BIPN194/BGGN284: Stem Cell Models in Neuroscience
Winter 2024

Professor: Hiruy Meharena
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Class Meeting Time: Wednesday 09:00AM-10:20AM
Location: York 3010
Course Canvas page: https://canvas.ucsd.edu/courses/53224

Office Hours: By appointment only and required for the presenting group of the week. The group should arrange to meet with me on Friday or Monday before your Wednesday presentation. Members of the presenting group must coordinate their schedules and then a representative should coordinate with me to find a time we can meet. I highly encourage you to share your contact information (email and phone numbers) with your group to facilitate scheduling. The meeting is intended to provide feedback on presentation materials and answer any questions about the paper to help in presentation preparation. Groups should come prepared having read the materials, have prepared a presentation, and know what they need help with. The best way to contact me is by e-mail to schedule your personal meetings. Please include "BIPN194 or BGGN248" in the subject line of emails concerning this class.

Course Website: There will be a Canvas site for the course (https://canvas.ucsd.edu/courses/45344). Announcements, updates, postings, required reading material and grades will be communicated on the course website using Canvas.

Prerequisites: This upper-division course is intended for junior/senior undergraduate students and Master's students. Prior to enrollment, BIPN 100 (Physiology I) or BIPN 140 (Cellular Neurobiology) must be completed.

Course Format: The first and second lectures will be instructor led. All other course meetings will be student-led discussions of primary research literature. All meetings will be very interactive, with all students expected to participate in discussions and presentation. **Expect to spend at least 4 hours/week on the assigned reading and summary preparation, and 10+ hours the week you are presenting a paper.**

Syllabus: (subject to change)

class	Date	Lecture Topic	Group #
1	**Jan 10**	**Introduction to course structure and Brain Cell Types**	
2	**Jan 17**	Generation of Pluripotent Stem Cells	
3	**Jan 24**	Organoids – Autism spectrum disorder	**1**
4	**Jan 31**	Genomics - Schizophrenia	**2**
5	**Feb 7**	Dopaminergic Neurons – Parkinson's Disease	**3**
6	**Feb 14**	Brain Cell Types – Alzheimer's Disease	**4**
7	**Feb21**	Oligodendrocytes – Multiple Sclerosis	**5**
8	**Feb 28**	Microglia – CRISPR	**6**
9	**Mar 6**	Human Mouse chimeras	**7**
10	**Mar 13**	**No class work on Final assignment due March 15th**	

Course Materials: No textbook is required. PDFs of the required readings will be posted on the course Canvas website. In addition, other papers will be recommended to give additional background on concepts covered in the required reading. Students may need to seek out other

resources if further background information is needed to help them understand the required readings. These additional readings can be found by searching PubMed (https://www.ncbi.nlm.nih.gov/pubmed/). Be sure to be logged into the UCSD server while searching PubMed in order to have access to most journal subscriptions.

Grading and Evaluations:

Attendance	8%	40pts (4ea)
In class participation (discussion 6/8 and 8 written evaluations)	12%	60pts (6.66/2.5)
Primary research article summary (8 total)	30%	150pts (18.75 ea)
Group presentation	30%	150pts
Final assignment: review article	20%	100pts
Total	100%	500pts

Grading Scale: Grades will be rounded to the nearest whole number. The class grades will not be curved.

%	Grade	%	Grade	%	Grade	%	Grade
>97	A+	87-89	B+	77-79	C+	60-69	D
93-97	A	83-86	B	73-76	C	0-59	F
90-92	A-	80-82	B-	70-72	C-		

Summary of due dates: Please upload your documents to Canvas.

Weekly Article Summary:	Due on **Wednesday** by 11:59pm (first one due April 12, 2023).
Weekly Presentation Evaluation:	Due on **Wednesday** following the Thursday presentation by 11:59pm (first one due April 19, 2023).
Final writing assignment:	Due **Sunday, June 11, 2023** by 11:59pm.
Group presentation:	Please submit *one copy per group* by 9am the day of your presentation.

Attendance and Participation: Attendance is mandatory. Students will be expected to participate in the discussion of assigned papers during class and to ask questions during the presentation. Unexcused absences or arriving late will impact your participation grade. If students are not participating on their own, **the instructor will randomly call on individuals to respond to questions and comments.**

Weekly written summary: Written summaries in Word or PDF format are due by **11:59pm the Wednesday before class**. *Late assignments will not be accepted*. Students are required to read the assigned paper and write a one-page summary (maximum) on the assigned article, **except** on the day you are presenting. Please use 1" margin, single space, Arial/Times font, and font size 11 for the writing assignment. Your summary should address the following points:

- What is the overall question being asked?
- Why is this question important?
- What were the specific hypotheses and how did the authors test them? Discuss the protocol/s used to generate the different 2D and 3D brain cell types.
- What conclusions did the authors arrive at from their experiments? (be sure to state the experiments)
- Did their results address their question?

- What is the next research question that follows from the author's findings in the paper (in your opinion)?
- What are the implications of the paper in the field/disease?
- What are three questions you have about the paper? These can be about a technique being used, why a certain experiment was done, confusion on interpreting data etc. Provide these in bullet points at the end of the document. These questions should allow you to participate in the discussions.

Presentation:
Groups will be determined and posted on canvas and mentioned in class two weeks in advance of the presentation but are subject to change depending on add/drops, with the exception of the first group that will be announced on canvas on Friday April 7th. Each group will have 40 minutes for the presentation and 15-20 minutes for questions and discussion. Each group member will have equal presentation time and should be prepared to answer questions and engage the class in discussions. Presentations will be graded using a rubric. Please see the end of the syllabus for a summary of the rubric.

Group meetings to prepare for presentations: Each group of presenters needs to exchange contact information (phone numbers and email information) and arrange meetings to discuss the overall presentation and how the presentation will be divided among group members. These meetings are essential. I will also meet with the entire group Wednesday, Thursday, or Friday the week before to discuss the presentation and help with questions. You are required to set this meeting with me ahead of time and the group should select one member to contact me after you find a time that works for all members. This is a mandatory meeting that will help with your presentation. Each group member should be prepared for this meeting and have read the paper and prepared ~4-5 slides each related to their section of the presentation. After our meeting, the group may wish to meet again to modify the presentation. Note that while the presentation should be cohesive, each group member will receive an individual grade that is reflective of their part in the project. Each group member should be very familiar with the paper and should be able to answer questions and lead the discussion if needed.

Presentation details: The group's entire presentation should be in one presentation document. Please use PowerPoint, Google slides, or Keynote file formats. Please make sure that all group members and I have a copy of the presentation in case there are technical issues. Your presentation should be uploaded to Canvas by 8am the day of the presentation. The presenting group should arrive to class promptly to ensure that the presentation and screen sharing is working properly.

Presentation Components:

1. *Background/Introduction*: Provide the necessary background for the audience to understand the overall research question(s), experimental methods, conclusions drawn from experimental data, and the significance of the research in the context of the field. Then, describe the biological question that the authors were addressing and the primary stem cell differentiation approach utilized.

2. *Results:* Present the experimental results in a logical order. How did the authors address their question? Explain the tools and methodology beyond the differentiation protocol that the authors use to address the question. What are the specific conclusions from their results? I recommend that the figures in the paper are split up between group members.

Most figures in papers have multiple panels. Many papers have supplementary figures that support the main figure and these are required reading for the paper. You will need to decide which of the panels in a figure to present and if any supplemental figures should be presented. For each figure you should explain what is being tested and why. Most figures have one or two main conclusions, be sure you are clear about these and can explain these to the class. Experiments require proper controls, also make sure you understand why the given controls were used. Discuss reservations, if any, about the data.

3. *Overall conclusions and implications*: Overall, what are the findings of this paper? Does the data support the conclusions? Are there alternative conclusions that could be drawn from the data? What are the next steps that follow from these experiments? What is the impact of the findings on the field?

Non-presenters: You are expected to read every paper before coming to class and be prepared to discuss and ask questions. During class you are expected to participate in discussion and ask questions. If students are not participating on their own, the instructor will randomly call on individuals to respond to questions and comments. **At the end of each class you will write a short (1-2 paragraphs),** constructive evaluation of the presentation, except on the day you are presenting. These evaluations need to address how the presentation helped clarify the paper and your questions, what aspects of the presentation were particularly good, and how the presentation could have been improved. These evaluations need to be constructive and are an important part of your participation grade. Your comments may be shared with the presenters. **Evaluations are due on the Wednesday by 11:59pm** the week following the presentation and are to be uploaded on Canvas in a Word Doc file.

Final writing assignment: Your final writing assignment will be due by **11:59pm** on Sunday, **June 11th**.
Find a paper that you would recommend for the class next year. Write a two-page, single spaced paper (references should be on a separate page) about the paper and why you chose it. Begin by stating the question that the authors are addressing. Include background on what was known regarding this research question prior to the publication of the paper you select. Describe the experiments that were performed and include information related to the methods used as well as the conclusions drawn from each experiment. Elaborate on the overall conclusion(s) of the paper and how it influenced, or will influence, future studies.
Finally, as a separate section, write a paragraph on the paper you most enjoyed this quarter and why. Upload the Word docs on Canvas. In addition to your paper, upload the PDF (and supplemental material) of the paper you are evaluating.

BGGN284 students: The course requirements are the same for you with the exception that your **final report is three pages**, with more details on significance and future directions. The background section should be longer and the section on potential implications/significance should be expanded. This should include a discussion of follow up experiments.

CLASSROOM CODE OF CONDUCT:

Technology Etiquette: Please refrain from engaging in personal internet or other communications during class and ensure that your cell phones and tablets are turned off. This is a participation-based course.

Academic Integrity: Integrity of scholarship and learning is fundamental to creating our classroom community and the academic community at large. The University expects that both students and faculty will honor this principle and in so doing protect the validity of University intellectual work. Therefore, Academic dishonesty will not be tolerated. This means that all academic work you submit for this course should be your own new original work**. Chatgpt or any AI/machine learning based technology IS NOT ALLOWED. Use of this technology on your assignments will be considered academic dishonesty.** To hold everyone accountable for their actions, any serious suspected instances of a breach of academic integrity will be reported to the Academic Integrity Office for review. For more information on academic integrity, please visit https://students.ucsd.edu/academics/academic-integrity/index.html.

Discussion Paper Summary

Week 1	How to read a paper, course overview, and introduction to cell types of the brain
Week 2	**Discussion paper**: Generation of Pluripotent Stem Cells (iPSCs) Takahashi et al. Differences and similarities between human and chimpanzee neural progenitors during cerebral cortex development (2007) Cell. Volume 131, Issue 5, 861-872. **Background reading**: 1. Takahashi and Yamanaka. Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors. Cell. Volume 126, Issue 4, 663-676.
Week 3	**Discussion Paper:** Organoids – Autism spectrum disorder Paulsen et al. Autism genes converge on asynchronous development of shared neuron classes. (2022) Nature. 602, 268–273. **Background reading**: 1. Santos et al. Modeling Autism Spectrum Disorders with Induced Pluripotent Stem Cell-Derived Brain Organoids. (2023) Biomolecules. 13(2): 260. 2. Zhang et al. Patterning of brain organoids derived from human pluripotent stem cells. (2022) Current Opinion in Neurobiology. 74:102536
Week 4	**Discussion Paper:** Genomics - Schizophrenia Rajarajan, et al. Neuron-specific signatures in the chromosomal connectome associated with schizophrenia risk. (2019) Science. 362(6420). **Background reading**: 1. Räsänen et. al. The iPSC perspective on schizophrenia. (2022) Trends in Neurosciences. Volume 45, Issue 1, 8-26. 2. Rao et. al. A 3D Map of the Human Genome at Kilobase Resolution Reveals Principles of Chromatin Looping. (2014) Cell. Volume 159, Issue 7, 1665-1680.
Week 5	**Discussion Paper**: Dopaminergic Neurons – Parkinson's Disease Woodard et al. iPSC-Derived Dopamine Neurons Reveal Differences between Monozygotic Twins Discordant for Parkinson's Disease. (2014) Cell Reports. Volume 9, Issue 4, 1173-1182. **Background reading**: 1. Liu and Cheung. Stem Cell-Based Therapies for Parkinson Disease. (2019) Int J Mol Sci. (21): 8060. 2. Schweitzer et al. Personalized iPSC-Derived Dopamine Progenitor Cells for Parkinson's Disease (2020) The New England Journal of Medicine. 382:1926-1932.
Week 6	**Discussion paper:** Brain Cell Types – Alzheimer's Disease Lin et al. APOE4 Causes Widespread Molecular and Cellular Alterations Associated with Alzheimer's Disease Phenotypes in Human iPSC-Derived Brain Cell Types. (2018). Neuron 98, 1141–1154. **Background reading**:

	1. Penney et al. Modeling Alzheimer's disease with iPSC-derived brain cells. (2020) Molecular Psychiatry. Volume 25, 148–167.
Week 7	**Discussion paper**: Oligodendrocytes – Multiple Sclerosis Plastini et al., Transcriptional abnormalities in induced pluripotent stem cell-derived oligodendrocytes of individuals with primary progressive multiple sclerosis. (2022). Front. Cell. Neurosci. Volume 16 - 2022. **Background reading:** 1. Livesey et. al. Maturation and electrophysiological properties of human pluripotent stem cell-derived oligodendrocytes. (2016) Stem Cells. 34(4): 1040–1053. 2. Albert et. al. Utilising Induced Pluripotent Stem Cells in Neurodegenerative Disease Research: Focus on Glia. (2021) Int J Mol Sci. 22(9): 4334.
Week 8	**Discussion paper**: Microglia – CRISPR Dräger et al. A CRISPRi/a platform in human iPSC-derived microglia uncovers regulators of disease states (2022) Nature Neuroscience. Volume 25, 1149–1162. **Background reading**: 1. Timmerman et al. An Overview of in vitro Methods to Study Microglia. (2018) Front. Cell. Neurosci. Volume 12 - 2018. 2. Hasselmann et al. Human iPSC-derived microglia: A growing toolset to study the brain's innate immune cells. (2020) Glia. 68(4): 721–739. 3. Paolicelli et al. Microglia states and nomenclature: A field at its crossroads. (2022) Neuron. Volume 110, issue 21, 3458-3483.
Week 9	**Discussion paper:** Human Mouse chimeras 1. Revah et. al. Maturation and circuit integration of transplanted human cortical organoids (2022) Nature. Volume 610, 319–326. **Background reading**: 2. Jgamadze et al. Structural and functional integration of human forebrain organoids with the injured adult rat visual system (2023) Nature. Cell Stem Cell 30, 137–152. 3. Mansour et al. An in vivo model of functional and vascularized human brain organoids (2018) Nature Biotechnology volume 36, 432–441.
Week 10	No class work on Final writing assignment-due March 15th

Rubric Summary

Talks will be scored on the following sections: Introduction, Data, and Conclusion.

Background/ Introduction	**Criteria**
Broad Introduction	Present all information that is required for listener's understanding of the research
Main research question	Clearly explain
Background	Clearly explains what others have done to set the stage for this research
Significance	Makes clear what motivates the authors to explore this question and potential

Results	**Criteria**
Logical Flow	Logically follows the data and each conclusion is clearly explained and justified
Methods	Clearly explains methods and how experiments address research question(s)
Results	Presents necessary data
Clarity	Clearly explains significant results and figures

Conclusion/ Implications	**Criteria**
Inferences	Explains what the work infers/means, competing explanations well addressed
Impact of work for field	Clearly explain and includes discussion of strength and weakness of the paper
Future research directions	Suggests what should be done next or points out new questions raised by work