Sample syllabus

# BME 459L
# Introduction to Nanomedicine and Drug Delivery

**Units:** 4
**Spring 2021 – Monday, Wednesday – 2:00-3:20 PM**
**Lecture Location:** virtual

**Lab Location: BHE B8, Wednesday – 12:00-1:50 PM**

**Instructor: Eun Ji Chung**
**Office:** virtual
**Office Hours:** Wednesdays 3:30-4:30 PM by email request
**Contact Info:** eunchung@usc.edu (response within 48 hours)

**Teaching Assistant:** TBD
**Office:** virtual
**Office Hours:** TBD
**Contact Info:** TBD

**Prerequisite:** Chem 322A: Organic Chemistry
**Recommended Preparation:** BISC 220L: Cell Biology and Phyisology

***"The reward of a thing well done, is to have done it." Ralph Waldo Emerson***

## Course Description

This course provides a comprehensive introduction to drug delivery as well as nanoscale materials and its applications in medicine. Applications of nanoengineered materials, including nanotechnology-based drug delivery systems, nano-based imaging and diagnostics, and nanotechnology-based tissue engineering approaches will be explored. Host response to nanomaterials and nanotoxicology will also be discussed. Research methods in nanomedicine will also be emphasized (i.e. critical analysis of scientific literature, effective oral and written communication). The course is lecture and lab-based with quizzes, exams, labs, throughout the semester, and a final project due at the end of the semester. Students will also be assigned homework based on reading and analyzing primary literature articles, as well as preparation for labs and lab reports.

## Course Learning Objectives

1. Understand the principles and concepts of effective drug delivery systems and the state-of-the-art in terms of nanoengineered materials research for applications in medicine.
2. Be able to critically read, summarize, and analyze scientific literature in nanomedicine.
3. Apply knowledge of engineering and biology to think critically about and propose solutions for current applications in medicine based on understanding of nanoscience fundamentals.
4. Be able to clearly represent ideas in written reports and oral presentations.
5. Synthesize and characterize nanoparticles

a. Nanoparticle synthesis: lipid film formation, drug loading
b. Nanoparticle materials testing: zeta potential, dynamic light scattering, transmission electron microscopy
c. In vitro testing: cell culture, sterile technique, biocompatibility/MTT assays, Live/Dead fluorescence assay, fluorescent microscopy, plate reader measurements
d. In vivo testing (theory): calculating nanoparticle therapeutic effectiness via measuring tumor size, tumor cell, morphology/histology/immunohistochemistry; calculating pharmacokinetic properties like the half-life of nanoparticles
e. Use Image J and Excel to analyze in vitro and in vivo histological images and calculate statistical significance

**BME Program Outcomes**
Students who complete successfully the Biomedical Engineering Program should have acquired:

1. an ability to identify, formulate, and solve complex engineering problems by applying principles of engineering, science, and mathematics
2. an ability to apply engineering design to produce solutions that meet specified needs with consideration of public health, safety, and welfare, as well as global, cultural, social, environmental, and economic factors
3. an ability to communicate effectively with a range of audiences
4. an ability to recognize ethical and professional responsibilities in engineering situations and make informed judgments, which must consider the impact of engineering solutions in global, economic, environmental, and societal contexts
5. an ability to function effectively on a team whose members together provide leadership, create a collaborative and inclusive environment, establish goals, plan tasks, and meet objectives
6. an ability to develop and conduct appropriate experimentation, analyze and interpret data, and use engineering judgment to draw conclusions
7. an ability to acquire and apply new knowledge as needed, using appropriate learning strategies.

a) an ability to apply knowledge of mathematics, science, and engineering
b) an ability to design and conduct experiments, as well as to analyze and interpret data
c) an ability to design a system, component, or process to meet desired needs within realistic
constraints such as economic, environmental, social, political, ethical, health and safety, manufacturability, and sustainability
d) an ability to function on multidisciplinary teams
e) an ability to identify, formulate, and solve engineering problems
f) an understanding of professional and ethical responsibility
g) an ability to communicate effectively
h) the broad education necessary to understand the impact of engineering solutions in a global, economic, environmental, and societal context
i) a recognition of the need for, and an ability to engage in life-long learning
j) a knowledge of contemporary issues
k) an ability to use the techniques, skills, and modern engineering tools necessary for engineering practice

Relationship of Course Objectives to Program Outcomes:

| BME Student Outcomes → Course Objectives ↓ | a | b | c | d | e | f | g | h | i | j | k |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | X | | | | X | X | | | | X | |
| 2 | | X | | | X | | X | | | X | |
| 3 | X | X | X | X | X | | X | | | X | |
| 4 | X | X | | X | X | | X | | | X | |
| 5 | X | X | X | X | X | X | X | | | X | X |

| BME Student Outcomes → Course Objectives ↓ | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| 1 | X | | | X | | | |
| 2 | X | | X | X | | X | |
| 3 | X | X | X | X | X | X | X |
| 4 | X | X | X | X | X | X | X |
| 5 | X | X | X | X | X | X | X |

**Course Notes**
Lecture slides in .pdf format will be posted on Blackboard. Grades will be posted on Blackboard as assignments are completed and graded.

**Required Readings and Supplementary Materials**
Through lectures, critical reading of primary literature and the textbook, homework assignments, exams, class presentations and a collaborative project, students will learn how nanomedicine can be applied to address medical needs.

**Required Textbook:**
Nanoparticles for Bomedical Applications (Chung, Leon, Rinaldi), Elsevier, ISBN 9780128166628

Reading assignments will be posted on Blackboard. The timeline on which the material will be covered is provided below and is subject to change, at the instructor's discretion.

**Quizzes**
Six quizzes will be given at the beginning of class throughout the semester. Quizzes will be ~15 minutes and will test comprehension of the reading assignment and lecture materials, as noted on the syllabus. Only five quizzes will count towards each student's final grade.

**Journal Club Articles**

1. Cellular uptake mechanism and intracellular fate of hydrophobically modified glycol chitosan nanoparticles. Nam et al. Journal of Controlled Release 135: 259, 2009.
2. Spherical nucleic acid nanoparticle conjugates as an RNAi-based therapy for glioblastoma. Jensen et al. Science Translational Medicine 5(209): 209ra152, 2013. Victor and Brock

3. Therapeutic cell engineering with surface-conjugated synthetic nanoparticles. Stephan et al. Nature Medicine, 16(9), 1035. 2010. Lucia and Lexie
4. Erythrocyte membrane-camouflaged polymeric nanoparticles as a biomimetic delivery platform. Hu et al. PNAS 108(27): 10980, 2011. Nina and Jeong
5. RGD peptide conjugated liposomal drug delivery system for enhance therapeutic efficacy in treating bone metastasis from prostate cancer. Wang et al. Journal of Controlled Release, 196:222, 2014.
6. Exosome encased spherical nucleic acid gold nanoparticle conjugates as potent microRNA regulation agents. Small 10(1): 186-192, 2013. Sebastian and Natalie
7. A brain tumor molecular imaging strategy using a new triple-modality MRI-photoacoustic-Raman nanoparticle. Kircher et al. Nature Medicine, 18(5): 829, 2012. Sean and David
8. Enhanced survival with implantable scaffolds that capture metastatic breast cancer cells in vitro. Rao et al. Cancer Research, 76(18), 2016. Jason and Zixian
9. Multifunctional nanoparticles facilitate molecular targeting and miRNA delivery to inhibit atherosclerosis in ApoE-/- mice, ACS Nano, 9(9): 8885-8897, 2015. Yi and Mher
10. Correlating animal and human phase 1a/1b clnical data with CALAA-01, a targeted, polymer-based nanoparticle containing siRNA. Zuckerman et al. PNAS, 111(31):11449-11454, 2014.

Professor Chung will present journal articles as part of lectures. All journal club articles will be made available on Blackboard at the beginning of the semester. Students will write a summary and critique of the article as homework (1 page maximum). A printed hard copy of the write-up is due at the beginning of class on the date listed on the syllabus. Use Arial font, size 12, single spaced, 1" margins (10 points each).

• Summarize the article (4 points):
  - What is the knowledge gap the authors are addressing?
  - What is the hypothesis and/or objective?
  - Briefly, what did they do? (Methods)
  - What are the key results?
  - What are the important take-home messages, limitations, and applications? (Discussion)
• Critique the article (3 points):
  - One positive comment – what did you think was especially clever, innovative, elegant, etc.?
  - One negative comment – what was lacking, sloppy, misleading, etc.?
  - Do not critique small technical issues in the paper, such as formatting of figures. Instead critique the science
• Future directions (2 points):
  - One suggestion for future experiments based on their findings
  - Suggestions should be unique and innovative, not incremental
• Formatting/writing style (1 points):
  - Follow formatting instructions
  - Writing should be clear, understandable, and scientific

**Final Project: Mini-Review Paper**

Students will work in groups of 3-5 to formulate a mini-review paper that extends a lecture topic or journal club article. The proposed work should use concepts described in class. Examples of appropriate topics include: targeting moieties for a specific disease model, a specific nanoparticle type (or types) for an application of interest, or a nanoparticle characteristic (e.g., size, shape, charge, etc) and it's implications in targeting or clearance. Students are required to meet with the instructor prior to deciding on their topic/outline for the final project. A 3-page outline of your paper (not including sources) with a list of at least

30 sources of information should be included. Groups will present their paper during the last week of class and submit the written document during Finals Week. Presentations should be done in PowerPoint (rubric will be handed separately). Papers must be between 10-15 pages single spaced (12 point font) excluding references, figures, and tables. If you use figures and tables, they should appear after the text and bibliography in the order they are referred to in the text. Figures, tables, and other graphic elements obtained from other sources must be appropriately cited. Grading will be based upon clarity, comprehensive inclusion of technical content, adherence to the requested format, and grammar and presentation. An example mini-review will be provided in class.

Presentations should be approximately 15-20 minutes long and include background and signficance with respect to nanomedicine and drug delivery, methods and technology, examples and applications, and challenges and future directions. Slides sould be clear and concise with proper headings. All students must attend all presentations or will lose 50% of their final presentation grade. No labtops or phones should be in use during presentations.

Final papers must be sent as e-mail attachments in PDF form and delivered in printed form. Your written work may be electronically tested for plagiarized content. Do not duplicate another person's work: this will result in a failing grade and disciplinary action.

Exams will be focused on lecture material and reading assignments. Midterm exams will not be cumulative.

**Pre-lab Assignment**
Pre-lab assignments regarding the next week's lab will be given. Late homeworks will not be accepted.

**Lab Performance/Participation**
Students must do the lab exercise and activities to receive credit. Professor Chung or the lab TA will assess each student/group progress.

**Lab Report**
Lab reports will be due 1 week after the lab exercise. Late lab reports will be accepted, but 10% points will be subtracted off the grade for every 24 hour period that passes after the due date.

**Grading Breakdown**

| **Assignment** | **% of Grade** |
|---|---|
| Quizzes | 10% |
| Journal Club Write Up | 10% |
| Midterm Exams (2 x 15%) | 30% |
| Final Proposal | Total: 25%<br>*Breakdown:*<br>*5% Outline and Bibliography*<br>*10% Presentation*<br>*10% Written document* |
| Lab | Total: 25%<br>*Breakdown:* |

| | |
|---|---|
| | *5% Pre-labs*<br>*10% Lab performance*<br>*10% Lab report* |

**Assignment Submission Policy**
All journal articles are available online. Homeworks are due at the beginning of class on their due date (see syllabus for due dates). Homeworks are to be typed and printed.

**Additional Policies**
Late homeworks will be accepted, but 10% points will be subtracted off the homework grade for every 24 hour period that passes after the due date.

Questions about homework, exams, etc. should be asked at office hours. Prof. Chung will not regularly answer questions over email. Regrade requests for homeworks or exams are due within one week of the date they are returned. Students must type or neatly hand-write an explanation for their regrade request and submit it to Prof. Chung, stapled to the original assignment.

**Lecture Schedule**

| **Date** | **Topic** | **Journal Club (write ups due beginning of class), Reading Assignments** |
|---|---|---|
| Monday<br>Week 1 | Lecture 1: Introduction to and Concepts of Drug Delivery and Nanomedicine | |
| Wednesday<br>Week 1 | Lecture 2: Transport and Diffusion<br>Reading Scientific Literature<br>Journal Club 1 assigned | Chapter 1 |
| Monday<br>Week 2 | **Martin Luther King Day, No Class** | |
| Wednesday<br>Week 2 | Lecture 3: Mechanisms of Cellular Internalization | Journal Club 1 |
| Monday<br>Week 3 | **Quiz 1**<br>Lecture 4: Routes of Administration<br>Journal Club 2 assigned | Chapter 6 |
| Wednesday<br>Week 3 | **Lecture 5: Barriers to Drug Delivery** | Journal Club 2<br>Chapter 2 |
| Monday<br>Week 4 | **Quiz 2**<br>Lecture 6: Pharmacokinetics, Biodistribution, Clearance Mechanisms<br>Journal Club 3 assigned | Chapter 8 |
| Wednesday<br>Week 4 | Lecture 7: Controlled and Targeted Drug Delivery<br>Journal Club 4 assigned | Journal Club 3<br>Chapter 3 |
| Monday<br>Week 5 | **No Class** | |
| Wednesday<br>Week 5 | Review | Journal Club 4 |
| Monday<br>Week 6 | **Midterm 1** | |

| | | |
|---|---|---|
| Wednesday Week 6 | Lecture 8: Nucleic Acid Delivery | |
| Monday Week 7 | **President's Day, No Class** | |
| Wednesday Week 7 | Lecture 9: Classes of Nanomaterials: Biological | |
| Monday Week 8 | **Quiz 3**<br>Lecture 10: Peptide and Protein Based Delivery<br>Journal Club 5 assigned | |
| Wednesday Week 8 | Lecture 11: Classes of Nanomaterials: Synthetic and Self-Assembled | Journal Club 5<br>Chapter 19 |
| Monday Week 9 | **Quiz 4**<br>Lecture 12: Nanoengineered Materials Characterization and Analysis Tools-Part 1<br>Journal Club 6 assigned | Chapter 9 |
| Wednesday Week 9 | Lecture 13: Nanoengineered Materials Characterization and Analysis Tools-Part 2<br>NanoBiophysics Core<br>Journal Club 7 assigned<br>(How to do a literature search and use EndNote) | Journal Club 6 |
| Monday | **Spring Break, No Class** | |
| Wednesday | **Spring Break, No Class** | |
| Monday Week 10 | Lecture 14: Nanobased Materials for Diagnostic Application<br>(How to do a literature search and use EndNote) | Journal Club 7 |
| Wednesday Week 10 | Meet with groups one-on-one to approve outline | Outline and Bibliography due |
| Monday Week 11 | **Quiz 5**<br>Lecture 15: Nanobased Materials for Therapeutic/Theranostic Application<br>Journal Club 8 assigned | |
| Wednesday Week 11 | Lecture 16: Implantable Drug Delivery Systems | Journal Club 8 |
| Monday Week 12 | **Quiz 6**<br>Lecture 17: Nanobased Materials in Regenerative Medicine<br>Pick order/days for presentations | |
| Wednesday Week 12 | Lecture 18: Nanotoxicology<br>Journal Club 9 assigned | |
| Monday Week 13 | Review | Journal Club 9 |
| Wednesday Week 13 | **Midterm 2** | |
| Monday Week 14 | Open day for editing final project | |
| Wednesday Week 14 | Lecture 19: FDA Regulation, Intellectual property, Commercialization/Presentations | |

| | | |
|---|---|---|
| Monday Week 15 | Presentations | |
| Wednesday Week 15 | Presentations | |
| Finals Week | Final Project (written) Due | |

**Lab Schedule**

| Date | Topic | Assignment Due (beginning of lab) |
|---|---|---|
| **Week 1** | Overview of experimental techniques | |
| **Week 2** | Liposome synthesis (thin film, sonication method, filtration), transmission electron microscopy preparation<br>-nanoparticle synthesis | Prelab 1 |
| **Week 3** | Liposome drug loading, dynamic light scattering and zeta potential measurements<br>-nanoparticle surface charge and size | Report 1<br>Prelab 2 |
| **Week 4** | Visit NanoBiophsics Core | Report 2 |
| **Week 5** | Cell culture introduction | |
| **Week 6** | Assess biocompatibility (Live/Dead assay, fluorescence assay) on human cells, prepare slide for fluorescence microscopy<br>-nanoparticle in vitro biocompatibility | Prelab 3 |
| **Week 7** | Analysis using Image J | Report 3 |
| **Week 8** | Visualize cells using fluorescence microscopy<br>-nanoparticle in vitro biocompatibility | Prelab 4 |
| **Week 9** | Gold nanoparticle characterization, prep TEM samples<br>-inorganic nanoparticle synthesis | Report 4<br>Prelab 5 |
| | Spring Break | |
| **Week 10** | Transmission electron microscopy facility<br>-nanoparticle size and morphology | Report 5 |
| **Week 11** | Animal testing introduction | |
| **Week 12** | Animal facility visit, plot tumor growth curves, half life<br>-in vivo biocompatibility, therapy, pharmacokinetics | Prelab 6 |
| **Week 13** | H and E staining and in vivo biocompatibility<br>-in vivo biocompatibility | Report 6<br>Prelab 7 |
| **Week 14** | Immunocytochemistry, analysis using Image J | Report 7<br>Prelab 8 |
| **Week 15** | Nanoparticles in the clinic, patent dissection, FDA approval, patient-derived sample testing | Report 8 |
| **Finals Week** | | |

## 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. 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:

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