SYLLABUS FOR TOPICS IN CELL BIOLOGY AND NEUROSCIENCE, 01:146:464, Spring 2023
Keck Center Conference Room, Nelson D-251, 2:00 – 3:20 pm

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Course Description
This course is intended for upper-level students pursuing a major in a Life Science field who are interested in learning research principles and experimental approaches helping them to understand how research leads to scientific discoveries with potential for therapy in clinical problems. Students should have taken basic cell biology or neurobiological courses to be prepared for the more intense research studies that will be covered in the course. This long story of research is designed to show how cutting-edge technology - it was the use of monoclonal antibodies at the time of research - can lead to important insights into the functions of the functions of the nervous system. The instructor with extensive research experience will introduce students to primary research publications addressing specific topics in cell biology or neuroscience and engage students in critical thinking and in-depth discussions. In the first weekly session for each topic (on a Tuesday), the instructor will present and discuss the indicated publications. In the second weekly session (on a Thursday), the assigned student will follow up on these publications with comments, critique and thoughts for future experiments. The whole class will be encouraged to participate. At the end of each class, the students are asked to rate the performance of the instructor by putting their comments on a plain piece of paper (without names) which will be collected in a box. These comments will be welcomed feedbacks. The grading policy will be based on class participation (20%), the students' presentations (30%) and the final exam (50%).

Title
Discoveries in Cellular and Molecular Neurobiology

Topic
The cell adhesion molecule L1 and its functions in the nervous system. Students will learn how this functionally seminal molecule was discovered and how its biological role has evolved from a cell adhesion molecule that contributes to nervous system development to one that is relevant to support recovery from injury, ameliorate neurodegenerative diseases, contribute to learning and memory and reduce tumor progression. Selected readings will illustrate how basic science insights into L1 functions have progressed to clinical potential.

Classes will focus on:
Introduction to the field of cell adhesion molecules.
Discovery of the L1 cell adhesion molecule.
L1 structure: member of the immunoglobulin superfamily.

L1 in neuronal migration and formation of neurites during neural development.
L1 in signal transduction.
L1 in synapse formation, synaptic plasticity or memory.
L1 in mitochondrial functions.
L1 as a co-transcription factor.
L1 in reducing the deficits of several neurodegenerative diseases in mouse and fish models.
Recovery from trauma using small organic compounds that act as agonistic L1 mimetics.
FDA-approved L1 agonist mimetic in ameliorating the L1 syndrome in afflicted individuals.
FDA-approved L1 antagonistic mimetics in inhibiting tumor cell migration and metastasis.

Learning Goals

The learning goals for this course are consistent with general goals set by the Department of Cell Biology and Neuroscience, as well as the Division of Life Sciences. They include:

1. Obtain factual and conceptual knowledge in neurodevelopment, neural trauma and regeneration, and exploring therapies for treating neural disease.
2. Develop an ability to summarize, integrate and organize scientific literature.
3. Use scientific logic and literature to develop a hypothesis for research related to course subjects.
4. Develop the ability to critique scientific literature from logical, feasible and ethical points of view for their relevance to human health and our society.
5. Learn from the instructor's very personal experience in dealing with professional setbacks, success, interactions with colleagues at national and international conferences as well as with students, technicians, postdoctoral fellows and the lay public.

Required Materials

There is no text for the course. Original publications covering the learning goals are available on Canvas. Lectures will be recorded and made available on Canvas. Students are requested to bring and use their own recording devices.

Grading Policy

The primary assignment for the course is to critically understand the literature and to experience the logical thread from the discovery of an adhesion molecule important in development to a molecule with potential in clinical settings. An example of the use of an FDA-approved agonist L1 mimetic with two boys affected by the L1 syndrome (not published) will be presented, but not graded. An example of the use of antagonistic FDA mimetics in a preclinical setting (not published) will be presented, but not graded. The grading policy will be based on class participation (20%), the students' presentations (30%) and the final exam (50%).

Grades are based on:

1. Student's presentation (with slides) in the second class of each week (30%).

Grades are based on the student's ability to understand the assigned papers, readiness to encourage and answer questions from other students and the instructor, and general

knowledge of cell biology and neurobiology. The presentation will be scored at the session and the student will be told the grade.

2. Final exam covering all the topics covered in the course (50%).

The final exam will consist of multiple-choice questions. A few examples of multiple-choice questions will be given each week to allow students to orient themselves for the final exam.

3. Class participation (20%). Participation will be counted.

Participation will be based on discussions during course sessions. Students showing poor participation will be encouraged to participate more or may be called upon to participate. Students' presence will be counted at each session.

Week	Date	Topic	References
1	January 17 and 19	Introduction to cell adhesion molecules Discovery of cell adhesion molecule L1	1. Sytnyk, V., Leshchyns´ka, I., and Schachner, M. (2017). Neural cell adhesion molecules of the immunoglobulin superfamily regulate synapse formation, maintenance and function. Trends Neurosci. 40, 295-308 2. Lindner, J., Rathjen, F.G., and Schachner, M. (1983). L1 mono- and polyclonal antibodies modify cell migration in early postnatal mouse cerebellum. Nature 305, 427-430. 3. Rathjen, F.G., and Schachner, M. (1984). Immunocytological and biochemical characterization of a new neuronal cell surface component (L1 antigen) which is involved in cell adhesion. EMBO J. 3, 1-10.
2	January 24 and 26	Structure of L1	1. Moos, M., Tacke, R., Scherer, K., Teplow, D., Früh, K., and Schachner, M. (1988). Neural adhesion molecule L1 as a member of the immunoglobulin superfamily with binding domains similar to fibronectin. Nature 334, 701-703. 2. Appel, F., Holm, J., Conscience, J.F., and Schachner, M. (1993). Several extracellular domains of the neural cell adhesion molecule L1 are involved in neurite outgrowth and cell body adhesion. J. Neurosci. 13, 4764-4775. 3. Holm, J., Appel, F., and Schachner, M., Several extracellular domains of L1 are involved in homophilic interactions. J. Neuosci. Res. 42, 9-20.
3	January 31 and February 2	L1 contributes to positioning of interneurons and to generating the action potential at the axon initial segment	1. Magyar-Lehmann, S., Frei, T., and Schachner, M. (1995). Fasciculation of granule cell neurites is responsible for the perpendicular orientation of small inhibitory interneurons. Eur. J. Neurosci. 1460-1471. 2. Valente, P., Lignani, G., Medrihan, L., Bosco, F., Contestabile, A., Lippiello, P.,

			Ferrea, E., Schachner, M., Giovedi, S., and Baldelli, P. (2016). Cell adhesion molecule L1 contributes to neuronal excitability regulating the function of voltage-gated Na+ channels. J. Cell Sci. 129, 1878-1891.
4	February 7 and 9	L1 induces signal transduction	1.Schuch, U., Lohse, M.J., and Schachner, M. (1969) Neural cell adhesion molecules influence second messenger systems. Neuron 3, 13-20. 2. Wang, Y., and Schachner, M. (2015). The intracellular domain of L1CAM binds to casein kinase 2α and is neuroprotective via inhibition of the tumor suppressors PTEN and p53. J. Neurochem. 133, 828-848. 3. Loers, G., Makhina, T., Bork, U., Dörner, A., Schachner, M., and Kleene, R. (2012). The interaction between cell adhesion molecule L1, matrix metalloproteinase 14 and adenine nucleotide translocator at the plasma membrane regulates L1-mediated neurite outgrowth. J. Neurosci. 32, 3917-3930.
5	February 14 and 16	L1 in the cell nucleus	1. Lutz, D., Wolters-Eisfeld, G., Joshi, G., Djogo, N., Jakovcevski, I., Schachner, M., and Kleene, R. (2012). Generation and nuclear translocation of sumoylated transmembrane fragment of cell adhesion molecule L1. J. Biol. Chem. 287, 17161-17175. 2. Girbes Minguez, M, Wolters-Eisfeld, G., Lutz, D., Buck, F., Schachner, M., and Kleene, R. (2020). The cell adhesion molecule L1 interacts with nuclear proteins via its intracellular domain. FASEB J. 34, 9869-9883.

6	February 21 and 23	L1 functions in the cell nucleus and in mitochondria	1. Kraus, K., Kleene, R., Henis, M., Braren, I., Kataria, H., Sharaf, A., Loers, G., Schachner, M., and Lutz, D. (2018). A fragment of adhesion molecule L1 binds to nuclear receptors to regulate synaptic plasticity and motor coordination. Mol. Neurobiol. 55, 7164-7178. 2. Kraus, K., Kleene, R., Braren, I., Loers, G., Lutz, D., and Schachner, M. (2018). A fragment of adhesion molecule L1 is imported into mitochondria and regulates mitochondrial metabolism and trafficking. J. Cell Sci. 8, 131-143.
7	February 28 and March 2	L1 promotes myelination	1. Seilheimer, B., Persohn, E., and Schachner, M. (1989). Antibodies to the L1 adhesion molecule inhibit Schwann cell ensheathment of neurons in vitro. J. Cell Biol. 109, 3095-3103. 2. Seilheimer, B., Persohn, E., and Schachner, M. (1989). Neural cell adhesion molecule expression is regulated by Schwann cell-neuron interaction in culture. J. Cell Biol. 108, 1009-1915. 3. Kim, S., Lee, D.W., Schachner, M., and Park, H.C. (2021). Small compounds mimicking the adhesion molecule L1 improve recovery in a zebrafish demyelination model. Sci. Rep. 11, 5878.
8	March 7 and 9	L1 expression is influenced by neural activity L1 and L1 promotes nervous system tumor progression	1. Itoh, K., Stevens, B., Schachner, M., and Fields, R.D. (1995). Regulated expression of the neural cell adhesion molecule L1 by specific patterns of neural impulses. Science 270, 1369-1372. 2. Nagaraj, V., Mikhail. M., Baronio, M., Gatto, A., Nayak, A., Theis, T., Cavallaro, U., and Schachner, M. (2022). Antagonistic L1 adhesion molecule mimetic compounds

			inhibit glioblastoma cell migration in vitro. Biomolecules 12, 439.
		Spring Recess, March 9-17	
9	March 21 and 23	L1 in synaptic plasticity	1. Lüthi, A., Laurent, J.P., Figurov, A., Muller, D., and Schachner, M. (1994). Hippocampal long-term potentiation and neural cell adhesion molecules L1 and NCAM. Nature 372, 777-779. 2. Law, J.W., Lee. A.Y., Sun, M., Nikonenko, A.G., Chung, S.K., Dityatiev. A., Schachner, M., and Morellini, F. (2003). Decreased anxiety, altered place learning, and increased CA1 basal excitatory synaptic transmission in mice with conditional ablation of the neural cell adhesion molecule L1. J. Neurosci. 23, 10419-10432.
10	March 28 and 30	L1 in learning and memory	1. Wolfer, D.P., Mohajeri, H.M., Lipp, H.P., and Schachner, M. (1998). Increased flexibility and selectivity in spatial learning of transgenic mice ectopically expressing the neural cell adhesion molecule L1 in astrocytes. Eur. J. Neurosci. 10, 708-717. 2. Tiunova, A., Anokhin, K.V., Schachner, M., and Rose, S.P.R. (1998). Three-time windows for amnestic effect of antibodies to cell adhesion molecule L1 in chicks. Neuroreport 9, 1645-1648.
11	April 4 and 6	L1 and nervous system diseases	1. Dahme, M., Bartsch, U., Martini, R., Anliker, B., Schachner, M., and Mantei, N. (1997). Disruption of the mouse L1 gene leads to malformations of the nervous system. Nat. Genet. 17, 346-349. 2. Sauce, B., Wass, C., Netrakanti, M., Saylor, J., Schachner, M., and Matzel, L.D. (2015). Heterozygous L1-deficient mice express an autism-like phenotype. Behav. Brain Res. 292, 432-442.

			3. Schmid, J.S., Bernreuther, C., Nikonenko, A.G., Ling, Z., Miles, G., Hossmann, K.A., Jakovcevski, I., and Schachner, M. (2013). Heterozygosity for the mutated X-chromosome-linked L1 cell adhesion molecule gene leads to increased numbers of neurons and enhanced metabolism in the forebrain of female carrier mice. Brain Struct. Funct. 218, 1375-1390.
12	April 11 and 13	L1 in spinal cord regeneration	1.Roonprapunt, C. Huang, W., Grill, R., Friedlander, D., Grumet, M., and Schachner, M. (2003). Soluble cell adhesion molecule L1-Fc promotes locomotor recovery in rats after spinal cord injury. J. Neurotrauma 20, 871-882. 2. Chen, J., Wu, J., Apostolova, I., Skup, M., Irintchev, A., Kugler, S., and Schachner, M. (2007). Adeno-associated virus-mediated L1 expression promotes functional recovery after spinal cord injury. Brain 130, 954-969.
13	April 18 and 20	L1 in spinal cord regeneration	1. Jakovcevski, I., Djogo, N., Hölters, L.S., Szpotowicz, E., and Schachner, M. (2013). Transgenic overexpression of the cell adhesion molecule L1 in neurons facilitates recovery after mouse spinal cord injury. Neuroscience 252, 1-12. 2. Wei, Z., Wang, Y., Zhao, W., and Schachner, M. (2017). Electro-acupuncture modulates L1 adhesion molecule expression after mouse spinal cord injury. Am. J. Chin. Med. 45, 37-52. 3. Xu, J.C., Bernreuther, C., Cui, Y.F., Jakovcevski, I., Hargus, G., Xiao, M.F., and Schachner, M. (2011). Transplanted L1 expressing radial glia and astrocytes enhance recovery after spinal cord injury. J. Neurotrauma 28, 1921-1937.

14	April 25 and 27	L1 agonistic small compound mimetics	1. Kataria, H., Lutz, D., Chaudhary, H., Schachner, M., and Loers, G. (2016). Small molecule agonists of cell adhesion molecule L1 mimic L1 functions in vivo. Mol. Neurobiol. 53, 4461-4483. 2. Xu, J., Hu, C., Jiang, Q., Pan, H., Shen, H., and Schachner, M. (2017). Trimebutine, a small molecule mimetic agonist of adhesion molecule L1, contributes to functional recovery after spinal cord injury in mice. Disease Models & Mechanisms 10, 1117-1128. 3. Loers, G., Appel, D., Lutz, D., Congiu, L., Kleene, R., Hermans-Borgmeyer, I., Schäfer, M.K.E., and Schachner, M. (2021). Amelioration of the abnormal phenotype of a new L1 syndrome mouse with L1 mimetics. FASEB J. 35, e21329.
	April 30 - May 1	Reading Days	
	To be announced (between May 2 and 8)	Final exam	

Schedule

The course will be conducted in person and will meet twice a week (80 min classes) for 14 consecutive weeks. Students are expected to attend the classes, to participate in discussions and interface with the instructor. Office hours will be available at scheduled times to maximally accommodate students' schedules. These meetings will be held in person or assisted through the Canvas conference portal. Students that require additional assistance will be able to schedule further appointments on an individual basis. Students are expected to have experience using Canvas and should seek help from the help desk, if necessary.

Class Organization

The course is designed for not more than 20 students to encourage lively interactions. Every week the instructor will present the publications in the first class of the week. In the second class of the week, one student will present the topic of the week, thereby encouraging discussions with questions and answers.

Curriculum

Course Policies and Resources

1. **Academic Integrity Policy**

http://academicintegrity.rutgers.edu/academic-integrity-policy
Violations include: cheating, fabrication, plagiarism, denying others access to information or material, and facilitating violations of academic integrity.

2. **Student-Wellness Services**

Just In Case Web App
http://codu.co/cee05e
Access helpful mental health information and resources for yourself or a friend in a mental health crisis on your smartphone or tablet and easily contact CAPS or RUPD.

Counseling, ADAP & Psychiatric Services (CAPS)
(848) 932-7884
17 Senior Street, New Brunswick, NJ 08901
www.rhscaps.rutgers.edu/
CAPS is a university mental health support service that includes counseling, alcohol and other drug assistance, and psychiatric services staffed by a team of professional within Rutgers Health services to support students' efforts to succeed at Rutgers University. CAPS offers a variety of services that include individual therapy, group therapy and workshops, crisis intervention, referral to specialists in the community and consultation and collaboration with campus partners.

Crisis Intervention
http://health.rutgers.edu/medical-counseling-services/counseling/crisis-intervention
Report a Concern: http://health.rutgers.edu/do-something-to-help

Violence Prevention & Victim Assistance (VPVA)
(848) 932-1181
3 Bartlett Street, New Brunswick, NJ 08901
www.vpva.rutgers.edu
The Office for Violence Prevention and Victim Assistance provides confidential crisis intervention, counseling, and advocacy for victims of sexual and relationship violence and stalking to students, staff, and faculty. To reach staff during office hours when the university is open or to reach an advocate after hours, call 848-932-1181.

Disability Services
(848) 445-6800

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Rutgers University welcomes students with disabilities into all University's educational programs. In order to receive consideration for reasonable accommodations, a student with a disability must contact the appropriate disability services office at the campus where you are officially enrolled, participate in an intake interview, and provide documentation: https://ods.rutgers.edu/students/documentation-guidelines. If the documentation supports your request for reasonable accommodations, your campus's disability services office will provide you with a Letter of Accommodations. Please share this letter with your instructors and discuss the accommodations with them as early in your courses as possible. To begin this process, please complete very carefully and precisely the Registration form on the ODS web site at: https://ods.rutgers.edu/students/registration-form

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