CELL AND TISSUE ENGINEERING (3 CREDITS)

Florida International University, Department of Biomedical Engineering
BME 4332 (3 credits), Fall 2020
MWF – 11 to 11.50 AM; Room: EC 1115
Instructor: Associate Professor Sharan Ramaswamy, PhD, *FAHA, FASME*
E-mail: sramaswa@fiu.edu
Office hours:

COURSE OVERVIEW:
This course will cover the physiology of cell growth and *in vitro* cultivation with basic techniques in biotechnology. Analysis of fundamental processes and engineering approaches on *in vitro* models for tissue growth will also be examined. Cell and Tissue engineering is an interdisciplinary and multi-disciplinary subject requiring knowledge of several biological as well as engineering concepts. At a fundamental level, the common thread for tissue engineering strategies involves cells and scaffolds. First, we will initially discuss the properties and methodologies of using various cell types (e.g. stem cells) and scaffold materials (e.g. degradable fabrics).

Next, we will then briefly cover Fundamental engineering concepts related to tissue engineering problems. The course will engage in detailed discussions of how biochemical (e.g. growth factors) and biomechanical treatments (e.g. fluid shear stress) are used in optimizing tissue formation. We will also discuss the use of computational models in tissue engineering, as well as contemporary topics in iPSC and gene editing technologies. In addition, we will cover some of the commonly used "tools" that are being used in the development and in the assessment of cell and tissue engineered constructs. Mid-way in the course, you will get hands-on experience working in our cell culture core in experiments devoted to engineering tissue constructs The latter portion of the course will focus on the various application areas (e.g. cardiovascular) within tissue engineering. Currently used cellular/tissue engineering treatments, followed by soon-expected-to-be clinically translatable areas (< 10 years) will be addressed.

Note: This is a Global Learning Discipline Specific course that counts towards your Global Learning graduation requirement.
absences are not excusable unless it is a documented emergency situation – kindly plan your time accordingly.

GLOBAL LEARNING OUTCOMES:
This is a Discipline-specific Global Learning (GL) course that counts towards your FIU Global Learning graduation requirement.

· Global Awareness: Students will be able to demonstrate knowledge of the interrelatedness of local, global, international and intercultural issues, trends, and systems. Global awareness-relevant materials - Items 1, 3 and 4 in the "COURSE MATERIALS" section.

· Course Learning Outcome: Students will demonstrate knowledge of the interrelated global dynamics (social-cultural, political, economic, etc.) that shape aesthetics, values, and authority on cell and tissue engineering, in diverse cultural contexts.

· Global Perspectives: Students will be able to develop a multi-perspective analysis of local, global, international, and intercultural problems. Global perspective-relevant materials - Items 1, 3 and 4 in the "COURSE MATERIALS" section.

· Course Learning Outcome: Students will be able to analyze the multiple global forces that shape their understanding of aesthetics, values, and authority on cell and tissue engineering — economic, political, sociological, technological, cultural, etc.

· Global Engagement: Students will be able to demonstrate a willingness to engage in local, global, international, and intercultural problem solving. Global engagement-relevant materials - Items 1, 3 and 4 in the "COURSE MATERIALS" section.

· Course Learning Outcome: Students will be able to develop solutions to local, global, international, and/or intercultural problems related to aesthetics, values, and authority.

· Assessments: (1) Overall assessment of student's understanding in global trends, perspectives and problem-solving within the interdisciplinary discipline of cell and tissue engineering along with sound scientific interpretations. (2) of student's logical arguments on subjective themes in cell and tissue engineering in a "for" and "against" context, with evidences from the world-wide scientific literature.

· GL-specific assignments: (1) 3-Page Paper – Top-Hat 3-page Write-up Assignment, as described in the "GRADING" section of this syllabus. (2) LAB REPORTS 1 and 2 as described in the "GRADING" section of this syllabus.

Fall 2020, Tentative Course Schedule:

WEEK	**TOPIC**
1	Intro. and origins in Tissue Engineering (TE); Challenges
2	Starting from cells; basis for growth; cell-ECM interactions
3	Cell adhesion, proliferation, migration, Growth factors
4	Cell Mechanobiology. Biomechanical cues, Bioreactor Design
5	Matrix molecules (e.g. Collagen) and their ligands
6	Stem Cells
7	Lab Session 1 – Cell culture
8	Lab Session 2 – Trypan blue live-dead assessment
9	Lab session 3 – Gel-based 3D cellular construct preparation
10	Lab session 4 – Viability-Necrosis-Apoptosis assessment
11	Lab session 5 – Soluble Collagen Assay
12	Gene-Editing (Lab Session 6 – BME6330 only; TBD)
13	Scaffolds: Design and Processing
14	Histology and Immunostaining; Biocompatibility
15	Clinical Cell and TE applications
16	Final Exam (Wed -12/11/2020: 9.45 to 11.45 AM – EC 1115)

COURSE MATERIALS:

1) *Fisher, Mikos and Bronzino, Tissue Engineering, CRC Press, Boca Raton, FL, 2007.*

The above book is a *recommended* text for this course. I will be referring to the above text for lectures. In addition, selected material in the text will be critical study material for the midterms and final exam. I will highlight selected material to read during the course.

2) *Another text for additional reading: Principles of Tissue Engineering, 4th Edition by Lanza R, Langer R and Vacanti JP. Academic Press, 2013.*

Regular class attendance and good lecture notes will not necessitate the purchase of the above texts and therefore strictly speaking, both texts are optional for this course.

3) *In this course we will be using **Top Hat** as an integrative teaching tool all semester. This is a required tool for this course.* You should have or will be soon be receiving an email from Top Hat in your FIU email with the invitation and sign up procedures. Once you have signed up and have gained access, you can participate in class via Smartphone (Apple and Android), IPad, Laptop or Tablet. Please bring a mobile or computing device to class so you can participate in the in-class discussions. You will also have access to any files that are uploaded onto our Top-Hat course website. Bring your own device.

Top Hat Course Name: Cell and Tissue Engineering Fall 2020
Direct URL to Top Hat Course Website: (Will be announced in class)

4) *Required Scientific Papers to Read:*

A. A. I. Caplan, J. E. Dennis, Mesenchymal stem cells as trophic mediators. *J Cell Biochem* 98, 1076-1084 (2006).

B. P. F. Davies, Flow-mediated endothelial mechanotransduction. *Physiol Rev* 75, 519-560 (1995).

C. F. G. Giancotti, E. Ruoslahti, Integrin signaling. *Science* 285, 1028-1032 (1999).

D. I. Martin, D. Wendt, M. Heberer, The role of bioreactors in tissue engineering. *Trends Biotechnol* 22, 80-86 (2004).

E. L. E. Niklason et al., Functional arteries grown in vitro. *Science* 284, 489-493 (1999).

F. S. Ramaswamy et al., The role of organ level conditioning on the promotion of engineered heart valve tissue development in-vitro using mesenchymal stem cells. *Biomaterials* 31, 1114-1125 (2010).

G. S. Rath, M. Salinas, A. G. Villegas, S. Ramaswamy, Differentiation and Distribution of Mesenchymal Stem Cells in Pulsatile Flow Environments Demonstrate Support of the Valvular Phenotype. *PLoS One* 10, e0141102 (2015).

H. K. Takahashi, S. Yamanaka, Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell* 126, 663-676 (2006).

B. J. Ulery, L. S. Nair, C. T. Laurencin, Biomedical Applications of Biodegradable Polymers. *J Polym Sci B Polym Phys* 49, 832-864 (2011).

J. B. Wehrle-Haller, B. A. Imhof, Actin, microtubules and focal adhesion dynamics during cell migration. *Int J Biochem Cell Biol* 35, 39-50 (2003).

K. G. Zhang, L. J. Suggs, Matrices and scaffolds for drug delivery in vascular tissue engineering. *Adv Drug Deliv Rev* 59, 360-373 (2007).

GROUPS:
You will be assigned a group number for working on TOP HAT assignments and the Labs. Note that you are encouraged to work with one another but each assignment and report you turn in must be your own – EVERYBODY turns in their own work. Each group will consist of ~ 6 to 7 students. When you receive the Email invitation from TOP HAT to sign up, **please enter your group number instead of your student ID number when prompted to enter your Student ID**. Group ID's will be notified to the class soon. Note that you will also be in groups for your lab sessions scheduled during weeks 7 through 11. Students will take turns to lead or assist during in each lab session to work effectively in teams, and to ensure that all students get an equal, yet rigorous hands-on experience in the lab under the direction of the teaching assistant (TA).

GRADING:
The final grade for this course will be computed from the results of the following:

Top-Hat In-Class Discussions and Debates – 10%

Topics will include but is not limited to both objective and subjective areas in: cell adhesion, cell signaling pathways, bioreactors, stem cells, scaffold processing, vascular tissue engineering, as well as other topics. Debates will be centered on the more subjective and culturally-specific themes that could be regionally-dependent (e.g., use of embryonic stem cells in different countries for scientific research). For example, if the debate topic is on "Should human embryonic stem cell therapies from approved clinical sources be approved for research and development purposes?", students will answer in real-time, YES or NO via the TOP HAT web-platform. The student responses could be based on scientific, ethical and/or culturally/religiously-centered viewpoints. Next, the instructor will review the real-time responses and call upon two groups of students (5 to 8 students/group), who in majority answered either YES or NO, to come to the front of the class to explain their answer, with for example, the students who said YES, going first (and subsequently followed by the students amongst the two groups who said NO). A debate will subsequently ensue. The discussion will then switch to the rest of the students in the class, i.e., the "audience members", who will actively participate on the explanations provided by the two student groups. This active in-class discussion will conclude by the instructor summarizing the different points-of-view and weighing-in. However, the students will be able to continue exploration of the topic, if they so choose, by selecting it as part of their 3-page write-up assignment (See section below). TOP HAT real time discussions/debates will occur every Wednesday unless otherwise notified.

Top-Hat 3-page Write-up Assignment – 10%

Assignment Instructions:
We have had 3 TOP-HAT "long-discussions" so far that were actively debated in-class and consisted of the following central questions:
Instructions on the 3-page write-up:

1) *Pick ONLY 1 out of the 3 debate topics as the basis for this assignment.*
2) *Please follow the following format: single space, 1" margins all around, Arial 11 font.*
3) *On the first line of the 1st page, type your name and panther ID. Leave the second line blank. On the 3rd line, enter the CENTRAL QUESTION that was asked for your assignment. Leave the 4th line blank. Begin the write-up on the 5th line of the page.*
4) *No more than 1 Figure within your 3-pages (Please note that the figure can have parts, such as Fig 1a, 1b, etc., if there is context to present in this manner).*
5) *The write-up must contain the following sections: 1) BACKGROUND, 2) RATIONALE FOR (YOUR) ARGUMENT, 3) ALTERNATIVE ARGUMENTS, 4) CONCLUSIONS and 5) REFERENCES.*

Note that all of the above sections, including the REFERENCES must be within the 3-page limit. For clarity in the write-up, you are encouraged to use, BOLD, underlines, tabs, etc., where needed to distinguish between different section, to emphasis a point, and so on. TOP HAT has some valuable publications posted under the "FILES" tab. Depending on which topic you selected, you can and should look into these publications that are relevant to your chosen topic and use them as references.

If you have any questions, you are encouraged to come and see me BEFORE the write-up is due.

Lab Report I (On sessions 1 and 2) – 10 %

Lab Report 1 Instructions:

Summary:

You have completed two lab sessions thus far for this course. In these sessions you were exposed to critical aspects of cell culture, which included, 1) cell culture, 2) cell plating in flasks, 3) cell expansion, 4) cell detachment using trypsin, 5) cell counting, 6) cell freezing/thawing, and 7) trypan blue cell viability assessment.

Specific Instructions:

You as an Individual need to submit YOUR lab report: However, you worked on the lab sessions in groups. Therefore, you are highly-encouraged to work together with your group members to discuss the labs and the data you collected, as well as analyze the data together. Specifically, this collaboration is highly-encouraged in the following activities: review of global scientific literature, raw data analyses into results, statistical analyses and last but not least, in the interpretation of the results. However, as already stated, the lab report that you submit needs to be YOURS and distinct in its writing from that of your group members.

Timely submission:

You are expected to turn in a hardcopy of a 5-page (MAXIMUM), typed, lab report a week after the completion of your 2nd lab session (at the start of your 3rd lab session), i.e., the week of October 21st. For example, if you completed lab 2 session on October 15th, your lab report 1 will be due in the lab when you initiate lab 3 session on October 22nd. No late reports will be accepted.

Report format:

The format of the report (font, margins, single versus double space, number of figures, number of references, single-sided versus double sided etc.) is entirely up to you. However kindly keep in mind that the 5 page limit includes figures, tables and references. We will ignore anything that exceeds 5 single-sides of printed material. The only additional requirement is that you please include a cover page with your name and panther ID along with the title "BME 4332/BME 6330, Lab Report 1". The cover page does not count to the 5 –page limit. Also please paginate all pages with printed material except for the cover page. Page 1 should be the first printed page of your lab report (not counting the cover page).

Report Sections:

Your lab report MUST consist of the following 5 sections (as listed in BOLD text below):

1) Introduction: Provide some background on the culture of cells you used, highlighting from the literature critical findings for optimizing culture conditions for these cells. Describe any unique aspects of culture expansion for these cells (e.g. stem cells vs. somatic cell sources).

2) Methods: Summarize the key parts of the protocol, focusing on the aforementioned 7 steps (in the summary above). Also include a sub-section in this section called "Data/Statistical Analyses".

3) Results: Provide in figure/table format all the results that you obtained from these lab sessions and a few lines explaining each figure/table. Any meaningful data/statistical analyses requiring additional post-processing of the data you collected are highly encouraged, i.e., beyond the obvious presentation of the results, and should also be included in this section. If included, its corresponding methodology should also be explained in the "Methods" section, i.e., 2) above, under the "Data/Statistical Analyses" sub-section.

4) Discussion and Conclusions: In the Discussion section, make sure to address the following: 1) what you interpret the results you obtained to mean, 2) your rationale for presenting results the way you did and how your results compare to those in the literature (describe similarities and differences) and 3) Any limitations of the way your lab sessions were done and limitations in your findings which would require further work. Please have a few lines of "conclusions" summarizing your work and the key learning milestones from these labs.

5) References: Please list your references in a proper scientific style in this section and ensure that if you list them here that they are cited appropriately in the text of your lab report.

Lab Report II (Summative, sessions 1 through 5, with emphasis on sessions 3 through 5) – 25 %

Lab Report 2 Instructions:

You are expected to turn in a 10-page (single side, all pages stapled), typed, report in class. *You as an Individual need to submit YOUR lab report: However, you worked on the lab sessions in groups. Therefore, you are highly-encouraged to work together with your group members to discuss the labs and the data you collected, as well as analyze the data together. Specifically, this collaboration is highly-encouraged in the following activities: review of global scientific literature, raw data analyses into results, statistical analyses and last but not least, in the interpretation of the results. However, as already stated, the lab report that you submit needs to be YOURS and distinct in its writing from that of your group members.* The report needs to adhere to strong scientific style as one would expect from a reputed, peer-reviewed journal publication. To get examples of proper scientific writing style, refer to the 2 journal papers "PLOS 1" and "Biomaterials" (both have been uploaded onto TOP HAT) that you will need to refer to for this lab report. No late reports will be accepted. The format of the report (font, margins, single versus double space, number of figures, number of references, single-sided versus double sided etc.) is entirely up to you. However kindly keep in mind that the 10-page limit includes the report text and figures but not references. Anything exceeding this page limit requirement will be ignored. The 10 pages represents a maximum limit, thus you can use less than 10 pages if you wish. There is no limit to the number of references. The only additional requirement is that you please include a cover page with your name and panther ID along with the title "BME 4332/BME 6330, Lab 2: "Engineered Tissues". The cover page does not

count to the 10 –page limit. Also please paginate all pages with printed materials except for the cover page. Page 1 should be the first printed page of your lab report (not counting the cover page).

Figures/Analysis required for this report:
From Session 4:
1) Include representative live-dead images for each of the 3 groups
2) Present viability data in terms of % live and % Dead cells for the specified culture duration.
3) Normalize your data with respect to the area of your imaging slices. Conduct some statistics to determine significance ($p < 0.05$) in cells/mm2, between the groups assessed. Make sure to justify your choice of statistical method.
4) Plot a bar chart for the Mean +/- standard error of the mean (SEM) for each group, A, B and C.
5) Compare your results to those presented "PLOS-One" paper in the form of a figure.
From Session 5:
1) Draw your standards curve (Absorbances versus Collagen content)
2) Plot a bar chart of your collagen for each sample
3) Compare your mean collagen content to those presented in the "Biomaterials" paper in the form of a figure. Make sure you make these comparisons objective. For example, The Biomaterials paper normalizes samples with respect to their weight. An objective comparison would require your samples then to also be normalized with corresponding dry weight.
Lab Report:
Your lab report MUST consist of the following 6 sections:
1) Abstract: Concise summary of the entire study, (No more than 300 words).
2) Introduction: Provide some background on tissue engineering in Agar gels, and the objectives of your study.
3) Materials and Methods: Summarize the key parts of Sessions 1 and 2. Next provide materials used and methodology of sessions 3, 4 and 5 using proper sentences. You need to adhere to proper scientific reporting style! Again, refer to the 'PLOS 1' and 'Biomaterials' papers. For the Session 5 you can also use the "Sircol Instruction" the same with the Collagen Assay kit as a reference (this document has been uploaded onto TOP HAT). Make sure to include a sub-section on "Statistical Analyses" reporting the Statistics Methodology. Specific instructions regarding reporting of Session 4 as applicable, will be e-mailed to those registered in BME 6330.
4) Results: Please include all results and figures asked for in the "Figures/Analysis" segment described above.
5) Discussion and Conclusions: Interpret what your results mean. What results are significant? what are not? when and where would data normalization be important? Compare and contrast the results of your assay with the corresponding "PLOS One" and "Biomaterials" paper results. Conclude by summarizing your main findings and any limitations.
6) References: Please list your references in a preferred scientific style in this section and ensure that if you list them here that they are cited appropriately in the text of your lab report.

Lab Mini-quizzes (5 total) – 10%

Final Exam (Comprehensive) – 15%

Additional formatting of and deadlines for assignments, lab reports as well as the exam dates will be announced in class ahead of time as needed.

BME 4332 Cell and Tissue Engineering

Course Learning Outcomes:

No.	Course Learning Outcome	Corresponding BSBME Program Learning Outcome
1	Ability to understand engineering principles applied to cellular morphology and behavior	1
2	Ability to employ techniques to primary cell culturing, including aseptic techniques, handling and disposal of waste, and laboratory safety	2,5,8
3	Ability to understand the use of various biomaterials in formulation of cell therapies (i,e., cell morphology and tissue formation)	1,4,5
4	Ability to communicate ideas effectively through required class assignments	7

BSBME Program Learning Outcomes

- 1. Ability to apply knowledge of mathematics (including differential equations and statistics), physical and life sciences, and engineering to carry out analysis and design to solve problems at the interface of engineering and biology;
- 2. Ability to design and conduct experiments as well as to measure, analyze and interpret data from living systems;
- 3. Ability to design a system, component, or process to meet desired needs, including systems that involve the interaction between living and non-living materials;
- 4. Ability to identify, formulate, and adapt engineering solutions to unmet biological needs,
- 5. Ability to use the techniques, skills, and modern engineering tools necessary for engineering practice, including the ability to model and analyze biological systems as engineering systems;
- 6. Ability to function on multi-disciplinary teams;
- 7. Ability to communicate effectively;
- 8. Awareness of the characteristics of responsible professional engineering practice, including ethical conduct, consideration of the impact of engineering solutions on society in a global and contemporary context, and the value of lifelong learning.

Policy regarding student misconduct: Students at Florida International University are expected to adhere to the highest standards of integrity in every aspect of their lives. Honesty in academic matters is part of this obligation. Academic integrity is the adherence to those special values regarding life and work in an academic community. Any act or omission by a student which violates this concept of academic integrity shall be defined as academic misconduct and shall be subject to the procedures and penalties established by the university. **Students violating academic integrity will receive a failing grade for the course and the incident will be forwarded to Student Academic Affairs.** Academic misconduct includes, but is not limited to, copying homework, copying work on exams either in-class or take-home, copying of projects, or plagiarism. Plagiarism is using others' ideas and words without clearly acknowledging the source of that information. This includes, but is not limited to, the internet, textbooks, journals, or any other material that is not your own work. It is the responsibility of students to report misconduct, which may include another student copying from your, or another student's exam, homework, projects or any other assignment. Therefore, if a student copies from you, it is your responsibility to report it, otherwise you are also responsible. **Under no circumstances will any student be permitted to leave and return to the classroom during an exam.**