AWARD NUMBER: W81XWH-17-1-0435

TITLE: Direct Targeting of the FKBP52 Cochaperone for the Treatment of Castration-Resistant Prostate Cancer

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REPORT DATE: August 2018

TYPE OF REPORT: Annual Report

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

DISTRIBUTION STATEMENT: Approved for Public Release;
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REPORT DOCUMENTATION PAGE

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OMB No. 0704-0188

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1. REPORT DATE
August 2018

2. REPORT TYPE
Annual

3. DATES COVERED
1 Aug 2017 - 31 Jul 2018

4. TITLE AND SUBTITLE

Direct Targeting of the FKBP52 Cochaperone for the Treatment of Castration-Resistant Prostate Cancer

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-17-1-0435

5c. PROGRAM ELEMENT NUMBER

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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8. PERFORMING ORGANIZATION REPORT NUMBER

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

U.S. Army Medical Research and Materiel 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

Prostate cancer affects one in seven men in the United States and is a major leading cause of cancer death among men. Current treatment strategies exploit the dependence of AR for hormone activation and current therapies are ineffective in castration resistant prostate cancer (CRPC). Based on this rationale, we are pursuing a unique non-AR based strategy. The folding, activation, and nuclear translocation of steroid hormone receptors involves no less than twelve proteins and at least four distinct complexes. At least one of these proteins, the FKBP52 cochaperone, is a highly promising therapeutic target for the disruption of a number of mechanisms important in prostate cancer. The proposed research is focused on the preclinical development of GMC1, a drug-like small molecule that targets FKBP52 regulation of steroid hormone receptor activity. During the first year of this award we have made progress in the hit-to-lead optimization process and have identified a number of novel derivatives with activity. We have also established protocols and assays for assessing lead drug effects in cellular and animal models.

15. SUBJECT TERMS

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

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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A. INTRODUCTION

Prostate cancer affects one in seven men in the United States and is a major leading cause of cancer death among men. Current treatment strategies exploit the dependence of AR for hormone activation and current therapies are ineffective in castration resistant prostate cancer (CRPC). Based on this rationale, we are pursuing a unique non-AR based strategy. The folding, activation, and nuclear translocation of steroid hormone receptors involves no less than twelve proteins and at least four distinct complexes. At least one of these proteins, the FKBP52 cochaperone, is a highly promising therapeutic target for the disruption of a number of mechanisms important in prostate cancer. The proposed research is focused on the preclinical development of GMC1, a drug-like small molecule that targets FKBP52 regulation of steroid hormone receptor activity. The major goals of this research are to perform hit-to-lead optimization of GMC1 to improve drug solubility and potency, investigate the drug binding site and molecular mechanism of action in cellular models of prostate cancer, and conduct pre-clinical evaluation of our most promising lead compounds in animal models of prostate cancer.

B. KEYWORDS

Prostate cancer, castration-resistant prostate cancer, androgen receptor, glucocorticoid receptor, progesterone receptor, testosterone, FKBP52, FKBP4, FKBP51, FKBP5, immunophilin, cochaperone, beta-catenin, anti-androgen, pre-clinical, FKBP inhibitor

C. ACCOMPLISHMENTS

C.1 Major Goals of the Project as Outlined in the Approved SOW

The major goals for year 1 of the project are outlined below.

Major Task 1: Conduct large-scale *in silico* screen against the FKBP52 PPIase pocket
1.1 Screen ZINC database with glide docking followed by eHiTS docking and retain hits with low RMSD score for further analysis (months 1-6)
1.2 Optimization by hit-based similarity search to develop more potent compounds and derive preliminary SAR information. (months 1-6)

Major Task 2: Functional screening of hit molecules and molecule modifications
2.1 Screen hits identified *in silico* for effects on FKBP52-regulated AR, GR and PR function (months 6-12)
2.2 Design and commercially synthesize GMC1 modifications with consultation from Dr. Cherkasov and screen in functional reporter assays to select most promising lead molecules for further analysis (months 1-12)
2.3 Independently verify lead molecules identified for effects in prostate cancer cells and assess cellular toxicity (months 1-12)

Major Task 3: Verify drug-binding site for the most promising lead molecules
3.1 Perform functional mutagenesis to assess drug binding to the FKBP52 PPIase pocket (months 6-12)

C.2 Accomplishments Under These Goals

University of Texas at El Paso Site (Cox, PI):

In the year 1 reporting period, we proposed to screen the novel GMC1 derivatives identified in the *in silico* hit-to-lead optimization being performed at the Vancouver Prostate Centre site (see below for more details) for anti-AR activity in order to identify new lead drug molecules with novel chemistry with which we can pursue composition of matter patents. In addition, we proposed to use functional mutagenesis to verify the drug target site on FKBP52. The outcomes detailed below correspond to **Major Task 2, subtasks 2.1 and 2.2; and Major Task 3, subtask 3.1** above.

Specific Aims

Aim 2: Perform a detailed evaluation of all candidate drug compounds in multiple cellular models of prostate cancer.

Major Task 2: Functional screening of hit molecules and molecule modifications

We have completed multiple rounds of SAR analysis in which each round informs the medicinal chemistry of the next round. A representative sample listing GMC1 derivatives and their IC50 values in AR-mediated luciferase reporter assays in MDAkb2 cells is shown in Table 1. This SAR data informed the design of the molecules in Table 2 below. It should be noted that all molecules listed in Table 2 are novel and would allow us to pursue composition of matter. We are currently in the process having the molecules in Table 2 commercially synthesized and testing them for activity. We currently have performed a preliminary screen of eight of the molecules, six of which have activity in the 50-100 µM range.

Table 1. Sampling of SAR Analysis of GMC1 derivatives in AR-Mediated Luciferase Reporter Assays in MDA-kb2 Cells

ID	Empirical Formula	Molecular Weight	IC_{50} (M)
GMC1- 1	C21H24N4O4S	428.51	2.04E-05
GMC1- 2	C19H20N4O3S	384.46	No activity
GMC1- 3	C18H17BrN4O2S	433.33	2.59E-05
GMC1- 4	C20H22N4O3S	398.49	No activity
GMC1- 5	C21H24N4O4S	428.51	2.74E-05
GMC1-6	C19H20N4O3S	384.46	4.61E-05
GMC1- 7	C18H18N4O3S	370.43	6.96E-05
GMC1- 8	C19H20N4O4S	400.46	No activity
GMC1-9	C20H22N4O4S	414.49	No activity
GMC1-10	C20H22N4O4S	414.49	No activity
GMC1-11	C22H18N4O2S	402.48	3.61E-05
GMC1-12	C20H22N4O2S	382.49	No activity
GMC1-13	C19H20N4O3S	384.46	No activity
GMC1-14	C19H20N4O4S	400.46	4.31E-05
GMC1-15	C20H20N4O5S	428.47	No activity
GMC1-16	C19H20N4O2S	368.46	No activity
GMC1-17	C17H15BrN4O2S	419.30	No activity
GMC1-18	C19H18N4O4S	398.44	No activity
GMC1-19	C18H18N4O2S	354.43	2.06E-05
GMC1-20	C18H18N4O2S	354.43	No activity

GMC1-21	C17H16N4O3S	356.40	No activity
GMC1-22	C18H18N4O3S	370.43	7.90E-05
GMC1-23	C19H20N4O2S	368.46	1.66E-05
GMC1-24	C19H20N4O4S	400.45	No activity
GMC1-25	C19H19N5O4S	413.45	No activity
GMC1-26	C19H20N4O3S	384.45	No activity
GMC1-27	C19H20N4O2S	368.46	3.69E-05
GMC1-28	C19H20N4O4S	400.45	8.72E-05
GMC1-29	C19H19N5O4S	413.45	No activity
GMC1-30	C19H18N4O4S	398.44	No activity
GMC1-31	C20H20N4O5S	428.46	No activity

Aim 2: Perform a detailed evaluation of all candidate drug compounds in multiple cellular models of prostate cancer.

Major Task 3: Verify drug-binding site for the most promising lead molecules

Given that GMC1 is predicted to target the FKBP52 PPIase pocket based on *in silico* predictive modeling, we aimed to verify that GMC1 targets the PPIase pocket and to establish protocols for assessing the binding of derivatives developed in this project. We previously performed fluorescence polarization assays to assess the ability of GMC1 to displace FK506 (Tacrolimus), which is a known FKBP52 PPIase-binding molecule. We were unable to observe competitive binding of GMC1 to FKBP52 in these experiments (data not shown). However, GMC1 is a much smaller molecule that is predicted to have only half of the binding affinity to the catalytic pocket compared to FK506. Thus, it is likely that GMC1 simply failed to displace FK506 from the PPIase pocket.

Alternatively, we proposed in this project to generate FKBP52 PPIase pocket mutants that retained the ability to regulate AR activity, and to use those mutants to demonstrate that alteration of the proposed GMC1 binding site affects GMC1 inhibitory activity. This would provide strong evidence that GMC1 does in fact target the PPIase pocket. We have identified D68, I87 and Y113 as three key residues within the FKBP52 PPIase pocket that form important hydrogen bond interactions with known ligands. GMC1 is predicted to bind through these specific residues within the catalytic pocket and induce re-orientation of the proline-rich loop disrupting the co-chaperone's interaction with steroid hormone receptors. The molecular docking models suggest that Val86 within the PPIase pocket is also predicted to form a close interaction with GMC1 although it does not create a hydrogen bond with the molecule. Thus, we generated FKBP52-D68A, V86A, I87A, and Y113A mutants via site-directed mutagenesis, and evaluated them in AR-mediated luciferase assays to confirm that these mutations within the PPIase pocket do not impair FKBP52-mediated potentiation of AR activity in 52KO mouse embryonic fibroblasts. Any mutants that did not obstruct the potentiation ability of FKBP52 were subsequently tested for the co-chaperone-enhanced receptor-mediated luciferase expression in the presence of GMC1. As shown in Figure 1, mutations at positions D68, V86, and I87 did not impair FKBP52 potentiation of the receptor function, but the Y113A mutant did. Therefore, only the FKBP52-D68A, V86A, and I87A mutants were further assessed for their effects on GMC1 inhibition. In comparison to the IC50 of GMC1 in assays of wild type FKBP52 (6.9 μM), the mutation at position D68 in the PPIase pocket decreased the GMC1 IC50 in FKBP52-regulated AR reporter assays by two-fold (13.2 μM). This demonstrates that alteration of the PPIase pocket can affect GMC1 activity, and strongly suggests GMC1 interaction within this pocket. These mutants will be used to assess the binding of GMC1 derivatives that are identified in the hit-to-lead optimization process.

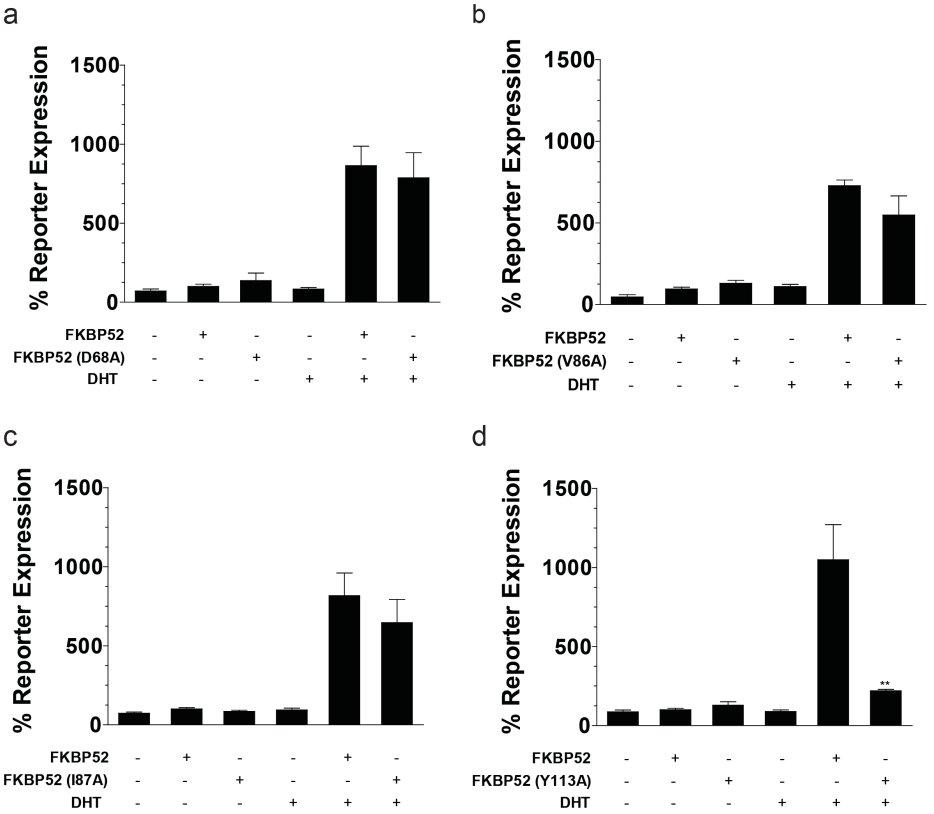


Fig. 1: FKBP52 PPIase pocket mutants retain the ability to potentiatiate AR function. (a-d) AR, the receptor-inducible reporter plasmid, and the constitutively active β-galactosidase reporter plasmids were co-transfected simultaneously with each of the plasmids indicated for the different treatment groups in 52KO MEFs. Cells were induced at 10 pM DHT or EtOH for 16-18 h. Following cell lysis, AR expression was assessed by luciferase assay. The data represents the averaged reporter expression (luciferase activity/β-galactosidase activity ± s.d.) of at least three replicates. The asterisks denote a statistically significant difference by comparing the FKBP52-mutants to WT with only the presence of DHT. $^{**}P \leq 0.01$ was calculated by One-Way ANOVA followed by Bonferroni's multiple comparison tests.

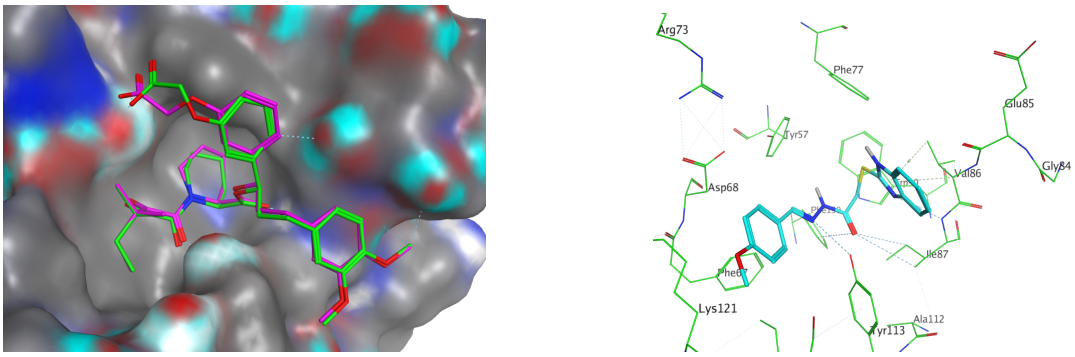
Vancouver Prostate Centre Site (Cherkasov, PI):

In the year 1 reporting period, we proposed to develop a novel drug based on GMC1. We aimed at the identification of a lead molecule that will be characterized in both cellular and animal models of prostate cancer. The Cherkasov group at VPC performed hit-to lead optimization and carried out a systematic study on the binding mode of the characterized hit molecule, GMC1, in the FKBP52 PPIase pocket, focusing on moving forward with commercially synthesized modification libraries based on GMC1 as an initial scaffold. The outcomes detailed below correspond to **Major Task 1, subtasks 1.1 and 1.2** above.

Specific Aims

Aim 1: Use structure-based drug design methodology and *in silico* library screening to identify small molecules targeting the FKBP52 PPIase pocket

We first evaluated if docking programs ICM, Glide-XP, and Glide-SP can reproduce the binding pose of a simplified analog of FK506 co-crystalized with FKBP52 in crystal structure 4LAY. Fig. 2A shows that ICM provided nearly perfect binding pose prediction of the co-crystalized ligand. Fig. 2B shows the predicted binding pose of GMC1, which is our current best hit molecule.



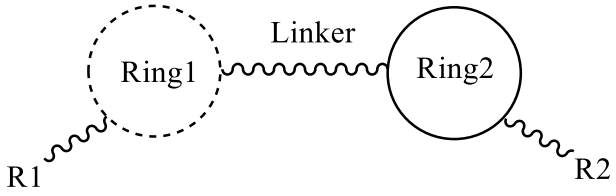
A B

Fig. 2 A). Co-crystalized FK506 analog is shown in green, ICM predicted binding pose is shown in pink. B). the predicted binding pose of the characterized hit of GMC1.

On the basis of current understanding of GMC1 binding, using substructure search starting from GMC1 core as a template, we found 148 compounds with substitutions of interests on the phenyl moiety and the benzimidazole moiety of GMC1 from 500M compounds in ZINC15. Those that are available are purchased. The lab results showed that none of these GMC1 derivatives demonstrate higher potency.

For further optimization of the GMC1-series, we employed structure-based drug design. A virtual library of 36 compounds were proposed. The ICM docking program were first employed to generate the binding pose of the proposed library. The predicted poses are subsequently subjected to a structure activity analysis by the advanced software SeeSAR for interactive and visual compound prioritization. SeeSAR prediction provides a computational estimate of potency range of each proposed compound. 21 compounds in Table 2 with predicted Ki range were quoted for synthesis. We are waiting these compounds to arrive for biological assays.

Table 2. Proposed medicinal chemistry compounds for SAR study



ID	R1	R2	SeeSAR_ESTIMATED_AFFINITY_Ki
1	H	H	25255578584 nM > Ki_Hyde > 254193011 nM
2	H	Cl	537241 nM > Ki_Hyde > 5407 nM
3	H	Me	328479 nM > Ki_Hyde > 3306 nM
4	H	Ethyl	15119924 nM > Ki_Hyde > 152179 nM
5	H	3-OMe	1042064 nM > Ki_Hyde > 10488 nM
6	H	2-OMe	16800267 nM > Ki_Hyde > 169092 nM
7	7-Me	4-OMe	6332170 nM > Ki_Hyde > 63732 nM
8	7-OMe	4-OMe	3080901 nM > Ki_Hyde > 31009 nM
9	7-F	4-OMe	13978315 nM > Ki_Hyde > 140689 nM
10	7-Cl	4-OMe	13680650 nM > Ki_Hyde > 137693 nM
11	7-Br	4-OMe	6286170 nM > Ki_Hyde > 63269 nM
12	7-I	4-OMe	352656 nM > Ki_Hyde > 3549 nM
13	CN	4-OMe	779211 nM > Ki_Hyde > 7843 nM
14	6-Me	4-OMe	54281 nM > Ki_Hyde > 546 nM

15	6-F	4-OMe	207185 nM > Ki_Hyde > 2085 nM
16	6-Cl	4-OMe	4609072 nM > Ki_Hyde > 46390 nM
17	6-Br	4-OMe	15386194 nM > Ki_Hyde > 154859 nM
18	6-I	4-OMe	74782 nM > Ki_Hyde > 753 nM
19	6-OMe	4-OMe	416924 nM > Ki_Hyde > 4196 nM
20	6-OH	4-OMe	688791 nM > Ki_Hyde > 6933 nM
21	7-OH	4-OMe	1501060 nM > Ki_Hyde > 15108 nM

We are also doing large scale virtual screening on the 11 million commercially available drug-like compound library of ZINC15 using our new pipeline (Fig. 3) of consensus docking of Glide, ICM and Hybrid docking programs using FKBP52 crystal structure 4LAY. We have first finished Glide-SP docking of the compound library, and will follow the screening pipeline to select ~100 compounds for lab screening assays.

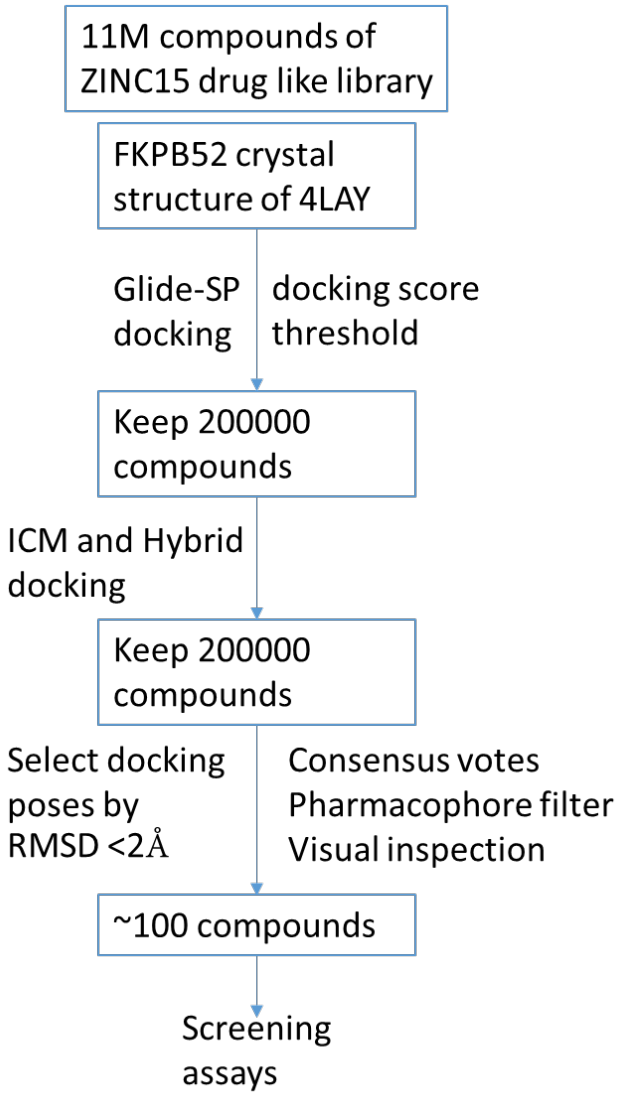


Fig. 3 Virtual screening pipeline

Clark Atlanta University Site (Chaudhary, PI):

In the year 1 reporting period, we proposed to use well established CRPC cell models such as VCaP, C4-2B and CW22Rv1. Extensive literature is available on these cell line models that will be used to establish the mechanism of action and response to FKBP52 inhibitors in context of AR activity and function. The following major tasks were accomplished:

1. In continuation with our preliminary studies, we used the CWR22Rv1 xenografts to understand the molecular changes in response to GMC1 treatment and optimize immuno-histochemistry of AR and AR target genes.
2. Obtained the cell lines from ATCC and performed molecular profiling to establish cell line authenticity.
3. Performed immune-cytochemistry on LNCaP cells to investigate the effect of GMC1 on AR translocation

The outcomes detailed below correspond to **Major Task 2, subtask 2.3** above.

Specific Aims

Subtask 2: Screen GMC1 modifications library for lead molecules with increased solubility and potency. To establish the screening of lead compounds, we first sought to establish the authenticity of the cell lines. We purchased LNCaP-Clone FGCP1, CW22Rv1 and VCaP prostate cancer cell lines from ATCC. Based on testing results obtained from analysis of 15 autosomal short tandem repeat (STR) loci and the gender identity locus amelogenin, the profile of the submitted samples CW22Rv1 is a 94.74% match with the reference profile CW22Rv1(ATCC CRL-2505). These results established the authenticity of CWR22Rv1 cells. In the case of LNCaP, the match was 72.73% with reference profile LNCaP clone FGC (ATCC CRL-1740) that was indicative of mycoplasma contamination. These results were disturbing that suggested we may have mycoplasma contamination in our cell culture facility. These results led us to extensive evaluation of mycoplasma detection in our cell culture (MycoAlert, Lonza) and subsequent treatment of affected cell lines with the mycoplasma inhibitor Plasmocin. In the meantime, we requested another batch of LNCaP cell from ATCC. The new cell was mycoplasma free and the treatment also rendered our earlier LNCaP cell line mycoplasma free. The genomic DNA from these cells and VCaP (ATCC) and C4-2B (available in house) have been send to Genetica Inc. for cell line authentication.

The basic IACUC protocol for the use of potential FKBP52 inhibitors has been prepared. The protocol will be submitted as soon as Dr. Cox's and Dr. Artem's lab determines the toxicity and PK/PD of the compounds.

While we continue our initial analysis on the FKBP2 inhibitors, we decided to establish the process and protocols for the immune-histochemistry on GMC1 treated CW22Rv1 xenografts from nude mice. These studies were designed generate preliminary data on the effect of GMC1 inhibitors on AR, AR activated genes/ proteins and underlying molecular mechanism. As shown in Fig. 4, GMC1 promoted nuclear localization of AR. Although the AR was nuclear, the activity of AR was severely impaired as seen by the decrease in AR target genes PSA and FKBP51. Interestingly, the expression of FKBP52 remained unchanged. The decrease in the tumor size (and weight) following GMC1 treatment (shown as preliminary results in the proposal) was due to decreased proliferation (decreased expression of proliferation marker Ki67 in GMC1 treated xenografts) and apoptosis (TUNEL, Brown staining, Fig. 5). These results are significant which suggest that GMC! Treatments blocks AR activity, the proposed outcome of the treatment. We expect to use the same techniques in our proposed study.

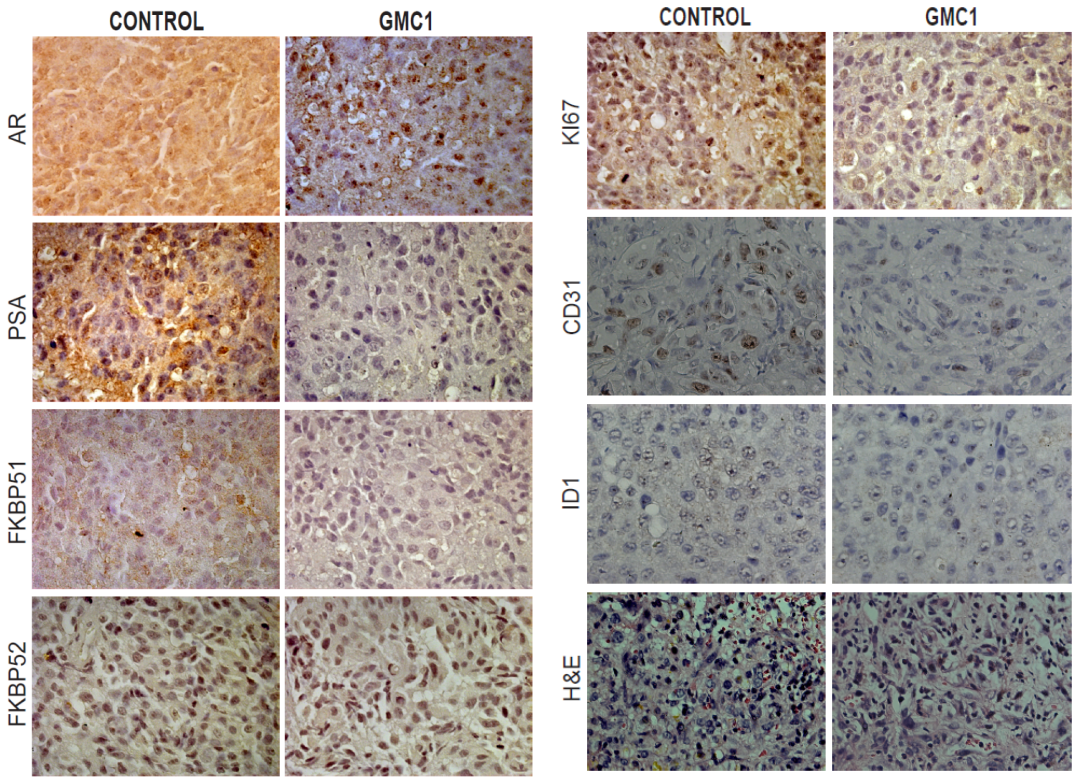


Fig. 4. IHC analysis of AR and AR target genes in CW22Rv1 on GMC1 treated mice xenografts. The expression of AR-target genes including PSA and FKBP51 were significantly attenuated in the GMC1 treated xenografts as compared to the untreated CW22RV1 tumors in vivo. The expression of Ki67 was significantly attenuated in the GMC1 treated xenografts as compared to untreated CW22RV1 tumors. Predominant human-specific Lamin A expression observed in the GMC1 treated/untreated CW22RV1 tumors further confirmed that increased tumor volume is due to the expansion of CW22RV1 cells and not due to mouse-derived stromal cells.

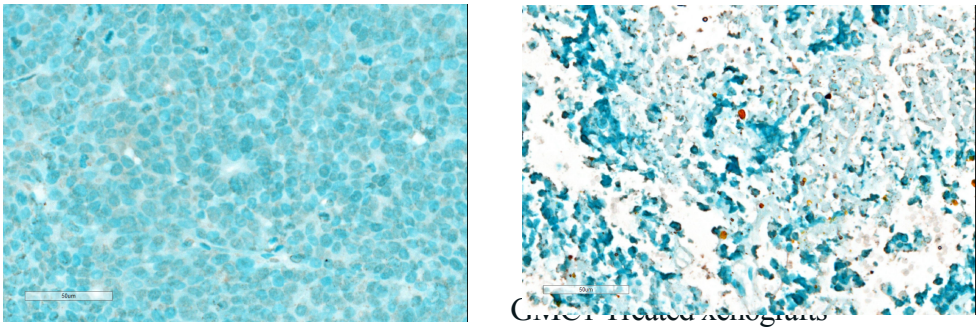


Fig. 5. TUNEL IHC staining of CW22Rv1 mice xenografts

C.3 Opportunities for Training and Professional Development

Nothing to report

C.4 Results Disseminated to Communities of Interest

Nothing to report

C.5 Plans for Next Reporting Period

University of Texas at El Paso Site (Cox, PI):

Early in year 2 of the project we will complete the screening of the novel compounds in Table 2, and ultimately settle on a few lead drug molecules to move forward for more detailed cellular and animal studies. We anticipate being able to pursue composition of matter protection of our lead molecules in year 2. In addition, we will continue to screen molecules that come out of the virtual screens being performed by the Cherkasov lab (Fig. 3) to identify any novel drug molecules to pursue. We will also perform a detailed characterization of lead drug effects in cellular models of prostate cancer including assessing their binding using the FKBP52 mutants described in Figure 1, and their ability to affect GR and PR activity, receptor stability, receptor translocation to the nucleus, endogenous receptor-mediated gene expression, and prostate cancer cell proliferation.

Vancouver Prostate Centre Site (Cherkasov, PI):

In year 2 we will continue the virtual screening detailed in Figure 2 above. In addition, we will apply for approvals for using animals in the study (to ACURO) and our local IACUC in preparation for the PK/PD studies on the lead molecules.

Clark Atlanta University Site (Chaudhary, PI):

In year 2 we will apply for approvals for using animals in the study (to ACURO) and our local IACUC. We will also complete the cell line authentication. The authenticated cells will then be used to develop the toxicity profiles of the lead molecules *in vitro.* In addition, we will perform *in vitro* studies on the lead compounds including MTT/ Annexin (PI), Matrigel transwell migration assay and anchorage-independent growth in a soft agar assay in a variety of androgen-sensitive and castration-resistant cell lines.

D. IMPACT

D.1 Impact on the Development of the Principle Discipline(s) of the Project

University of Texas at El Paso Site (Cox, PI): Nothing to report
Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report
Clark Atlanta University Site (Chaudhary, PI): Nothing to report

D.2 Impact on Other Disciplines

University of Texas at El Paso Site (Cox, PI): Nothing to report
Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report
Clark Atlanta University Site (Chaudhary, PI): Nothing to report

D.3 Impact on Technology Transfer

University of Texas at El Paso Site (Cox, PI): Nothing to report
Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report
Clark Atlanta University Site (Chaudhary, PI): Nothing to report

D.4 Impact on Society Beyond Science and Technology

University of Texas at El Paso Site (Cox, PI): Nothing to report
Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report

Clark Atlanta University Site (Chaudhary, PI): Nothing to report

E. CHANGES/PROBLEMS

E.1 Changes in Approach and Reasons for Change

University of Texas at El Paso Site (Cox, PI): Nothing to report
Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report
Clark Atlanta University Site (Chaudhary, PI): Nothing to report

E.2 Changes that Had a Significant Impact on Expenditures

University of Texas at El Paso Site (Cox, PI): Nothing to report
Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report
Clark Atlanta University Site (Chaudhary, PI): Nothing to report

E.3 Significant Changes in Use or Care of Human Subjects, Vertebrate Animals, Biohazards, and/or Select Agents

University of Texas at El Paso Site (Cox, PI): Nothing to report
Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report
Clark Atlanta University Site (Chaudhary, PI): Nothing to report

F. PRODUCTS

University of Texas at El Paso Site (Cox, PI):

The following review article references support from this award:

Mazaira, G.I., Zgajnar, N.R., Lotufo, C.M., Daneri-Becerra, C., Sivils, J.C., Soto, O.B., Cox, M.B., and Galigniana, M.D. (2018) The Nuclear Receptor Field: A Historical Overview and Future Challenges. *Nuclear Receptor Research*. **5**: Article ID 101320, 21 pages.

Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to Report
Clark Atlanta University Site (Chaudhary, PI): Nothing to report

G. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

G.1 Individuals Who Have Worked on the Project

University of Texas at El Paso Site (Cox, PI):

Name: Dr. Marc B. Cox
Project Role: PI
Researcher Identifier: https://orcid.org/0000-0001-7854-2676
Person months worked: 2.8
Contribution to Project: Dr. Cox provided oversight of the project, provided guidance and consultation to Ashley Payan, and assisted with the analysis and interpretation of data.
Funding Support: This project only

Name: Ashley Payan
Project Role: Graduate Student

Researcher Identifier: N/A
Person months worked: 12
Contribution to Project: Ashley conducted all experiments (reporter assays for screening derivatives, mutagenesis and assessment of drug effects on mutants), and collected and analyzed data.
Funding Support: This project only

Vancouver Prostate Centre Site (Cherkasov, PI):

Name: Dr. Artem Cherkasov
Project Role: PI
Researcher Identifier:
Person months worked: 2
Contribution to Project: Dr Cherkasov oversees all aspects of computational drug design, molecular modeling and bioinformatics, provides guidance and consultation to Dr. Ban, and assists with the analysis and interpretation of data.
Funding Support: Salary 100% covered by the University of British Columbia (no salary paid from this grant.

Name: Dr. Fuqiang Ban
Project Role: Post-doctoral Fellow
Researcher Identifier:
Person months worked: 2
Contribution to Project: Dr. Ban conducted and/or supervised Dr. Kriti and the Masters student in computational drug design, molecular modeling and bioinformatics studies to generate novel derivatives to be tested. He also assisted with the analysis and interpretation of data.
Funding Support: salary fully covered by other sources (no salaried paid from this grant)

Name: Dr. Kriti Singh
Project Role: Post-doctoral Fellow
Researcher Identifier:
Person months worked: 6
Contribution to Project: Dr. Kriti conducted computational drug design, molecular modeling and bioinformatics studies under the supervision of Dr. Ban.
Funding Support: This project only

Name: Godwin Woo
Project Role: Master's Student
Researcher Identifier:
Person months worked: 2
Contribution to Project: Mr. Woo worked alongside Dr. Kriti on computational drug design, molecular modeling and bioinformatics studies.
Funding Support: This project only

Clark Atlanta University Site (Chaudhary, PI):

Name: Dr. Jaideep Chaudharry
Project Role: PI
Researcher Identifier: https://orcid.org/0000-0002-4440-6585
Person months worked: 1
Contribution to Project: Dr. Chaudhary provided oversight of the project, provided guidance and consultation to Dr. Komaragiri, and assisted with the analysis and interpretation of data.

Funding Support: This project only

Name: Dr. Shravan Kumar Komaragiri
Project Role: Post-doctoral Fellow
Researcher Identifier: https://orcid.org/0000-0003-0889-9906
Person months worked: 12
Contribution to Project: Dr. Kumar established experimental protocols (cell culture, immune-histochemistry etc.), collected and analyzed data and managed the supply chain.
Funding Support: This project only

G.2 Changes in Active Other Support of the PD/PI(s) or Senior/Key Personnel Since the Last Reporting Period

University of Texas at El Paso Site (Cox, PI):

The following grant has been activated since negotiation and setup of this award:

Cox (PI) 6/1/2018-5/31/2019
Lizanell and Colbert Coldwell Foundation $70,000
A Novel Approach to Treating Castration Resistant Prostate Cancer
The overall goal of this project is to further our understanding of the mechanisms by which FKBP52 and beta-catenin regulate unique androgen-regulated, genome-wide transcriptional programs and define how targeting this mechanism affects those transcriptional programs.

Vancouver Prostate Centre Site (Cherkasov, PI): Nothing to report

Clark Atlanta University Site (Chaudhary, PI): Nothing to report

H. SPECIAL REPORTING REQUIREMENTS

This report is for a collaborative award (partnering PI option), and was prepared jointly by the three PIs. The tasks are clearly for each responsible Pi and project performance site are clearly marked.

I. APPENDICES

None