



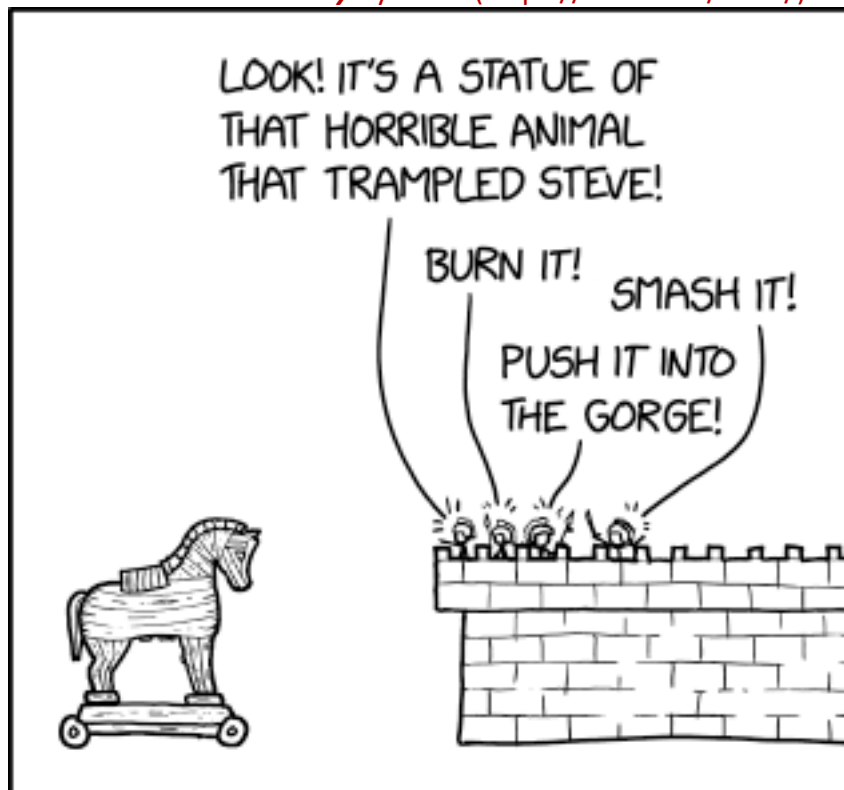
# USC

## 599: Viral Immunology & Viral Vector Engineering

**Units:** 2  
**Semester:** Spring 2023  
**Date – Time:** Wednesday – 16:00-17:50  
**Location:** SOS B38  
**Office Hours:** Wednesday – 15:00-15:50 or anytime  
(by email request with > 24h advance notice)

**Instructor:** Jennifer Treweek  
**Office Hours:** MCB 240A, Zoom  
**Contact:** [jtweek@usc.edu](mailto:jtweek@usc.edu), (213) 821-3478  
**Syllabus:** schedule overview enclosed, see Bb for weekly syllabus

*Viral Vector Immunity* by XKCD (<https://xkcd.com/2406/>)



HOW VACCINE FAILURE DUE TO  
VIRAL VECTOR IMMUNITY WORKS

## Course Description

In-depth survey of current topics in viral immunology and of pioneering technologies for detecting virus infection, engineering patient immunity (e.g., vaccine platforms), and harnessing virus properties for noninvasive gene delivery in the treatment of human disease.

### Expanded Course Description

The first module of this class will introduce key principles in virology and immunology, including: the mechanism of virus infectivity, human immunology with respect to virus infection, and the pathogenesis of virus infection-associated disease in humans. We will review assays and devices that can be used to measure virus titer and infectivity in-lab, as well as track virus infection in humans/biological specimens. The second module will cover topics in viral vector engineering, including strategies for designing viral vectors and biomedical applications to which viral vectors have been applied. The third module will delve into vaccine-based strategies for preventing virus infection and/or attenuating the disease pathology. Herein, the focus will be on the use of viruses in vaccines, from live-attenuated or inactivated viruses, to virus-inspired vaccines such as virus-like particles and viral vectored vaccine platforms. We will also spend a small amount of time reviewing pharmacological, immunological, and vector-based modalities for modifying immune system function (i.e., immunoengineering) so as to treat disease. This module will conclude with a review of the FDA approval process for drugs and biologics, as this has crucial implications in the use of viral vectors in vaccination and in gene therapy.

Finally, the fourth module will entail more active in-class discussion of applied topics within viral vector engineering. Specifically, we will discuss the promise of viral vectors as delivery vehicles for gene editing technologies, and review the critical limitations of current viral vectors (e.g., cargo capacity) – and what engineering steps must be undertaken so as to overcome these barriers. Herein, students will have the opportunity to lead the discussion of a journal article on a relevant current topic in viral vector engineering, such as machine-learning approaches to AAV capsid design, noninvasive gene delivery with viral vectors, clinical studies on virus vectored vaccines or gene therapy, etc.

Although this 2-unit lecture-based course can be taken as a standalone course on virology and viral vector applications, it has been designed to integrate seamlessly with a concurrent 2-unit lab-based course on viral vector production. The latter course allows students to gain exposure to adeno-associated virus (AAV) genome design; AAV vector production, purification, and titering; and AAV vector delivery in rodents. Because AAV vectors have received FDA approval as disease treatments in the US, and because AAV vectors hold tremendous promise in gene editing strategies, the accompanying lab course provides real-world background on the design, production, and in vivo administration of AAV-based therapeutics. Enrollment in both courses provides a well-rounded education in viral vector engineering *in theory* and *in practice*.

### Learning Objectives

Students will learn:

- 1) the core principles of virology, including virus structure and genome, virus classification, and steps of the infectious cycle that are pertinent to virus infection of humans and transmission in human populations
- 2) the basic concepts in viral immunology and virus-associated disease in humans
- 3) the different modalities for combatting virus-host infection, virus replication, and virus-associated immunopathology and disease in humans, with a focus on virus/vector-based modalities
  - a. active vaccination strategies (e.g., inactivated or live-attenuated virus vaccines, protein subunit vaccines, viral vectored vaccines, nucleic acid vaccines, etc)
  - b. passive immunization strategies (e.g., monoclonal antibodies, vector delivery of immune system modulators)
  - c. modern immune-engineering approaches (i.e., what will be the “next” vaccine platform?)
  - d. FDA approval and regulatory processes for next-generation therapies – from vaccines to gene therapy
- 4) the focus areas in viral vector engineering and gene therapy, including:
  - a. in vivo versus ex vivo therapies
  - b. viral approaches for gene transfer or modification (viral vectors that have been used preclinically to combat disease)
  - c. capsid engineering to create clinically viable vectors for gene delivery in humans
  - d. next-generation approaches to gene therapy

## Course Outcomes

- 1) Apply course teachings (on the virological and immunological mechanisms that enable virus infection and host immunosurveillance, respectively) to brainstorming novel biomedical engineering approaches for the diagnosis, prevention, and treatment of viral infection and disease.
- 2) Interpret and critique data from published journal articles on viral immunology, vaccine design, viral vector engineering, and vector-based gene delivery.
- 3) Collaborate with classmates to communicate important findings from research articles.
- 4) Use engineering/math to design and evaluate assays and devices for measuring complex biological/virological processes – such as viral infectivity, viral replication, viral load or titer, etc. Parameterize assay/device efficacy in terms of specificity or sensitivity of detection, etc.
- 5) Summarize the current state of the FDA approval process for viral vectored therapeutics.
- 6) Evaluate the ethical implications, government responsibilities in topics concerning population-wide vaccination, gene therapy, etc.

## Recommended Preparation

Previous coursework in one or more of the following is a plus: molecular or cell biology, immunology, virology, biochemistry, genetics, or neuroscience.

## Course Notes

Copies of lecture slides, video-recorded lectures, and other class information will be posted on Blackboard (Bb) or Design2Learn (D2L) course website.

## Technological Proficiency and Hardware/Software Required

For remote instruction, students will be required to use an internet-enabled device with browser capabilities, such as a laptop. The course will be delivered in-person (DEN accessibility, if applicable) or potentially by Zoom, depending on the evolving pandemic situation. Bb or D2L will be used for important class announcements, written assignment submission, claiming JC articles, and student discussion board posts.

## Required Readings and Supplementary Materials

Although the course will not be taught chapter-by-chapter from a single textbook, students will be assigned peer-reviewed journal articles. Although not mandatory, background reading may be suggested from the following textbooks:

- Principles of Virology (4<sup>th</sup> or 5<sup>th</sup> Ed.) by Jane Flint, Vincent R. Racaniello, Glenn F. Rall, *et al.* (4<sup>th</sup> Ed. available electronically through USC library)
- Molecular Biology of the Cell, by Bruce Alberts *et al.* (4<sup>th</sup> Ed. available electronically through USC library and on NCBI)
- Cellular and Molecular Immunology (8<sup>th</sup> Ed.), by Abul K. Abbas, Andrew H. H. Lichtman, Shiv Pillai, Saunders (available electronically through USC library)

Students should read the assigned materials (e.g., journal articles, textbook excerpts flagged as mandatory, etc; posted on Bb or D2L) before each class meeting so that they are prepared to take productive notes during lecture and actively participate during in-class discussion.

## Description of Assignments

**Quizzes:** Throughout the semester, three at-home quizzes (~ 60-minute) will be assigned to take online (Bb/D2L) in order to access student comprehension of “big-picture” ideas, and/or to ensure that reading assignments are completed in a timely fashion. Each quiz will be closed-book, closed notes, and closed “internet”. They will be a mix of true/false, fill-in-the-blank, multiple choice, and short-answer questions. Quiz answers will be reviewed in lecture during the class following the quiz due date; quiz answer keys will not be provided, but students can schedule an appointment to view quiz answers in-person.

**Journal Club (JC) Presentation:** Throughout the semester, each student or student group (1-3 students) will be responsible for leading a single journal article discussion during the the last two course meetings. Presenters are expected to provide background information on the journal article (introduce the topic, explain the experimental methods, review the article findings (figures), and critique the results (holes in study, future directions of research, etc). Student presentations (including asking/answering questions) should be < 30-40 minutes in length. Suggested journal articles are claimed on a first-come first-serve basis, via email to the professor (TA cc'd). If a student/group does not select a JC article before the start of Module 4 (Week 13), the instructor will assign a journal article to the student/group; this is to ensure that classmates have time to read selected journal articles before their discussion in-class.

**In-Class Work:** Class time will often be used for topic discussion; and the latter class periods will consist entirely of journal article presentation and discussion. As such, regular attendance is “highly recommended”. For the latter class meetings, attendance is MANDATORY (i.e., during JC presentations). Thus, if a student knows in advance that he/she/they will be absent on the day of a JC presentation for an important occasion or non-emergency situation (at the discretion of the instructor), notify the instructor by email as soon as possible ( $\geq 2$  weeks beforehand) to discuss possible accomadations. Except under the scenario of health/family emergency or pre-excused absence, NO MAKE-UP WORK FOR JC PRESENTATIONS OR FOR JC PARTICIPATION WILL BE ACCEPTED.

**Participation:** The overall participation grade will be based on measures of engagement, including preparation for and participation in class discussions. Participation will be assessed over the course of the term on an informal 3-point scale: no credit (0) = rarely attends class in real time, 1 = frequently absent from class, 2 = regularly attends class, 3 = regularly attends class and demonstrates intellectual engagement (e.g., through asking/answering questions in-class, through active participation on the class discussion board, or through one-on-one meetings with the professor to dicuss course topics). Participation during Weeks 14-15 during JC Presentations is mandatory, and the participation grade will be weighted to reflect whether a student asks/answers during each JC presentation.

**Final Exam:** A cumulative Final Exam will be administered during the scheduled final exam slot for the course. It will be the equivalent of a “super-quiz” that encompasses major topics tested on the three prior quizzes. Structure-wise, it will consist solely of short-answer and short-essay questions to test “big picture comprehension”; it will not contain any true-false/multiple-choice questions on “definitions” or memorized facts. SORRY, NO MAKE-UPS OR LATE TURNS CAN BE ACCEPTED – PLAN ACCORDINGLY!

### **Assignment Submission Policy**

**Submission guidelines:** For all written/at-home assignments (e.g., quizzes, JC presentation slides), a single file should be uploaded to the assignment link on the Bb or D2L site by the due date and time. No late turn-ins will be accepted – plan accordingly. Within 24 hours following an in-class JC presentation, the presenting student(s) should submit an electronic copy of their presentation (e.g., PDF of slides) to the JC presentation assignment file upload on Bb/D2L; it is encouraged that JC presenters explicitly “write-out” the questions that they formulate for in-class discussion on these slides.

**Late Policy for Quizzes and Assignments:** Late assignments will only be accepted in cases of extremely extenuating circumstances (e.g., family or health emergency); under non-emergency situations, there will be no make-ups for missed quizzes or assignments. Planned absences (e.g., sports, conference travel, interviews, and other non-emergency situations, etc) must be communicated to the professor at least two weeks in advance in order to arrange for make-up work, at the discretion of the instructor. Otherwise, no grade or feedback will be provided on assignments submitted late.

### **Assessment and Grading Policies**

**Grading Timeline:** Quiz grades are provided within two weeks of their completion. Journal Club Presentations will be graded after all students have presented; and participation will involve cumulative assessment throughout the term to generate a final participation score. *Students are encouraged to discuss their performance and approximate grade at any point during the semester with the instructor during office hours or by individual appointment.*

**Regrade Policy:** All regrading requests are due within one week of their return. The requester must email Prof. Treweek about this regrade, providing a clear explanation for the regrade and attaching the original graded assignment.

**Grading Breakdown:** (assignment-specific rubrics will accompany individual assignment instructions)

Assessment Tool (assignments)	% of Grade
Quizzes (3)	45
Journal Article Presentation	25
In-class work (JC participation)	10
Final Exam	20
<b>TOTAL</b>	100

**Grading Scale:** Final letter grades are not assigned based on absolute percentage values, but they are curved to generate a reasonable grade distribution (e.g., Z-score, with mean and standard deviation of approximately  $88 \pm 12$ ). Students can expect their final grades to loosely align with the following scale:

A	95-100
A-	90-94
B+	87-89
B	83-86
B-	80-82
C+	77-79
C	73-76
C-	70-72
D+	67-69
D	63-66
D-	60-62
F	59 and below

### Additional Policies

**Technology Policy:** During class, devices should only be used to participate in activities guided by the instructor or for note-taking. Use of devices for other purposes (email, web-surfing, social media, A/V-recording) is not permitted, wherein any non-academic use of such devices that distracts the instructor or students will result in no credit for in-class work for the day. Photographing or audio/video-recording of lecture material and/or slides is strictly prohibited, as is uploading course content to third-party sites for viewing and/or distribution.

**Communication Policy:** To promote independence and critical thinking, students are encouraged to work through the following process for obtaining answers to questions on course content and policy *before contacting the instructor*. (1) consult the course syllabus and course policies. If you do not find the answer you need, (2) consult a classmate directly or through D2L/Bb "Discussion" boards. If you are still not satisfied with the answer, (3) review recent lecture slides and announcements posted on D2L/Bb for class updates, (4) email/ask your TA (if applicable), (5) ask the instructor at office hours. Finally, after you have exhausted these methods, (6) email the instructor. In your email, please indicate the steps you have undertaken to seek the answer. Assuming that you have followed the aforementioned criteria (steps 1-5), your question will be answered within 48 hours between 9am-5pm, but response may be delayed on the weekend or holidays. Please use USC email for all correspondence with the section TA and instructor, and list the course ID (and section, where applicable) in the subject line. The instructor does not respond to questions pertaining to assignments during the 24 hours before an assignment due date. Emails that require a long response (at the discretion of the instructor) will not be answered over email. Instead, the student will be directed to office hours.

**Office Hours:** *Students are strongly encouraged to take advantage of office hours.* Herein, a preset time and location for office hours (OH) will be identified at the beginning of second session of the class (after compiling student input

on timing). Given the ongoing COVID-19 situation in LA county, OH will likely be held in a hybrid fashion, both online via Zoom (meeting ID and password will be provided by email) and in-person by advance request.

For Zoom OH or for scheduling a meeting outside of normal office hours, students are to email [jtweek@usc.edu](mailto:jtweek@usc.edu) at least 24-hr in advance to request a 10-min, 20-min, 30-min, or 60-min time block on a given day. Professor Treweek will then give each student a specific time to log-in to the Zoom meeting (or to arrive at her office). This will ensure that no students are caught waiting indefinitely in the Zoom waiting room for "admission" into weekly OH, and it allows all students to have privacy during OH for discussing a personal matter/sensitive issue/grades during OH. To reiterate, Professor Treweek is happy to meet outside of normal OH, however she can only accommodate requests if they are made > 24-hour in advance.

**Attendance Policy:** When a class session includes active student participation (e.g., student journal club presentation), attendance for class is mandatory and will only be excused in case of an emergency, at the discretion of the instructor. For absence due to non-emergency situations, the student must notify the instructor at least 2 weeks in advance, and appropriate make-up work will be arranged (at the discretion of the instructor).

**Policies on teamwork:** Collaboration is not only permitted but it is also highly encouraged when students are completing reading assignments and JC presentations. This includes the discussion of concepts, exchange of information, and soliciting feedback. Depending on course enrollment, JC presentations may be completed in groups of 1-3 students. However, each student is responsible for contributing to and for fully understanding the work product that their group submits. This class has a no-tolerance policy on academic integrity violations – direct copying of a fellow students' work, transcribing or "paraphrasing" online/published resources without proper attribution, misrepresenting one's own intellectual contribution on an assignment, and/or corroborating on quizzes are all forms of cheating. Review USC's Integrity Policies (see below, and <http://www.usc.edu/student-affairs/SJACS/docs/AcademicIntegrityOverview.pdf> and <http://www.usc.edu/student-affairs/SJACS/docs/GradIntegrity.pdf>), as they will be strictly enforced. Violations of this policy will result in an automatic F in the class and filing of an academic misconduct report to the Office of Student Conduct.

## Course Schedule (Tentative)

		Topics/Daily Activities	Deliverables
<b>Week 1</b>	11-Jan	Review of course plan and policies; Overview of pandemic viruses and introduction to virology	
<b>Module 1: Viral Immunology</b>			
<b>Week 2</b>	18-Jan	What is a virus? Virus genetics and “life cycle”	
<b>Week 3</b>	25-Jan	NO Class – Treweek at conference Lecture video: Chronology of viral infection and the host (human) immune response	
<b>Week 4</b>	1-Feb	Structure-function of adaptive immunity, part 1: B cells, part 2: T cells	
<b>Week 5</b>	8-Feb	Development of immunity vs virus immune evasion strategies	
<b>Week 6</b>	15-Feb	Experimental methods for assaying host-virus and host-vector interactions with respect to immunity and immunopathology	<b>Quiz 1</b>
<b>Module 2: Viral Vector Engineering</b>			
<b>Week 7</b>	22-Feb	Quiz & Module 1 Review; Introduction to viral vector engineering	
<b>Week 8</b>	1-Mar	Viral Vector Engineering: AAV production I	
<b>Week 9</b>	8-Mar	Viral Vector Engineering: AAV purification II	<b>Quiz 2</b>
<b>Spring Recess</b>	15-Mar	<i>No class</i>	
<b>Module 3: Engineering Viruses and Engineering Immunity</b>			
<b>Week 10</b>	22-Mar	Applications of Viruses: Engineering Novel Viral Vectors	
<b>Week 11</b>	29-Mar	History of Vaccination and Vaccine Platforms	
<b>Week 12</b>	5-April	Immunotherapeutic platforms for attenuating virus infection/replication and treating disease pathology	<b>Quiz 3</b>
<b>Module 4: Biomedical Applications of Viral Vectors</b>			
<b>Week 13</b>	12-Aprt	“Next generation” Viral Vectors and Engineering Approaches	
<b>Week 14</b>	19-Apr	Journal Club presentations #1-3	JC presentations
<b>Week 15</b>	26-Apr	Journal Club presentations #4-6	JC presentations
<b>Finals Week</b>		Final Exam	

## Statement on Academic Conduct and Support Systems

### Academic Conduct:

Plagiarism – presenting someone else’s ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in SCampus in Part B, Section 11, “Behavior Violating University Standards” [policy.usc.edu/scampus-part-b](https://policy.usc.edu/scampus-part-b). Other forms of academic dishonesty are equally unacceptable. See additional information in SCampus and university policies on scientific misconduct, [policy.usc.edu/scientific-misconduct](https://policy.usc.edu/scientific-misconduct).

### Support Systems:

*Counseling and Mental Health - (213) 740-9355 – 24/7 on call*

[studenthealth.usc.edu/counseling](https://studenthealth.usc.edu/counseling)

Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

*National Suicide Prevention Lifeline - 1 (800) 273-8255 – 24/7 on call*

[suicidepreventionlifeline.org](https://suicidepreventionlifeline.org)

Free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week.

*Relationship and Sexual Violence Prevention and Services (RSVP) - (213) 740-9355(WELL), press “0” after hours – 24/7 on call*

[studenthealth.usc.edu/sexual-assault](https://studenthealth.usc.edu/sexual-assault)

Free and confidential therapy services, workshops, and training for situations related to gender-based harm.

*Office of Equity and Diversity (OED)- (213) 740-5086 | Title IX – (213) 821-8298*

[equity.usc.edu](https://equity.usc.edu), [titleix.usc.edu](https://titleix.usc.edu)

Information about how to get help or help someone affected by harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants. The university prohibits discrimination or harassment based on the following *protected characteristics*: race, color, national origin, ancestry, religion, sex, gender, gender identity, gender expression, sexual orientation, age, physical disability, medical condition, mental disability, marital status, pregnancy, veteran status, genetic information, and any other characteristic which may be specified in applicable laws and governmental regulations. The university also prohibits sexual assault, non-consensual sexual contact, sexual misconduct, intimate partner violence, stalking, malicious dissuasion, retaliation, and violation of interim measures.

*Reporting Incidents of Bias or Harassment - (213) 740-5086 or (213) 821-8298*

[usc-advocate.symplicity.com/care\\_report](https://usc-advocate.symplicity.com/care_report)

Avenue to report incidents of bias, hate crimes, and microaggressions to the Office of Equity and Diversity | Title IX for appropriate investigation, supportive measures, and response.

*The Office of Disability Services and Programs - (213) 740-0776*

[dsp.usc.edu](https://dsp.usc.edu)

Support and accommodations for students with disabilities. Services include assistance in providing readers/notetakers/interpreters, special accommodations for test taking needs, assistance with architectural barriers, assistive technology, and support for individual needs.

*USC Support and Advocacy - (213) 821-4710*

[uscса.usc.edu](https://uscса.usc.edu)

Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.



*Diversity at USC - (213) 740-2101*

[diversity.usc.edu](https://diversity.usc.edu)

Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

*USC Emergency - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call*

[dps.usc.edu](https://dps.usc.edu), [emergency.usc.edu](https://emergency.usc.edu)

Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

*USC Department of Public Safety - UPC: (213) 740-6000, HSC: (323) 442-120 – 24/7 on call*

[dps.usc.edu](https://dps.usc.edu)

Non-emergency assistance or information.