



Course Code-Name	BTEC 536 Stem Cell 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	Monday 14:00 – 16:50 @ C554												
Laboratory	None												
Office Hours	Monday 11:00 – 13:00 <i>by appointment only</i>												
Course Description	An introduction to stem cell technologies												
Course Objectives	The course will cover topics in the basic biology of embryonic, fetal and adult stem cells; the tools, methods and experimental protocols needed to study and characterize stem cells; as well as the application of stem cells to treat specific human diseases. The course is intended for master's degree students in the Biotechnology Program of Yeditepe University. Students are expected to acquire knowledge and understanding of the basic biology of embryonic and tissue specific stem cells, the potential application of stem cell for the treatment of human diseases and different experimental approaches used to study and characterize stem cells.												
Required Textbook & Supplementary Materials	Essentials of Stem Cell Biology, Robert Lanza and Anthony Altala, 2nd Edition Cell Stem Cell www.cell.com/cell-stem-cell/home												
Grading	<table> <tr> <td>Class Participation:</td> <td>10%</td> </tr> <tr> <td>Presentation 1:</td> <td>15%</td> </tr> <tr> <td>Presentation 2:</td> <td>15%</td> </tr> <tr> <td>Midterm Exam:</td> <td>20%</td> </tr> <tr> <td>Final Exam:</td> <td>40%</td> </tr> <tr> <td>TOTAL:</td> <td>100%</td> </tr> </table> <p>If you achieve less than 50% overall in the class, you will automatically get an “F”.</p>	Class Participation:	10%	Presentation 1:	15%	Presentation 2:	15%	Midterm Exam:	20%	Final Exam:	40%	TOTAL:	100%
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Make-up Exams	There is no planned make-up for any missing examination. You must demonstrate a valid excuse to re-take a missed exam. 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. Midterm and final exams will utilize written short essay format questions. <i>Each student is required to give lecture presentations of assigned research articles related to stem cell biology.</i>												
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

Take Home Midterm Exam	Monday, Apr. 11 th	Take Home Midterm Exam due.
Final Exam	May 23, 2015	14:00 – 16:50 @ C554

Course Outline

Week		Lecture	Module	Topics
Week 1	Feb 8	1	Module 1	Course introduction
Week 2	Feb 15	2	Module 1	Overview of basic and translational research of stem cells
Week 3	Feb 22	3	Module 1	Human embryonic stem cells
Week 4	Feb 29	4	Module 1	Generation of pluripotent stem cells,
Week 5	Mar 7	5	Module 1	Origin of primordial germ cells and embryonic germ cells, Trophoblast stem cells, Extraembryonic endoderm stem cells.
Week 6	Mar 14	6	Module 2	Neural stem cells, Hematopoietic stem cells, retinal stem cells, hair follicle stem cells
Week 7	Mar 21	7	Module 2	Vascular progenitors, skeletal muscle stem cells, cardiac stem cells, kidney stem cells
Week 8	Mar 28	8	Module 2	Mesenchymal stem cells,
Week 9	Apr 4	9	Module 2	Stem cells in the liver, pancreas, intestine, and teeth
Week 10	Apr 11	10	Module 1-2	Take Home Midterm Exam Due date
Week 11	Apr 18	11	Module 3	Tissue engineering with mesenchymal stem cells, Therapeutic potential of neural stem cells
Week 12	Apr 25	12	Module 3	Preclinical studies using stem cells to treat heart disease, β -cell replacement therapy, Embryonic stem cells in tissue engineering
Week 13	May 2	13	Module 3	Stem cells for the treatment of muscular dystrophy, Regeneration of epidermis from adult keratinocyte stem cells, Application of stem cells to bone regeneration
Week 14	May 9	14	Module 3	Stem cell gene therapy, Viral and non-viral vectors, Genetically corrected stem cells and their use for gene therapy



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Research Paper Presentation: You will be given 2 research topics related to stem cell technology, prepare powerpoint presentations and explain assigned research papers 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 25 minutes, followed by 5 minutes of discussion. Actual length of presentations and number of presented papers will depend on total number of participating students.

Powerpoint presentation and a question related to the discussed topic will be submitted to the instructor. Due by the presentation date.

MODULES

Module 1: Pluripotent Stem Cells

Chapters: 1-11, 35-51

Topics: Overview of basic and translational research of stem cells, Pluripotent stem cells; murine embryonic stem cells, human embryonic stem cells, Induced pluripotent stem cells, and primordial and germ cells, amniotic fluid derived cells, and methods in stem cell biology.

Module 2: Tissue Specific Stem Cells

Chapters: 16-34

Topics: Neural, Hematopoietic, Retinal, Hair Follicle, Vascular, Skeletal Muscle, Kidney, Liver, Pancreas, Intestine, Dermal, Mesenchymal Stem Cells.

Module 3: Therapeutical Applications of Stem Cells

Chapters: 52-69

Topics: Use of stem cells to treat various disorders including; nervous system disorders, heart disease, muscular dystrophy, diabetes. Applications of stem cells in bone and epidermis regeneration, tissue engineering and stem cell gene therapy, regulation and ethics of stem cells

Final Exam will cover chapters from Modules 1-3

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. **Trophoblast stem cells**
 - a. Bencherit, Hana, et al. "Extensive Nuclear Reprogramming Underlies Lineage Conversion into Functional **Trophoblast** Stem-like Cells." *Cell stem cell* 17.5 (2015): 543-556.
 - b. Kubaczka, Caroline, et al. "Direct Induction of **Trophoblast** Stem Cells from Murine Fibroblasts." *Cell stem cell* 17.5 (2015): 557-568.
2. **Leukemia stem cells**
 - a. Ye, Min, et al. "**Hematopoietic** Differentiation Is Required for Initiation of Acute Myeloid **Leukemia**." *Cell stem cell* 17.5 (2015): 611-623.
 - b. Iwasaki, Masayuki, et al. "CD93 Marks a Non-Quiescent Human **Leukemia** Stem Cell Population and Is Required for Development of MLL-Rearranged Acute Myeloid Leukemia." *Cell stem cell* 17.4 (2015): 412-421.
3. **Megakaryopoiesis and Lymphoid Regeneration**
 - a. Haas, Simon, et al. "Inflammation-Induced Emergency **Megakaryopoiesis** Driven by Hematopoietic Stem Cell-like Megakaryocyte Progenitors." *Cell stem cell* 17.4 (2015): 422-434.
 - b. Menon, Tushar, et al. "**Lymphoid** Regeneration from Gene-Corrected SCID-X1 Subject-Derived iPSCs." *Cell stem cell* 16.4 (2015): 367-372.
4. **ESC Self renewal**
 - a. Ho, Lena, et al. "ELABELA Is an Endogenous Growth Factor that Sustains **hESC** Self-Renewal via the PI3K/AKT Pathway." *Cell stem cell* 17.4 (2015): 435-447.
 - b. Zhao, Bo, et al. "Filia Is an **ESC**-Specific Regulator of DNA Damage Response and Safeguards Genomic Stability." *Cell stem cell* (2015).
5. **ESC Function**
 - a. Ohgushi, Masatoshi, Maki Minaguchi, and Yoshiki Sasai. "Rho-signaling-directed YAP/TAZ activity underlies the long-term survival and expansion of human **embryonic** stem cells." *Cell stem cell* 17.4 (2015): 448-461.
 - b. Morey, Lluís, et al. "Polycomb regulates mesoderm cell fate-specification in **embryonic** stem cells through activation and repression mechanisms." *Cell stem cell* 17.3 (2015): 300-315.
6. **Neurogenesis**
 - a. Llorens-Bobadilla, Enric, et al. "Single-cell transcriptomics reveals a population of dormant **neural** stem cells that become activated upon brain injury." *Cell stem cell* 17.3 (2015): 329-340.
 - b. Sierra, Amanda, et al. "Neuronal Hyperactivity Accelerates Depletion of Neural Stem Cells and Impairs Hippocampal **Neurogenesis**." *Cell stem cell* 16.5 (2015): 488-503.
7. **Induced pluripotent stem cells**
 - a. Zhao, Tongbiao, et al. "Humanized mice reveal differential immunogenicity of cells derived from autologous **induced pluripotent stem cells**." *Cell stem cell* 17.3 (2015): 353-359.
 - b. Young, Jessica E., et al. "Elucidating Molecular Phenotypes Caused by the SORL1 Alzheimer's Disease Genetic Risk Factor Using Human Induced **Pluripotent** Stem Cells." *Cell stem cell* 16.4 (2015): 373-385.
8. **Skin stem cells**
 - a. Nelson, Amanda M., et al. "dsRNA Released by Tissue Damage Activates TLR3 to Drive **Skin** Regeneration." *Cell Stem Cell* 17.2 (2015): 139-151.
 - b. Peterson, Shelby C., et al. "Basal Cell Carcinoma Preferentially Arises from Stem Cells within **Hair Follicle** and Mechanosensory Niches." *Cell stem cell* 16.4 (2015): 400-412.
9. **Hematopoietic stem cells maintenance**
 - a. Yamashita, Masayuki, Eriko Nitta, and Toshio Suda. "Asp1 preserves **hematopoietic** stem cell pool integrity and prevents malignant transformation." *Cell stem cell* 17.1 (2015): 23-34.
 - b. Prashad, Sacha Leandra, et al. "GPI-80 Defines Self-Renewal Ability in **Hematopoietic** Stem Cells during Human Development." *Cell stem cell* 16.1 (2015): 80-87.
10. **Hematopoietic stem cells function**
 - a. Luo, Min, et al. "Long Non-Coding RNAs Control **Hematopoietic** Stem Cell Function." *Cell stem cell* 16.4 (2015): 426-
 - b. Thambyrajah, Roshana, et al. "GFI1 proteins orchestrate the emergence of **haematopoietic** stem cells through recruitment of LSD1." *Nature cell biology* 18.1 (2016): 21-32.
11. **Regulation of Hematopoietic stem cells**
 - a. Cai, Xiongwei, et al. "Runx1 deficiency decreases ribosome biogenesis and confers stress resistance to **hematopoietic** stem and progenitor cells." *Cell stem cell* 17.2 (2015): 165-177.



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- b. Laurenti, Elisa, et al. "CDK6 Levels Regulate Quiescence Exit in Human **Hematopoietic** Stem Cells." *Cell stem cell* 16.3 (2015): 302-313.

12. Pluripotent stem cells

- a. Sasaki, Kotaro, et al. "Robust in vitro induction of human germ cell fate from **pluripotent stem cells**." *Cell stem cell* 17.2 (2015): 178-194.
- b. Park, Chul-Yong, et al. "Functional correction of large factor VIII gene chromosomal inversions in hemophilia A patient-derived **iPSCs** using CRISPR-Cas9." *Cell stem cell* 17.2 (2015): 213-220.

13. Colon cancer stem cells

- a. Wu, ZhengMing, et al. "TPO-induced metabolic reprogramming drives liver metastasis of colorectal cancer CD110+ **tumor-initiating cells**." *Cell stem cell* 17.1 (2015): 47-59.
- b. Shah, Manasvi S., et al. "Comparative effects of diet and carcinogen on microRNA expression in the stem cell niche of the mouse **colonic** crypt." *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease* 1862.1 (2016): 121-134.

14. Blood production

- a. Pietras, Eric M., et al. "Functionally Distinct Subsets of Lineage-Biased Multipotent Progenitors Control Blood Production in Normal and Regenerative Conditions." *Cell stem cell* 17.1 (2015): 35-46.
- b. Nai, Antonella, et al. "The second transferrin receptor regulates red blood cell production in mice." *Blood* 125.7 (2015): 1170-1179.

15. Artificial Blood production

- a. Giarratana, Marie-Catherine, et al. "Proof of principle for transfusion of in vitro-generated red blood cells." *Blood* 118.19 (2011): 5071-5079.
- b. Jobaliya, Chintan D., et al. "Targeted Application of Human Genetic Variation Can Improve Red Blood Cell Production from Stem Cells." *Cell Stem Cell* 18 (2016): 1-6.

16. Gene Editing in Stem Cells

- a. Hoban, Megan D., et al. "Correction of the sickle cell disease mutation in human hematopoietic stem/progenitor cells." *Blood* 125.17 (2015): 2597-2604.
- b. Wang, Jianbin, et al. "Homology-driven genome editing in hematopoietic stem and progenitor cells using ZFN mRNA and AAV6 donors." *Nature biotechnology* 33.12 (2015): 1256-1263.

17. Cardiac regeneration

- a. Wu, Haodi, et al. "Epigenetic Regulation of Phosphodiesterases 2A and 3A Underlies Compromised β -Adrenergic Signaling in an iPSC Model of Dilated Cardiomyopathy." *Cell stem cell* (2015).
- b. Dutta, Partha, et al. "Myocardial Infarction Activates CCR2+ Hematopoietic Stem and Progenitor Cells." *Cell stem cell* 16.5 (2015): 477-487.

18. Retinogenesis

- a. Hiler, Daniel, et al. "Quantification of retinogenesis in 3D cultures reveals epigenetic memory and higher efficiency in iPSCs derived from rod photoreceptors." *Cell stem cell* 17.1 (2015): 101-115.
- b. Farber, Debora B., and Diana Katsman. "Embryonic Stem Cell-Derived Microvesicles: Could They be Used for Retinal Regeneration?." *Retinal Degenerative Diseases*. Springer International Publishing, 2016. 563-569.

19. Mesenchymal stem cells and cancer

- a. Wang, Shihua, et al. "Lung cancer exosomes initiate global long non-coding RNA changes in mesenchymal stem cells." *International journal of oncology* 48.2 (2016): 681-689.
- b. Cui, Benjamin G., et al. "MSC-Regulated MicroRNAs Converge on the Transcription Factor FOXP2 and Promote Breast Cancer Metastasis." *Cell stem cell* 15.6 (2014): 762-774.

20. Skeletal stem cells

- a. Choi, Ji Suk, et al. "Exosomes from differentiating human **skeletal** muscle cells trigger myogenesis of stem cells and provide biochemical cues for skeletal muscle regeneration." *Journal of Controlled Release* 222 (2016): 107-115.
- b. Ryall, James G., et al. "The NAD⁺-dependent SIRT1 deacetylase translates a metabolic switch into regulatory epigenetics in skeletal muscle stem cells." *Cell stem cell* 16.2 (2015): 171-183.

21. Small Molecules and stem cells

- a. Zhang, Lei, et al. "**Small Molecules** Efficiently Reprogram Human Astroglial Cells into Functional Neurons." *Cell stem cell* 17.6 (2015): 735-747.
- b. Yu, Chen, et al. "Small molecules enhance CRISPR genome editing in pluripotent stem cells." *Cell stem cell* 16.2 (2015): 142-147.

22. Cancer-initiating stem cells in Skin and Osteosarcoma

- a. Beck, Benjamin, et al. "Different levels of Twist1 regulate skin tumor initiation, stemness, and progression." *Cell stem cell* 16.1 (2015): 67-79.



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- b. Martins Neves, Sara R., et al. "Osteosarcoma Stem Cells Have Active Wnt/ β -catenin and Overexpress SOX2 and KLF4." *Journal of cellular physiology* 231.4 (2016): 876-886.

23. Cancer-initiating stem cells in Liver and AML

- a. Wang, Yanying, et al. "The Long Noncoding RNA lncTCF7 Promotes Self-Renewal of **Human Liver Cancer Stem Cells** through Activation of Wnt Signaling." *Cell stem cell* 16.4 (2015): 413-425.
- b. Bruedigam, Claudia, et al. "Telomerase inhibition effectively targets mouse and human **AML stem cells** and delays relapse following chemotherapy." *Cell stem cell* 15.6 (2014): 775-790.

24. Intestinal stem cells and cancer

- a. Schuijers, Jurian, et al. "Ascl2 Acts as an R-spondin/Wnt-Responsive Switch to Control Stemness in **Intestinal Crypts**." *Cell stem cell* 16.2 (2015): 158-170.
- b. Asfaha, Samuel, et al. "Krt19+/Lgr5- cells are radioresistant cancer-initiating stem cells in the colon and intestine." *Cell stem cell* 16.6 (2015): 627-638.

25. Airway Basal Stem/Progenitor Cells and fibrosis

- a. Pardo-Saganta, Ana, et al. "Injury Induces Direct Lineage Segregation of Functionally Distinct **Airway Basal Stem/Progenitor Cell Subpopulations**." *Cell stem cell* 16.2 (2015): 184-197.
- b. Kramann, Rafael, et al. "**Perivascular** Gli1+ progenitors are key contributors to injury-induced organ fibrosis." *Cell stem cell* 16.1 (2015): 51-66.

26. CRISPR in Human Gene Therapy

- a. 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.
- b. 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.

27. Endometrial Stem Cells

- a. Thiruchelvam, Uma, Mary Wingfield, and Cliona O'Farrelly. "Increased uNK Progenitor Cells in Women With Endometriosis and Infertility are Associated With Low Levels of Endometrial Stem Cell Factor." *American Journal of Reproductive Immunology* (2016).
- b. Shoaee Hassani, Alireza, et al. "Differentiation of human endometrial stem cells into urothelial cells on a three-dimensional nanofibrous silk-collagen scaffold: an autologous cell resource for reconstruction of the urinary bladder wall." *Journal of tissue engineering and regenerative medicine* 9.11 (2015): 1268-1276.