

Reading Material for Biomedical Engineering Graduate Student Exam

Exam period:

Start: Friday October 27th at 12 pm (noon)

Due: Sunday October 29th at 12 pm (noon)

Format: Take home exam. Open book and on-line resources.

Exam Goal: Students will be given a task that will involve 2D or 3D cultures of human induced pluripotent stem cells (*h*-iPSC) which will require experimental tissue engineering design, interpretation of data and possible artefacts, and design of an assay using the system that has been designed. The exam will test the student's scientific reasoning in designing and interpreting experiments not in their specific expertise.

I. Overview of iPSC models for Alzheimer's disease (AD)

1. Barak, M., Fedorova, V., Pospisilova, V. *et al.* Human iPSC-Derived Neural Models for Studying Alzheimer's Disease: from Neural Stem Cells to Cerebral Organoids. *Stem Cell Rev and Rep* **18**, 792–820 (2022). <https://doi.org/10.1007/s12015-021-10254-3>

II. Experimental Procedures for 3D Neuron-Microglia cultures from h-iPSCs

1. Abud EM, Ramirez RN, Martinez ES, Healy LM, Nguyen CHH, Newman SA, Yeromin AV, Scarfone VM, Marsh SE, Fimbres C, Caraway CA, Fote GM, Madany AM, Agrawal A, Kaye R, Gyls KH, Cahalan MD, Cummings BJ, Antel JP, Mortazavi A, Carson MJ, Poon WW, Blurton-Jones M. iPSC-Derived Human Microglia-like Cells to Study Neurological Diseases. *Neuron*. 2017 Apr 19;94(2):278-293.e9. doi: 10.1016/j.neuron.2017.03.042
2. Haenseler W, Sansom SN, Buchrieser J, Newey SE, Moore CS, Nicholls FJ, Chintawar S, Schnell C, Antel JP, Allen ND, Cader MZ, Wade-Martins R, James WS, Cowley SA. A Highly Efficient Human Pluripotent Stem Cell Microglia Model Displays a Neuronal-Co-culture-Specific Expression Profile and Inflammatory Response. *Stem Cell Reports*. 2017 Jun 6;8(6):1727-1742. doi: 10.1016/j.stemcr.2017.05.017.
3. Walsh RM, Harschnitz O, Ciceri G, Sneeboer M, Mazutis L, Setty M, Zumbo P, Betel D, de Witte LD, Pe'er D, Studer L. Fully defined human pluripotent stem cell-derived microglia and tri-culture system model C3 production in Alzheimer's disease. *Nat Neurosci*. 2021 Mar;24(3):343-354. doi: 10.1038/s41593-020-00796-z.

III. Potential Experimental Artefacts

1. Yuan C, Gao J, Guo J, Bai L, Marshall C, Cai Z, Wang L, Xiao M. Dimethyl sulfoxide damages mitochondrial integrity and membrane potential in cultured astrocytes. *PLoS One*. 2014 Sep 19;9(9):e107447. doi: 10.1371/journal.pone.0107447.

2. Brunner JW, Lammertse HCA, van Berkel AA, Koopmans F, Li KW, Smit AB, Toonen RF, Verhage M, van der Sluis S. Power and optimal study design in iPSC-based brain disease modelling. *Mol Psychiatry*. 2023 Apr;28(4):1545-1556. doi: 10.1038/s41380-022-01866-3.

IV. Metabolic Shuttles of the CNS and AD

1. Mason S. Lactate Shuttles in Neuroenergetics-Homeostasis, Allostasis and Beyond. *Front Neurosci*. 2017 Feb 2;11:43. doi: 10.3389/fnins.2017.00043.
2. Monsorno, K., Ginggen, K., Ivanov, A. *et al.* Loss of microglial MCT4 leads to defective synaptic pruning and anxiety-like behavior in mice. *Nat Commun* **14**, 5749 (2023). <https://doi.org/10.1038/s41467-023-41502-4>