July 27, 2021

Final Investigation Report
Allegations of Research Misconduct against Janina Jiang, M.D., Ph.D.

This report is being submitted in response to a request from Roger Wakimoto, Ph.D., Vice Chancellor for Research (VC Wakimoto), who serves as the campus Research Integrity Officer (RIO), to investigate allegations of research misconduct brought against Janina Jiang, M.D., Ph.D., (Respondent), in accordance with UCLA Policy 993, "Responding to Allegations of Research Misconduct" (Policy 993). Respondent conducted the research in question while working as an Assistant Researcher in the Department of Pathology & Laboratory Medicine in the David Geffen School of Medicine at UCLA. VC Wakimoto charged the Investigation Committee with determining whether research misconduct occurred pursuant to the definitions and evidentiary standards set forth in Policy 993.

BACKGROUND

Complainant reported the suspected scientific misconduct committed by Respondent in a letter, dated January 10, 2019, to Ann Pollack, Associate Vice Chancellor-Research. According to the letter, Complainant provided financial support for Respondent, who had experience in evaluating vaccine immune responses in mice, to evaluate two vaccines he was developing in collaboration with other colleagues between February 2015 and June 2018. Respondent completed 6 HIV vaccine studies and 2 HPV vaccine studies during that time. Complainant became suspicious when Respondent failed to provide the raw flow cytometry data. Respondent eventually provided the raw data for only 2 ½ HIV vaccination experiments and the 2 HPV vaccination experiments. Complainant asked another staff research scientist with expertise in flow cytometry to review the primary data. After a review and re-analysis of the raw flow cytometry data, the staff research scientist identified irregularities with Respondent's work. Respondent's results were used in several grant applications before anyone became aware of these irregularities.

Description of the Research

The research in this case focused on examining mice for their immune responses to vaccines directed to proteins in the human immunodeficiency virus (HIV) and human papillomavirus (HPV). The vaccines were "Vault" vector vaccines. Vault Nanocapsules were developed by Leonard Rome, Ph.D., a Distinguished Professor in the Department of Biological Chemistry in the David Geffen School of Medicine at UCLA. Mice were injected with the HIV and HPV vaccines and vaccine controls, and the animals were euthanized at different time points post-vaccination at which time the mononuclear cells were collected from the mouse spleens. Flow Cytometry was used to measure intracellular cytokine production (Interleukin-2 and Interferon-gamma) in vitro in CD4+ and CD8+ T lymphocytes (T cells) in response to 15-mer overlapping HIV and HPV peptides. Cellular immune responses to the vaccines in response to the peptides were measured by cytokine production. Live cells were gated in the analysis of the flow cytometry data to provide the comparison between T cells that produced cytokines in response to the peptides compared to non-peptide controls.

Institutional Inquiry

A preliminary assessment determined an inquiry must be conducted. VC Wakimoto subsequently notified Respondent of the allegations and his determination to convene an inquiry in a letter dated April 17, 2019. Associate Vice Chancellor Pollack and Claudia Modlin, Associate Director, Research Policy & Compliance, hand delivered the letter to Respondent on the same day. Respondent stated that she did not have any materials to provide for sequestration since she had changed jobs, and no longer had access to the

computer at her prior work. Nevertheless, on April 18, 2019, Respondent contacted Ms. Modlin and provided some raw data on a USB device. The device (4GB USB) is kept under lock and key in the Office of the Vice Chancellor for Research, [redacted]. In addition, Complainant provided electronic copies of the raw data for the experiments in his possession. These materials are currently stored in a password protected BOX folder maintained by the Office of the Vice Chancellor for Research.

The Inquiry Committee, established on April 25, 2019, by VC Wakimoto, consisted of [redacted]. The Inquiry Committee met on May 15, 2019 to officially receive its charge of determining whether sufficient evidence existed to open a formal investigation.

The Inquiry Committee examined the following allegations:

Iris Cantor Women's Center/ UCLA CTSI proposal titled, "A Novel Therapeutic Vaccine to Clear Early Cancerous Cervical HPV Infection" (NCATS UCLA CTSI Grant # UL1TR000124; PI: Yang, Otto). *[Proposal has been funded.]*

1. Data were falsified and/or fabricated in Figure 6 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health, National Cancer Institute SBIR proposal titled, "CTL Based Therapeutic Vaccine to Prevent or Interrupt HPV Mediated Oncogenesis" (R43CA228629; PI: Kickhoefer, Valerie (Vault Nano)). *[Proposal has been funded.]*

2. Data were falsified and/or fabricated in Figure 2 by reporting immune response results that are incompatible with the raw data files.
3. Data were falsified and/or fabricated in Figure 3 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health, National Institute of Allergy and Infectious Diseases proposal titled, "Defining Factors Controlling HIV Rebound" (P01AI131294; PI: Zack, Jerome). *[Proposal has been funded.]*

4. Data were falsified and/or fabricated in Figure 8 (Project 3) by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" (R21AI131451-01; PI: [redacted] *[Proposal has not been funded.]*

5. Data were falsified and/or fabricated in Figure 8 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" (R21AI131451-01A1 (resubmission); PI: [redacted] *[Proposal has not been funded.]*

6. Data were falsified and/or fabricated in Figure 9 by reporting immune response results that are incompatible with the raw data files.
7. Data were falsified and/or fabricated in Figure 10 by reporting immune response results that are incompatible with the raw data files.
8. Data were falsified and/or fabricated in Figure 11 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health SBIR Phase II proposal titled, "Novel Pan-Serovar Vaccine for Chlamydia" (R44AI126960-01; PI: [redacted] *[Proposal has not been funded.]*

9. Data were falsified and/or fabricated in Figure 9 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health SBIR Phase I proposal titled, "A Novel Pan-Serovar Vaccine for Chlamydia" (R43AI136224-01; PI: [redacted] *[Proposal has not been funded.]*

10. Data were falsified and/or fabricated in Figure 3 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health proposal titled, "A Novel Cellular Immune Zika Vaccine" (R21AI131013; PI: [redacted] *[Proposal has not been funded.]*

11. Data were falsified and/or fabricated in Figure 9 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health proposal titled, "A Recombinant Human Vault CTL-Based HIV Vaccine Component" (R01AI126914; PI: [redacted] *[Proposal has not been funded.]*

12. Data were falsified and/or fabricated in Figure 7 by reporting immune response results that are incompatible with the raw data files.
13. Data were falsified and/or fabricated in Figure 14 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health SBIR I/II Fast-Track proposal titled, "Design of a Novel CTL Retargeting Therapeutic HIV Vaccine" (R44AI128983, PI: [redacted])). *[Proposal has not been funded.]*

14. Data were falsified and/or fabricated in Figure 7 by reporting immune response results that are incompatible with the raw data files.
15. Data were falsified and/or fabricated in Figure 13 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" (R21AI142068-01; PI: [redacted]). *[Proposal has not been funded.]*

16. Data were falsified and/or fabricated in Figure 8A and B by reporting immune response results that are incompatible with the raw data files.

17. Data were falsified and/or fabricated in Figure 8C by reporting immune response results that are incompatible with the raw data files.
18. Data were falsified and/or fabricated in Figure 9 by reporting immune response results that are incompatible with the raw data files.
19. Data were falsified and/or fabricated in Figure 10 by reporting immune response results that are incompatible with the raw data files.

On May 1, 2020, the Preliminary Inquiry Report was sent to Respondent, who was asked to provide any comments to the report by May 15, 2020. After requesting and receiving extensions, Respondent submitted her comments to the report on June 9, 2020. The Inquiry Committee completed its final report on June 23, 2020. VC Wakimoto wrote to Respondent on July 2, 2020 to inform her that he had accepted the report and its findings that there was sufficient evidence of alleged research misconduct to warrant a formal investigation with respect to allegations 1-19 [Exhibit 01].

ALLEGATIONS

The allegations under investigation involve falsification of data used to generate figures in the grant proposals listed below.

Iris Cantor Women's Center/ UCLA CTSI proposal titled, "A Novel Therapeutic Vaccine to Clear Early Cancerous Cervical HPV Infection" (NCATS UCLA CTSI Grant # UL1TR000124; PI: Yang, Otto). *[Proposal has been funded.]* The allegation is as follows:

1. It is alleged that Respondent falsified data used in Figure 6 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health, National Cancer Institute SBIR proposal titled, "CTL Based Therapeutic Vaccine to Prevent or Interrupt HPV Mediated Oncogenesis" (R43CA228629; PI: Kickhoefer, Valerie (Vault Nano)). *[Proposal has been funded.]* The allegations are as follow:

2. It is alleged that Respondent falsified data used in Figure 2 by reporting immune response results that are incompatible with the raw data files.
3. It is alleged that Respondent falsified data used in Figure 3 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health, National Institute of Allergy and Infectious Diseases proposal titled, "Defining Factors Controlling HIV Rebound" (P01AI131294; PI: Zack, Jerome). *[Proposal has been funded.]* The allegation is as follows:

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National Institutes of Health proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" (R21AI131451-01; PI: [redacted]). *[Proposal has not been funded.]* The allegation is as follows:

5. It is alleged that Respondent falsified data used in Figure 8 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" (R21AI131451-01A1 (resubmission); PI: [redacted] *[Proposal has not been funded.]* The allegations are as follow:

6. It is alleged that Respondent falsified data used in Figure 9 by reporting immune response results that are incompatible with the raw data files.
7. It is alleged that Respondent falsified data used in Figure 10 by reporting immune response results that are incompatible with the raw data files.
8. It is alleged that Respondent falsified data used in Figure 11 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health SBIR Phase II proposal titled, "Novel Pan-Serovar Vaccine for Chlamydia" (R44AI126960-01; PI: [redacted] ([redacted])). *[Proposal has not been funded.]* The allegation is as follows:

9. It is alleged that Respondent falsified used data in Figure 9 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health SBIR Phase I proposal titled, "A Novel Pan-Serovar Vaccine for Chlamydia" (R43AI136224-01; PI: [redacted] ([redacted])). *[Proposal has not been funded.]* The allegation is as follows:

10. It is alleged that Respondent falsified used data in Figure 3 by reporting immune response results that are incompatible with the raw data files.

National Institutes of Health proposal titled, "A Novel Cellular Immune Zika Vaccine" (R21AI131013; PI: [redacted]). *[Proposal has not been funded.]* The allegation is as follows:

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National Institutes of Health proposal titled, "A Recombinant Human Vault CTL-Based HIV Vaccine Component" (R01AI126914; PI: [redacted]). *[Proposal has not been funded.]* The allegations are as follow:

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National Institutes of Health SBIR I/II Fast-Track proposal titled, "Design of a Novel CTL Retargeting Therapeutic HIV Vaccine" (R44AI128983, PI: [redacted] [redacted]). *[Proposal has not been funded.]* The allegations are as follow:

14. It is alleged that Respondent falsified data used in Figure 7 by reporting immune response results that are incompatible with the raw data files.
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National Institutes of Health proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" (R21AI142068-01; PI: [redacted]). *[Proposal has not been funded.]* The allegations are as follow:

16. It is alleged that Respondent falsified data used in Figure 8A and B by reporting immune response results that are incompatible data incompatible with the raw data files.
17. It is alleged that Respondent falsified data used in Figure 8C by reporting immune response results that are incompatible with the raw data files.
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19. It is alleged that Respondent falsified data in Figure 10 by reporting immune response results that are incompatible with the raw data files.

INSTITUTIONAL INVESTIGATION: PROCESS

On July 2, 2020, VC Wakimoto wrote to Alexander Runko, Ph.D., Director, Division of Investigative Oversight, Office of Research Integrity (ORI), to notify him that UCLA was in the process of establishing a committee to investigate this matter. In a letter dated July 6, 2020 to VC Wakimoto, Dr. Runko acknowledged receipt of the inquiry report and assigned a Division of Investigative Oversight number (DIO 7163) to the case. Dr. Runko noted the deadline for completing the investigation was October 30, 2020, however, ORI granted UCLA an extension. On October 28, 2020, Ranjani Prabhakara, Ph.D., ORI Scientist Investigator, granted an extension until February 26, 2021. On February 18, 2021, a further extension to June 27, 2021 was requested from ORI and granted by Dr. Anuj Sharma. A final extension was granted until August 26, 2021.

Before officially convening an investigation committee, VC Wakimoto wrote to Respondent on July 27, 2020 to disclose the identities of the proposed panel. Since Respondent did not object to any of the members, VC Wakimoto established the Investigation Committee on August 4, 2020. The Committee included [redacted] Professor, Molecular, Cell and Developmental Biology; [redacted] Professor, Microbiology, Immunology & Molecular Genetics; and [redacted] Pathology & Laboratory Medicine. Professor [redacted] chaired the Committee.

On August 10, 2020, Alexander Runko, Ph.D., Director of the Division of Investigative Oversight, Office of Research integrity (ORI), wrote to [redacted] and to [redacted], [redacted], [Exhibit 02] to inform them that UCLA was conducting an investigation, and that some of the allegations of possible research misconduct involved 4 grants submitted by [redacted] (1 was funded) and 1 grant submitted by [redacted] Associate Vice Chancellor Pollack and Associate Director Modlin met, via Zoom, with [redacted] on September 1, 2020. At that time, [redacted] agreed that UCLA should take the lead with regard to the research misconduct proceeding [Exhibit 03]. On September 2, 2020, Associate Vice Chancellor Pollack and Associate Director Modlin met, via Zoom, with [redacted] also agreed that UCLA should take the lead with regard to the research misconduct proceeding [Exhibit 04].

The Investigation Committee met on September 24, 2020 to officially receive its charge. They were instructed that the purpose of the investigation is to develop a factual record and examine the evidence to determine whether research misconduct occurred for each of the allegations and, if so, to determine

the responsible person(s). The Committee was expected to take reasonable steps to ensure an impartial and unbiased process.

As part of their investigation, the Committee interviewed the following individuals:

- [redacted]

Respondent's appointment at UCLA ended on August 31, 2020. Emails were sent to her last known email address requesting an interview with the Investigation Committee. When she did not respond to the emails, Associate Director Modlin sent a letter, dated November 5, 2020, to Respondent's home address requesting an interview and asking her to respond by November 19, 2020 [Exhibit 05]. The letter was sent via UPS and delivered on November 6, 2020 [Exhibit 06]. Respondent did not respond.

INSTITUTIONAL INVESTIGATION: ANALYSIS

Institutional Policy & Considerations

Policy 993 and the Public Health Services (PHS) Policies on Research Misconduct, 42 CFR Part 93, define research misconduct as fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. It does not include honest error or differences of opinion. Both policies provide the following definitions for fabrication and falsification:

> Fabrication is making up data or results and recording or reporting them.
>
> Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Policy 993 II; 42 CFR § 93.103(a); 42 CFR § 93.103(b).

For an investigation committee to make a recommendation of research misconduct, it must find that the alleged research misconduct, "1) represents a significant departure from accepted practices of the relevant research community; 2) was committed intentionally, knowingly, or with reckless disregard of the facts; and 3) was proven by a Preponderance of the Evidence." Policy 993 IV.G; 42 CFR § 93.104.

PHS Policies on Research Misconduct state, "The respondent has the burden of going forward with and the burden of proving, by a preponderance of the evidence, any and all affirmative defenses raised. In determining whether HHS or the institution has carried the burden of proof imposed by this part, the finder of fact shall give due consideration to admissible, credible evidence of honest error or difference of opinion presented by the respondent." 42 CFR § 93.106(a)(2).

Although the terms intentionally, knowingly and recklessly are not defined by federal regulations or UCLA Policy, the National Science Foundation, Office of the Inspector General, provides the following definitions:

> **Reckless**: The subject did not exercise the care a reasonable person similarly situated would have exercised under the circumstances, and did so with a conscious awareness of, or indifference to, the risk of adverse consequences of his actions and the potential resulting harm.
>
> **Knowing**: The subject had an awareness or understanding of his actions. Knowing is essentially synonymous with consciously.
>
> **Intentional**: The subject acted with a specific purpose in mind. Intentional is essentially synonymous with purposeful or willful.[1]

In addition, HHS Departmental Appeals Board, Civil Remedies Division, *ORI v. Kreipke*, Docket No. C-16-402, Decision No. CR5109, May 31, 2018, defines recklessness as, "Used materials without exercising proper care or caution and disregarding or showing indifference to the risk that the materials were false, fabricated or plagiarized thereby causing harm to the integrity of the research process or waste of public funds ..."

Responsible Conduct of Research

National Academy of Sciences, *On Being a Scientist*, provides:

> The scientific enterprise is built on a foundation of trust… Society trusts that scientific research results are an honest and accurate reflection of a researcher's work. Researchers equally trust that their colleagues have gathered data carefully, have used appropriate analysis and statistical techniques, have reported their results accurately, and have treated the work of other researchers with respect….[2]

In *ORI Introduction to the Responsible Conduct of Research*, the author discusses ownership of data, reinforcing the principle that although the institution owns the data, individual researchers have myriad responsibilities for integrity in the collection, recording and storage process:

> The rules of the road for research therefore need to be supplemented with good judgment and a strong sense of personal integrity. When meeting deadlines, you can cut corners by filling in a few missing data points without actually running the experiments or adding a few references to your notes that you have not read. You can resist sharing data with colleagues or leave some information on method out of a publication to slow down the competition. You can ignore your responsibilities to students or a mentor in order to get your own work done. You can do all of these things and more, but should you?

[1] National Science Foundation, Office of the Inspector General. *Assessing Intent in Research Misconduct Investigations*. Retrieved from https://nsf.gov/oig/outreach/RM-intent.pdf

[2] National Academy of Sciences, National Academy of Engineering and Institute of Medicine Committee on Science, Engineering, and Public Policy. *On Being a Scientist: A Guide to Responsible Conduct in Research: Third Edition*. Washington, DC: National Academies Press; 2009. doi: 10.17226/12192

> In the final analysis, whatever decision you make when you confront a difficult decision about responsibility in research, you are the one who has to live with the consequences of that decision. If you are uncertain whether a particular course of action is responsible, subject it to one simple test. Imagine what you are preparing to do will be reported the next day on the front page of your local newspaper. If you are comfortable having colleagues, friends, and family know what you did, chances are you acted responsibly, provided, of course, you also understand your responsibilities as a researcher, as described in the rules of the road covered in the rest of the *ORI Introduction to RCR*.[3]

When discussing data collection, the author states:

> There is no one best way to collect data. Different types of research call for different collection techniques. There are, however, four important considerations that apply to all data collection and that will help ensure the overall integrity of both the process and the information collected.
>
> **Appropriate methods.** Reliable data are vitally dependent on reliable methods. If you use a test that can detect an effect in one of every 100 samples to find an effect that may not occur more frequently than 1 in every 1,000 cases, your results will not be reliable. Failure to find the effect could be due to either your experimental design or the lack of an effect, but you will not know which is true. The common saying, "garbage in, garbage out," applies to research methods.
>
> Although the need for appropriate methods might seem obvious, studies have suggested that researchers sometimes use inappropriate statistical tests to evaluate their results… Methods can also be compromised by bias—choosing one method or set of experimental conditions so that a particular conclusion can be drawn—or sloppy technique. Whatever the origin, the use of inappropriate methods in research compromises the integrity of research data and should be avoided. Responsible research is research conducted using appropriate, reliable methods.
>
> **Attention to detail.** Quality research requires attention to detail. Experiments must be set up properly and the results accurately recorded, interpreted, and published. A failure to pay attention to detail can result in mistakes that will later have to be corrected and reported…[4]

<u>Background on the Respondent</u>

Respondent was an Assistant Researcher in Professor [redacted]'s lab in the Department of Pathology and Laboratory Medicine at UCLA's David Geffen School of Medicine (DGSOM) between 2010-2020. [redacted]'s research was focused on mucosal immunology in the female reproductive tract. Respondent and [redacted] have several publications together on Chlamydia immunity and vaccine development. In 2017, Respondent began collaborating actively with Dr. [redacted], who also supported Respondent's salary through grants that were based, in part, on preliminary data from Respondent. [redacted] research focuses on mechanisms of HIV escape from T cells, determinants of T cell antiviral function, and vaccines and other therapeutic strategies against HIV infection.

Respondent received post-doctoral training in the [redacted] between 2009-2010. She received an M.D. degree from Tongji Medical University, in Wuhan, China in 1988, a Master's degree from the University

[3] Steneck, Nicholas H. *ORI Introduction to the Responsible Conduct of Research*. Rockville, MD: U.S. Department of Health and Human Services; 2007, pp 14-15.
[4] Steneck (2007), pp 90-91.

of Ottawa in 2001, and a Ph.D. from McMaster University, in Hamilton, Canada in 2005. Prior to coming to UCLA, she was a post-doctoral fellow in the Department of Gastroenterology at Stanford University between 2005-2008 [Exhibit 07]. She published over 20 peer-reviewed manuscripts, reviews and book chapters, focusing on understanding immunity with Chlamydia and other infectious diseases that affect the reproductive track, and aiming to develop vaccines against them. She specialized in flow cytometry techniques and in developing multicolor methods for isolating and analyzing immune cells. She served as a co-investigator on several grants that utilize her expertise in multi-color flow cytometry to study immunity and vaccine development and has given several lectures and meeting presentations on these topics. She collaborated with Vault Nano on vaccine testing since 2015 and worked with [redacted] until 2018.

Interview of [redacted] *November 18, 2020* ***[00:02:51.270-00:04:23.940]***[5]*:*

> **[00:02:54.030]** Janina came to work [redacted] in **[00:02:57.930]** March of 2010, and she was there **[00:03:03.450]** until 2018 when our grant funding was gone. Then in the end of 2015, we had a grant application in with Vault Nano with Lenny and Val, and **[00:03:20.520]** this was all on our chlamydia work, and so she was already working with Vault Nano…, **[00:03:42.210]** since she was working with Vault Nano, **[00:03:45.870]** I believe it was Dr. Rome or whatever. I don't know exactly how it was. But Dr. [redacted] then said he would help extend her salary for six months, so she could work on it. **[00:04:01.560]** And since he was contributing the, I think it was $50,000 or whatever for her, that she would do some projects for him in his lab, which was fine because **[00:04:13.470]** we were kind of in between, you know, grants and stuff. And so that was fine with me. And that's pretty much all I knew about. I knew about it. **[00:04:23.940]**

Interview of [redacted] *December 9, 2020* ***[00:09:46.680-00:20:00.210]:***

> It was my understanding that when she was hired, when she was hired by Kathy Kelly that she was an expert in doing flow cytometry, and especially in doing multi flow cytometry where you use **[00:10:00.660]** multiple different colors. You know…

[redacted] was asked whether Respondent ever raised concerns about the analysis of the data:

> No. And when we did there was not until [redacted] brought it up, then at some point when [redacted] brought it up. And then, especially when [redacted] redid this analysis. I had a meeting with [redacted] and [redacted] to **[00:10:36.810]** ask about the various gating, and she claimed that her gating was acceptable, or this was the way she had been shown to gate. And she had **[00:10:49.740]** I'm not sure what lab it was which she had come out of a pretty well-known lab up at Stanford. And yes, and so [redacted] **[00:10:59.430]** was not able to reproduce the results she had. And I think the problem with the gating is it made it, made it look like with the way [redacted] gated made it look like we had a really robust CD8 response and that, and this led us to doing with [redacted] a **[00:11:22.860]** monkey experiment with a group that he works with. And in that experiment, and for those experiments, I actually did the preparation of all the vault particles for that for the gags. And there we never thought **[00:11:39.870]** we did not see any of these results, which brought back to them going to trying to repeat and do the ELISpot analysis, which it is my understanding the ELISpot is should be more sensitive. **[00:11:53.670]**

[5] Bracketed numbers are citations to where the testimony can be found in the recorded interview and transcript.

[00:19:10.950] I would say that she was **[00:19:14.250]** somewhat. It was a while ago, but I would say she was a bit defensive about her position and that and that she felt that this was a potential. I can't say that she exactly stated that she **[00:19:31.350]** this was the way somebody taught her, or the way she's always done it or anything like that. **[00:19:38.370]** But I did feel that that was a very uncomfortable meeting for [redacted] and myself. **[00:19:48.960]** And that and trying to ask her about these things. She did not back down and say, oh, no, I should have done it a different way, if that's **[00:19:59.130]** what you're asking. **[00:20:00.210]**

Interview of [redacted] *12, 2020,* ***[00:04:52.530-00:05:47.790]:***

[redacted] was asked whether Respondent was qualified to do the work and whether she had experience in flow cytometry in the [redacted] lab:

She was very experienced. She said she was confident she could get it done.

She had published flow cytometry experiments with Dr. [redacted], though the numbers were not as positive. These were done by [redacted] lab) and Janina. [redacted]'s numbers were a fraction of Janina's.

Well, at the time, she, Dr. [redacted] was running out of funding, and she [Respondent] was going to have to leave so she **[00:04:52.530]** expressed a great deal of interest in staying, in working, and said that she wanted to, she was hoping that the, the vault work would take off and that she could continue to be involved in it. So, you know, there was no explicit **[00:05:10.200]**, you know agreement of any sort, but **[00:05:13.590]** I think she felt under pressure that, that she was going to have to leave because Dr. [redacted] had run out of funding, but that's just speculation. I don't know for sure. **[00:05:27.060]**

You know, one thing that **[00:05:33.810]** I think could be interesting or useful **[00:05:37.260]**. So, I think I sent you everything so you can see. And I think you'd see, like those dose responses to me, in particular are, I see no way that it could be accidental **[00:05:47.790]** that you would get a beautiful dose response curve over, and it would be repeated multiple times.

<u>Background on Flow Cytometry and the Research</u>

The goal of the experiments performed by Respondent was to evaluate the efficiency of different vaccines (HIV or HPV) in murine models. To accomplish this, vaults were administered to mice and T lymphocytes from different organs and were analyzed 6 weeks later by flow cytometry for the intracellular expression of cytokines (IFNg and IL2) in response to the corresponding peptide stimulation. If a vaccine is efficient, the T cells are expected to release cytokines at a high level when they are in the presence of the vaccine-specific peptide.

Two types of negative control arms were used:

1. The administration of control (empty) vaults into the mice, in which case the T cells should not respond whether in the absence or the presence of any peptide.
2. The stimulation with "no peptide" in which case neither the T cells from animals injected with the control vault nor those from animals injected with experimental vaults should respond.

These negative controls are meant to set up the basal level of cytokine expression from T cells without any specific activation which should be close to zero.

The technique used in the figures to evaluate the cytokine release by the T lymphocytes is an intracellular flow cytometry staining. After activation, the cells are first stained with antibodies to cell surface molecules (here CD4, CD8 and CD3) to be able to identify the T cells and then fixed and permeabilized. The permeabilization step is necessary for the antibodies against the cytokines to enter the cytoplasm of the cell. The cells are then stained with the cytokine antibodies, washed, and analyzed by flow cytometry.

An operator with skills in flow cytometry knows that the fixation/permeabilization may affect cell morphology and that a fixable viability dye is recommended to be able to gate on live cells. This dye was not used here. Importantly, a technical negative control should always be added to the set of experimental tubes, where no intracellular antibodies are added. The indispensable technical negative control sets the negative parameters for the flow cytometer. That control was not included in these experiments.

When performing flow cytometry analysis, the control arms (control vault and no peptide control) are compared to the experimental arms. It is necessary to analyze the live cells in both arms. Of note, the stimulation might induce the cells to proliferate more and to increase their size, but the gate should still be set on live cells on both non-stimulated and stimulated samples.

An important point is that there is an alternative and more sensitive assay to measure the cytokine release by the T cells and does not involve gating live cells: the ELISpot assay. The assay was done, but the results confirmed that there was no cytokine release as observed by flow cytometry. This result fits with the fact that no actual cytokine release was seen by flow cytometry in any of these experiments.

Interview of [redacted] *December 17, 2020* ***[00:04:59.790]- [00:16:15.930]:***

> Yeah. Well, it was, **[00:04:59.790]** it was surprising to me. I mean, I usually work in a T cell stimulation with peptide libraries. Actually, right now I'm running this premise for [redacted] with mouse vaccination. So, it was pretty surprising at the time to find out that vaccinating these mice **[00:05:21.510]** with vaults that will contain a collection of peptides, HPV, if I remember correctly, **[00:05:30.030]** could give a positive signaling interferon like 80% of the T cells responding to the vaccine. I was, I was just casually commenting to my P.I., [redacted], at the time and now also. **[00:05:47.730]** And I was telling him, okay, well that's surprising. In fact, we were surprised by that we commented on maybe these mice are super naïve so never encountered any antigen, so you put an antigen in them and they just triggered the whole thing. I was okay. It was **[00:06:06.150]** okay, it was surprising. It was outstanding to **[00:06:09.030]** understand 80% of the T cell, **[00:06:12.420]** CD8 T cell, responding to this peptide collection. It is outstanding. **[00:06:17.580]**
>
> But well at the beginning, it was like that. So, it wasn't until maybe the third meeting when someone asked me. **[00:06:27.000]** Hey, why don't you take a look at the data because, in fact, yeah. Before we go ahead, and maybe just to take an independent look at the data. And I said, well, you know it's pretty uncomfortable to analyze data for another scientist, but well, okay, I will do that. And then we start finding **[00:06:49.860]** some things. Yeah. So basically, should I say what I found, or should you want to ask me? I don't know how to proceed? **[00:06:58.620]**…

Well, basically what I found is that in some samples the gates were, the forward versus side scatter gates, were moved like one order of manner to the left or to the right. **[00:07:29.460]** She's kind of **[00:07:31.380]** not to do thing because obviously when you do this kind of experiment you designed your gating strategy and then you make your template and then you do a batch analysis. **[00:07:43.710]** Or maybe you have to collect sometimes some gates because obviously sometimes there's some that are a little bit off but not by that stand. So, I comment to my P.I., I said, okay, you know what I found, sometimes this gate is not where I think it should be, but **[00:08:05.100]** we have to be kosher with these things, and he told me, he asked me to look for a pattern **[00:08:11.550]** in this gating strategy. **[00:08:15.330]** And then I found that mostly **[00:08:20.910]** in non-stimulated samples the gates falling to the left, on the left **[00:08:28.560]** forward/side scatter, forward scatter which corresponds to usually dead cells on very small or very small cells. On in a stimulated sample, the gate was falling to lymphocyte gate, where they should be full of **[00:08:45.300]** the samples. This obviously here renders a very different result **[00:08:49.770]** from one to the other. **[00:08:51.990]**

The Committee asked: …what was your understanding of her expertise in doing this kind of experiments? **[00:11:29.430]** Did she have a long history on working on FACS analysis or this kind of experiments or was this kind of a new **[00:11:38.310]** type of situation for her, do you know, or what was your take on? **[00:11:43.620]:**

I don't know. I don't know her. I just, obviously, I know her. But I had never been personal, or we had been working in the same program even, never. **[00:11:55.650]** I don't know how new she was to the to the technique. I understand she was not totally new. And I understand, she has some background, I don't know. After I did what I did I, as you said, probably you have my document, I elaborated a document about my findings [Exhibit 08], and I made my opinion. **[00:12:16.500]** I know I didn't judge, but I was asked to meet her. **[00:12:23.310]** And to, **[00:12:25.200]** there was a meeting, you probably know about this also, it was a meeting with her and with a researcher from [redacted] laboratory, **[00:12:36.840]** just to see how we could put together my analysis and her analysis. Just see if maybe I was missing something. Because I mean, maybe, I don't know, maybe I can learn. I don't know. **[00:12:55.140]** And we had a meeting, and my feeling was that, **[00:13:00.450]** I don't know how to say that. I'm not here to judge her, you know, I mean this is just the feeling I had is that she was not **[00:13:13.860]** well aware on how to proceed with the analysis. **[00:13:17.640]** Let's say that. **[00:13:19.320]**

The Committee asked about Respondent's response to [redacted] analysis [Exhibit 08].**[00:13:30.120]**

Yeah, I asked her, I told her that when you do this kind of experiment or this kind of analysis; what you have to do, you cannot move the gates all over the place because **[00:13:40.380]** flow cytometry can be very subjective. I don't know. Probably you are familiar with this technique. **[00:13:46.590]** I mean, I don't know who I am speaking to. **[00:13:48.690]** But I mean, it is more, **[00:13:52.470]** if you have a very rare response, and you move your access left or right, you can have different results. And that's great, it's very tricky. **[00:14:03.360]** What I do is usually I **[00:14:06.030]** set up my gating strategy, and I set up my template and do a batch analysis, and then I come back and I see sample by sample if everything is okay. **[00:14:16.260]** And again, last week I did an experiment for [redacted] and I worked, had a hundred tubes and I had to move the gate slightly, the gates in three or four. **[00:14:26.970]** So, but I asked her why she was moving this, and she told me that her answer was that you have to use different gates for every single sample. **[00:14:37.950]**

The Committee inquired whether [redacted] asked Respondent if she was aware of the problems with gating on the dead cells. **[00:14:47.310]**

> Yeah, I told her. **[00:14:50.460]** I told her that the gates she was analyzing in the, let's say left gate. **[00:14:57.990]** They were probably dead cells that don't respond, and in some cases, they act like sponges for antibodies. They have autofluorescence, and they, I mean, they create all kinds of trouble. Actually, now we have all established using a live **[00:15:16.860]** probe, but at the time, she didn't do that. And she told me that. **[00:15:22.920]** I don't know. Actually, I don't remember what she answered. **[00:15:26.700]**

The Committee asked whether he or anybody else did more experiments to try to replicate the results independently. **[00:16:01.620]**

> I don't think we did any other experiment. I run, I actually now, I run the same kind of experiments for the same lab. But not exactly the same HPV experiments. **[00:16:15.930]**

Interview of [redacted] *November 18, 2020* ***[00:22:17.340-00:27:46.170]:***

> The Committee asked, **[00:22:19.230]** did you ever have **[00:22:21.810]**, did you use any know vital dyes in order to exclude dead cells in your experiments? Or was it just done on, on gating to exclude that cells? **[00:22:34.770]**
>
> Yeah, we had used PI [Propodium iodide] like when we did a few experiments where we looked at **[00:22:41.670]** types of cytokines. One of the big questions **[00:22:46.470]** at the time was, you know, were these cells that were stimulated naturally producing a certain kind of cytokine pattern. Versus if you immunize them, could you like **[00:23:02.250]** change the cytokine pattern so that would be more effective at clearing the infection. So we had to look at gamma interferon production, and in order to do that, it was best to use live cells, you know, vital dyes so we could gate on the live cells **[00:23:22.980]** for those experiments. For this experiment, we didn't, we didn't use the vital dye, but some of them we did when we looked at cytokine responses. A lot of times we did. **[00:23:37.230]**
>
> And PI was in one. I think there was, there were a couple others that that we had looked at as well. But again, it depends, you know, you're looking at 8, as you know, 8 to 10 different colors, you're kind of limited with what, with what dyes you can use. **[00:24:00.600]**
>
> The Committee asked about a figure represented in Nov 18 slides.pptx slide #5 [Exhibit 09] which was an example of the vital dye. **[00:24:16.800]… [00:24:31.140]** and whether this was not an established kind of a way to continue in other experiments? **[00:24:40.770]**
>
> What do you mean established? **[00:24:47.790]**
>
> The Committee asked whether if it was used successful[ly] here in this nice published paper that that this didn't become the standard how to do these kind of experiments in the, **[00:25:02.970]** in follow up projects. **[00:25:06.990]**

Oh, for chlamydia vaccine in mice? And the particular type of mice we were using? Yeah, that would be standardized for that. **[00:25:18.960]** Again, you know, would depend on **[00:25:21.990]** the particular mice at that time. You know, they don't always read the experimental protocol. Sometimes they work better than other times. But yeah, it's pretty much standard and you know for an experiment, **[00:25:40.920]** for a project or paper. But then, you know, with the question was different for the project than the gating scheme and **[00:25:51.060]** probably the way we would look at it would be just a little bit different, just depending on the question and the markers that you're using. And **[00:26:02.460]** I guess that's why it's research, it's never **[00:26:06.570]** the same. And for the clinical lavish (labs), it should be the same **[00:26:10.890]**

The Committee asked: And for the, because… it was intracellularly FACS. **[00:26:19.860]** Do you know if she was using any control like an isotype control or no antibody control to be able to gate the positive versus negative population properly? **[00:26:30.540]**

Yeah. So, this, of course, there is always a control, this one, you'll see [redacted] was on it. He's a big immunologist and at the time he was at the University of Minnesota. And he, he, we would use, actually used, his gating scheme **[00:26:46.650]** for a lot of these because this was tetramer experiment. So, you would use in like it. This is not cytokine staining, a tetramer staining. So, you would use another **[00:26:59.010]** nonspecific tetramer as a control. So, you know you, we would always use whatever was the appropriate for the control. So, and this is another one of the cases where we would consult with him. His lab actually made the tetramer. **[00:27:19.470]** So, you know, if it was a cytokine you would use a whatever the appropriate isotype control for would be in this particular case it was tetramer. So, it was a nonspecific tetramer, **[00:27:43.770]** non chlamydia specific **[00:27:46.170]** antigen.

Findings

Allegation 1 concerns the following: Iris Cantor Women's Center/ UCLA CTSI grant titled, "A Novel Therapeutic Vaccine to Clear Early Cancerous Cervical HPV Infection" [NCATS UCLA CTSI Grant # UL1TR000124; PI: [redacted]

Allegation 1: It is alleged that Respondent falsified data used in Figure 6 by reporting immune response results that are incompatible with the raw data files.

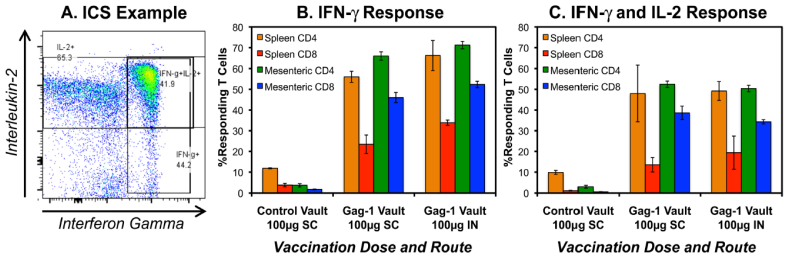


Figure 6. Vaults containing a short region of HIV-1 Gag yield systemic and mucosal polyfunctional T cell responses. Mice (C57BL6) were given subcutaneous injections (SC) or intranasal instillations (IN) of human recombinant vaults (100µg) containing the $Gag_{148-214}$ sequence or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. **A**. Example of intracellular cytokine staining after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning the stretch in Gag. Percentages of $CD4^+$ and $CD8^+$ T cells producing: **B**. interferon-γ or **C**. interferon-γ and interleukin-2 are plotted as means and standard deviations (three mice per group).

Analysis: In their final report [Exhibit 10], the Inquiry Committee noted:

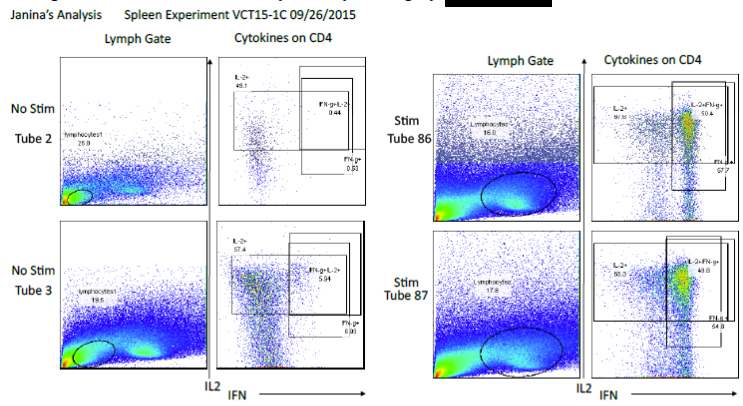
> Allegation 1 refers to Figure 6 of the grant, data that relate to HIV peptides ("Gag") even though they appear in an HPV grant.
>
> Figure 6A: As shown in Exhibit 01, data calculated show IFNg, IL2, and IL2/IFNg positive cells well above reported values (10ug S.Q. MLN tissue), with and without stimulation (1ug). Generated graphs resemble reported graphs, and gating strategy is similar. Of note is the observation that virtually no difference was found between control "empty" vault treated tissues and Gag-1 vault (10ug) treated tissues.
>
> Figure 6B and 6C: As shown in Exhibit 01, data calculated show little difference in IL2 and IL2/IFNg secreting CD4+ T cells comparing empty vault (SC) and Gag-1 vault (SC, 100ug) in spleen, and mesenteric lymph nodes. Other differences were noted between the reported and calculated data; however, most noteworthy is the observation that control vault treatment showed high IFNg and IL2 secreting T cells, whether of the CD4 or CD8 type.
>
> Furthermore, in stimulated (1ug) samples, similar observations were noted. CD4+ T cells that secrete IFNg or IL2/IFNg were higher in control empty vault experiments than in Gag-1 vault experiments. This is in stark contrast to the reported results.

Please refer to the **Background on Flow Cytometry and the Research** section above. The Committee found that the experiments had not been performed properly. Dr. [redacted] and the Committee used the raw data [Exhibit 12] to rerun the analysis, which showed results different from what Respondent provided. [redacted] were surprised by Respondent's results. Dr. [redacted] performed a blind analysis for three or four experiments. Respondent provided Dr. [redacted] with the analysis she did, and they compared this analysis. (See Interview of [redacted] December 17, 2020 [00:10:32.910]- [00:11:15.270])

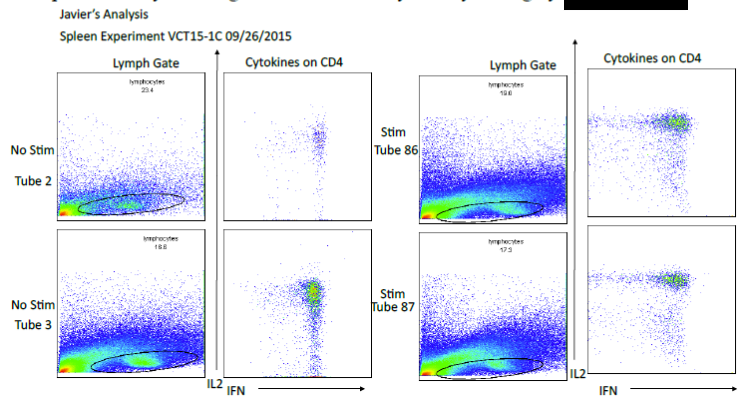
Interview of [redacted] *December 17, 2020* ***[00:16:54.720]- [00:26:25.440]:***

> The Committee asked… do you think in her analysis and all the samples she had in her, in her files, did she have the right controls to be able to gate under the right positive? Or if it was, as you said, a lot of reasons or you maybe you don't remember that? **[00:16:54.720]**
>
> [redacted]: What I remember of the scatters, in fact I was looking **[00:16:59.850]** at the analysis right now **[00:17:02.640]** because I was kind of nervous about this meeting. And I was looking at what I saw, is a very, very **[00:17:09.240]** typical scatter. I mean, you had, she had a very nice, very nice. Most of the tubes, obviously, most of the tubes **[00:17:18.780]** in the spleen. Okay. **[00:17:21.510]** Because if I remember correctly, they were analyzing **[00:17:23.430]** three kind of tissues. **[00:17:25.260]**
>
> The Committee asked to look at the December 17 pptx, slide #3 [Exhibit 11]:

Examples of Inconsistent Flow Cytometry Gating by [redacted]



Examples of Analysis Using Consistent Flow Cytometry Gating by [redacted]



[redacted]: Yeah. **[00:18:14.070]** I recognize that one, yeah… **[00:18:14.850]** But yeah, so when you see this is a spleen. **[00:18:20.400]** I think.

[redacted] You see the, the cluster down right, close to the x-axis like. **[00:18:31.170]**

[redacted] Those are lymphocytes. **[00:18:35.340]**

[redacted] Yeah, so I mean, I don't see, I don't see, quite frankly, I don't see anyone not recognizing that.

[redacted] So, and what, what she used to do was, do you see the left? She used to gate the non-stimulated on the left, on the big cluster you have in the corner of the axis. Those are dead cells. In fact, it is very typical for the spleen cell, this splenocyte **[00:19:03.360]** *(inaudible)* in our hands. When you isolate these cells, you have about 80% viability **[00:19:10.920]** because they **[00:19:12.030]** are previously treated and still. And then after overnight stimulation on, on all the thing, your viability can drop to somewhere around 70 or 60 percent. That means you have a big, big cluster of dead cells. **[00:19:27.690]**

So that's why she'd argue that that were the right thing. I mean, I couldn't. I honestly don't remember any coherent response answered to

why she was gating in that thing. Because anyone that has seen a flow cytometry scatter knows this.

The Committee asked whether there any other individuals from her lab who had done similar experiments or was anybody else able to provide any kind of rational[e], like this is how it's done, or something or, or were, was only communications with, with her? **[00:20:08.340]**

[redacted]: No, in [redacted]'s laboratory, no one has any expertise in flow cytometry. **[00:20:19.680]** I know because **[00:20:24.240]** I helped them with this. **[00:20:26.160]**

Committee: And some, something I wanted to ask you is non-stimulated, they shouldn't express an interferon gamma. So, I guess this, this population that we see here on the non-stability when we use the right gates that you draw, **[00:20:41.340]** this should be moved to the left because it should be negative. **[00:20:45.570]** So, I guess *[crosstalk]*

[redacted] Oh yeah. **[00:20:47.370]** Yeah, I don't remember how I did the analysis. I remember that it was kind of a, it felt like a bomb. Yeah, because I found nothing. **[00:21:04.080]**

Well, I don't want to be, yes, but it was not very nice. No. **[00:21:15.600]** Because I mean you have to tell these people what someone has done wrong. And then they ask are you sure, and you are sure to a point, but there is a point where you start doubting yourself. **[00:21:29.220]**

You know, you say, okay, maybe I'm wrong. That's why we had this meeting with Janina. And I say, okay, okay, I will meet her, I will meet her. **[00:21:41.100]** Okay, I have no problem. If she's right, she's right. At the end, this is not my project, this is not my experiment. I have nothing to do with this. **[00:21:49.980]** And I **[00:21:52.860]** asked a basic question, why she was moving the gate to the left. No, I had to leave the meeting because it was really, **[00:22:13.020]** very tense meeting. **[00:22:16.440]**

Committee: And that, that's another set of experiments with dose response. **[00:22:24.180]** I don't know if you remember, it was like one microgram versus ten microgram, hundred microgram, and when she analyzed it, she had those beautiful graphs with the perfect dose response. **[00:22:38.160]** And this is what you, you should actually, that's when it's gating them with the same consistent gates. There is no difference with any of the dose. **[00:22:48.330]** So, for these, do you, I'm sorry you have to go back to all this old, old stuff. But do you remember seeing how she gated to, to increase the, the response of the dose, did she really move around that gate to have that kind of result? **[00:23:04.020]**

[redacted] I cannot answer to that. If it is really necessary, I could go to my files and try to answer that question. **[00:23:12.270]** I don't remember if she did selectively move progressively to the right, or to the left the gates to have that. If this is what you mean. **[00:23:24.450]** I can't answer to that. **[00:23:27.930]** I don't know.

Committee: Okay. **[00:23:29.340]** Yeah, because I did. I had access to the raw files not the FloJo files. And that's, yeah, what I, what I saw, actually, is that if you gate on live cells that population that you showed us. It is the lymphocytes. **[00:23:45.780]** When it's an empty vault with a peptide, it shouldn't be activated, and it's everything is move[d] to the right. **[00:23:54.660]** But then if I analyze the same sample the same gating as you probably did, I see absolutely no difference with

them, with either ten microgram or hundred micrograms. So, I was just wondering, we were wondering how she would have put her gate to, to see an increase in the, in each. **[00:24:12.840]** Yeah, to, to draw those, those graphs are same problem with these graphs. **[00:24:18.300]**

[redacted] I know, I know. I don't know. It was a lot of trouble. At the time, I have to say, I don't know how good or bad I did, but I can tell you, I did this analysis like three times. **[00:24:28.050]** Because I wanted to be hundred percent sure that I was doing it right. So, what I did is analyzed to create an Excel spreadsheet to keep clean, forget for a couple of three days, **[00:24:44.850]** and to come back and compare both of the spreadsheet. To me there was no doubt. **[00:24:51.240]**

Committee: If you, if you draw the gate **[00:25:06.930]** where it's supposed to be negative, with no stimulation on that HIV experiment, and then you check the stimulation with the peptide the, there is no, no more. Yeah, nothing happening in those gates. Everything is negative. **[00:25:19.590]**

[redacted] No. **[00:25:20.760]** No, I even did, sometimes I did, **[00:25:25.440]** as you say, well, you should put to the right of the negative control, your gate. But I even did the analysis, drawing with a background. **[00:25:36.720]** Just saying, okay, maybe it's a really small signaling, and we analyzed the, the histogram for the fluorescence intensity to see maybe the intensity moves too. I mean I never saw such a thing, but this is prob, possible that the, the intensity of the fluorescence channel increases, **[00:26:00.210]** or the background. But, no, no. **[00:26:02.970]**

[redacted] Yeah, because there are some markers that are for clusters to the right, that only they move. So, you have to analyze the histogram. It is not the case for intracellular staining. **[00:26:25.440]**

In addition, the Committee found that Respondent had extensive training and many years of experience in flow cytometry.

Interview of [redacted]*, November 18, 2020* ***[00:02:51.270-00:21:51.960]****:*

So, **[00:28:05.970]** I would think that they [redacted] and Jiang] planned them [the experiments] together, you know. **[00:28:12.510]** We would always plan these together, I would write an outline, or I'd have her [Jiang] write an outline. She'd give it to me. And then we need to tweak it a little bit, make sure she had the proper controls and this and that. And then, you know, the experiment would be okay and then **[00:28:28.710]** they would carry it out. **[00:28:30.510]** I'm sure that's how it's done in his [Yang] lab, like I said, I don't know, because I have never really worked with them or so I didn't really understand how their **[00:28:43.260]** work functions. But she was really good of course, she was a senior scientist in in my lab. And so I would always have her, you know, design the experiment at the beginning and then we would talk about it and then you know if anything had to be modified or whatever we would do that. **[00:29:02.700]**

[redacted] was asked whether Respondent ever expressed any concerns about technical challenges with the work or sample quality that would have made it challenging to do the experiments:

[00:18:33.600] …for our stuff, yeah, there was. I mean, you know, any experiment. Yeah. You know, sometimes it works the first time. Generally, not. There's always little things that you'd have to tweak them so, **[00:18:46.440]** you know, we always, if there was a problem, she'd let me know, we'd talk about it, work through it. I think one of the projects we also did we were **[00:18:57.000]** consulting with someone in Texas, I forget which university. So, you know if there was ever a technical issue that we couldn't solve, we usually would talk to somebody else. **[00:19:10.080]**

[redacted] did not have any concerns about Respondent and her skills:

[00:19:20.550] No, see she worked for me for like eight years. And we had other technicians and graduate students and **[00:19:31.110]** like research assistants, volun… like not volunteers, like rotation, you know, rotation students summer projects. And they all came up with, everybody came up with the similar type of data. So, I was never, **[00:19:47.490]** I never had any concerns **[00:19:50.820]** on her data. **[00:19:54.270]** It all matched everything else the other people in the lab we're doing and independently of her. **[00:20:00.960]** So, I had no reason to ever **[00:20:04.020]** think that there was anything wrong. **[00:20:07.350]**

[redacted] was asked whether receiving funding for the grants in question would have allowed Respondent to maintain her position. She responded as follows:

Yes. **[00:21:11.190]** Yeah, because she was a Research Scientist, Step III. I think. So, she had a fairly sizable salary. And so it was, you know, one of those where you, and she you know of course she did a lot, a lot of the **[00:21:26.580]** head work, writing, and things like that as well. So, I mean, it was warranted. But it was one of those things that well you needed funding for in order to **[00:21:38.790]** separate keep her on board. And that's why it was so kind when Vault Nano and Dr. Yang kicked in $50,000 just to keep her on for a half a year. It was like, yay. **[00:21:51.960]**

Interview of [redacted] *M.D., November 12, 2020,* ***[00:09:51.210]-[00:10:50.100]***

[redacted] was asked whether Respondent had ever communicated concerns about the data analysis or asked for help in understanding the data:

She was sure of herself. Yeah, she never did **[00:09:51.210]**. I guess one other aspect that I sort of forgot was, which also had raised alarm bells, was that **[00:09:59.280]** we asked her, I asked her to do ELISpot **[00:10:02.820]** experiments. Right. So, ELISpots are just another way of measuring T cell release of cytokines. And so, we asked her to do interferon gamma ELISpots. And they never were **[00:10:17.490]**, she couldn't get them to work, she couldn't get them to show anything **[00:10:21.270]**. So that that was one other piece of information for what kind of raise the alarm bells because ELISpot is technically easier and faster and much more sensitive than flow cytometry. **[00:10:36.870]**

And it's, and you can, right, it [ELISpot] doesn't involve gating. And it's not possible to fabricate the results because you have the plates right there, with the spots right there. **[00:10:50.100]**

The Investigation Committee noted, in the material above, that the flow cytometry had been conducted incorrectly and could not be validated by ELISpot. This occurred despite Respondent's extensive training, which leads to evidence that Respondent had an awareness or understanding of her actions. As such, the first two prongs are satisfied: a significant departure from accepted practices in the research community and an awareness of the risk caused by her actions. Both have been proven by a preponderance of the evidence as shown above. Thus, the Committee has determined that the Respondent knowingly committed research misconduct by falsification with regard to Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was by moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted and required practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data was knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 6 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 1.

Allegations 2-3 concern the following: National Institutes of Health, National Cancer Institute SBIR grant titled, "CTL Based Therapeutic Vaccine to Prevent or Interrupt HPV Mediated Oncogenesis" [R43CA228629; PI: [redacted]].

Allegation 2: It is alleged that Respondent falsified data used in Figure 2 by reporting immune response results that are incompatible with the raw data files.

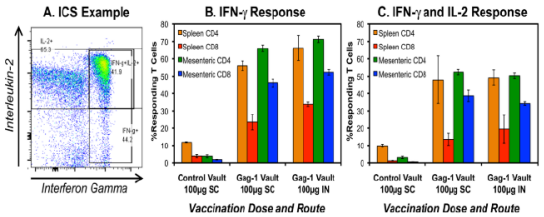


Fig. 2. Robust cellular immune response to HIV vaults. The HIV-1 Gag vaults were administered to groups of three C57BL/6 mice IN at weeks 0, 2, and 4. At 6 weeks, mice were sacrificed and mononuclear cells were harvested from spleen or mesenteric lymphatics for assessment of Gag responsiveness using overlapping 15-mer peptides and intracellular cytokine staining. Means and standard deviations are plotted.

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 2 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 2.

Allegation 3: It is alleged that Respondent falsified data used in Figure 3 by reporting immune response results that are incompatible with the raw data files.

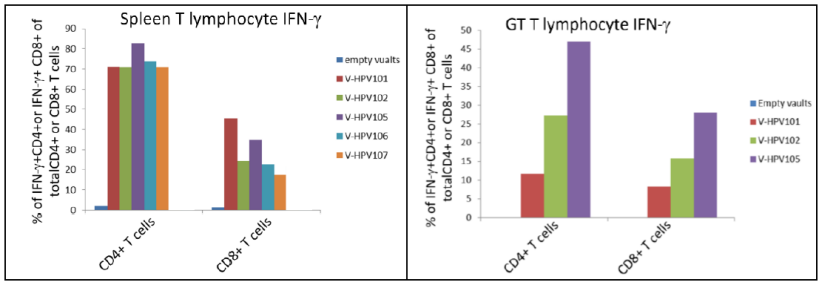
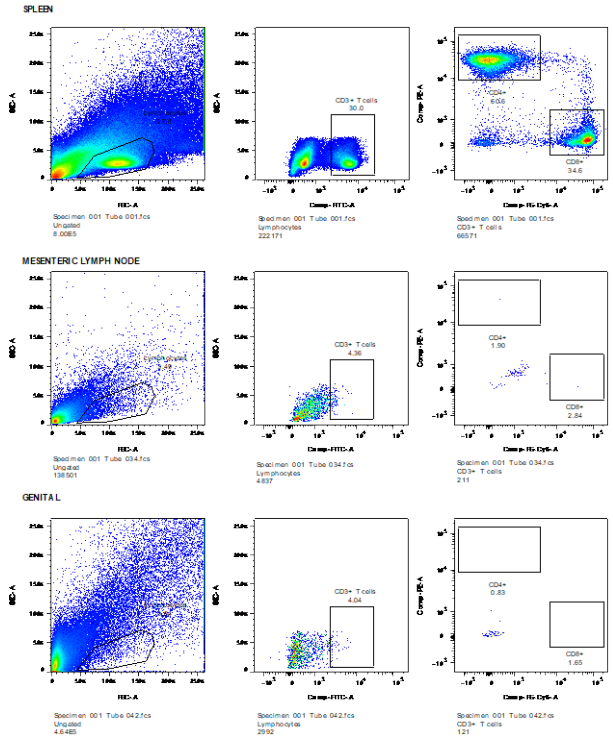


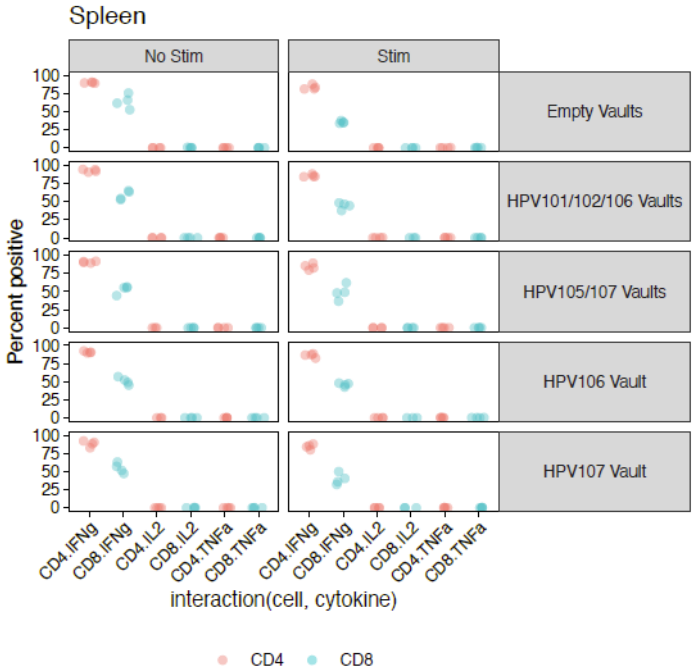
Fig. 3. Robust cellular immune response to HPV prototype vaults. The HPV vaults described in Table II below, were administered to groups of three C57BL/6 mice IN at weeks 0, 2, and 4. At 6 weeks, mice were sacrificed and mononuclear cells were harvested from spleen or genital tract lymphatics for assessment of HPV responsiveness using over-lapping 15-mer peptides and intracellular cytokine staining. Means and standard deviations are plotted.

Analysis: In their final report [Exhibit 10], the Inquiry Committee noted:

> Figure 3 data are for HPV responses. The data refer to the "HPV 2" dataset [Exhibit 02]. There are major problems with this dataset. Many of the samples analyzed by flow cytometry do not appear to be viable. Samples from the spleen were largely fine in this regard. Samples from the mesenteric lymph node were mostly compromised and samples from "genital" were highly compromised, with very few cells in the viable, lymphocyte gate. See examples below, created by the Committee using the data:



Spleen samples showed very high levels of IFN-γ (80+%) regardless of whether they were unstimulated or stimulated, and regardless of whether the immunization was a vault containing HPV peptides or an "empty" vault. *These results are incompatible with the data presented in the grant Figure 3 titled, "Spleen T lymphocyte IFN-γ."*



Please refer to the **Background on Flow Cytometry and the Research** section above. The Investigation Committee found that when gating on live cells as [redacted]) did when re-analyzing the data [Exhibit 13], the expression of cytokines was very high in both the negative control (no stim) and the experimental tubes. This shows that the parameters of the flow cytometer were not set up properly because the negative control should show no or very little cytokine expression. That is where the "no antibody" negative control would be needed. The cytokine expression profile was equivalent in both the control and experimental arms and the bar graphs should show no difference.

The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data.

Please also refer to the **Background on the Respondent** noting that Respondent had been highly trained in performing flow cytometry. Unfortunately, as the Committee has found, her gating strategy and her lack of controls were improper. Respondent could not validate her work by ELISpot. Others who tried could not either.

Please refer to Allegation 1 for further discussion and analysis.

The Investigation Committee noted, in the material above, that the flow cytometry had been conducted incorrectly and could not be validated by ELISpot. This occurred despite Respondent's extensive training, which leads the Committee to find that Respondent had an awareness or understanding of her actions. As such, the first two prongs are satisfied: a significant departure from accepted practices in the research community and an awareness of the risk caused by her actions. Both have been proven by a preponderance of the evidence as shown above. Thus, the Committee has determined that the Respondent knowingly committed research misconduct by falsification with regard to Allegation 3.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions, and her lack of control and inappropriate gating strategy. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 3 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 3.

Allegation 4 concerns the following: National Institutes of Health, National Institute of Allergy and Infectious Diseases grant titled, "Defining Factors Controlling HIV Rebound" [P01AI131294; PI: [redacted]

Allegation 4: It is alleged that Respondent falsified data used in Figure 8 (Project 3) by reporting immune response results that are incompatible with the raw data files.

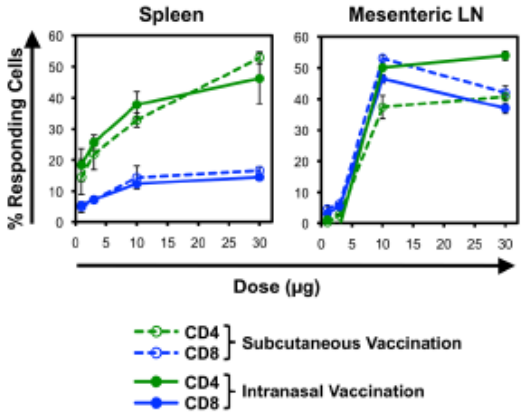


Figure 8. Immunogenicity of recombinant human vaults packaged with Gag 148-214 delivered to C57BL6 mice. Vaults were administered to mice by subcutaneous injection or intranasal instillation at varying doses at weeks 0, 2, and 4. At week 6, splenocytes and mesenteric lymphocytes were assessed for responses against overlapping peptides spanning Gag 148-214 by intracellular cytokine staining for gamma IFN and IL-2. The mean percentages of responding cells are plotted for groups of 3 mice.

Analysis: In their final report [Exhibit 10], the Inquiry Committee noted:

> Figure 8 was generated from data in Experiment 3 [Exhibit 03]. However, there is no experiment staining key for this experiment as there are for the others. Looking at the data and analyzing, based on the assumption that the same antibody-fluorochrome combinations that were used in other experiments were used here as well, shows inconsistent results with what should appear in the spleen, e.g. distinct CD4 and CD8 T cell subsets.
>
> This experiment included ~96 samples, 48 spleen and 48 mesenteric lymph node samples. The spleen samples were of good quality with more than enough events to allow for analysis. The lymph node samples, on the other hand, were of poor quality with few events to analyze. The Committee does not consider data from these samples to be interpretable.
>
> Without an experiment key to determine staining parameters, the Committee relied on a process of elimination to analyze the data and make the following observations:
>
> - The calculated values show no difference between treatment groups in either treatment route or tissues analyzed.
> - Some experiments show very few if any cells to analyze, particularly at the highest amount of Gag proteins.
> - The reported values (grant figures) demonstrate an exemplary dose response curve, however, that was not observed by this analysis. Data generated from this analysis is included as Exhibit 04.

Please refer to the **Background on Flow Cytometry and the Research** section above. Based on the evidence and interviews, the Committee found that the experiments were not performed properly. Dr. [redacted] and the Committee used the raw data to rerun the analysis using generally accepted techniques and analysis, which showed results different from what Respondent provided. [redacted] were surprised by Respondent's results at the time.

The Investigation Committee found that when gating on live cells as [redacted] did when re-analyzing the data, the expression of cytokines was very high in both the negative control (no stim) and the experimental tubes. This shows that the parameters of the flow cytometer were not set up properly because the negative control should show no or very little cytokine expression. That is the reason the "no antibody" negative control would be needed. The cytokine expression profile was equivalent in both the control and experimental arms and the bar graphs should show no difference.

The Committee found that only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data.

There are figures showing a dose dependent curve (Allegations #4, 17) [Exhibit 14]. The above comments all apply to these as well. No difference was observed between control and experimental arms with any of the doses of the vaults. In this case, the values in the graphs are unsupported by the data. The Committee found that Respondent's actions to create these curves were intentional and purposeful.

Please also refer to the **Background on the Respondent** who was said to be highly trained in performing flow cytometry. Unfortunately, as the Committee has found, her gating strategy and her lack of controls were not proper. Respondent could not validate her work by ELISpot. Others who tried could not either. The Committee could not find any logical reason to explain how the raw data [Exhibit 14] could be used to generate the graphs presented**.**

Please refer to Allegation 1 for further discussion and analysis.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Applying the correct gating strategy is an accepted (required) practice in the field. Respondent's actions appear to be specific and purposeful, showing an intense dose response while providing data that cannot be interpreted. Respondent had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were intentionally falsified. The Committee finds that data provided by Respondent and used in Figure 8 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 4.

Allegation 5 concerns the following: National Institutes of Health grant proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" [R21AI131451-01; PI: [redacted]

Allegation 5: It is alleged that Respondent falsified data used in Figure 8 by reporting immune response results that are incompatible with the raw data files.

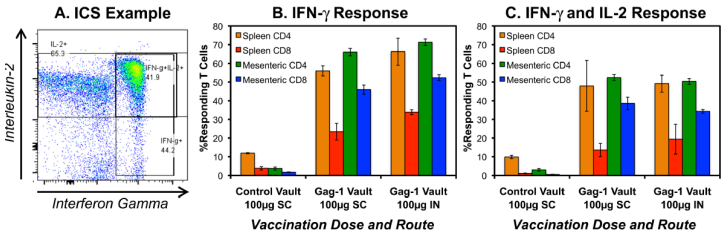


Figure 8. Vaults containing a short region of HIV-1 Gag yield remarkably high frequency systemic and mucosal polyfunctional Th1 cellular immune responses. Mice (C57BL6) were given subcutaneous injections (SC) or intranasal instillations (IN) of human recombinant vaults (100µg) containing the $Gag_{148-214}$ sequence or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. **A**. Example of intracellular cytokine staining after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning the stretch in Gag. Percentages of $CD4^+$ and $CD8^+$ T cells producing: **B**. interferon-γ or **C**. interferon-γ and interleukin-2 are plotted as means and standard deviations (three mice per group). Thus vaults deliver antigen with adjuvant-like potency to elicit Th1-biased cellular immunity.

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 8 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 5.

Allegations 6-8 concern the following: National Institutes of Health grant proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" [R21AI131451-01A1 (resubmission); PI: [redacted]

Allegation 6: It is alleged that Respondent falsified data used in Figure 9 by reporting immune response results that are incompatible with the raw data files.

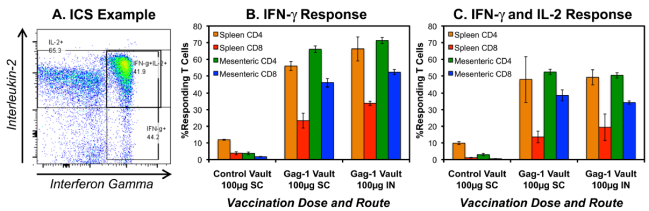


Figure 9. Vaults containing a short region of HIV-1 Gag yield remarkably high frequency systemic and mucosal Th1 cellular immune responses. Groups of three C57BL/6 mice were given subcutaneous (SC) or intranasal (IN) administration of human recombinant vaults containing the $Gag_{148-214}$ sequence or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric mononuclear cells at week 6. **A**. Example of intracellular cytokine staining after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning Gag 148-214. Percentages of $CD4^+$ and $CD8^+$ T cells producing: **B**. interferon-γ or **C**. interferon-γ and interleukin-2 are plotted as means and standard deviations. Subsequent titration experiments reveal that the frequency of responses reach plateaus between 3 to 10 µg dosing (not shown).

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 9 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 6.

Allegation 7: It is alleged that Respondent falsified data used in Figure 10 by reporting immune response results that are incompatible with the raw data files.

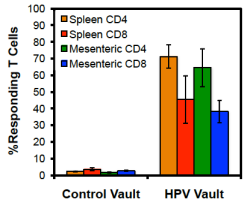


Figure 10. Vaults containing HPV-16 $E6_{33-84}$ are highly immunogenic in mice. Groups of four C57BL/6 mice were given intranasal instillations (IN) of human recombinant vaults (14µg) containing the HPV-16 $E6_{33-84}$ sequence (**Figure 7**) or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. Percentages of $CD4^+$ and $CD8^+$ T cells producing interferon-γ are plotted as means and standard deviations. The dose of 14µg was chosen to deliver the same number of antigen molecules as 10µg of the MVP-fused Gag148-214 vaults in **Figures 4 and 9**.

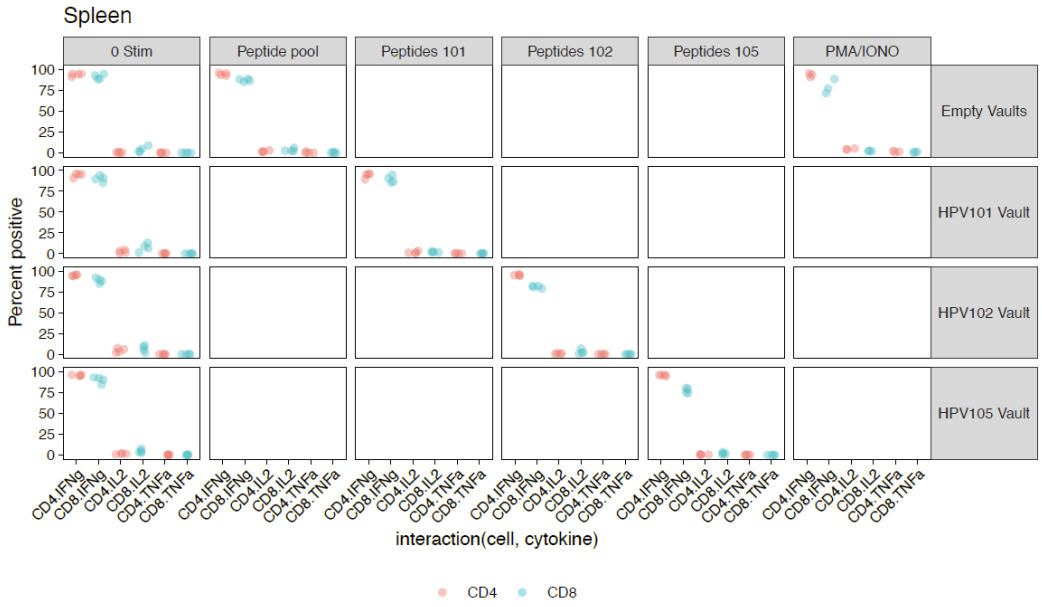
Analysis: See Allegation 1 for analysis.

In their final report [Exhibit 10], the Inquiry Committee noted:

> These data refer to the "HPV 1" dataset [Exhibit 05]. There are major problems with this dataset. Many of the samples analyzed by flow cytometry do not appear to be viable. Samples from the spleen were largely fine in this regard. Samples from the mesenteric lymph node were about half

compromised and samples from "genital" were highly compromised, with very few cells in the viable, lymphocyte gate. The figure in the proposal shows only mesenteric and spleen.

Spleen samples showed very high levels of IFN-γ (80+%) regardless of whether they were unstimulated or stimulated, and regardless of whether the immunization was a vault containing HPV peptides or an "empty" (also "control") vault. See chart below, created by the Committee using the data. *These results are incompatible with the data presented in Figure 10.*



Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data [Exhibit 15] provided by Respondent and used in Figure 10 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 7.

Allegation 8: It is alleged that Respondent falsified data used in Figure 11 by reporting immune response results that are incompatible with the raw data files.

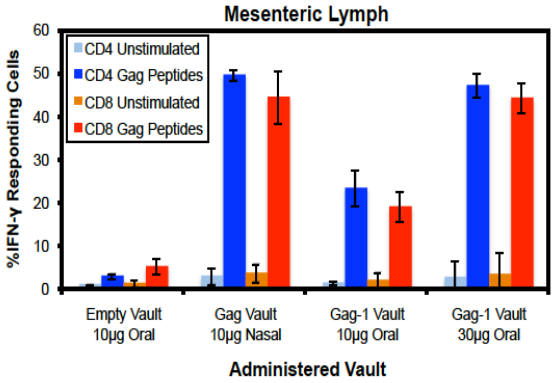


Figure 11. Immunogenicity of orally administered vaults. The HIV-1 Gag vaults from **Figures 4 and 9** were administered to groups of three C57BL/6 mice. Oral (fed in a sucrose solution) or intranasal administration was performed at weeks 0, 2, and 4. At 6 weeks, mice were sacrificed and mononuclear cells were harvested from spleen or mesenteric lymphatics for assessment of Gag 148-214 responsiveness using overlapping 15-mer peptides and intracellular cytokine staining. Means and standard deviations are plotted.

Analysis: See Allegation 1 for analysis.

In their final report [Exhibit 10], the Inquiry Committee noted:

> Allegation 8 refers to Figure 11 of the grant proposal, data that relate to HIV peptides ("Gag") even though they appear in an HPV proposal.
>
> Data for Figure 11 were generated from experiment "HIV5 Gag-1 oral vaccination and durability experiment." Based on the staining key [Exhibit 06] and experiment layout [Exhibit 07] provided, the Committee could not obtain results that support Respondent's conclusions [Exhibit 08]. With regard to CD4 positive T cells and examining interferon-gamma response, which was one of the main output readings taken for this grant proposal, it was impossible to determine where responsiveness was determined from. It appears that regardless of treatment, stimulation, or vault condition, the results were nearly identical. Examination of CD8 T cell populations demonstrated similar results. Overall, sample quality and data quality were very good with distinct and typical lymphocyte population profiles. Based on the evidence available, it would seem that either a) all cells responded to vaccination regardless of amount or stimulation, or b) the vaccination elicited no response. In either case, such results are inconsistent with the published results.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data [Exhibit 16] provided by Respondent and used in Figure 11 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 8.

Allegation 9 concerns the following: National Institutes of Health SBIR Phase II grant proposal titled, "Novel Pan-Serovar Vaccine for Chlamydia" [R44AI126960-01; PI: [redacted]].

Allegation 9: It is alleged that Respondent falsified data used in Figure 9 by reporting immune response results that are incompatible with the raw data files.

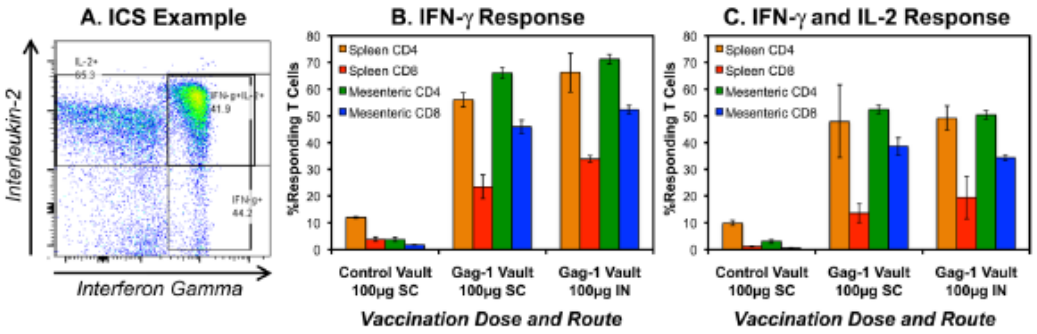


Figure 9. Vaults containing a short region of HIV-1 Gag yield systemic and mucosal polyfunctional T cell responses. Mice (C57BL6) were given subcutaneous injections (SC) or intranasal instillations (IN) of human recombinant vaults (100µg) containing HIV-1 Gag-1 148-214 or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. A. Example of intracellular cytokine staining after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning the stretch in Gag. Percentages of $CD4^+$ and $CD8^+$ T cells producing: B. interferon-γ or C. interferon-γ and interleukin-2 are plotted as means and standard deviations (three mice per group).

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent

appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 9 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 9.

Allegation 10 concerns the following: National Institutes of Health SBIR Phase I grant proposal titled, "Development of A Novel Pan-Serovar Vaccine for Chlamydia" [R43AI136224-01; PI: [redacted])].

Allegation 10: It is alleged that Respondent falsified data used in Figure 3 by reporting immune response results that are incompatible with the raw data files.

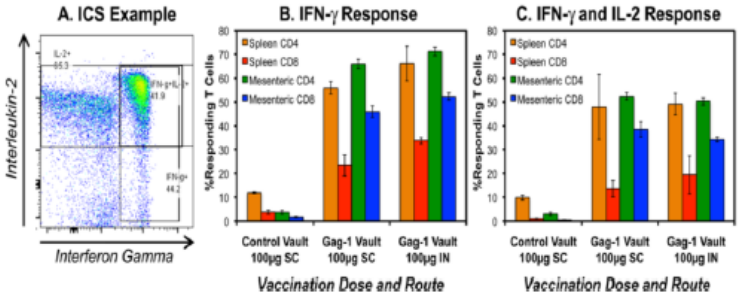


Fig. 3 Robust cellular immune response to HIV vault. Robust cellular immune responses were seen following subcutaneous (SC) or intranasal (IN) delivery of the Gag vault to wild-type mice (Yang et al. unpublished).

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The

Committee finds that data provided by Respondent and used in Figure 3 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 10.

Allegation 11 concerns the following: National Institutes of Health grant proposal titled, "A Novel Cellular Immune Zika Vaccine" [R21AI131013; PI: [redacted]

Allegation 11: It is alleged that Respondent falsified data used in Figure 9 by reporting immune response results that are incompatible with the raw data files.

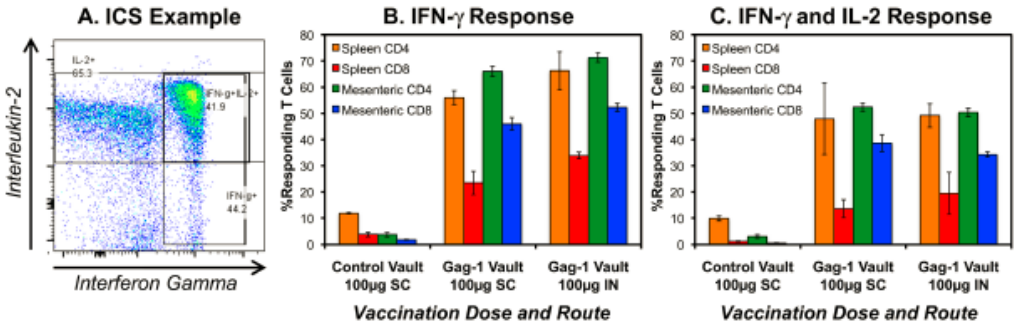


Figure 9. Vaults containing a short region of HIV-1 Gag yield remarkably high frequency systemic and mucosal polyfunctional Th1 cellular immune responses. Mice (C57BL6) were given subcutaneous injections (SC) or intranasal instillations (IN) of human recombinant vaults (100µg) containing the $Gag_{148-214}$ sequence or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. **A**. Example of intracellular cytokine staining after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning the stretch in Gag. Percentages of $CD4^+$ and $CD8^+$ T cells producing: **B**. interferon-γ or **C**. interferon-γ and interleukin-2 are plotted as means and standard deviations (three mice per group). Thus vaults deliver antigen with adjuvant-like potency to elicit Th1-biased cellular immunity.

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 9 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 11.

Allegations 12 and 13 concern the following: National Institutes of Health grant proposal titled, "A Recombinant Human Vault CTL-Based HIV Vaccine Component" [R01AI126914; PI: [redacted]

Allegation 12: It is alleged that Respondent falsified data used in Figure 7 by reporting immune response results that are incompatible with the raw data files.

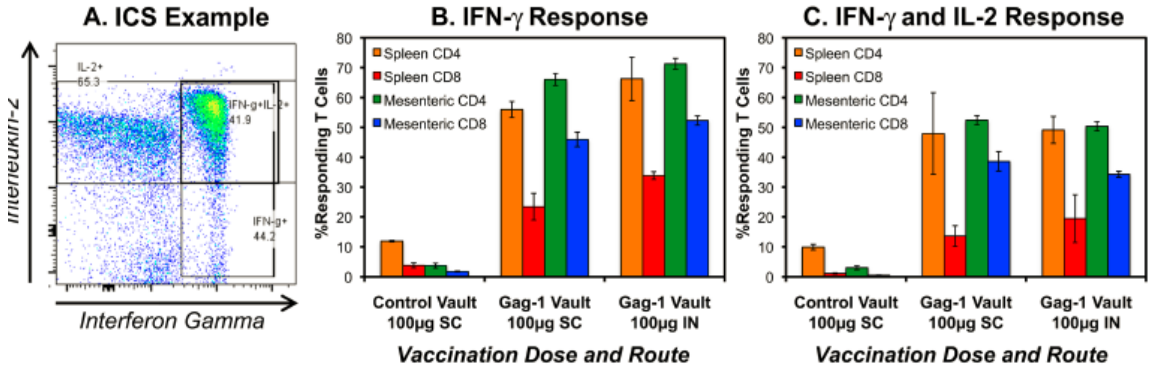


Figure 7. Vaults containing a short region of HIV-1 Gag yield systemic and mucosal polyfunctional T cell responses. Mice (C57BL6) were given subcutaneous injections (SC) or intranasal instillations (IN) of human recombinant vaults (100µg) containing the cGag-1 sequence or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. **A**. Example of intracellular cytokine staining after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning the stretch in Gag. Percentages of $CD4^+$ and $CD8^+$ T cells producing: **B**. interferon-γ or **C**. interferon-γ and interleukin-2 are plotted as means and standard deviations (three mice per group).

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 7 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 12.

Allegation 13: It is alleged that Respondent falsified data used in Figure 14 by reporting immune response results that are incompatible with the raw data files.

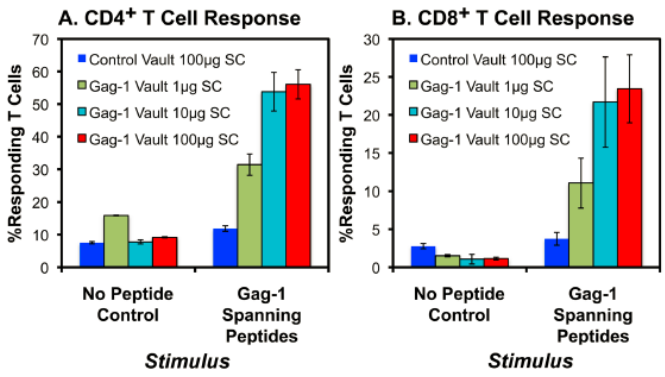


Figure 14. Dose response of mouse vaccination with the recombinant human vault delivering cGag-1. Mice were vaccinated as described in **Figure 7**. Percentages of cells expressing IFN-γ in response to no peptide or Gag-1 spanning peptides are plotted.

Analysis: See Allegation 1 for analysis.

In their final report [Exhibit 10], the Inquiry Committee noted:

> Figure 14A and B: Contrary to data shown in Exhibit 01, data calculated for this inquiry show small, if any, difference between no peptide control and Gag-1 spanning peptide treated samples. Looking at both CD4 and CD8 T cells that secrete IL2, IFNg, or IFNg/IL2 at all doses reported (1ug, 10ug, and 100ug) with and without peptide stimulation (1ug), most groups show very modest differences. In addition, comparison within groups (e.g. no peptide stimulation or Gag-1 spanning peptide stimulation) showed no difference with increased Gag-1 protein amount.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 14 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 13.

Allegations 14 and 15 concern the following: National Institutes of Health SBIR I/II Fast-Track grant proposal titled, "Design of a Novel CTL Retargeting Therapeutic HIV Vaccine" [R44AI128983, PI: [redacted])].

Allegation 14: It is alleged that Respondent falsified data used in Figure 7 by reporting immune response results that are incompatible with the raw data files.

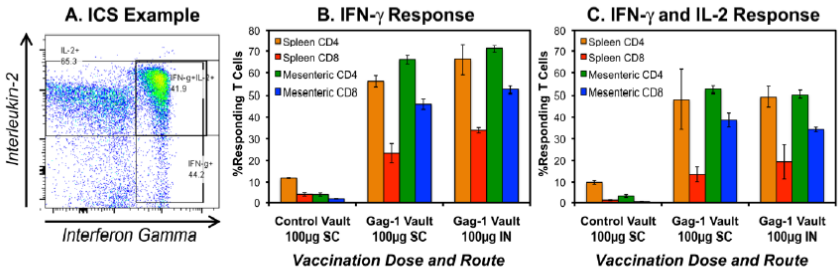


Figure 7. Vaults containing a short region of HIV-1 Gag yield systemic and mucosal polyfunctional T cell responses. Mice (C57BL6) were given subcutaneous injections (SC) or intranasal instillations (IN) of human recombinant vaults (100µg) containing the cGag-1 sequence or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. **A**. Example of intracellular cytokine staining after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning the stretch in Gag. Percentages of $CD4^+$ and $CD8^+$ T cells producing: **B**. interferon-γ or **C**. interferon-γ and interleukin-2 are plotted as means and standard deviations (three mice per group).

Analysis: See Allegation 1 for analysis. These figures are identical to those in Allegation 1.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 7 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 14.

Allegation 15: It is alleged that Respondent falsified data used in Figure 13 by reporting immune response results that are incompatible with the raw data files.

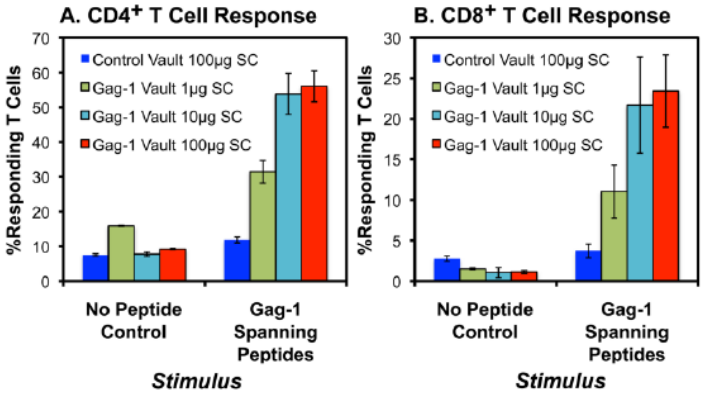


Figure 13. Dose response of mouse vaccination with the recombinant human vault delivering cGag-1. Mice were vaccinated as described in **Figure 10**. Percentages of splenocyte T cells expressing IFN-γ in response to no peptide or Gag-1 spanning peptides are plotted.

Analysis: See Allegation 1 for analysis.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 13 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 15.

Allegations 16-19 concern the following: National Institutes of Health grant proposal titled, "A Novel Therapeutic Vaccine for HPV Oncogenesis" [R21AI142068-01; PI: [redacted]].

Allegation 16: It is alleged that Respondent falsified data used in Figure 8A and B by reporting immune response results that are incompatible with the raw data files.

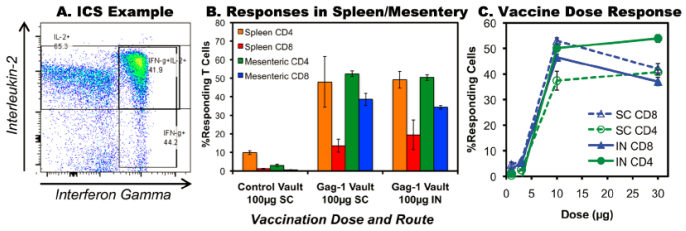


Figure 8. Vaults containing a short region of HIV Gag yield remarkably high frequency systemic and mucosal Th1 cellular immune responses, maximized at a dose of 3 to 10µg per vaccination. Groups of three C57BL/6 mice were given subcutaneous (SC) or intranasal (IN) administration of human recombinant vaults containing the HIV $Gag_{148-214}$ sequence or no insert, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric mononuclear cells at week 6. **A**. Example of measuring antigen-specific responses by intracellular cytokine staining (ICS) after stimulation of mesenteric $CD8^+$ T cells with overlapping 15-mer peptides spanning Gag 148-214. **B**. Percentages of responding $CD4^+$ and $CD8^+$ T cells producing interferon-γ and interleukin-2 are plotted as means and standard deviations for spleen (systemic) and mesenteric (gut mucosal) compartments. **C**. Frequencies of responding cells in the mesenteric compartment across varying doses via SC or IN routes of vaccination are shown from a separate experiment.

Analysis: See Allegation 1 for analysis.

In their final report [Exhibit 10], the Inquiry Committee noted:

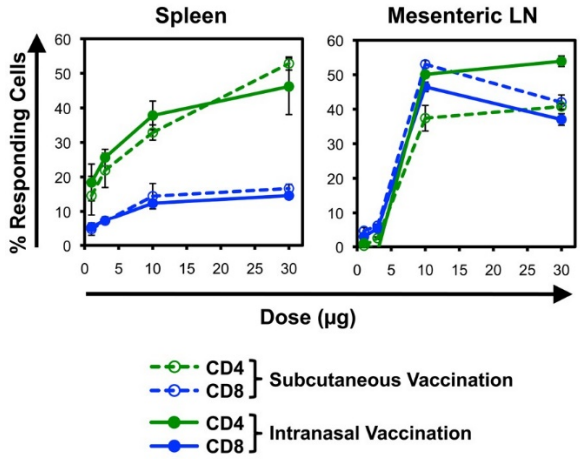
> Allegation 16 refers to Figure 8A and 8B of the grant proposal, data that relate to HIV peptides ("Gag") even though they appear in an HPV proposal.
>
> Figure 8A: As shown in Exhibit 01, data calculated show IFNg, IL2, and IL2/IFNg positive cells well above reported values (10ug S.Q. MLN tissue), with and without stimulation (1ug). Generated graphs resemble reported graphs, and gating strategy is similar. Of note is the observation that virtually no difference was found between control "empty" vault treated tissues and Gag-1 vault (10ug) treated tissues.
>
> Figure 8B: As shown in Exhibit 01, data calculated show little difference in IL2 and IL2/IFNg secreting CD4+ T cells comparing empty vault (SC) and Gag-1 vault (SC, 100ug) in spleen, and mesenteric lymph nodes. Other differences were noted between the reported and calculated data; however, most noteworthy is the observation that control vault treatment showed high IFNg and IL2 secreting T cells, whether of the CD4 or CD8 type.
>
> Furthermore, in stimulated (1ug) samples, similar observations were noted. CD4+ T cells that secrete IFNg or IL2/IFNg were higher in control empty vault experiments than in Gag-1 vault experiments. This is in stark contrast to the reported results.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the

live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data provided by Respondent and used in Figure 8A and B were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 16.

Allegation 17: It is alleged that Respondent falsified data used in Figure 8C (see Allegation 16 above) by reporting immune response results that are incompatible with the raw data files.



Analysis: Please refer to Allegation 1 for further discussion and analysis. Also, please refer to the **Background on Flow Cytometry and the Research** section above. Based on the evidence and interviews, the Committee finds, that the experiments were not performed properly. Dr. [redacted] and the Committee used the raw data to rerun the analysis using generally accepted techniques and analysis, which showed results different from what Respondent provided. Drs. [redacted] and [redacted] were surprised by Respondent's results at the time. The Investigation Committee found that when gating on live cells as Dr. [redacted] (and Dr. [redacted]) did when re-analyzing the data, the expression of cytokines was very high in both the negative control (no stim) and the experimental tubes. This shows that the parameters of the flow cytometer were not set up properly because the negative control should show no or very little cytokine expression. That is the reason the "no antibody" negative control would be needed. The cytokine expression profile was equivalent in both the control and experimental arms and the bar graphs should show no difference.

The Committee found that the only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data.

There are figures showing a dose dependent curve (Allegations #4, 17) [Exhibit 14]. The above comments all apply to these as well. No difference was observed between control and experimental arms with any

of the doses of the vaults. In this case, the values in the graphs are unsupported by the data. The Committee found that Respondent's actions to create these curves were intentional and purposeful.

Please also refer to the **Background on the Respondent** who was said to be highly trained in performing flow cytometry. Unfortunately, as the Committee found, her gating strategy and her lack of controls were not proper. Respondent could not validate her work by ELISpot. Others who tried could not either. The Committee could not find any logical reason to explain how the raw data [Exhibit 14] could be used to generate the graphs presented**.**

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Applying the correct gating strategy is an accepted (required) practice in the field. Respondent's actions appear to be specific and purposeful, showing an intense dose response while providing data that cannot be interpreted. Respondent had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were intentionally falsified. The Committee finds that data provided by Respondent and used in Figure 8C were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 17.

Allegation 18: It is alleged that Respondent falsified data used in Figure 9 by reporting immune response results that are incompatible with the raw data files.

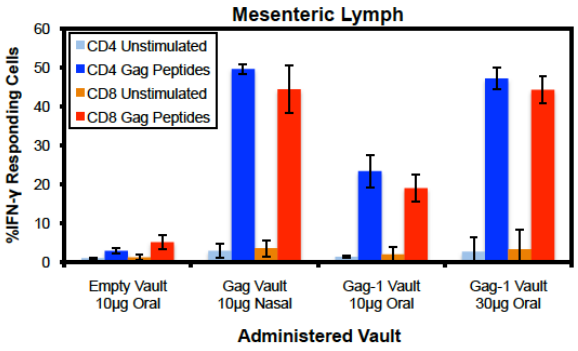


Figure 9. Immunogenicity of orally administered vaults. HIV-1 $Gag_{148-214}$ vaults were administered to groups of three C57BL/6 mice. Oral (fed in a sucrose solution) or IN administration was performed at weeks 0, 2, and 4, followed by ICS analysis at 6 weeks. Means and standard deviations are plotted.

Analysis: See Allegations 1 and 8 for analysis.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

The Investigation Committee notes that these criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data [Exhibit 16] provided by Respondent and used in Figure 9 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 18.

Allegation 19: It is alleged that Respondent falsified data used in Figure 10 by reporting immune response results that are incompatible with the raw data files.

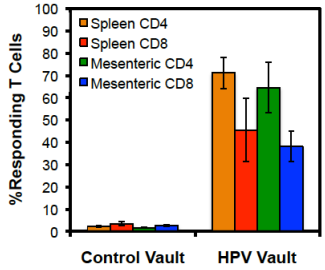


Figure 10. Vaults containing HPV-16 $E6_{33-84}$ are highly immunogenic in mice. Groups of four C57BL/6 mice were vaccinated with human recombinant vaults (14µg, selected to contain equal copy number of antigen to 10µg of the HIV $Gag_{148-214}$ vault) containing the HPV-16 $E6_{33-84}$ sequence (**Figure 7**) or no insert IN, at weeks 0, 2, and 4, followed by harvesting of splenic and mesenteric T cells at week 6. Percentages of responding $CD4^+$ and $CD8^+$ T cells producing interferon-γ against overlapping peptides are plotted as means and standard deviations.

Analysis: See Allegations 1 and 7 for analysis.

Conclusion: 42 CFR §93.104 provides: "A finding of research misconduct made under this part requires that (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence."

These criteria have been satisfied. Respondent's conduct of the research, by improperly conducting the flow cytometry experiments, represents a significant departure from accepted practices in the research community. Although these experiments are complicated, there are accepted ways of conducting them. The Investigation Committee interviewed various witnesses and replotted the experiments. Respondent appears to have an inappropriate gating strategy. The only way the bar graphs presented in the figures (Allegations #1, 2, 3, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19) could be generated was via moving the live cell gate to the dead cell/debris population only in the case of the negative control. For the experimental samples, the gate was set on the live cell population. This is not the appropriate way of analyzing that type of data. Since applying the correct gating strategy is an accepted (required) practice in the field, Respondent had to know that there was a substantial risk associated with her actions. This is so, because she had extensive experience in this field and understood what she was doing. Thus, the preponderance of the evidence points to the conclusion that these data were knowingly falsified. The Committee finds that data [Exhibit 15] provided by Respondent and used in Figure 10 were falsified by reporting immune response results that are incompatible with the raw data files. Therefore, the Committee makes a finding of research misconduct regarding Allegation 19.

CONCLUSION

The Committee concludes the preponderance of the evidence supports a finding that Respondent committed research misconduct in connection with Allegations 1-19.

ADDENDUM

The Preliminary Investigation Report was sent to Respondent on June 22, 2021 [Exhibit 17] via email and UPS with return receipt. The report was delivered on June 23, 2021 [Exhibit 18] to Respondent's home address. Respondent was asked to provide any comments to the report within 30 days, by July 22, 2021. Respondent did not respond or provide any comments. Therefore, the conclusions of the Final Investigation Report are unchanged.

[redacted]