BIPN194/BGGN284 Advanced Topics in Physiology/Neurobiology: "Synapse and Autism"

Wednesdays 10-11:20 am, York 3010

Professor Yishi Jin
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[*please include BIPN194 in subject line of any emails concerning the class*]
Office Hours: Mon 4-5 pm, in person @ Bonner Hall 2418, or via zoom by appointment.

Brief outline of the course:

Apr 5: Introduction to class organization, and assignment of discussion groups.

Apr 12: Introduction lecture on synapses and autism (Jin)

Apr 19: pre-synaptic terminal/group 1

Apr 26: post-synaptic terminal/group 2

May 3: synaptic adhesion/group 3

May 10: autism genetics/group 4

May 17 autism genetics/group 5

May 24: autism genetics /group 6

May 31: roundtable presentation preparation

June 7: final presentation and discussion

(June 8*:* back-up presentation)

Prerequisites: *This course will assume strong knowledge of molecular biology, genetics, cell biology, and neurobiology.* BICD 100 (Genetics), BIPN 100 (Mammalian Physiology), BICD 110 (Cell Biology), and BIPN140 (cellular neurobiology) are strongly recommended.

General Description of the Course
Synapses are where the actions in the nervous system take place! Many neurological diseases are associated with synapse dysfunction. Recent genetic studies of Autism or Autism spectral disorders (ASD) have implicated many mutations affecting genes that function in synapses. The goals of the course are to provide basic knowledge on how synapses are formed and regulated, and to discuss cutting-edge research on understanding the causative associations of genes in Autism. Specifically, we will first focus on the key studies that reveal the tripartite components of the synapse. We will

then discuss representative research on understanding autism-associated genetic mutations on synapses and behaviors using animal models.

After the introductory lectures by the instructor, each class will be student-led presentation and discussion of primary research literature. The course is highly interactive, and everyone must speak and give feedback to each other!

Evaluation: There is NO final exam. Your grade will be based on:

(1) Your performance in your group presentation.
(2) Your attendance and audible participation in each class.
(3) Your presentation and participation in roundtables (last two classes)
(4) Your constructive feedback to presenters.

Bonus: ***Submit at least one question, prior to the start of the class,*** *on the discussion paper when you are NOT a presenter.* Questions can range from clarification of scientific concepts or hypothesis, research jargon, data analysis, experimental procedure, authors' conclusions.

Readings
All reading materials are primary research papers and review articles, which are freely available online through UCSD library, so along as you use a UCSD IP address to access the research papers. For reading, PDFs of the papers are convenient; hard copies will not be provided. For your presentation, nearly all data figures can be downloaded as ppt or equivalent format. To find any primary papers, use Pubmed (https://www.ncbi.nlm.nih.gov/pubmed/) or Google Scholar (scholar.google.com).

There is no textbook for this course. Use your textbooks from other classes (such as BIPN140) for general knowledge on neuroscience. Scholar review articles are recommended to help understanding the general background.

Expect to spend at least 4 hours a week on the reading, 8-10 hours when you are presenting a paper.

Group presentations
PRESENTERS:
Each of you is a member of a presentation group (3-4 students), and everyone will present twice in this class. Each presentation is on one of the assigned research papers, and the total presentation should be 45-50 minutes. Try to insert 2-3 breakout time during presentation to discuss questions with non-presenters. Each member of the group should be prepared to answer questions and engage class discussion of their portion of the presentation.

NONPRESENTERS:
You are expected to read **EVERY** discussion paper **before** coming to class and to be prepared to discuss it. During the class presentation you are expected to actively participate in discussion, and meet the presenters in breakout. After each presentation (except your own), you will submit a short and constructive evaluation of the

presentation.

PRESENTATION FORMAT

Each member of a group should prepare between 3-5 slides (in ppt or a format agreeable by the entire group). The entire presentation (made as power point or keynote or other web-format) should be on one computer and uploaded to class website after presentation. Presenting group should be in classroom ~ 5 minutes early to set up.

PRESENTATION CONTENT

1. *Background/Introduction*: What is the *biological problem*? What are the authors attempting to show? How does this work fit into the overall findings of the field? What tools or methodologies are going to be used to approach the problem?
2. *Results /data*: recommend that each group member present one or two Figures/Tables each. For each Figure or experiment, address (a) what is being shown, and (b) why and how was this experiment done, in the context of the paper. Discuss reservations or questions you have about the data. It is required that you read and understand all the data, including those in "supplemental information", which is often in a separate file from the pdf of the article.
3. *Conclusions/Discussions:* What are the conclusions? How strong does the data support the model or hypothesis? What are the 'next steps' or remaining questions?

GROUP MEETINGS PRIOR TO PRESENTATION

It is essential that all members of the group meet prior to the presentation.
Group members should exchange phone numbers and e-mail addresses and arrange to meet at least twice to prepare for the presentation. Research papers are complicated, and the level of background knowledge among classmates varies. By working as a team you can give an effective presentation.
I will meet with the entire group at the end of class on Wednesday to guide organization of presentation.

PEER EVALUATIONS

After each presentation, non-presenters will fill out a short evaluation of the presentation. Did the presentation and discussion clarify the work? Were your questions answered? Do you have suggestions for improving the quality of the presentations? Comments should be constructive. This is a very important factor in your course participation.

ATTENDANCE

You are expected to attend ALL class meetings (sign in at each class). Late arrival (i.e.>5 minutes) will likely cause grade reduction. Acceptable excuses for missing a class are: documented medical emergency and family emergency; university sponsored events. Vacation, oversleeping, or deadlines or demands from other courses/exams are not acceptable excuses for missing this class.

READING LIST (please download pdf from PubMed: http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=search&db=pubmed)

General readings for the entire course

The autism sequencing consortium: large-scale, high-throughput sequencing in autism spectrum disorders. Buxbaum JD, Daly MJ, Devlin B, Lehner T, Roeder K, State MW; Autism Sequencing Consortium. *Neuron.* 2012 Dec 20;76(6):1052-6. DOI: 10.1016/j.neuron.2012.12.008

Current knowledge on the genetics of autism and propositions for future research. Bourgeron T. *C R Biol.* 2016 Jul-Aug;339(7-8):300-7. DOI: 10.1016/j.crvi.2016.05.004

Autism spectrum disorder: neuropathology and animal models. Varghese M, Keshav N, Jacot-Descombes S, Warda T, Wicinski B, Dickstein DL, Harony-Nicolas H, De Rubeis S, Drapeau E, Buxbaum JD, Hof PR. Acta Neuropathol. 2017 Oct;134(4):537-566. DOI: 10.1007/s00401-017-1736-4.

Weekly topics and discussion papers

Apr 5: Introduction and organization of the course: Jin

Apr 12: Introduction lecture: Jin

Apr 19: presynaptic terminal/group I

Presenters:

Background reading:

A molecular machine for neurotransmitter release: synaptotagmin and beyond.

Südhof TC. *Nat Med.* 2013 Oct;19(10):1227-31.

Discussion paper:

Synaptotagmin I: a major Ca2+ sensor for transmitter release at a central synapse.

Geppert M, Goda Y, Hammer RE, Li C, Rosahl TW, Stevens CF, Südhof TC. *Cell.* 1994 Nov 18;79(4):717-27. doi: 10.1016/0092-8674(94)90556-8.

Apr 26: postsynaptic terminal/group 2

Presenters:

Background reading:

The Shank family of scaffold proteins.

Sheng M, Kim E. *J Cell Sci.* (2000) v113:1851-6.

Discussion paper:

A preformed complex of postsynaptic proteins is involved in excitatory synapse development.

Gerrow K, Romorini S, Nabi SM, Colicos MA, Sala C, El-Husseini A. *Neuron.* 2006 Feb 16;49(4):547-62. DOI: 10.1016/j.neuron.2006.01.015

May 3: synaptic adhesion/group 3

Presenters:

Background reading:

Neuroligins and neurexins link synaptic function to cognitive disease.

Südhof TC. *Nature.* 2008 Oct 16;455(7215):903-11.

Discussion paper:

Neurexin mediates the assembly of presynaptic terminals.

Dean C, Scholl FG, Choih J, DeMaria S, Berger J, Isacoff E, Scheiffele P. *Nat Neurosci.* 2003 Jul;6(7):708-16. DOI: 10.1038/nn1074

May 10: autism genetics/group 4

Presenters:

Background reading:

The autism sequencing consortium: large-scale, high-throughput sequencing in autism spectrum disorders.

Buxbaum JD, Daly MJ, Devlin B, Lehner T, Roeder K, State MW; Autism Sequencing Consortium. *Neuron.* 2012 Dec 20;76(6):1052-6.

Discussion papers:

Mutations of the X-linked genes encoding neuroligins NLGN3 and NLGN4 are associated with autism.

Jamain S, Quach H, Betancur C, Råstam M, Colineaux C, Gillberg IC, Soderstrom H, Giros B, Leboyer M, Gillberg C, Bourgeron T; Paris Autism Research International Sibpair Study. *Nat Genet.* 2003 May;34(1):27-9. doi: 10.1038/ng1136.

Autism-related neuroligin-3 mutation alters social behavior and spatial learning. Jaramillo TC, Liu S, Pettersen A, Birnbaum SG, Powell CM. *Autism Res.* 2014 Apr;7(2):264-72. DOI: 10.1002/aur.1362

May 17: Shank autism genetics/group 5.

Presenters:

Background reading:

The emerging role of SHANK genes in neuropsychiatric disorders. Guilmatre A, Huguet G, Delorme R, Bourgeron T. *Dev Neurobiol.* 2014 Feb;74(2):113-22.

Discussion paper:

Mice with Shank3 Mutations Associated with ASD and Schizophrenia Display Both Shared and Distinct Defects.

Zhou Y, Kaiser T, Monteiro P, Zhang X, Van der Goes MS, Wang D, Barak B, Zeng M, Li C, Lu C, Wells M, Amaya A, Nguyen S, Lewis M, Sanjana N, Zhou Y, Zhang M, Zhang F, Fu Z, Feng G. *Neuron.* 2016 Jan 6;89(1):147-62.
DOI: 10.1016/j.neuron.2015.11.023

May 24: Neuroligin autism therapy /group 6

Presenters:

Background reading:
Oxytocin as Treatment for Social Cognition, Not There Yet.
Erdozain AM, Peñagarikano O. Front Psychiatry. 2020 Jan 9;10:930.
doi: 10.3389/fpsyt.2019.00930.

Discussion paper:

Rescue of **oxytocin** response and social behaviour in a mouse model of autism.

Hörnberg H, Pérez-Garci E, Schreiner D, Hatstatt-Burklé L, Magara F, Baudouin S, Matter A, Nacro K, Pecho-Vrieseling E, Scheiffele P. Nature. 2020 Aug;584(7820):252-256. doi: 10.1038/s41586-020-2563-7.

May 31: round-table presentation preparation
June 7: final presentation-discussion