal of this study was to examine some of the potential mechanisms by which PSMA may contribute to prostate cancer progression. Cell cycle analysis and cell doubling were utilized in prostate cancer cell lines expressing vector alone or PSMA to determine the effect on cell growth. The microbiological, *Lactobacillus casei*, assay aided in the determination of intercellular folate concentration content in these cell lines. Subcellular fractionation was used to examine the cell lines for PSMA localization and mitochondria folate levels. We found that while expression of PSMA promoted growth in the BPH1 cell line, cells expressing PSMA had twice as much folate in their mitochondria as the same cell line with vector alone ($P \leq 0.001$). These findings begin to shed some light on how PSMA contributes to prostate carcinogenesis, and furthermore, suggest a novel role for PSMA in mitochondrial one-carbon metabolism.

This work was supported by the Department of Defense grant #PC080566.

ERK MAPK Activity Coincides With Prostate Cancer Cell PC3 Mesenchymal to Epithelial Transition

Kimberly Myers¹, Bo Ma², and Alan Wells²

Tuskegee University, Department of Biology, Tuskegee, AL¹, University of Pittsburgh School of Medicine, Department of Pathology, Pittsburgh, PA²

Prostate Cancer is the second leading cause of cancer deaths in men. A large number of men are diagnosed each year with this cancer. Current therapies for metastatic prostate cancer are not curative and prolong survival by only a year even in patients with metastatic disease; critically overt metastatic disease is generally resistant to treatments. To understand the mechanisms that metastatic prostate cancers use to survive from treatments will be very helpful to save life. The previous data from this lab, along with reports in the literature, suggest that E-cadherin, an indicator of the cell phenotype, dictates dissemination and metastatic survival. The inhospitable microenvironment induces prostate cancer cells to re-express E-cadherin and undergo a mesenchymal to epithelial transition (MET). However, it is still unclear which mechanisms during MET are responsible for making metastatic prostate cancer cells more resistant to chemotherapies. Extracellular signal-regulated kinases (ERK) and phosphatidylinositol 3-kinases (PI3K) activities are involved in the cells' survival. P38 is responsible for cell death and tumor suppression, as well as the development of malignance. By utilizing the PC3 cell line, the "classical" prostatic cancer cell line originally derived from advanced androgen independent bone, we induced PC3 cells to undergo MET after treatment with the EGFR inhibitor PD153035 *in vitro*. A correlation between the level of E-cadherin re-expression and cell confluence was detected in this project. Moreover, the level of E-cadherin re-expression was induced at different durations (0, 6, 24, 48 hours) and was assayed. The

activities of ERK in PC3 cells after EGF stimulation before and after MET were also assessed in this project.

This work was supported by the Department of Defense grant #PC080566.

The Effects of ELL2 Loss in Murine Prostate on Vascularity or Angiogenesis Epithelial Defects

LeeKira Smith¹ and Laura Pascal²

Tuskegee University, Department of Biology, Tuskegee, AL¹, University of Pittsburgh School of Medicine, Department of Urology, Pittsburgh, PA²

All tumors rely on an adequate blood supply in order to grow beyond one cubic mm in size. Tumors can secrete signaling molecules, which promote the increased formation of new blood vessels, a process called angiogenesis. Tumors also can encourage normal cells to give off that same signaling resulting in even more blood vessels being produced. When the new blood vessels are produced they feed the growing tumor with oxygen and other nutrients. This makes it possible for cancer cells to spread and grow, and eventually to metastasize. When cancer cells metastasize they spread from one location to the next. Angiogenesis is a process that facilitates the growth and progression of prostate cancer. New blood vessels not only provide nourishment for the tumor but they also act as a mode of transportation to different locations in the body. ELL2 and EAF2 are two proteins, which have been implicated in both angiogenesis as well as prostate cancer. Prostate cancer is the second leading cause of cancer death in American men. Prostate cancer occurs mainly in older men. Nearly two thirds are diagnosed in men sixty-five or older. The effects of the loss of ELL2, eleven-nineteen lysine-rich leukemia protein 2, and EAF2, an ELL associated factor 2, on vascularity in murine prostate were observed in this experiment. In addition, the correlation of EAF2 loss and increased vascularity was examined in human prostate tumor specimens. Scientists believe that cutting off the blood supply or inhibiting the chemical responses used in spreading the tumor will inhibit the growth of the tumor.

This work was supported by the Department of Defense grant #PC080566.