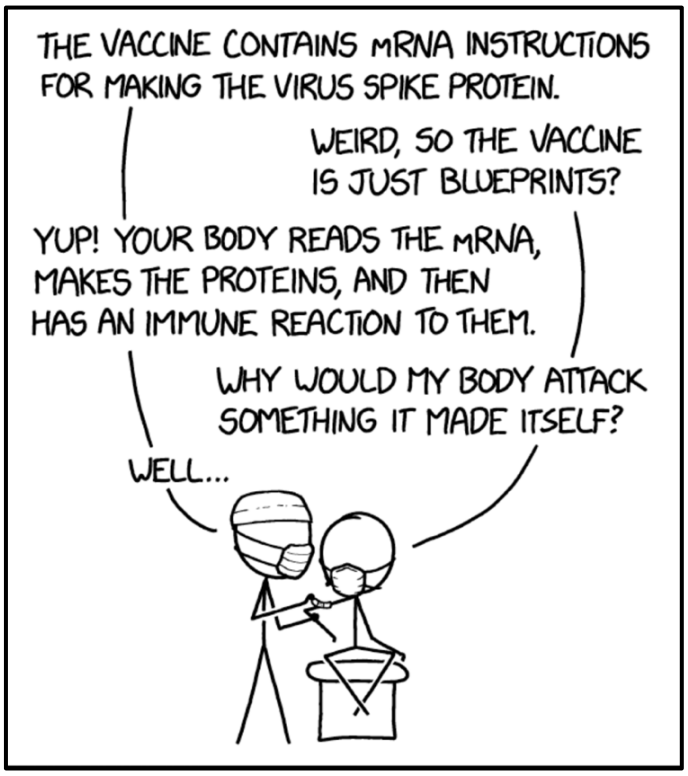
Please refer to the USC Center for Excellence in Teaching for current best practices in syllabus and course design. This document is intended to be a customizable template that primarily includes the technical elements required for the Curriculum Office to forward your proposal to the UCOC.

USC University of Southern California

**Viral immunology and Gene Therapy BME 499**

Units: 2
Term - Lecture Day - Time/Location: Spring 2022 - TBA

**Instructor: Jennifer Treweek**
Office: DRB 172, Zoom
Office Hours: TBA (schedule in advance for Zoom meeting time), or by appointment
Contact Info: jtreweek@usc.edu, (213) 821 - 3478 (no voicemail)




## Course Description

From COVID-19 to the CRISPR Nobel – reimagining viruses in the age of immune-engineering and viral-vector-based gene transfer.

## Technological Proficiency and Required Hardware

If we return to remote instruction, students will be required to use an internet-enabled device with browser capabilities, such as a laptop or tablet.

The course will be delivered in-person (or over Zoom upon any pandemic-related mandate), with the occasional use of supplemental online lectures (posted on Bb as homework) so as to allow time for in-class group discussion, etc. Bb will be used for written assignment submission.

## Grading Breakdown – subject to change

Grades will be recorded in Bb and updated weekly after assignment due dates; delays may occur following late turn-ins. JC presentations will be graded after *all* students/groups have presented; students are invited to ask the professor for immediate informal feedback following in-class presentations.

| Assignment | % of Grade |
|---|---|
| Quizzes (10% each, in-class and/or take-home) | 60 |
| Journal Article Presentation (once per student or student group) | 20 |
| In-class participation in JC discussion | 5 |
| Final Exam | 15 |
| **Total** | **100** |

**Course Schedule: Topics and Reading**

An overview of topics to be covered in each lecture (Tues 8-10am) and background reading to be completed for that week's lecture or assignments.

**Syllabus Abbreviations**

| | |
|---|---|
| L | Lecture topic for the week |
| B | Background textbook reading to support that week's lecture material or facilitate completion of assignments (JC presentation and discussion, quizzes) |
| J | Journal article reading assignments, either to support lecture material, or to be discussed directly in-class or in JC presentations |
| JC# | JC presentations by students (1-2 ppl/group); 30-40 minute presentation, including Q&A and discussion |

Students should read the assigned materials (i.e., "B", "JC", as listed on the Bb syllabus) before each class meeting so that they are prepared to take productive notes during lecture and actively participate during in-class discussion.

- Additional background reading and resources will be uploaded to the course syllabus and/or Bb discussion board as we progress through the course; likewise, some readings may be postponed or canceled based on lecture pace and student comprehension. Thus, the current syllabus does not provide an exhaustive list of all reading materials, but instead highlights what we will try to cover in terms of important textbook chapters and mandatory JC articles. *You should check the course website (in particular, the Bb announcement/discussion board) regularly to verify weekly content.*

- To reiterate, because the pacing of JC presentations and in-class discussion can be variable, this syllabus is subject to change. I will refine background reading assignments as the course progresses based on what we cover in-class. *Please check the syllabus regularly.*

- Occasionally, I will list textbook chapters alongside assigned JC articles – these chapters are to be used as a point-of-reference when reading JC articles. They are not intended to be read from start-to-finish.

**Course Resources and Important Notes**

Although the course will not be taught chapter-by-chapter from a single textbook, students will be assigned peer-reviewed journal articles as well as background reading from:

- *Principles of Virology* (4th or 5th Ed.) by Jane Flint, Vincent R. Racaniello, Glenn F. Rall, et al. (4th Ed. available electronically through USC library)

Background reading (B) from this textbook (PoV = Principles of Virology) is intended to enhance your understanding of the day's lecture material, assigned journal articles, and JC discussion. *You are not expected to memorize every detail* of an assigned book chapter or journal article, but to grasp the major ideas and broader mechanisms of how viruses work and of how our body/immune system reacts to viral infection, vaccine administration, and the delivery of gene therapies.

I will try to mention which chapter "sub-sections" to skip… generally, you can ignore anything on "oncolytic viruses". Focus on subsections that are more generic to virology, or that are specific to viruses that we explicitly cover (e.g., RNA viruses, viruses relevant to engineering viral vectors – for list, see PoV2 Ch9: Gene Therapy).

*Note bene: For students with a weak background in molecular and cell biology and biochemistry, please use the following textbook for background reading of key principles (e.g., the structure and function of major cellular organelles, the mechanisms of DNA replication and of gene expression – transcription, translation, etc.):*

- *Molecular Biology of the Cell,* by Bruce Alberts et al. (4th Ed. available electronically through USC library and on NCBI)

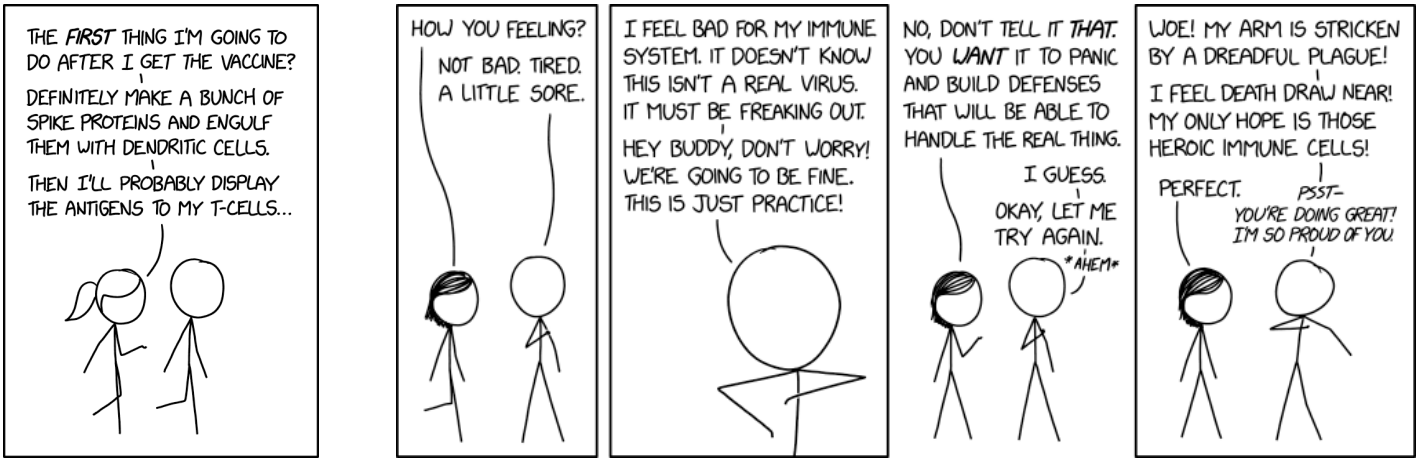
| | Topic and Readings | Deliverable |
|---|---|---|
| **Week 1** 10-Jan | L: Introduction to course plan and policies; Overview of the COVID-19 pandemic; What is a virus and how do we study them? | |
| | B: verify that you can access **PoV** - *Principles of Virology* (4th or 5th Ed.) by Jane Flint, Vincent R. Racaniello, Glenn F. Rall, et al. (4th Ed. available electronically through USC library);<br>B: some lecture figures taken from PoV1 Ch2 | |
| | JC: review Course Info, Course Syllabus, and list of JC presentation articles | |
| **Module 1:** Viral Immunology | | |
| **Week 2** 17-Jan | L: Introduction to Virology: viruses associated with past pandemics (PoV1 Ch1), traits of respiratory viruses, and the virus life cycle | Email instructor re. JC group: individual or 2-ppl! |
| | B: PoV1 Ch2 (infectious cycle), Ch3 (Genomes & Genetics);<br>B: quickly skim PoV2 Ch1 (History and Epidemiology), Ch11 (Emergence) | |
| | J: "The proximal origin of SARS-CoV-2" - https://www.nature.com/articles/s41591-020-0820-9, see PoV2 – Ch11 (Emergence)<br>O: A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270–273. https://doi.org/10.1038/s41586-020-2012-7 | |
| **Week 3** 24-Jan | L: Part 1 – Infection basics, Part 2 - Structure-function of the human immune system | Quiz 1* |
| | B: PoV1 – Ch5 (Attachment and Entry), Ch6 (RNA viruses); PoV2 – (Ch1), Ch2 – Barriers to infection | |
| | JC: SARS- CoV-2 review - https://doi.org/10.1038/s41579-020-00468-6 | |
| **Week 4** 31-Jan | L: Viral Immunology: Parts 1-2, pathogenesis and transmission; Part 3, host immune response | Quiz 2 |
| | B, Part 1-2: PoV2, Ch2 – Barriers to Infection<br>B, Part 3: PoV2, Ch3 - Innate Immunity, Ch4 - Adaptive Immunity **these are important chapters** | |
| | JC: (for both articles, just review abstract, intro, discussion) Longitudinal analyses reveal immunological misfiring in severe COVID-19. Nature 584, 463–469 (2020). https://doi.org/10.1038/s41586-020-2588-y;<br>A critical role for the sphingosine analog AAL-R in dampening the cytokine response during influenza virus infection, PNAS 106, 1560-1565 (2009). www.pnas.org/cgi/doi/10.1073/pnas.0812689106 | |
| **Week 5** 07-Feb | L: Development of immunity/immunopathology, virus immune evasion strategies<br>JC #1: SARS-CoV-2 Disrupts Splicing, Translation, and Protein Trafficking to Suppress Host Defenses, https://doi.org/10.1016/j.cell.2020.10.004 | JC #1 |
| | B: review RNA virus and retrovirus genome replication for JC #1<br>PoV2 Ch5 (Mechanisms of Pathogenesis) – Box 5.1-5, 5.9; Fig 5.1, 5.3, 5.5; skim "Persistent Infections" intro & "Latent Infections" intro paragraphs; skim: "Viral Virulence"; PoV2 Ch6 Box 6.9 (Transformation by remote control?); skim/flip through Ch10 (Virus Evolution): skip "The Origins of Viruses" and "Lessons from Paleovirology"; Ch11 (Emergence) **Fig 11.3, Box 11.2 | |
| | J: Commentary on current "mutation", see PoV2 – Ch10 (virus evolution) | |
| **Module 2:** TETRIS – *Test*, trace, isolate | | |
| **Week 6** 14-Feb | L: Overview of diagnostic tests and devices to detect viral infection or disease. | Quiz 3 |
| | B: review PoV2 Ch1 (Infections of Populations: History and Epidemology), Ch2 (Barriers to infection);<br>B: PoV2 Ch4: Box 4.10, section "The Humoral (Antibody) Response, Immunological Memory<br>B: PoV2 Ch5: Intro, Animal Models of Diesease, Patterns of Infection (start through Acute Infection, especially **Box 5.5, mathematical methods**), Viral Virulence, Pathogenesis, Perspectives | |
| | J: (articles discussed in lecture: Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. DOI: 10.1016/j.Cell.2020.05.015. Cross-reactive memory T cells and herd immunity to SARS-CoV-2. DOI: 10.1038/s41577-020-00460-4) | |
| **Week 7** 21-Feb | L: Experimental methods for assaying host-virus interactions with respect to adaptive immunity;<br>Overview of the FDA approval process for drugs, biologics, and diagnostic tests to treat or detect disease<br>JC #2: SARS-CoV-2 RapidPlex: A Graphene-Based Multiplexed Telemedicine Platform for Rapid and Low-Cost COVID-19 Diagnosis and Monitoring. https://doi.org/10.1016/j.matt.2020.09.027 | JC #2 |
| | B: PoV2 Ch4: Box 4.6-Measuring the anti-viral cellular immune response, Figure 4.4-4.6; PoV2 Ch9: Fig 9.1-9.2, 9.8, sections: 'Introduction' through 'The Difference between "R" and "D"', Boxes 9.3, 9.5-9.6)<br>B: Janeway's Immunobiology Methods & T-cell Immunity (Bb 'Content' folder) | |
| | J: Antigen-Specific Adaptive Immunity to SARS-CoV-2 in Acute COVID-19 and Associations with Age and Disease Severity. Cell (2020). DOI: 10.1016/j.cell.2020.09.038) | |
| **Week 8** 28-Feb | L: Overview of the FDA approval process during the pandemic: where do the CDC and HHS fit in?<br>JC #3: CRISPR–Cas12-based detection of SARS-CoV-2. https://doi.org/10.1038/s41587-020-0513-4 | JC #3 |
| | B: Color EUA (saved in Bb 'JC Topic-2: Detection' folder) | |

| | Topic and Readings | Deliverable |
|---|---|---|
| | J: (refer to the following articles for methods on T-cell profiling if you are still confused after Week 6-7 lectures: Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. Science 370, 89-94 (2020). DOI: 10.1126/science.abd3871; Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science (2021). DOI: 10.1126/science.abf4063) | |
| **Week 9** 07-Mar | L: Pharmacotherapies and other approaches for treating pathogenesis, disease pathology | Quiz 4 |
| | B: PoV1 Ch6: review 'Mechanisms of RNA Synthesis' section to appreciate how Inhibitors of viral nucleic acid synthesis work; PoV1 Ch12: sections 'Introduction' and 'Assembly in the Nucleus', Fig 12.1; PoV2 Ch9: Fig 9.1-2, 9.10-11, 9.15, sections: 'Approved Inhibitors of Viral Nucleic Acid Synthesis' and 'Expanding Target Options for Antiviral Drug Development', Boxes 9.2-9.3, 9.5-9.7<br>B: (for quiz, review PoV1 Ch2 (i.e., boxes on experimental methods) and PoV2 Ch4 and PoV2 Ch9 (see Week 7 assignments); for lecture, review PoV2 Ch9, Boxes 9.2-9.4, 9.6, Figs. 9.2, 9.8) | |
| | J: The Strange Tale of Remdesivir and a Black-Market Cat Drug - The Atlantic (Bb Content folder)<br>J: The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. https://doi.org/10.1016/j.antiviral.2020.104787 (and in Bb Content folder) | |
| **Mar 13-20: Spring Recess** | | |
| **Week 10** 21-Mar | L: Immunotherapies and other approaches for attenuating virus infection/replication/transmission and attenuating/blocking disease pathology<br>JC #4: Basis of mRNA vaccine design for Sars-CoV2 (MERS spike immobilization). DOI: 10.1073/pnas.1707304114 | JC #4 |
| | B: PoV2 – Ch8 (Vaccines); PoV2 Ch9 Boxes 9.3, 9.6<br>B: The Sputnik Vaccine (New Yorker article, JC Vaccine folder) | |
| | J: Vaccines against parasites: https://doi.org/10.1016/j.pt.2018.07.005 | |
| **Module 3:** Therapeutic strategies for addressing Sars-CoV-2 infection and Covid-19 disease | | |
| **Week 11** 28-Mar | L: Combatting virus transmission and vaccine design, part 1<br>JC #5: "Structure-guided multivalent nanobodies block SARS-CoV-2 infection and suppress mutational escape" (https://science.sciencemag.org/content/371/6530/eabe6230.long) | JC #5 |
| | B: PoV2 – Ch8 (Vaccines); PoV2 Ch 10 (Evolution): Boxes 10.1-10.5, Figs. 10.2, 10.4, sections 'Classic Theory of Host-Parasite Interactions', 'How Do Virus Populations Evolve?';<br>B: PoV1 Ch6: review section 'Origins of Diversity in RNA Virus Genomes', Box 6.8;<br>B: PoV1 Ch9: review section 'Origins of Diversity in DNA Virus Genomes' | |
| | J: SARS-CoV-2 vaccines in development, https://doi.org/10.1038/s41586-020-2798-3;<br>Unbiased Screens Show CD8+ T Cells of COVID-19 Patients Recognize Shared Epitopes in SARS-CoV-2 that Largely Reside outside the Spike Protein, https://doi.org/10.1016/j.immuni.2020.10.006 (just skim) | |
| **Week 12** 04-Apr | L: Combatting virus transmission and vaccine design, part 2<br>Optional: Preparing for the next pandemic: What is the role of WHO? How is Operation Warp Speed doing? Should the role of NIH, BARDA, etc be expanded? | Quiz 5 |
| | B: PoV2 Ch11: sections 'Encountering New Hosts: Ecological Parameters', 'Expanding Viral Niches: Some Well-Documented Examples', 'Notable Zoonoses', 'Host Range Can Be Expanded by Mutation, Recombination, or Reassortment', 'What's Next?' | |
| | J: tba | |
| **Module 4:** Gene Therapy (tentative schedule) | | |
| **Week 13** 11-Apr | L: Developing and applying engineered viral vectors to human gene therapy, part 1 | |
| | B: PoV2 5th ed., Ch9 (Therapeutic Viruses – pdf on Bb): skip "Oncolytic Animal Viruses", Ch12 (HIV): Prospects for Treatment and Prevention | |
| | J: (background) A multifunctional AAV–CRISPR–Cas9 and its host response. Nat Med (2016) doi:10.1038/nmeth.3993 | |
| **Week 14** 18-Apr | L: Developing and applying engineered viral vectors to human gene therapy, part 2<br>JC #7: an article on gene therapy mechanism and/or barriers *(see JC folder)* | JC #7 |
| | B: PoV, Ch3; PoV2 Ch8 – sections covering drug development/testing/pricing | |
| | J: tba | |
| **Week 15** 25-Apr | L: Student presentations (Quiz 6); New technologies for gene therapy (as time permits) | Quiz 6*<br>JC #8 (opt) |
| | B: n/a | |
| | JC *#8*: an article on FDA-approved gene therapy *(see JC folder)* | |
| **Exam** | **Exam - TBA** | |

| | Topic and Readings | Deliverable |
|---|---|---|
| ***Quiz 1 - Each student must choose a pathogenic virus and give a 5-minute presentation to describe: virus type/structure, its (proposed) host, its mechanism of infection, route of transmission, pathogenicity, etc**<br>***Quiz 6 – Each student must choose (a) a vaccine or (b) a gene therapy and give a 5-minute presentation to describe: (for a) vaccine type/structure, its virus target, the vaccine mechanism of action, and an overview of its use/efficacy/success; (for b) gene therapy and mode of delivery, the targeted gene(s) or disease phenotype, the role of the gene and how the gene therapy functions mechanistically, and an overview of its use/efficacy/success**<br><br>**For quiz 1 and 6, students must claim a virus and a vaccine/therapy by 8am-Monday on the week of the assigned quiz by posting their selection on the corresponding Bb discussion board topic for each quiz. No virus or vaccine duplications allowed.**<br><br>**Additional information about Quiz 1/6 is available on Bb in the Assignments folder – both within the individual quiz and associated grading rubric.** | | |

xkcd

**A WEBCOMIC OF ROMANCE, SARCASM, MATH, AND LANGUAGE.**



## Expanded Course Description

Motivated by the recent Covid-19 pandemic, this course, which is divided into four thematic modules, will provide a comprehensive introduction to viruses – both "how they can hurt you" and "how they can help you". In the first module, the basics of viral immunology (i.e., viruses associated with past pandemics, chronology of virus replication, and dynamics of the corresponding host immune response and development of immunity/immunopathology, virus immune evasion strategies) will be reviewed, particularly in relation to the respiratory viruses that launched pandemics of the 20$^{th}$ -21$^{st}$ centuries. In the second module, the course will shift to an in-depth analysis of the various technologies and devices used in detecting active virus infection, or in assaying the outcome of host-viral interactions (i.e., innate and adaptive immunity). Profiting from the USC BME department's current strength in medical device design and regulatory approval, this module will ask students to critically assess current Covid-19 medical device EUAs for in vitro diagnostics, and to brainstorm design modifications. The third module will cover therapeutic strategies for addressing the current Covid-19 pandemic – namely, approaches to treating Sars-CoV-2 infection (pharmacological agents and biologics, such as monoclonal antibodies and plasma therapy, for modulating the host immune system or counteracting virus replication); as well as preventative measures for combatting virus transmission (i.e., vaccine design). With respect to the latter, the design and use of viruses in vaccines, from live-attenuated or inactivated viruses, to virus-inspired vaccines such as virus-like particles and viral antigen-containing or antigen-encoding vaccines will be discussed in detail, incorporating real-time coverage of pre-prints and press releases on the status of Operation Warp Speed vaccine candidates, wherein results of Stage 2-3 clinical trials are anticipated to be released throughout winter 2020 – spring 2021. This discussion of virus-based vaccine platforms will serve as a springboard for the fourth module, which will broadly introduce students to "viruses that can help you" – focusing on the recent progress in developing and applying engineered viral vectors to human gene therapy.

## Learning Objectives

1) Describe the major concepts in viral immunology that are pertinent to virus infection, virus transmission, and virus-associated disease in humans
2) Describe key design considerations for the development and fabrication of novel assays and devices for the rapid, cost-effective, and scalable detection of viral infection in humans
3) Describe the different pharmacological and immunological strategies for combatting virus-host infection and replication, and for treating virus-associated immunopathology and disease in humans
4) Describe the biomedical/manufacturing/safety constraints for applying virus-based technologies to vaccine design and to human gene therapy.
5) Describe the regulatory affairs surrounding clinical testing and FDA approval of new devices/diagnostics and pharmacological agents/biologics
6) Describe, compare, and contrast the broader roles and responsibilities that: (1) government agencies, (2) international organizations, and (2) private industry should play in future pandemic preparedness and pandemic responses

## Course Outcomes

1) Apply course teachings (on the biophysical structures and immunological mechanisms that enable virus infection and host immunosurveillance, respectively) to brainstorming novel biomedical engineering approaches for the diagnosis and treatment of viral infection and virus-associated disease.
2) Interpret and critique data from research papers related to viral immunology, virus-associated disease and their corresponding immunopathology in humans, immunotherapeutic strategies, and vaccine design.
3) Apply teachings from other BME coursework (BME 302 Medical Electronics, BME 415/416 Development and Regulation of Medical Electronics) to the re-design of test platforms for viral infection – and learn how to evaluate device efficacy (specificity vs sensitivity) and clinical safety (with respect to applying for FDA approval and/or Emergency Use Authorization)
4) Collaborate with classmates on evaluating the ethical implications of population-wide vaccination mandates, gene therapy research, and pandemic preparedness funding; and debate how these endeavors should be regulated at the local, state and federal levels

**Recommended Preparation**: Previous coursework in one or more of the following is a plus: molecular or cell biology, immunology, biochemistry, genetics, or bioorganic chemistry. For Undergraduates, this could include coursework in biology, genetics, or biochemistry (e.g., BISC 220, BISC 325, or BISC 330, respectively).

## 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 or tablet. The course will be delivered over Zoom, with the occasional use of breakout rooms for group work and/or small-group discussion in-class. Bb or D2L will be used for in-class quizzes, written assignment submission, and group work.

## 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 as well as background reading from:

- Principles of Virology ($4^{th}$ or $5^{th}$ Ed.) by Jane Flint, Vincent R. Racaniello, Glenn F. Rall, *et al.* ($4^{th}$ Ed. available electronically through USC library)
- Molecular Biology of the Cell, by Bruce Alberts *et al.* ($4^{th}$ Ed. available electronically through USC library and on NCBI)

Students should read the assigned materials (e.g., journal articles, excerpts of chapters from the aforementioned textbooks, 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 and Assessment of Assignments

**In-class Quizzes**

Throughout the semester, in-class quizzes (< 60-minute) will be assigned on Bb or 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.

**Journal Club (JC) Presentation**

Throughout the semester, each student group (1-3 students) will be responsible for leading a single journal article discussion during the semester. 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 no one claims a given JC assignment, a student will be randomly selected approximately 5 days prior to the scheduled presentation.

**In-Class Work and Participation**

Class time will often be used for in-class individual and group discussions. Thus, attendance for class is mandatory and will only be excused in case of an emergency, at the discretion of the instructor. If a student knows in advance that he/she/they will be absent on the day of a quiz or presentation for an important occasion or non-emergency situation (at the discretion of the instructor), notify the instructor by email as soon as possible (≥ 2 weeks beforehand). Except under the scenario of health/family emergency or pre-excused absence, NO MAKE-UP WORK/QUIZZES WILL BE ACCEPTED.

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 a 3-point scale: 0 = routinely absent from class, 1 = regularly attends class, 2 = regularly attends and participates in class.

**Final Exam**

A final exam in the style of a "super-quiz" will be administered during the scheduled final exam time period. SORRY, NO MAKE-UPS OR LATE TURN-INS WILL BE ACCEPTED – PLAN ACCORDINGLY!

## Assignment Submission Policy

**Submission guidelines**

For all written assignments, a single file (e.g., a slide deck in PDF format) should be uploaded to the assignment link on the Bb site by the due date and time. 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 on Bb; it is encouraged that JC presenters explicitly "write-out" the questions that they formulate for in-class discussion on these slides.

**Late Policy for Assignments**
Late assignments (e.g., quizzes, presentations, etc) will only be accepted in cases of extremely extenuating circumstances (e.g., family or health emergency); under non-emergency scenarios (e.g., sports, conference travel, interviews, etc.), permission should be obtained from the instructor 2 weeks before the deadline; any make-up work is assigned at the discretion of the instructor. Otherwise, a 25% reduction in maximum points possible will be subtracted for each day that the assignment is late, starting immediately after the assignment deadline.

## 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; students may 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 Scale**
Final letter grades are not assigned based on absolute percentage values, but they are curved to generate a reasonable grade distribution. 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 Bb "Discussion" boards. If you are still not satisfied with the answer, (3) review recent lecture slides and announcements posted on 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, including the course # in the subject line. In your email, please indicate the steps you have undertaken to seek the answer. *Only* if you have followed the aforementioned criteria (steps 1-5) will your question be answered by the instructor within 2 business days. The response may be delayed on holidays. Please use USC email for all correspondence with the section TA and instructor. 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**
For Treweek office hours (OH) during remote instruction, OH will be held in DRB 172 or on Zoom in a re-occurring Zoom meeting (meeting ID and password to be announced during the first week of class). Students are to email jtreweek@usc.edu *at least 24-hr in advance* to request a 10-min, 20-min, 30-min, or 60-min meeting time-block (either within or outside of OH). This will ensure that no students are caught waiting indefinitely in the Zoom waiting room or outside her office for weekly OH, and it allows all students to have privacy during OH for discussing a personal matter/sensitive issue or grades during OH. Professor Treweek is happy to meet outside of normal OH, again by > 24-hour advance appointment.

**Attendance Policy**
When a class session includes in-class work (e.g., quiz) or active student participation (e.g., student journal club presentation and discussion), 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 two students (or up to three students with permission of instructor). However, each student is responsible for contributing to and for fully understanding the work product that their group submits/presents.

Review the university Integrity Policies (links below); they will be strictly enforced. This class has a no-tolerance policy on academic integrity violations – copying fellow students' work, directly transcribing online/published resources, and corroborating on in-class quizzes or exam answers are all forms of cheating. Quizzes and the final exam, which will consist of short problems (multiple choice, true-false) and essay-style questions, will be closed-book/closed-technology. Plagiarism, cheating, or other forms of academic misconduct will result in a zero grade for the assignment and will be reported to USC's Office of Student Judicial Affairs and Community Standards

**Statement on Academic Conduct and Support Systems**

**Academic and Professional Conduct (Ostrow SPPEC):** Should there be any suspicion of academic, professional or ethical dishonesty, students are referred to the Ostrow Student Professional Performance Evaluation Committee (SPPEC). The review process can be found in the Code of Ethics and Behavioral Guidelines on the School intranet.

**Emergencies (Ostrow):** If an officially declared emergency makes travel to campus infeasible, USC Emergency Information http://emergency.usc.edu/will provide safety and other updates, including ways in which instruction will be continued by means of blackboard, teleconferencing, case library, intranet, email listserv, and other technology. In addition, the Herman Ostrow School of Dentistry provides the case library, intranet, email listserv, and other technologies specific to the school. Ostrow students should access the Ostrow School of Dentistry Intranet for additional specific information in the event of an emergency.

**In the Event of Technical Breakdowns (Ostrow):** Students may submit assignments to the instructor via e-mail by the posted due date. Remember to frequently back up your work, post assignments once completed, load files onto a digital drive, and keep a hard copy of papers/projects.

**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. Other forms of academic dishonesty are equally unacceptable. See additional information in SCampus and university policies on scientific misconduct, policy.usc.edu/scientific-misconduct.

**Support Systems:**

***Student Health Counseling Services - (213) 740-7711 – 24/7 on call***

engemannshc.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
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 Services (RSVP) - (213) 740-4900 – 24/7 on call***
engemannshc.usc.edu/rsvp
Free and confidential therapy services, workshops, and training for situations related to gender-based harm.

***Office of Equity and Diversity (OED) | Title IX - (213) 740-5086***
equity.usc.edu, titleix.usc.edu
Information about how to get help or help a survivor of 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.

***Bias Assessment Response and Support - (213) 740-2421***
studentaffairs.usc.edu/bias-assessment-response-support
Avenue to report incidents of bias, hate crimes, and microaggressions for appropriate investigation and response.

***The Office of Disability Services and Programs - (213) 740-0776***
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***
studentaffairs.usc.edu/ssa
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
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, 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
Non-emergency assistance or information.

**Sample JC Presentation Articles**

1. Special topics in Virology, with respect to major human pathogens (JC Presentation #1-2)
    - **SARS-CoV-2 RNA reverse-transcribed and integrated into the human genome. doi: https://doi.org/10.1101/2020.12.12.422516**
    - Antigenic shift/drift, constraints on viral evolution, virus fidelity vs variant diversity
        - Mutational Analysis of Measles Virus Suggests Constraints on Antigenic Variation of the Glycoproteins. Cell (2015) http://dx.doi.org/10.1016/j.celrep.2015.04.054
        - Escape from neutralizing antibodies by SARS-CoV-2 spike protein variants. eLife 2020;9:e61312. DOI: https://doi.org/10.7554/eLife.61312
        - **Articles by Jesse Bloom on antibody escape could fit in this topic, or in the vaccines/antibodies topics**. For example: A human coronavirus evolves antigenically to escape antibody immunity. bioRxiv preprint doi: https://doi.org/10.1101/2020.12.17.423313 or Complete Mapping of Mutations to the SARS-CoV-2 Spike Receptor-Binding Domain that Escape Antibody Recognition, https://doi.org/10.1016/j.chom.2020.11.007.

      *(greyed entries are "less-preferred" for JC)*
        - Mapping the Antigenic and Genetic Evolution of Influenza Virus. Science (2004) DOI: 10.1126/science.1097211
        - Antibody landscapes after influenza virus infection or vaccination (redundant with Bjorkman). Science (2014) DOI: 10.1126/science.1256427
        - Fidelity: A single mutation in poliovirus RNA-dependent RNA polymerase confers resistance to mutagenic nucleotide analogs via increased fidelity. PNAS (2003) www.pnas.org/cgi/doi/10.1073/pnas.1232294100
        - Quasispecies: Quasispecies diversity determines pathogenesis through cooperative interactions in a viral population. Nature (2006) doi:10.1038/nature04388
    - Any paper providing an interesting/rigorous clinical assessment or immunological mechanism of SARS-CoV2 infection and/or COVID-19 pathology, such as:
        - SARS-CoV-2 Disrupts Splicing, Translation, and Protein Trafficking to Suppress Host Defenses. Cell (2020) https://doi.org/10.1016/j.cell.2020.10.004
        - Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science (2021) DOI: 10.1126/science.abf4063
        - Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. Nat Neurosci (2020). https://doi.org/10.1038/s41593-020-00758-5
2. Detection (JC Presentation #2-3)
    - Sherlock:
        - Clinical validation of a Cas13-based assay for the detection of SARS-CoV-2 RNA. Nat Biomed Eng (2020) https://doi.org/10.1038/s41551-020-00603-x ***or*** CRISPR–Cas12-based detection of SARS-CoV-2. Nat Biotech (2020) https://doi.org/10.1038/s41587-020-0513-4
        - Nucleic acid detection with CRISPR-Cas13a/C2c2. Science 356, 438–442 (2017)
        - Field-deployable viral diagnostics using CRISPR-Cas13. Science 360, 444–448 (2018) DOI: 10.1126/science.aas8836.
    - Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. Cell 181, 1489-1501 (2020) https://doi.org/10.1016/j.cell.2020.05.015. (follow-up paper: 10.1126/science.abd3871)
    - A serological assay to detect SARS-CoV-2 seroconversion in humans: Nat Med 26(7):1033-1036 (2020). doi: 10.1038/s41591-020-0913-5.
    - SARS-CoV-2 RapidPlex: A Graphene-Based Multiplexed Telemedicine Platform for Rapid and Low-Cost COVID-19 Diagnosis and Monitoring: https://doi.org/10.1016/j.matt.2020.09.027
    - Shotgun Transcriptome and Isothermal Profiling of SARS-CoV-2 Infection Reveals Unique Host Responses, Viral Diversification, and Drug Interactions - https://doi.org/10.1101/2020.04.20.048066
    - Any paper on devices or engineered systems to study the immune system, such as:
        - Acute Lymph Node Slices Are a Functional Model System to Study Immunity Ex Vivo: https://dx.doi.org/10.1021/acsptsci.0c00143
3. Vaccine Design (JC Presentation #4-5)

- Basis of mRNA vaccine design for Sars-CoV2 (MERS spike immobilization): https://doi.org/10.1073/pnas.1707304114; corresponding study for nCoV spike: DOI: 10.1126/science.abb2507
- Provide class with overview of Moderna's clinical study protocol and results: https://www.modernatx.com/sites/default/files/mRNA-1273-P301-Protocol.pdf ***or*** Provide class with overview of BioNTech/Pfizer's clinical study protocol and results: Phase 1/2 - https://doi.org/10.1038/s41586-020-2639-4, Phase 3 - https://www.nejm.org/doi/full/10.1056/NEJMoa2034577
- Phage escape libraries for checkmate analysis: https://doi.org/10.1073/pnas.0705362104

4. Antibodies and Passive Immunization (JC Presentation #6-7)
    - Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity. Science (2020) DOI:10.1126/science.abc8378 (2020)
    - SARS-CoV-2 neutralizing antibody structures inform therapeutic strategies. Nature (2020) https://doi.org/10.1038/s41586-020-2852-1
    - Structure-guided multivalent nanobodies block SARS-CoV-2 infection and suppress mutational escape: Science (2021)DOI: 10.1126/science.abe6230
    - Antibody-enhanced disease (also – vaccine-associated respiratory distress/disease)
        - Anti-spike IgG causes severe acute lung injury by skewing macrophage responses during acute SARS-CoV infection. DOI: 10.1172/jci.insight.123158
        - Immunodominant SARS Coronavirus Epitopes in Humans Elicited both Enhancing and Neutralizing Effects on Infection in Non-human Primates. DOI: 10.1021/acsinfecdis.6b00006
        - Antibody-dependent enhancement of influenza disease promoted by increase in hemagglutinin stem flexibility and virus fusion kinetics. www.pnas.org/cgi/doi/10.1073/pnas.1821317116
5. Viral Vectors and Gene Therapy (JC Presentation #7-8)
    - Engineered AAVs for efficient noninvasive gene delivery to the central and peripheral nervous systems. Nat Neuroscie (2017) DOI: 10.1038/nn.4593 ***or*** Multiplexed Cre-dependent selection yields systemic AAVs for targeting distinct brain cell types. Nat Methods 17, 541–550 (2020) https://doi.org/10.1038/s41592-020-0799-7
    - An article of your choosing on a virus, engineered vector, or virus-like particle being used to deliver a gene therapy
    - A long-term study of AAV gene therapy in dogs with hemophilia A identifies clonal expansions of transduced liver cells. Nature Biotech (2021) https://doi.org/10.1038/s41587-020-0741-7
    - Gene therapy for muscular dystrophy and for spinal muscular atrophy
        - Long-term evaluation of AAV-CRISPR genome editing for Duchenne muscular dystrophy
        - Postnatal genome editing partially restores dystrophin expression in a mouse model of muscular dystrophy
        - Zolgensma for SMA: DOI: 10.1056/NEJMoa1706198; https://www.novartis.com/news/media-releases/zolgensma-data-shows-rapid-significant-clinically-meaningful-benefit-sma-including-prolonged-event-free-survival-motor-milestone-achievement-and-durability-now; https://www.curesma.org/avexis-receives-fda-approval-of-zolgensma-a-gene-therapy-for-spinal-muscular-atrophy-for-patients-under-two-years-of-age/
    - AAV therapies
        - Safety and tolerability of gene therapy with an adeno-associated virus (AAV) borne GAD gene for Parkinson's disease- an open label, phase I trial
        - Dual AAV-mediated gene therapy restores hearing in a DFNB9 mouse model. www.pnas.org/cgi/doi/10.1073/pnas.1817537116
        - (Zolgensma for SMA) Single-Dose Gene-Replacement Therapy for Spinal Muscular Atrophy. NEJM (2017) DOI: 10.1056/NEJMoa1706198
    - Pre-existing adaptive immunity to Cas9 proteins
        - Identification of preexisting adaptive immunity to Cas9 proteins in humans. Nat Med (2019) https://doi.org/10.1038/s41591-018-0326-x
        - High prevalence of Streptococcus pyogenes Cas9-reactive T cells within the adult human population. Nat Med (2019) https://doi.org/10.1038/s41591-018-0204-6
6. An article of your own choosing!!!

| Abbreviations – to be cont'd | |
|---|---|
| AB (mAB, pAB) | Antibody (monoclonal, polyclonal) |
| APC | Antigen presenting cell |
| DC | Dendritic cell |
| RBD | Receptor Binding Domain |
| "CoV2" | SARS-CoV-2, i.e., severe acute respiratory syndrome coronavirus 2 |
| "SARS" | The original SARS-CoV, or SARS-CoV-1 |
| "MERS" | MERS-CoV, i.e., Middle East Respiratory Syndrome coronavirus |
| COVID-19 | Coronavirus disease 2019 |
| N501Y | An amino acid substitution in the SARS-CoV-2 spike protein RBD… in which the amino acid asparagine, at the 501 position, has been replaced by tyrosine. This substitution has been documented in several SARS-CoV-2 variants circulating in the UK and elsewhere. It is also present in the mouse-adapted SARS-CoV-2 recombinant virus developed in the Baric lab (https://doi.org/10.1038/s41586-020-2708-8) |
| $S_1/S_2$ and $S_2'$ | The two protease cleavage sites present in the SARS-CoV-2 S protein |
| VP | Virus particle |
| MOI | Multiplicity of infection |
| VLP | Virus-like particle |
| AAV | Adeno-associated virus |
| ELISA | enzyme-linked immunosorbent assay |
| PCR (qPCR) | Polymerase chain reaction (quantitative or real-time PCR) |
| RT-PCR | Reverse transcription polymerase chain reaction |
| PFU (per ul) | Plaque-forming units (often used as proxy measurement of # VPs in certain volume) |
| VG (per ul) | Viral genomes (often used in context of virus titer, as calculated via qPCR) |
| CTL | Cytotoxic T-lymphocyte |
| TLR | Toll-like receptor |
| flu | Influenza A,B virus |
| RdRp | RNA-dependent RNA polymerase |
| RdDp | RNA-dependent DNA polymerase (aka. reverse transcriptase) |