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TITLE: Characterization of Novel Vaccine Targeting Follicle-Stimulating Hormone Receptor in Ovarian Cancer

PRINCIPAL INVESTIGATOR: David Weiner, Ph.D.

CONTRACTING ORGANIZATION: The Wistar Institute of Anatomy & Biology

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14. ABSTRACT

Ovarian cancer has a high burden of disease and death. More than 50% of women diagnosed with ovarian cancer have just a 5-year survival rate. Many respond initially to traditional treatment; however, recurrence is high. Interesting post treatment there is little disease and the tumor burden is low, presenting an important opportunity for the use of immunotherapy to improve treatment for this disease. We focused on a two-pronged approach for immunotherapy of ovarian cancer. 1) The use of active immunization to drive antibody and T cell immunity against antigens expressed specifically in ovarian disease targeting the native follicle-stimulating hormone receptor (FSHR). We developed a therapeutic vaccine for the FSHR antigen and demonstrated that it activates the immune system in mice and improves survival in animals. We have been studying the induced immune responses as per the grant in detail and observed that the novel immunogen generated novel T cell responses that are important for impacting the tumor. We are studying additional tumor specific epitopes to increase the immune effect of the vaccine and improve T cell breadth. 2) We observed that the vaccination induced antibodies that target the native FSHR structure. This was important as the FSHR antigen is a 7 transmembrane molecule which is difficult to fold in vivo limiting generation of native immune responses. We are studying this response of the humoral immune response combining the vaccine with targeted FSHR immunotherapy to provide additional impact. We have generated genetically modified antibodies as tools. In this progress update we describe development of mAb that are potent for human FSHR that were developed using the unique FSHR vaccine immunogen. This provides us with dual targeting for ovarian tumor therapy. In addition, we continue to focus on development of multivalent immunization for Ovarian cancer to complement our FSHR vaccination strategy.

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1. **INTRODUCTION:**

The follicle-stimulating hormone receptor (FSHR) is an antigen that is selectively expressed in women in the ovarian granulosa cells(18) and at low levels in the ovarian endothelium(19). Most importantly, this protein is expressed in 50-70% of ovarian carcinomas(20-26). Given that oophorectomy is a standard procedure in the treatment of ovarian cancer, targeting the FSHR should not cause damage to healthy tissues. Therefore, **FSHR represents an ideal vaccine and immunotherapy target to prevent recurrence of post diagnosis and treatment**. ***Our central hypothesis is that a SynCon FSHR DNA vaccine or DNA immunotherapy would be able to itself impact tumors. We have data that now shows the synergy with immunotherapies such as Mab including CPI. We also have demonstrated increased survival in humanized animal challenge models. We have established the potency of the FSHR immunogen for generating antibodies that target the native FSHR. We isolated antibodies targeting FSHR as described below. These are new tools of potential for targeted immunotherapy of ovarian cancer. To bridge them to engage T cells we engineered bispecifics during the delay period for animal work, and then studied their potential as immunotherapeutics for treatment of FSHR tumors.*** We have created genetically enhanced versions of MAb targeting the external domain of FSHR for study in vitro and in animal models. We also added a novel Xcellegence based assay which allows for more quantitative and visual assessment of tumor impact. This assay is highly informative and is animal sparing using human immune cells. It is a highly valuable update to the program that provides new level of detail for immune targeting while improving throughput. We have demonstrated that MAbs we generated are specific and can target ovarian tumors with potency. These were engineered to also engage the T cell component of the immune system and be delivered by DNA inoculation. The combination of genetic active immunization and genetic delivery for FSHR ovarian cancer for potential treatment of this difficult cancer. We also developed a more focused Ag string neoAg like immunogen cassette for testing improved induction of T cell responses as proof of principal regarding the T cell impact for ovarian cancer therapy and observed tumor impact in mice. Such combination approaches could have importance for human immunotherapy of patients.

We were delayed for 9 months due to covid and have resumed animal ordering and invovo work after this delay. Shipments have been slow due to global supply shortages, and mice have been more limited especially humanized mice so we focused on the constuct design and invitro work during this period but as shown below significantly advanced the program. We have developed new assays. Nevertheless we have produced data in both regular mouse models and now humanized mice as outlined below advancing the program goals.

2. **KEYWORDS:** FSHR, Immunization, DNA Vaccination, FSHR targeted Immunotherapy, Cancer Immunotherapy, Ovarian Cancer

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

Goal(s)	Anticipated completion time	Complete (Y (date) or N)
Specific Aim 1. Determine whether FSHR DNA immunogen or FSHR Immunotherapy is effective and synergizes with combination therapy with checkpoint inhibitors.		
Major Task 1. Investigate the effect of combination strategies between DNA FSHR immunotherapy & checkpoint inhibitors.	Months	1-18
Local IRB/IACUC Approval	1-2	**Yes** Wistar IACUC protocol #201326 approved 1/17/2020 However COVID shut down impacted animal work April 2020
Subtask 1. Submit IACUC approval documentation.	1-2	**Yes**
Subtask 2. Study the combination of anti FSHR DNA immunotherapy with checkpoints in vitro. Groups: DNA FSHR Immunotherapy +IgG control, 2) DNA FSHR Immunotherapy+anti-PD-1, 3) DNA FHSR+anti-CTLA4. We developed new more quantitative Xcelligence assays for this task. This subtask is mostly complete. We observed that the combination approach improves tumor killing and that DNA anti-FSHR immunotherapy can complement PD-1 for killing tumor cells.	18-28	Yes
Subtask 3. Study the impact of invivo DNA FSHR immunotherapy in mice and measure tumor growth. Animal Studies were performed exvivo to measure killing more quantitatively on targets in Xcelligence assays. Groups: 1) No therapy controls 2) DNA FHSR immunotherapy. Killing is assayed 10 and 14 post immunotherapy on human ovarian cancer lines. Killing is observed in the DNA FSHR inoculated groups, and not in control groups. Data targeting multiple ovarian tumor lines has been demonstrated.	20-30	No
Subtask 4. Study the effect of the combination of FSHR Immunotherapy and its effects on the tumor microenvironment of unresectable cohort (same groups	18-30	No

as Subtask 2). 10 mice per group. Resection of tumor and spleen. Work In progress.		
Specific Aim 2. Determine the effectiveness of human DNA FSHR Immunotherapy against human ovarian cancer in humanized mice. *Animal work is not initiated until approved Wistar IACUC is also approved by ACURO.*	28-36	No
Major Task 2. Demonstrate immunogenicity of DNA FSHR immunotherapy and impact in humanized mice. **We have performed tumor challenge in humanized mice who were treated with DNA FSHR immunotherapy vs vector control and non specific immunotherapy controls.**	17-36	Partially Complete
Major Task 3. Demonstrate anti-tumor effectiveness DNA FSHR immunotherapy in humanized mice plus check point inhibitors.	24-36	No

The major goals of this project were to develop a synthetic DNA vaccine/immunotherapy targeting FSHR for treatment of ovarian cancer. We proposed to generate both humoral and cellular immunity to support this approach including study the antibody responses induced by DNA vaccine cassettes for their functions and then study the effects of these approaches in mice for ovarian cancer immunotherapy. Once we had proof of concept in invitro and in mice, we would then move to mice reconstituted with human T cells to further study tumor impact in humanized mouse models.

Our time lines were affected by COVID. We were not able to work for a time on this project and then we were *limited* in regards to mouse studies due to the the shut-down March 2020 till the winter of 2020. We were used this period to expand the T cells invitro studies and focus on characterization of the antibody approaches and molecular designs which were not as impacted. We have made major progress in spite of this impact due to rearranging our focus on specific experiments to fit available reagents and the colony limitations for cancer animal work. We also were able to purchase with in the laboratory a new Xcellegence devices which allows exvivo characterization with immune cells and serum thus saving animals and expanding the work flow. Its quantitative nature enhanced our studies. We focused on dissection of the induced immune response to the vaccine. We generated data that the vaccine is impactful in mouse models and we built on this using the monoclonals derived from the mice. We developed T cell epitope strings for ovarian cancer and showed that T cell elements alone particularly CD8 epitopes, were impactful in controlling tumors. Based on the isolation of native antibodies which bind human FSHR engineered some of the MAbs to increase effector functions by adding their ability to Target T cells directly. This is a novel approach for FSHR and for ovarian cancer linking dual targeting of humoral and cellular immunity. We have generated data showing high impact of these bispecific DNA molecules for tumor killing.

What was accomplished under these goals?

We have several important accomplishments under this grant, we believe these are of significant importance. We have demonstrated that the synthetic DNA vaccine for FSHR generates potent T cells and antibodies which can impact ovarian cancer in mouse model challenges. The antibody response appears to be an important additional contributor to tumor impact. We isolated spleens from animals that were vaccinated with the syncon FSHR plasmid vaccine. This immunogen is unique in that it is modified to break tolerance and was designed to be processed and folded in native form in vivo. We observed that we could transfer tumor impact of the vaccine using T cells isolated from immunized animals. However, we also observed induction of IgG that bound to the surface of ovarian tumors. This was a benefit of this vaccine antigen as it is expressed and likely folds into the true 7 transmembrane antigen structure allowing B cells to recognize native FSHR.

FIGURE 1

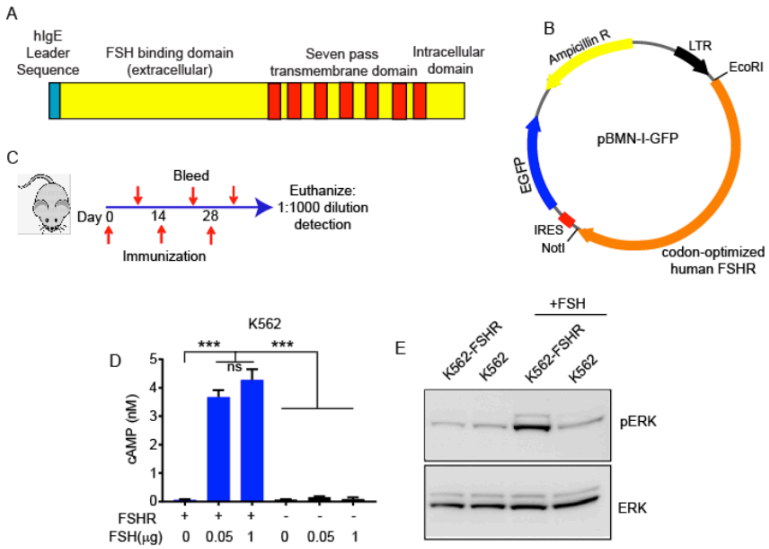

Figure 1. Generation of anti-human FSHR antibodies. (**A**)Depiction of FSHR structure. (**B**) Cloning strategy into pBMN-I-GFP1 expression vector. (**C**) Mouse immunization scheme. (**D**) cAMP response to different doses of FSH hormone of K562 and K562-FSHR. (**E**) Western blot of phospho-Phospho-p44/42 (Erk1/2) and p44/42 (Erk1/2) 20 minutes after stimulation of K562 and K562-FSHR cells using 1µg/ml FSH. ANOVA. *** p<0.001.

To study if the antibodies induced have relevance, we collected spleens from immunized mice and developed hybridomas to analyze the B cell responses. Using this approach, we also developed a unique screening assay using transfected cells expressing the synconFSHR antigen on the surface and screened the hybridomas by high throughput Intellicyt platform screening assay which we developed for this purpose.

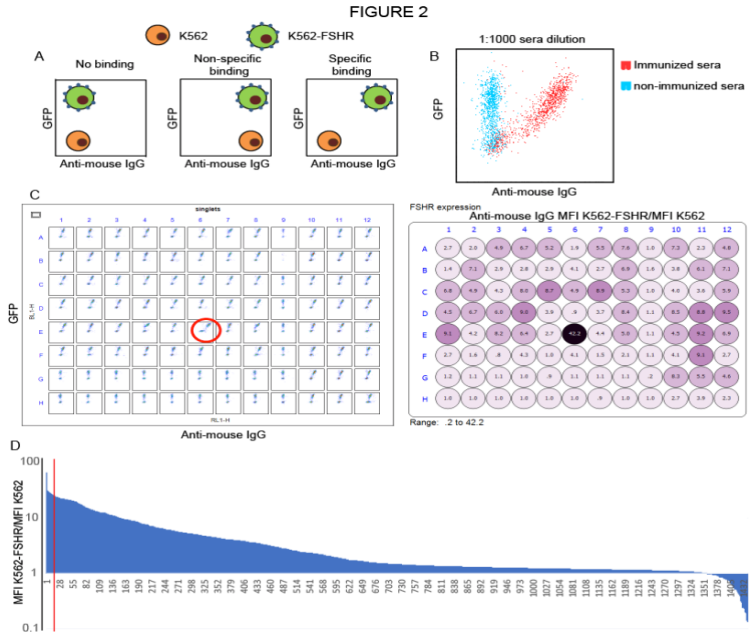

Figure. Screening of anti-human FSHR antibodies. (**A**) Scheme of flow cytometry plots representing the potential outcomes in the screening process with K562 and K562-FSHR. (**B**) Flow cytometry plot of K562 (GFP-)/K562-*Fhsr* (GFP+) cells stained with sera from mice immunized with human FSHR or empty vector at 1:1000 dilution and anti-mouse IgG APC. (**C**) Representative of flow cytometric screening output strategy for detection of FSHR binding antibodies from hybridomas as flow plot and fold mean fluorescent intensity of K562-FSHR/K562 (**D**) Waterfall plot depicting the hybridoma supernatant binding to FSHR measured as fold-MFI K562-FSHR/K562. After the first round of screening we went forward with the top 20 clones (left of the red bar)

We have been studying the most potent of these antibodies for targeting FSHR positive ovarian cancer (figure 3 below). As can be observed in the data set below the MAbs are highly specific and bind to several important ovarian tumor lines through recognizing FSHR in its native form on tumor surface. These reagents are potentially important tools for ovarian cancer studies. A MAb 9H11 was studied in additional detail due to its robust reactivity.

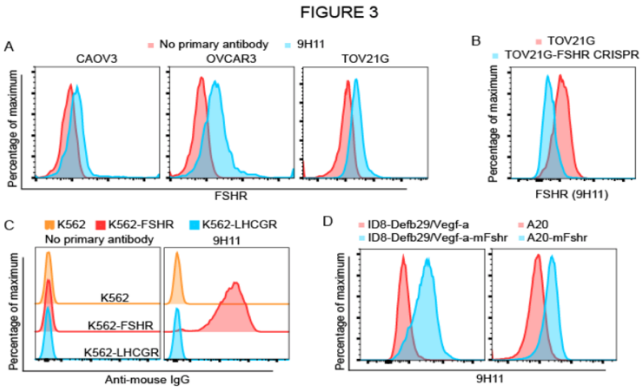

Figure 3. 9H11 binds human and murine FSHR. (**A**) Flow cytometry plot of CAOV3, OVCAR3 and TOV-21G stained with 9H11 or no primary antibody followed secondary APC labelled antibody. (**B**) Flow cytometry plot of TOV-21G parental or after CRISPR of FSHR stained with 9H11. (**C**) Flow cytometry plot of K562, K562-FSHR and K562-LHCGR 21G stained with 9H11 or no primary antibody followed secondary APC labelled antibody. (**D**) Flow cytometry plot of A20(GFP-)/A20-*Fhsr* (GFP+) and ID8-*Defb29/Vegf-a* vs. ID8-*Defb29/Vegf-a-Fshr* cells stained with 9H11 (both cell lines transfected with murine FSHR

To further characterize the ability of 9H11 to target human ovarian cancer we performed immunochemistry analysis. This antibody reacts with frozen sections as well as marks the surface of human FSHR expressing cells (figure 4) below.

FIGURE 4

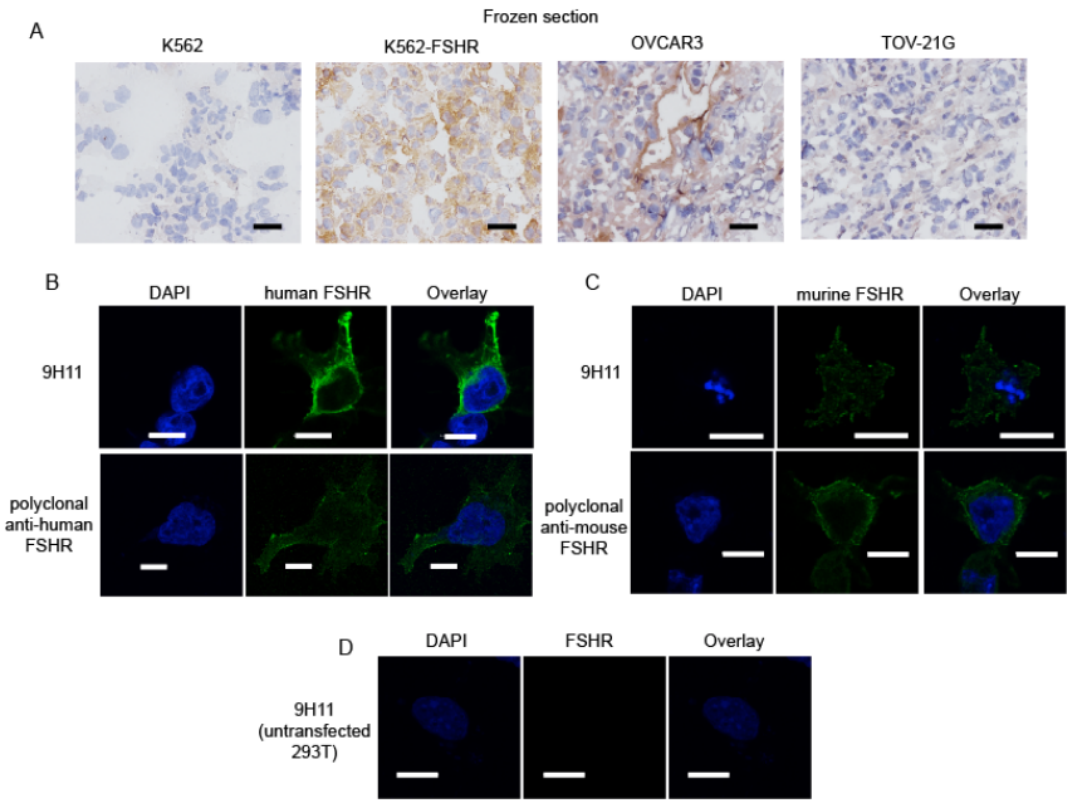

Figure 4. 9H11 binds to FSHR in immunohistochemistry and immunocytochemistryA) Immunohistochemistry images from frozen sections of tumors derived from K562, K562-FSHR, OVCAR3 and TOV-21G cell lines stained with 9H11. 40X, Scale bar 50µm. **(B)** Immunofluorescence images of 293T cells transfected with human FSHR and stained with either mouse anti-human FSHR or 9H11 antibodies followed by secondary anti-mouse IgG. **(C)** Immunofluorescence images of 293T cells transfected with murine FSHR and stained with either mouse anti-mouse FSHR or 9H11 antibodies followed by secondary anti-mouse IgG. **(D)** Immunofluorescence images of 293T cells transfected with pVax empty vector and stained with 9H11 antibodies followed by secondary anti-mouse IgG. B-D: Scale bar 10 µm.

We next tested the functionality of this antibody in ADCC assays which would support part of the anti-tumor activity we observed in the polyclonal responses. 9H11 is a potent activator of ADCC against human OVACAR3 ovarian cancer cells, supporting the role for this effector arm in possible immune treatment of ovarian disease (figure 5).

FIGURE 5

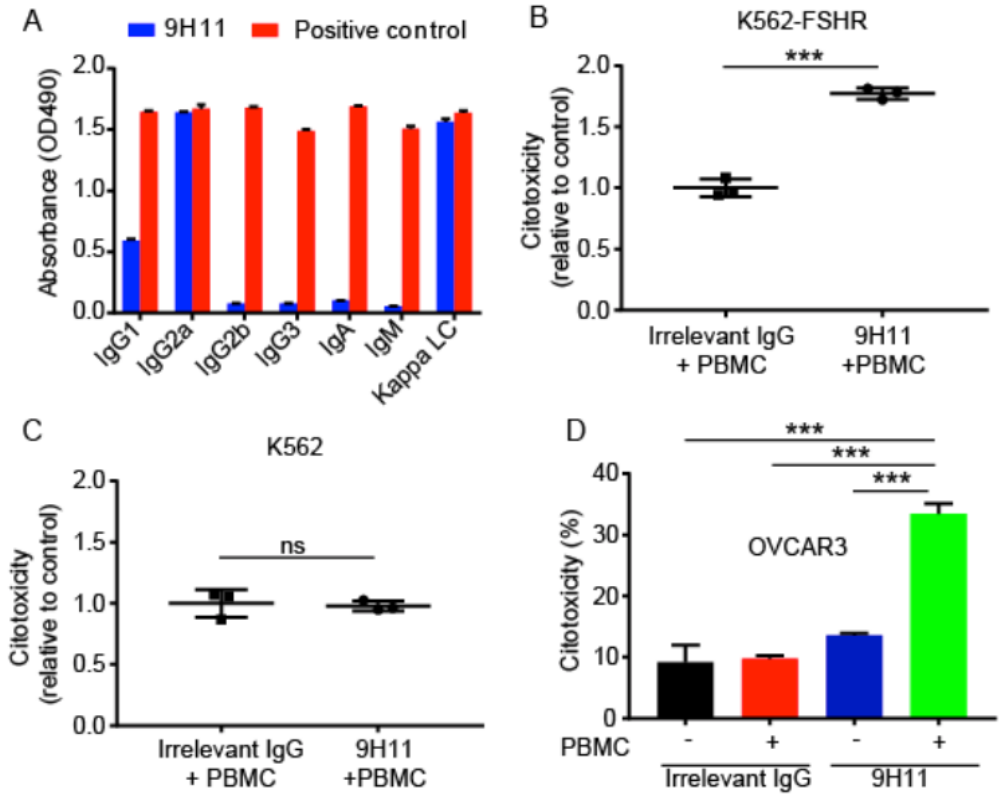

Figure 5. 9H11 induces antibody-dependent cell mediated cytotoxicity. (**A**) Absorbance values of isotype ELISA performed on 9H11 antibody. (**B**) Cytotoxicity mediated by ADCC of 9H11 or irrelevant mouse IgG2a (C1.18.4) against K562-FSHR. (**C**) Cytotoxicity mediated by ADCC of 9H11 or irrelevant mouse IgG2a (C1.18.4) against K562. (**D**) Cytotoxicity mediated by ADCC of 9H11 or irrelevant mouse IgG2a (C1.18.4) against OVCAR3 cells. t-test, ANOVA. ***p<0.001, ns not significant.

We are very excited by this data as it extends the immune mechanism for the immunization approach we developed, and it provides novel reagents for studying and possibly treating ovarian cancer. We continue to characterize additional antibodies developed from this screening. We are also writing up this work for publication later this year.

Enhanced MAb function by T cell engagement:

Based on immune potency we next designed a FSHR-9h11 CD3 FAB fusion as a bispecific DNA immunotherapy (Figure 5b). The FSHR Bispecific binds to FSHR, and to human T cell expressed CD3. It is highly potent to activate T cells in the presence of FSHR positive ovarian cancer. The Bispecific kills CaOV3 ovarian cancer with nanogram potency in a quantitative xCelligence assay.

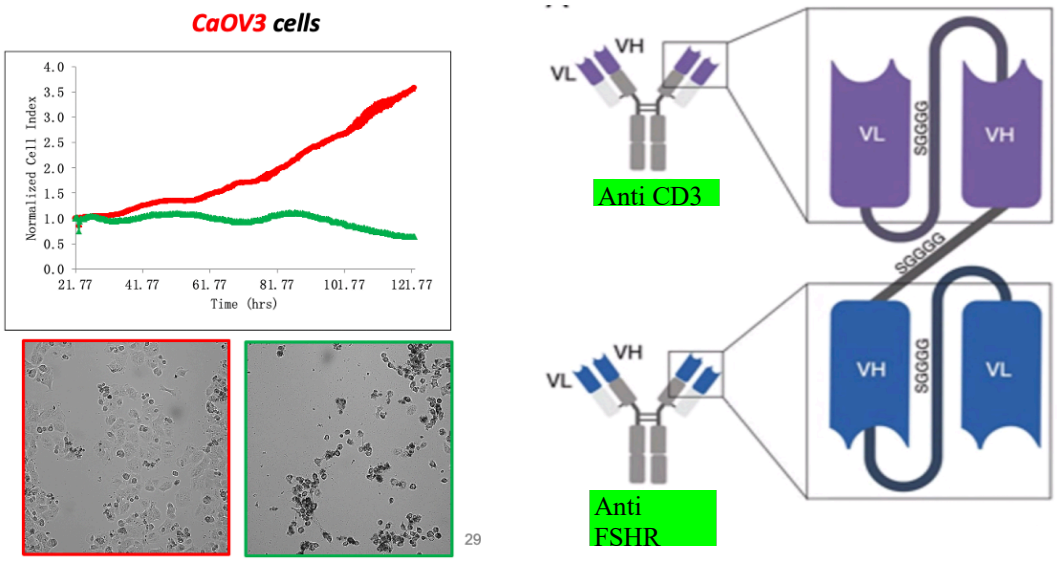

Figure 5b

Additional study of this potential important new approach in combination with T cell immunogens to impact FSHR positive ovarian cancer is an important application for this program.

Epitope T cell studies:

Analysis of the vaccine induced T cell responses supports the induction of new T cells from the syncon FSHR immunogen. New responses are similar in nature to neoAg responses that CPI therapies respond to. We were studying T cell epitope strings of responses as denovo T cell responses through a collaboration and based on the syncon data this would allow us to confirm and extend the relevance of strictly the T cell component for tumor impact. We this work has implications for specific immune therapy of ovarian and other cancers as well as combination T cell immunotherapy immunogens such as FSHR + Ag strings. We then tested this theory using a synDNA designed to carry 40 neoantigens expressed by two important cells line the ID8 ovarian cancer line and TC-1, epithelial tumor model cell line. We observed that arranging the antigens from the lines in strings generated reproducible induction of CD4 and CD8 T cell immunity. These responses would be supplemental to those expanded by CPI therapy, as these like the SynconFSHR would include denovo responses. The immune responses from the synthetic Ag collection were able to control tumor challenge, as well as rechallenge (Figure 6). This data provides a unique insight into the design of Syncon Ags for FSHR as part of an immune therapy cocktail. We are generating a manuscript on this work. This work developed as a collaboration with an industry group (Geneos) which supported their side of the collaborative study.

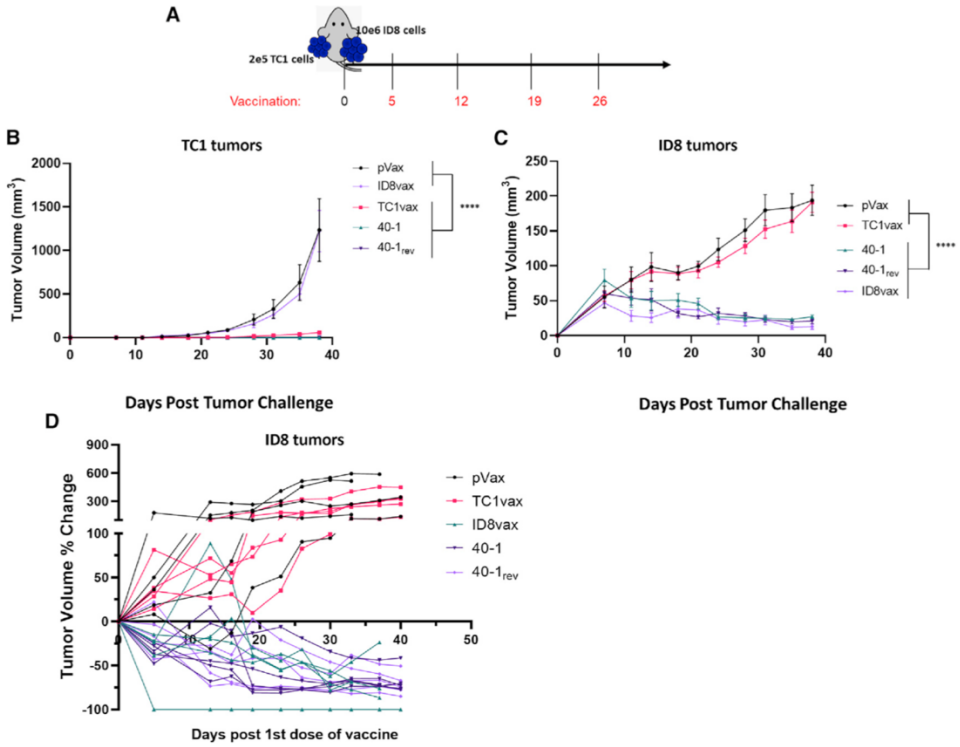

Figure 6: The syncon epitope vaccines control multifocal tumors (Ovarian & Epithelial) with unique mutation profiles (A) Schematic to explain tumor challenge experiments in (B)–(D). (B and C) Mean tumor sizes of TC1 (B) and ID8 (C) tumors in mice vaccinated with pVax (50 mg), TC1vax (25 mg)+pVax (25 mg), ID8vax (25 mg)+pVax (25 mg), 40-1 (50 mg), or 40-1rev (50 mg). (D) % of ID8 tumor size change after vaccination with pVax (50 mg), TC1vax (25 mg)+pVax (25 mg), ID8vax (25 mg)+pVax (25 mg), 40-1 (50 mg), or 40-1rev (50 mg). Error bars represent mean + SEM. Two-way ANOVA. ****p < 0.0001

Summary: We have advanced the goals of immunotherapy for Ovarian cancer. The FSHR work identified new T cell responses, neo Ag like responses, that were associated with tumor control and this has been extended to a synAg specific study clearly identifying the contribution of the epitope collections in Ags as playing a major role in tumor control. We have also determined that the antibodies induced by the FSHR vaccine have a role in immune control of the tumors as well, and define using new antibody reagents, that ADCC appears to be an important mechanism. We continue to propose that the dual induction of the specific humoral and cellular response to immunotherapy of ovarian cancer driven by specific antigens that break tolerance is likely to pay dividends. We expect at least 2 manuscripts describing portions of this work this year to be published over the next few months.

Summary of accomplishments:

1) **T cell killing of ovarian cancer by DNA immunogen**
2) **Identification of humoral potency induced by the DNA vaccine**
3) **Tumor impact in mouse tumor studies**
4) **Impact shown in humanized mice with human tumors**
5) **Generated novel MAbs that recognize native FSHR on ovarian cancer**
6) **Created novel highly potent bispecifics with high potency for killing ovarian cancer.**
7) **Two manuscripts in progress**
8) **Combination studies in progress**

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

Training opportunities were provided for two persons on this grant.

The first is an early post-doctoral fellow Devi Bordoloi, who was supported under this grant. She was trained in the lab in B cell and T cell immune assays and then performed analysis of the Ig responses to FSHR including screening and cloning of hybridomas resulting in the exciting new clones discussed. She has been invited to present her work at training meetings at Wistar, which were virtual due to COVID-19. She has also presented her work at lab meetings and workshops. As the restrictions around COVID are lifted she will be encouraged to attend meetings in person. She also will be given a summer trainee to help her develop her leadership skills. She has been working on writing up one of the described manuscripts.

The second person is Pratik Bhojnagarwala, a graduate student who was supported on this grant. He was trained in molecular and cellular immunology and studied the T cell responses to syncon FSHR, as well as then developed the ovarian neoAg DNA strings. He presented his work at training meetings at Wistar, which were virtual due to COVID-19. He has also presented her work at lab meetings and workshops. He also was invited to present his work at UPENN trainees cancer meeting. As the restrictions around COVID are lifted he will be encouraged to attend meetings in person. Pratik has had a undergraduate student assigned to help him grow his leadership skills, He is working on one manuscript for this program.

How were the results disseminated to communities of interest?

Presentations were limited during Covid. We are working on finishing up the FSHR work included in this report on identification of a functional anti-tumor antibody induced by a synconDNA FSHR immunogen. We also have generated a manuscript on the syncon Ovarian Ag studies and will look to have another manuscript published in the next few months. We plan on presenting this work at meetings in talks and posters.

What do you plan to do during the next reporting period to accomplish the goals?

Our focus will be to continue to focus on the novel and now expanded anti-FSHR DNA tools for impacting ovarian cancer in vitro and in vivo in animal challenge models. We will expand our work on the FSHR Bispecific and explore its potential for translational advancement. Our focus is to continue to combine both T cell effector function and humoral effector function as a combined immunotherapy for ovarian cancer. Our ultimate goal is combined T cell and humoral impact to control or eradicate specific ovarian cancer

4. IMPACT:

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

These studies are impactful in several ways. They support that synthetic DNA immunogens for FSHR can impact ovarian cancer in vitro as well as in animal challenge models. Our studies do not show on target off tumor unwanted effects. The data are supportive that we can drive new T

responses, as well as structurally important B cell responses which are capable of targeting and highly relevant for treating ovarian tumors. We show that increasing the numbers of epitopes in the vaccine is important as they provide a diverse pool of T cells that can coordinately control ovarian cancer immune escape. We also have evidence that the diversity of epitopes driven by the vaccine is important for potential control. Our observation of humoral anti-FSHR activity playing a role in tumor control led to development of potent anti-FSHR hybridomas which recognize cell expressing human FSHR. These antibodies have a role in immune control through induction of ADCC, thus providing an additional tool for both diagnostic studies, and importantly for possible treatment of this difficult disease. Dual immune engagement is an important observation from these studies for ovarian cancer. The combination of humoral and cellular anti-tumor immunity as an important combined approach for ovarian cancer, and possibly other cancers is supported by our work.

What was the impact on other disciplines?

While the work was focused on ovarian cancer, the concepts that induction of new T cell responses are valuable in cancer using tolerance breaking vaccines has potentially broad implications. The concept of combining humoral and cellular immunity to prevent cancer recurrence has potentially broad implications. This grant does not focus on diagnostics, however, the new hybridomas that target FSHR specifically, may be important as tools for diagnosis and staging of ovarian cancer, which could be studied. The FSHR antibodies as well as bispecific represent exciting tools for possible development for treatment of FSHR positive ovarian cancers.

What was the impact on technology transfer?

While the work was focused on ovarian cancer, the concepts that induction of new T cell responses are valuable in cancer using tolerance breaking vaccines has potentially broad implications. The concept of combining humoral and cellular immunity to prevent cancer recurrence has potentially broad implications. This grant does not focus on diagnostics, however, the new hybridomas that target FSHR specifically, may be important as tools for diagnosis and staging of ovarian cancer, which could be studied. The FSHR antibodies as well as bispecific represent exciting tools for possible development to treat FSHR positive ovarian cancers.

What was the impact on society beyond science and technology?

Our studies provide new immune insights into nucleic acid vaccines in general and their ability to drive protection against pathogenic cells for treatment of human disease in general. Establishing the importance of dual immune activity is likely important for targeting other tumors of epithelial nature. In addition, native structure immunogens appear important as immunotherapy tools. We have a paper that was accepted on a collaborative work for T cell immunization using DNA cassettes for ovarian cancer (see below).

5. CHANGES/PROBLEMS:

The change driven by the pandemic is an increased effort for molecular assay systems to pick up for the slow shipments and development of mice. Mice are a bit more limited during this time.

Changes in approach and reasons for change

Actual or anticipated problems or delays and actions or plans to resolve them
We were delayed by COVID especially for the animal studies. This allowed us to refocus on the laboratory assays and put more time up front into the characterization of mapping the T cell responses and the monoclonal antibody studies. These studies have substantially advanced the program as described above.

Changes that had a significant impact on expenditures
The costs overall have not changed in a significant way due to the minor adjustments described above. In addition, the cost of all biologic materials has increased during COVID, so we pay significant attention when ordering.

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
None

Significant changes in use or care of vertebrate animals
None in principle; in practice the supply of animals is a bit more limited. We will use our other assays to supplement for this issue.

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

6. PRODUCTS:

- **Publications, conference papers, and presentations**

  A synthetic DNA vaccine targeting multiple neoantigens induced robust, long-term T cell immunity which prevents tumor recurrence in a mouse lung cancer model
  Pratik S. Bhojnagarwala[1], Alfredo Perales-Puchalt[2], Neil Cooch[2], Niranjan Y. Sardesai[2] and David B. Weiner[1*] Mol Ther Oncolytics. 2021 Jun 25; 21: 278–287.
  Published online 2021 Apr 16. doi: 10.1016/j.omto.2021.04.005
  Support was acknowledged for this grant.

  Books or other non-periodical, one-time publications.
  Nothing to report

  Other publications, conference papers and presentations.
  Nothing to report

- **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:	David B. Weiner, Ph.D.
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	*0000-0002-22B2-8512*
Nearest person month worked:	*1*
Contribution to Project:	*Project oversight and guidance.*
Funding Support:	This award

Name:	*Pratik Bhojnagarwala, M.S.*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*0000-0002-9403-5276*
Nearest person month worked:	*6*
Contribution to Project:	Performs experiments
Funding Support:	This award

Name:	*Devivasha Bordoloi*, Ph.D.
Project Role:	*Postdoc Researcher*
Researcher Identifier (e.g. ORCID ID):	*0000-0002-3485-8369*
Nearest person month worked:	*4*
Contribution to Project:	Performs experiments
Funding Support:	This award

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

Dr. Muthumani left to take a position in pharma.

Termination of Gates Foundation OPP1180809
Termination of Gates Foundation OPP1201239
Termination of Gates Foundation OPP1189362
Activation of Sumitomo Dainippon Pharma Oncology Research Agreement - FAP
Activation of Sumitomo Dainippon Pharma Oncology Research Agreement - FSHR
Activation of Gates Foundation INV-023020
Activation of HR0011-21-9-0001
Activation of Inovio SRA21-04
Activation of Inovio SRA21-05

What other organizations were involved as partners?
None

8. SPECIAL REPORTING REQUIREMENTS

AWARD CHARTS: See Appendix.

9. APPENDICES: Award Chart attached.

OC180118: Characterization of Novel Vaccine Targeting Follicle-Stimulating Hormone Receptor in Ovarian Cancer

PI: David Weiner, The Wistar Institute, PA

Budget: $781,699

Topic Area: Ovarian Cancer

Mechanism: OCRP-IIRA

Research Area(s): 0806 - Therapeutic Vaccines, 0502 - Tumor Immunology

Award Status: 5/15/19-5/14/22

Study Goals:

Major Task 1. Investigate the effect of combination strategies between SynCon FSHR therapeutic/vaccine & checkpoint inhibitors.
Major Task 2. Demonstrate immunogenicity of SynCon FSHR therapeutic/vaccine in humanized mice.
Major Task 3. Demonstrate anti-tumor effectiveness SynCon FSHR DNA/Immunotherapy in humanized mice.

Specific Aims:

Specific Aim 1. Determine whether SynCon FSHR DNA therapy/vaccine synergizes with combination therapy with checkpoint inhibitors for ovarian cancer.

Specific Aim 2. Determine the effectiveness of human SynCon FSHR DNA vaccine/therapeutic against human ovarian cancer in humanized mice.

Key Accomplishments and Outcomes

T cell killing of ovarian cancer by DNA immunogen
Identification of humoral potency induced by the DNA vaccine
Tumor impact in mouse studies
Impact shown in humanized mice for human tumors
Generated MAbs from the vaccine Ag that recognize native FSHR on ovarian cancer and studied their tumor impact

Wistar and Acuro IACUC approval - January 2020

Publications: 1 manuscript published and one in preparation
Patents: none to date
Funding Obtained: Collaborative study on DNA t cell epitope cassettes as strings for ovarian cancer is a collaboration with Geneos biotechnology.