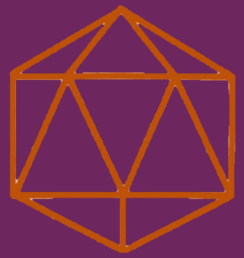
Society for Viral Studies



GBM #2
October 17th, 2022

Welcome New Members!

Please sign in using the QR Code for attendance!

What is the Society for Viral Studies?

We aim to encourage scientific discussion, research, and exploration with UF's undergraduate students who are interested in a career in science! We host a variety of meetings, guest lectures, socials, volunteer events, and trips with the common goal of developing the next generation of scientists. There is no major requirement to be involved and we do not charge dues.

UF SOCIETY FOR VIRAL STUDIES

Travel | Research | Mentorship | Volunteering | Leadership

Active Member Requirements

01

Be a UF Student

02

Attend ~ ⅔ of meetings

03

Attend ~ ⅓ of events

Benefits

- Priority for trip sign-ups
- Priority for committee positions

Meet Our Faculty Advisor

Dr. Niam Montazeri

Assistant Professor of Food Virology

Department of Food Science and Human Nutrition

Meet the Officers!

Brianna Garcia
President

Antonia LoFranco
Vice President

Erica Roberts
Treasurer

Michele Himadi
Secretary

Kira Kazi
Event Director

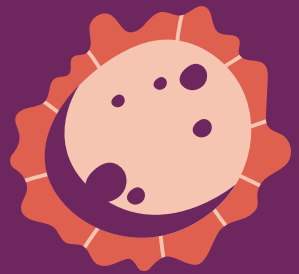
Sophie Penafiel
Public Relations Director

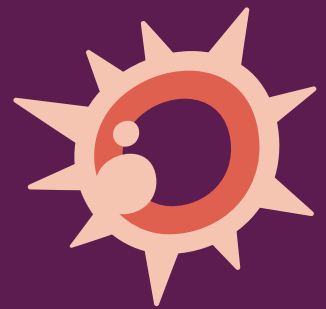
Urvi Patel
Trip Director

Middle School Outreach

- Ms. Winant of Howard Bishop Middle school is looking for our help in her 6th-8th grade classes!
- Connected us with 6th Grade teacher Ivy Grob
- Cellular Respiration-8th grade: Pushed back to Spring
- January: Pathology-6th grade
- March-May: Ecosystems-7th grade

In November, Ms. Grob will be teaching topics of air pressure and particle motion with her class instead of Cellular Respiration (pushed back to Spring). This opportunity will be an all day commitment and will require transportation to Howard Bishop Middle (carpooling can be coordinated).





Homecoming Festival

Thank you for coming out everyone!

Merch and Other Cool Stuff

- Our NEW T-shirts are for sale!
  - $20 each
- We still have some of our special stickers!
  - $3 each
- Rep SVS with logo stickers and buttons!
  - $1 each
- Grad cords will be available for active members who are graduating.
  - $10 each
- For all purchases you can Venmo @ericaroberts or pay in cash :)

How to find research...

Our biggest tips:

Take BCH4905 Science for Life Seminar!

If your schedule can accommodate it, this class will get your foot in the door and provide a streamlined path to working in a lab.

Attend Research Fairs/Events

Going to these events let's you speak to research coordinators directly and allows you to explore a variety of research opportunities!

Utilize CURBS & Personal connections

Use the CURBS website to look into position postings in areas of research that interest you. Use your connections! Don't be afraid to ask for help from peers, mentors, advisors and teachers!

https://cur.aa.ufl.edu/research-search/

Be persistent!

Of course, be polite, but show your enthusiasm.
If you're interested in a specific lab or paper– try contacting all the authors that worked on the paper or ar in the lab you see yourself joining.

Email Examples

My name is Kira Kazi and I am a freshman at the University of Florida enrolled in a course called Science for Life Seminar. As a part of the course, I will be writing a report on a UF faculty member's research after interviewing them and was wonderfing if you would be open to speaking to me about your current research at your lab? I think your research is interesting and integral to opening eyes to the detriments of pollution and would love to learn more.

I hope you are doing well and staying healthy! First and foremost, I want to again say thank you so much for your time in meeting with me to discuss your research and lab for my report. Talking about the type of research you do in your lab and learning more about the technology used to collect data using zebrafish as a model at the university level compared to what I had done in high school was really interesting and one of the highlights of my first semester! You had told me you had room for one more in the lab for the spring, but unfortunately I will not be moving to Gainesville until the fall 2021 semester, so I won't be able to be involved in the spring. I really appreciate the opportunity and your advice on getting involved in research at UF in general as well!

Have a wonderful day,
Kira Kazi

Dear [redacted]

I hope this email finds you well. My name is Brianna Garcia, and I am a Microbiology and Cell Science major in CALS. I am contacting you regarding the posting about a research lab position on the CURBS Undergraduate research website for Dr. Lam's Lab. I saw that you work with Dr. Lam as a Graduate Student after reading the research profile on UFCD.

I believe that antimicrobial resistance is a concerning issue that has risen in prevalence over the decades. Being able to understand the virulence of these bacterial pathogens such as *Enterococci* and *Streptococcus* mutans is necessary work.

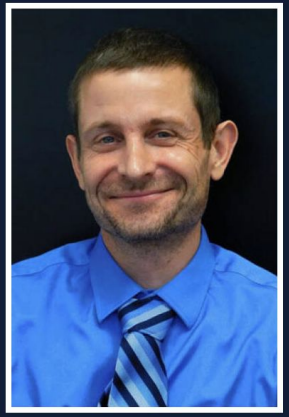
There is so much for me to learn in this area, and **I would love the opportunity to volunteer as an undergraduate research assistant in your lab.** Please let me know if you have any availability in your lab for the Spring 2022 semester.

Thank you for taking the time to read this. I hope we can work together in the future.

Sincerely,

Brianna Garcia

Our future speakers...



Andrew B Allison,
Assistant Professor – Veterinary Virology

DEPARTMENT:
Department of Comparative, Diagnostic & Population Medicine

BUSINESS PHONE:
(352) 294-4127

BUSINESS EMAIL:
aallison1@ufl.edu

Robert J Ossiboff, DVM, PhD, DACVP
Clinical Associate Professor – Aquatic Pathology/Anatomic Pathology

DEPARTMENT:
Department of Comparative, Diagnostic & Population Medicine

BUSINESS EMAIL:
rossiboff@ufl.edu

CV:
View Curriculum Vitae

Journal Article Presentation

- We will now go over a relevant journal article covering ongoing research on diseases, pathology, and how viruses can be utilized as a potential cure.
- The topic?
    - Using the same platform the Covid-19 vaccines were built on to cure/prevent cancer!

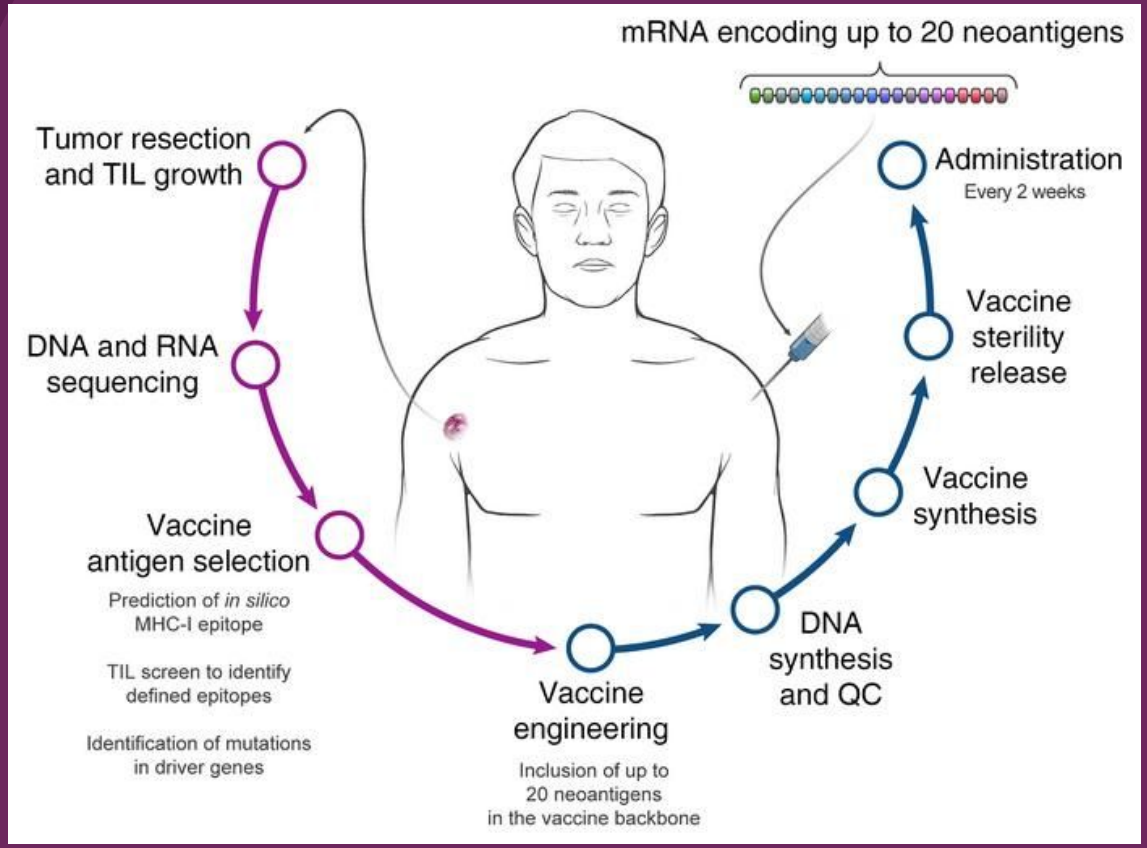
But First...

Kahoot!

General Research Article Structure

1. Abstract
    a. A concise summary for reader to determine usefulness
2. Introduction
    a. Provides context
    b. Outlines the upcoming topics
3. Middle (Body)
    a. Actual dive into information, data analysis, etc.
    b. Separated into multiple paragraphs and subheadings
4. Discussion (Conclusion)
    a. Discusses the results, data, and information,
    b. Highlights the limitations of the study/experiment,
    c. Outlines what future research should focus on

Abstract


mRNA encoding up to 20 neoantigens
Tumor resection and TIL growth
DNA and RNA sequencing
Vaccine antigen selection
Prediction of *in silico* MHC-I epitope
TIL screen to identify defined epitopes
Identification of mutations in driver genes
Vaccine engineering
Inclusion of up to 20 neoantigens in the vaccine backbone
DNA synthesis and QC
Vaccine synthesis
Vaccine sterility release
Administration
Every 2 weeks

Article Analysis (Preview)

mRNA vaccine–induced neoantigen-specific T cell immunity in patients with gastrointestinal cancer

Gal Cafri,[1,2] Jared J. Gartner,[1] Tal Zaks,[3] Kristen Hopson,[3] Noam Levin,[1] Biman C. Paria,[1] Maria R. Parkhurst,[1] Rami Yossef,[1] Frank J. Lowery,[1] Mohammad S. Jafferji,[1] Todd D. Prickett,[1] Stephanie L. Goff,[1] Christine T. McGowan,[1] Samantha Seitter,[1] Mackenzie L. Shindorf,[1] Anup Parikh,[1] Praveen D. Chatani,[1] Paul F. Robbins,[1] and Steven A. Rosenberg[1]

[1]Surgery Branch, National Cancer Institute (NCI), NIH, Bethesda, Maryland, USA. [2]Sheba Medical Center, Ramat Gan, Israel. [3]Moderna Inc., Cambridge, Massachusetts, USA.

BACKGROUND. Therapeutic vaccinations against cancer have mainly targeted differentiation antigens, cancer-testis antigens, and overexpressed antigens and have thus far resulted in little clinical benefit. Studies conducted by multiple groups have demonstrated that T cells recognizing neoantigens are present in most cancers and offer a specific and highly immunogenic target for personalized vaccination.

METHODS. We recently developed a process using tumor-infiltrating lymphocytes to identify the specific immunogenic mutations expressed in patients' tumors. Here, validated, defined neoantigens, predicted neoepitopes, and mutations of driver genes were concatenated into a single mRNA construct to vaccinate patients with metastatic gastrointestinal cancer.

RESULTS. The vaccine was safe and elicited mutation-specific T cell responses against predicted neoepitopes not detected before vaccination. Furthermore, we were able to isolate and verify T cell receptors targeting $KRAS^{G12D}$ mutation. We observed no objective clinical responses in the 4 patients treated in this trial.

CONCLUSION. This vaccine was safe, and potential future combination of such vaccines with checkpoint inhibitors or adoptive T cell therapy should be evaluated for possible clinical benefit in patients with common epithelial cancers.

TRIAL REGISTRATION. Phase I/II protocol (NCT03480152) was approved by the IRB committee of the NIH and the FDA.

FUNDING. Center for Clinical Research, NCI, NIH.

Introduction

Introduction

Protective vaccination against infectious diseases has proven to be one of the most effective health measures in medicine; however, therapeutic vaccination against established diseases such as persistent infections and cancer has proven more challenging. Cancer vaccines are designed to target antigens that can elicit selective immune responses against cancer cells and not normal cells. Until recently, therapeutic vaccines against nonviral tumors mainly targeted differentiation antigens, cancer-testis antigens, and/or overexpressed antigens, but with little clinical impact (1).

In recent years, our group and others have extensively studied the importance of neoantigens as targets for immunotherapy (2–7). It is now clear that neoantigen-specific T cells are present in most cancers. Neoantigens derived from somatic mutations offer a specific and highly immunogenic target for vaccination, and the recent development of rapid and relatively inexpensive technologies for DNA sequencing has facilitated the identification of those targets (2).

Several studies recently reported the vaccination of melanoma patients with neoantigen vaccines (8–10). Although T cell responses could be elicited against a subset of the candidate neoantigens evaluated in these trials, functional validation, including analysis of the ability of T cells to recognize naturally processed and presented antigens, was only carried out for a limited number of reactivities. Although these trials demonstrated the feasibility, safety, and immunogenicity of such vaccines, clear evidence of their clinical efficacy is lacking. An immunogenic vaccination platform capable of encoding multiple tumor-relevant antigens that can be manufactured in a personalized setting is essential for developing neoantigen vaccines for patients with the common epithelial cancers. Furthermore, the selection of vaccine neoantigens that are relevant and immunogenic remains a major hurdle. Here, we developed a pipeline for the selection of defined vaccine neoantigens expressed by the autologous cancer and recognized by the patient's tumor-infiltrating lymphocytes (TILs) that were functionally tested for their immunogenicity. This vaccine, named mRNA-4650, is composed of an mRNA back-

Conflict of interest: TZ is an employee of Moderna and holds equity in the company. KH was an employee of Moderna during the time this study was being conducted. SAR, GC, NL, and RY are inventors on a patent application (no. E-165-2020-0-US-01).

Submitted: November 11, 2019; **Accepted:** July 29, 2020; **Published:** October 5, 2020.
Reference information: *J Clin Invest*. 2020;130(11):5976–5988.
https://doi.org/10.1172/JCI134915.

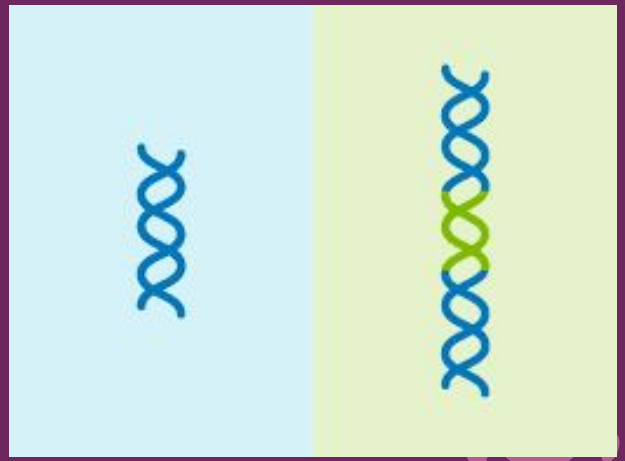
Checkpoint

- Why would mRNA be preferred as the sequence of choice over DNA?

Checkpoint

- Why would mRNA be preferred as the sequence of choice over DNA?
  - mRNA (+) can be directly translated by cellular machinery (ribosomes)
  - DNA would have to cross nuclear membrane (nucleus) for transcription, then translation
  - Once DNA is in membrane,

    can be mutagenic and insert into genome



Checkpoint

- Why are these experiments and methods even important? What is so special about immunotherapy?

Checkpoint

- Why are these experiments and methods even important? What is so special about immunotherapy?
  - Cancer is constantly evolving
  - Specifically mutated to rapidly replicate
  - Adapts extremely well to current conventional treatments (radiation, chemotherapy)
  - Will over or under express membrane receptors to evade immune cells

Methods and Results

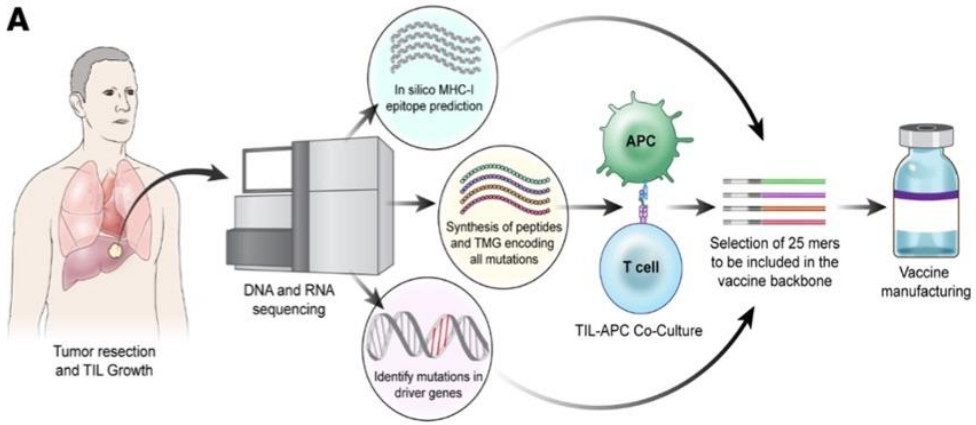


Figure 2. Vaccine design, prior treatments, and safety. (**A**) Illustration of the pipeline used to select the vaccine antigens. (**B**) The basic concatemer vaccine structure. (**C**) Overview of the vaccination schedule and immune monitoring. W_n, week number. (**D**) Patient-specific timeline of clinical trial progression. (**E**) Summary of preexisting, immunogenic, and nonimmunogenic vaccine antigens. (**F**) Percentage of neoantigen-specific $CD8^+$ and $CD4^+$ T cells from all patients. (**G**) Number of neoantigen-specific reactivities found in each patient.

Results

Patients and methods. Between March 29, 2018, and November 13, 2019, four patients with metastatic gastrointestinal (GI) cancer were treated with an mRNA

Methods and Results

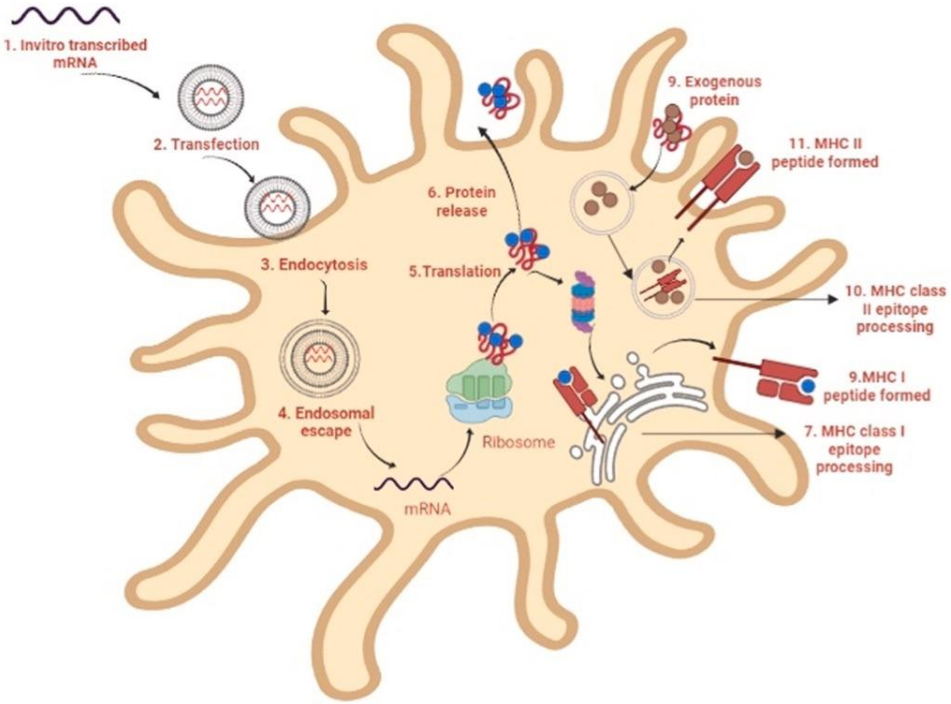


Fig. 2. Mechanism of action of mRNA vaccines. 1. In a cell-free system, mRNA is in vitro transcribed (IVT) from a DNA template. 2. IVT mRNA is then transfected into dendritic cells (DCs) by the process of (3) endocytosis. 4. Endosomal escape allows entrapped mRNA to be released into the cytoplasm. 5. The mRNA is translated into antigenic proteins using the ribosome translational mechanism. After post-translational modification, the translated antigenic protein is ready to act in the cell where it was produced. 6. The protein gets secreted by the host cell. 7. Antigen proteins are digested in the cytoplasm by the proteasome and transferred to the endoplasmic reticulum, where they are loaded onto MHC class I molecules (MHC I). 8. MHC I-peptide epitope complexes with loaded MHC I-peptide epitopes produced, resulting in induction. 9. Exogenous proteins are taken up DCs. 10. They are degraded in endosomes and delivered via the MHC II pathway. Furthermore, to obtain cognate T-cell help in antigen-presenting cells, the protein should be routed through the MHC II pathway. 11. The generated antigenic peptide epitopes are subsequently loaded onto MHC II molecules.

Methods and Results

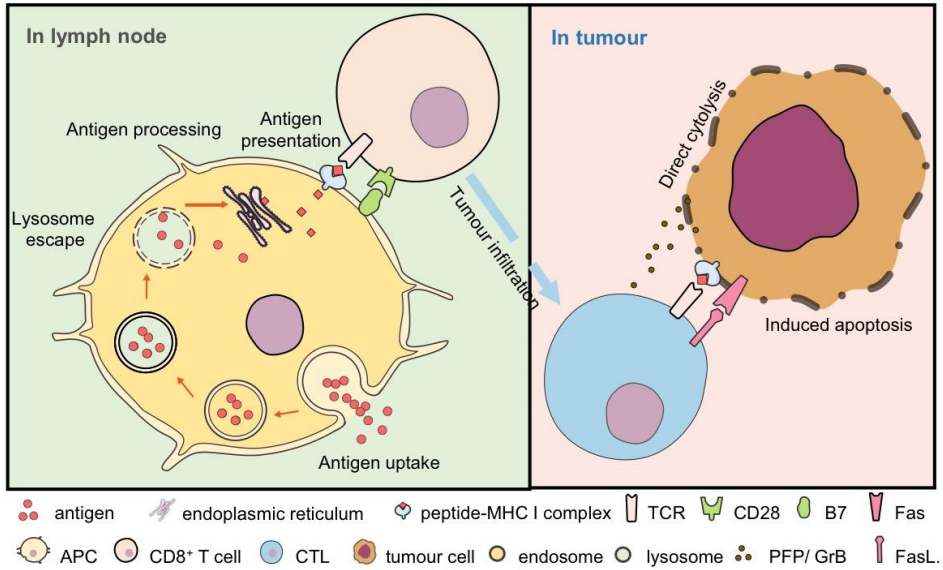
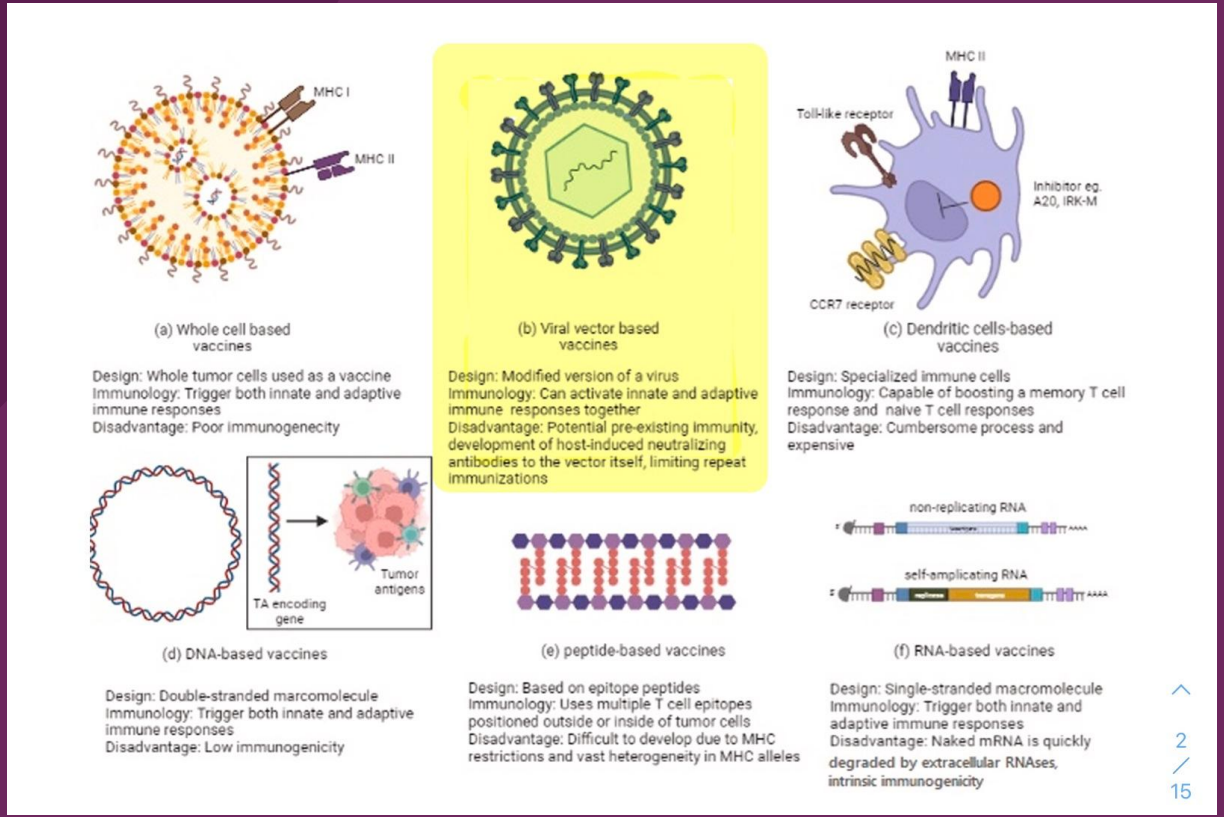


Fig. 1. Illustration of the mechanism of action of PCVs in vivo. The main processes are described, including antigen uptake, lysosome escape, antigen presentation, expression of co-stimulation molecules, T cell activation, cytotoxic T cell infiltration and killing tumour cells by induced apoptosis and direct cytolysis. MHC: major histocompatibility complex. TCR: T cell receptor. APC: antigen-presenting cell. CTL: cytotoxic T lymphocyte. PFP: pore-forming protein. GrB: Granzyme B.

How Can Viruses Play A Role?



- Act as a delivery vector for mRNA
- Have advantages as well as drawbacks
  - Are great at infecting cells
  - Immune tolerance varies (prior infection)

Results

Conclusions

Nucleotide based prostate cancer immunotherapy with RNActive® based compounds such as CV9104 offers a high specificity as only antigen positive tissues are subject to the therapeutic effect. Transient expression of RNActive®-based mRNA gives precise control of the pharmacokinetics and dose levels with high safety as RNActive®-based mRNA does not exhibit genomic integration. The self-adjuvanted prostate cancer vaccine induces a balanced immune response comprising of a dual activation of the immune system encoding antigens and simultaneously stimulate the innate immune system, effector and memory responses.

The first clinical studies of CV9103 indicate a favorable safety profile of RNActive® vaccines and prove their effectiveness. Ongoing clinical trials are set to demonstrate the utility of application in more defined clinical settings. Noteworthy, RNActive®-based vaccines can be produced in a highly flexible and versatile process.

- Personalized Cancer Vaccine (PCV) for prostate cancer demonstrated proof of concept
- 80% higher levels of Cytotoxic T-Cells (tumor infiltrating)
- Overall Survivability was extended by 7 months

Viral Outreach

- Thanks to everyone who came to our viral outreach button designing event! Everyone made really great designs!
- We will have a button making event soon in the Arts & Crafts Center in the Reitz basement, date TBA
- Counts for volunteer hours
- If you would like to be added to the viral outreach channel, please reach out to Erica on Slack

Upcoming Events

Halloween Party

Thursday, Oct. 27th at 7:30pm
Location TBD

GBM 4

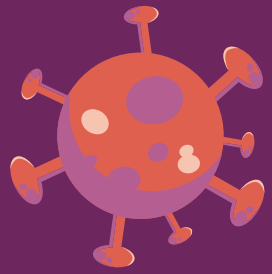
Monday, Nov. 14th at 7:30pm
Reitz Room 2350 or Zoom
https://ufl.zoom.us/j/98737398845

GBM 5

Monday, Nov. 21st at 7:30pm
Reitz Room G330 or Zoom
https://ufl.zoom.us/j/98737398845

Blaze Pizza Fundraiser

Monday, Nov. 21st 7-10pm
Blaze Pizza on SW Archer Road or Mobile Order
Bring your friends!



General Information

For more information about active member requirements, ordering viral merchandise, or a calendar of events, please refer to our website or see an officer!

virologyuf.weebly.com

Balance your PIES (physical, intellectual, emotional, sleep)
Remove “um” from your vocabulary
Question everything
When everyone says you can’t, keep going
Don’t limit yourself; keep your options open
Don’t be scared to ask for help

–Dr. Jim Maruniak , SVS Founder

Join Slack via this QR code!

Final Announcements

SVS GBM SCHEDULE

Join us in person or on Zoom at 7:30 PM!

GBM 1: 9/19 REITZ 2335

GBM 2: 10/3 on Zoom

GBM 3: 10/17 REITZ G330

GBM 4: 11/14 REITZ 2350

GBM 5: 11/21 REITZ G330

Zoom ID: 966 6229 4853

Questions?

Thanks for coming!

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