YEDITEPE UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

COURSE SYLLABUS
2016/2017-Fall

Course Code-Name	BTEC 643 Gene Editing Technologies

Instructor	Assist. Prof. Dr. Fatih Kocabaş, Department of Genetics and Bioengineering, Room B504, 0-216-578 0618 fatih.kocabas@yeditepe.edu.tr
Course Schedule	Friday 09:00 – 11:50 @ B0501 Seminar Room
Laboratory	None
Office Hours	Tuesday 11:00 – 13:00 *by appointment only*
Course Description	Advanced topics in gene editing technologies
Course Objectives	This course will cover the gene editing technologies including but not limited to Cre-lox system, Zinc Finger Nucleases, TALENS, and CRISPR/Cas9 system. It will provide description of genome editing tools, their pros and cons, their potential use in regenerative medicine, with focus on correction of genetic mutations in stem cells. It will provide alternatives for increased efficacy and specificity of gene editing tools and protocols to assess gene editing in human cells. In addition, breakthroughs including the correction of iPSCs and hematopoietic stem cells (HSCs) for regenerative medicine will be discussed.
Required Textbook & Supplementary Materials	Methods in Enzymology (special focus on genome editing techniques), Volume 546 # 2014 Elsevier Inc. ISSN 0076-6879 http://dx.doi.org/10.1016/B978-0-12-801185-0.00001-5 CRISPR 101:A Desktop Resource. Created and Compiled by Addgene January 2016 (1st Edition)
Grading	Class Participation: **25%** Presentation 1: **25%** Presentation 2: **25%** Final Exam: **25%** TOTAL: **100%** **If you achieve less than 50% overall in the class, you will automatically get an "F".**
Make-up Exams	There is no planned make-up for any missing examination or presentations. You must demonstrate a valid excuse to re-take a missed exam or presentations. In addition, the school policies will be taken into account in cases when you miss a scheduled examination.
Homework / Quizzes	Students are expected to read assigned textbook sections in advance of class, and will be expected to participate actively in class discussion. Final exams will utilize written short essay format questions. *Each student is required to give two lecture presentations related to recent developments in gene editing technologies.*
Attendance	If you fail to attend less than **80%** of the lectures from the beginning of the semester, you will get "FA" in the course and have no right to take BUTUNLEME exam. In addition, tardiness to class may incur a penalty of loss of marks.
Academic Integrity	Adherence to the University Academic Integrity policy is expected. No breach of this policy will be tolerated. Any offenders, explicit or complicit, will be dealt with in accordance with the established University procedures.

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Exam Schedule

Final Exam	Exact time and date will be announced later	Exact time and date will be announced later

Course Outline

Week		Lecture	Topics
Week 1	Sep 19-24	1	An Overview of Gene Editing Tools
Week 2	Sep 26-30	2	Gene editing by Cre-lox system
Week 3	Oct 3-7	3	Gene editing by Zinc Finger Nucleases
Week 4	Oct 10-14	4-5	Gene editing by TALENs and CRISPR/Cas9
Week 5	Oct 17-21	-	No planned lectures or class (THD Congress)
Week 6	Oct 24-28	-	Republic Holiday
Week 7	Oct 31-Nov 4	6-7	Targeted Genome Editing & Determining the Specificities of TALENs, Cas9, and Other Genome-Editing Enzymes
Week 8	Nov 7-11	8	Genome Engineering with Custom Recombinases
Week 9	Nov 14-18	-	Holiday (Tanıtım Gezileri)
Week 10	Nov 21-25	9	Genome Engineering in Human Cells
Week 11	Nov 28-Dec 2	10	Genome Editing in Human Stem Cells
Week 12	Dec 5-9	11	Genome Editing Using Cas9 Nickases
Week 13	Dec 12-16	12	Assaying Break and Nick-Induced Homologous Recombination in Mammalian Cells Using the DR-GFP Reporter and Cas9 Nucleases
Week 14	Dec 19-23	13	The iCRISPR Platform for Rapid Genome Editing in Human Pluripotent Stem Cells
Week 15	Dec 26-30	14	Gene Editing of Human Hematopoietic Stem Cells for Gene Therapy of Sickle Cell Anemia and Related Diseases

Active Student Participation: This class emphasizes on active student participation. You are supposed to define a very specific research topic within the field of gene editing technologies and perform an exhaustive literature search. You will present the specific topic in as a presentation.

Research Paper Presentation: You will be given research papers related to gene editing technologies, prepare a powerpoint presentation and explain this paper along with relevant studies in detail in class. One or two slides should indicate the general theme of the paper. All used methods and potentially unknown terminology should be explained in detail. All results should then be explained and critically evaluated. The presentation should take approximately 20-25 minutes, followed by 10 minutes of discussion. Actual length of presentations and number of presented papers will depend on total number of participating students.

Powerpoint presentation and one question regarding the research paper will be submitted to the instructor via email. This is due by the date of your presentation date. Please email to fatih.kocabas@yeditepe.edu.tr

Disclaimer: This syllabus provides a general plan and subject to change. The instructor reserves the right to make modifications in content and schedules as necessary to promote the best education possible within the prevailing conditions affecting this course. It is the student's responsibility to note the changes that may occur during the semester

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Topics and Assigned Readings: Assigned Readings will be discussed in class. Please read and be prepared to participate in class discussion.

1. Tebas, Pablo, et al. "Gene editing of CCR5 in autologous CD4 T cells of persons infected with HIV." *New England Journal of Medicine* 370.10 (2014): 901-910.
2. Sato, Kenya, et al. "Generation of a Nonhuman Primate Model of Severe Combined Immunodeficiency Using Highly Efficient Genome Editing." *Cell Stem Cell* 19.1 (2016): 127-138.
3. Zhu, Zengrong, et al. "Genome Editing of Lineage Determinants in Human Pluripotent Stem Cells Reveals Mechanisms of Pancreatic Development and Diabetes." *Cell stem cell* 18.6 (2016): 755-768.
4. Parfitt, David A., et al. "Identification and Correction of Mechanisms Underlying Inherited Blindness in Human iPSC-Derived Optic Cups." *Cell stem cell* 18.6 (2016): 769-781.
5. Hockemeyer, Dirk, and Rudolf Jaenisch. "Induced Pluripotent Stem Cells Meet Genome Editing." *Cell stem cell* 18.5 (2016): 573-586.
6. Zhang, Haojian, et al. "TGF-β Inhibition Rescues Hematopoietic Stem Cell Defects and Bone Marrow Failure in Fanconi Anemia." *Cell stem cell* 18.5 (2016): 668-681. **and** Tummala, Hemanth, and Inderjeet Dokal. "TGF-β Pathway Inhibition Signals New Hope for Fanconi Anemia." *Cell stem cell* 18.5 (2016): 567-568.
7. Young, Courtney S., et al. "A Single CRISPR-Cas9 Deletion Strategy that Targets the Majority of DMD Patients Restores Dystrophin Function in hiPSC-Derived Muscle Cells." *Cell stem cell* 18.4 (2016): 533-540.
8. Mandegar, Mohammad A., et al. "CRISPR Interference Efficiently Induces Specific and Reversible Gene Silencing in Human iPSCs." *Cell stem cell* 18.4 (2016): 541-553.
9. Giani, Felix C., et al. "Targeted application of human genetic variation can improve red blood cell production from stem cells." *Cell stem cell* 18.1 (2016): 73-78.
10. Lombardo, Angelo, et al. "Gene editing in human stem cells using zinc finger nucleases and integrase-defective lentiviral vector delivery." *Nature biotechnology* 25.11 (2007): 1298-1306.
11. Li, Ting, et al. "High-efficiency TALEN-based gene editing produces disease-resistant rice." *Nature biotechnology* 30.5 (2012): 390-392.
12. Liang, Puping, et al. "CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes." *Protein & cell* 6 (2015): 363-372.
13. Hu, Wenhui, et al. "RNA-directed gene editing specifically eradicates latent and prevents new HIV-1 infection." *Proceedings of the National Academy of Sciences* 111.31 (2014): 11461-11466.
14. Chu, Van Trung, et al. "Increasing the efficiency of homology-directed repair for CRISPR-Cas9-induced precise gene editing in mammalian cells." *Nature biotechnology* 33.5 (2015): 543-548.
15. Brooks, Christopher, et al. "Efficient gene editing in tomato in the first generation using the clustered regularly interspaced short palindromic repeats/CRISPR-associated9 system." *Plant physiology* 166.3 (2014): 1292-1297.
16. Tabebordbar, Mohammadsharif, et al. "In vivo gene editing in dystrophic mouse muscle and muscle stem cells." *Science* 351.6271 (2016): 407-411.
17. Smith, Cory, et al. "Whole-genome sequencing analysis reveals high specificity of CRISPR/Cas9 and TALEN-based genome editing in human iPSCs." *Cell stem cell* 15.1 (2014): 12.
18. Manjunath, N., et al. "Newer gene editing technologies toward HIV gene therapy." *Viruses* 5.11 (2013): 2748-2766.
19. Li, Dali, et al. "Heritable gene targeting in the mouse and rat using a CRISPR-Cas system." *Nature biotechnology* 31.8 (2013): 681-683.
20. Wu, Yuxuan, et al. "Correction of a genetic disease by CRISPR-Cas9-mediated gene editing in mouse spermatogonial stem cells." *Cell research*25.1 (2015): 67-79.
21. Baltimore, David, et al. "A prudent path forward for genomic engineering and germline gene modification." *Science* 348.6230 (2015): 36-38.
22. Smurnyy, Yegor, et al. "DNA sequencing and CRISPR-Cas9 gene editing for target validation in mammalian cells." *Nature chemical biology* 10.8 (2014): 623-625.
23. Liu, Guang-Hui, et al. "Targeted gene correction of laminopathy-associated LMNA mutations in patient-specific iPSCs." *Cell stem cell* 8.6 (2011): 688-694.
24. Cheng, Ranran, et al. "Efficient gene editing in adult mouse livers via adenoviral delivery of CRISPR/Cas9." *FEBS letters* 588.21 (2014): 3954-3958.
25. Chou, Chungjung, and Alexander Deiters. "Light-Activated Gene Editing with a Photocaged Zinc-Finger Nuclease." *Angewandte Chemie* 123.30 (2011): 6971-6974.
26. Osborn, Mark J., et al. "Fanconi anemia gene editing by the CRISPR/Cas9 system." *Human gene therapy* 26.2 (2014): 114-126.

27. Wu, Yuxuan, et al. "Correction of a genetic disease in mouse via use of CRISPR-Cas9." *Cell stem cell* 13.6 (2013): 659-662.
28. Gori, Jennifer L., et al. "Delivery and specificity of CRISPR/Cas9 genome editing technologies for human gene therapy." *Human gene therapy* 26.7 (2015): 443-451.
29. Esvelt, Kevin M., et al. "Orthogonal Cas9 proteins for RNA-guided gene regulation and editing." *Nature methods* 10.11 (2013): 1116-1121.
30. Cong, Le, et al. "Multiplex genome engineering using CRISPR/Cas systems."*Science* 339.6121 (2013): 819-823.
31. Gaj, Thomas, Charles A. Gersbach, and Carlos F. Barbas. "ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering." *Trends in biotechnology* 31.7 (2013): 397-405.
32. Hwang, Woong Y., et al. "Efficient genome editing in zebrafish using a CRISPR-Cas system." *Nature biotechnology* 31.3 (2013): 227-229.
33. Fu, Yanfang, et al. "High-frequency off-target mutagenesis induced by CRISPR-Cas nucleases in human cells." *Nature biotechnology* 31.9 (2013): 822-826.
34. Sebastiano, Vittorio, et al. "In situ genetic correction of the sickle cell anemia mutation in human induced pluripotent stem cells using engineered zinc finger nucleases." *Stem cells* 29.11 (2011): 1717-1726.
35. Sun, Ning, and Huimin Zhao. "Seamless correction of the sickle cell disease mutation of the HBB gene in human induced pluripotent stem cells using TALENs." *Biotechnology and bioengineering* 111.5 (2014): 1048-1053.
36. Cradick, Thomas J., et al. "CRISPR/Cas9 systems targeting β-globin and CCR5 genes have substantial off-target activity." *Nucleic acids research*(2013): gkt714.
37. Sankaran, Vijay G., and Mitchell J. Weiss. "Anemia: progress in molecular mechanisms and therapies." *Nature medicine* 21.3 (2015): 221-230.
38. Cheng, Ranran, et al. "Efficient gene editing in adult mouse livers via adenoviral delivery of CRISPR/Cas9." *FEBS letters* 588.21 (2014): 3954-3958.
39. Naito, Yuki, et al. "CRISPRdirect: software for designing CRISPR/Cas guide RNA with reduced off-target sites." *Bioinformatics* (2014): btu743.
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