**Neur 353 Neuroregeneration**

**Spring 2024**

**Instructor:** Dr. Tamara Stawicki

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**Class Meetings:** Tuesdays and Thursdays 1:15-2:30pm, Oechsle Hall 211

**Office Hours:** Mondays and Thursdays 3:00-4:00pm, Oechsle Hall 309A or by

 appointment: <https://calendly.com/stawickt/meeting-with-dr-stawicki>

**Course Website:** <https://moodle.lafayette.edu>

All assignments and readings will be posted on the course website. You should make sure to check the website regularly to keep up with the class material.

Moodle privacy statement: Moodle contains student information that is protected by the Family Educational Right to Privacy Act (FERPA).  Disclosure to unauthorized parties violates federal privacy laws.  Courses using Moodle will make student information visible to other students in this class.  Please remember that this information is protected by these federal privacy laws and must not be shared with anyone outside the class.  Questions can be referred to the Registrar's Office.

**Course Description:** Our neuronal tissues are particularly sensitive to injury and in many cases, are not able to repair themselves. This course explores the problem of neuronal regeneration through in class discussions and an analysis of primary research literature. We will investigate invertebrates and amphibians with remarkable regenerative capabilities as well as regeneration of axons and sensory cells in both mammalian and non-mammalian systems.

**Course Objectives:**

Through completing the assigned readings, assignments and class activities students will:

* Analyze primary literature articles in the field of neuroregeneration
* Generate hypotheses and design experiments to test them
* Discuss ethical issues involved in science and medical research
* Relate individual papers to a larger picture of how regeneration works

**Course Learning Outcomes:**

At the end of this course students will be able to:

* Describe some of the molecular and cellular processes required for different neuronal cell types to regenerate following injury.
* Compare and contrast systems where neuronal regeneration does or does not occur naturally.
* Use existing data to develop a model for how regeneration occurs or why it does not occur effectively.
* Interpret and analyze scientific data presented in primary research articles.
* Develop a hypothesis based on existing scientific data and design an experiment to test that hypothesis.

**Class format:**

The majority of the class sessions will focus on the analysis and discussion of primary research literature. This analysis will occur both in small groups and as a whole class. All assigned readings will be available through perusall. You will be expected to complete the assigned readings before class and come prepared to discuss them in class. You will read the Introduction and Methods sections of assigned papers for Tuesday’s class and the Results and Discussion for Thursday. It is expected that all students will be active participants in class.

Most weeks we will discuss two papers that are related in some way. For example, they may show how understanding of a topic has progressed with time, or are investigating a similar process in two different model organisms. You will be asked both to analyze the individual papers and think about how they relate to one another and the bigger scientific picture. Tuesday’s class will focus primarily on discussion of the background of that week’s topic and the methods used in the papers whereas Thursday’s class will focus on the results and conclusions that can be made from those results.

**Attendance Policy:**

As a discussion based course, class attendance is a key part of the learning experience. As such students are expected to attend all class sessions in person. If you cannot attend a class session due to illness or a reasonable conflict it is your responsibility to notify me before class so we can come up with an alternative plan for you to earn participation credit for the missed class. A failure to do so will negatively impact your grade. Repeated absences will require a dean’s excuse.

**Evaluation and Grading:**

Grades will be assessed based on a combination of assignments and in class participation as outlined below.

Paper Perusall Discussions and Quizzes (20%): For each assigned primary research article you will be expected to participate in a Perusall discussion prior to the class period in which we will be discussing the paper to help prepare you for the in-class discussions on the paper. These will be graded. Additionally, as the semester progresses you will also have a few quiz questions associated with a subset of papers to help prepare you for the final exam.

Class Participation (15%): Your participation grade will be based on attending class and **actively** participating in in-class discussions and in-class work activities.

Experiment Plans (30%): This course is divided into thirds (tissue regeneration weeks 2-5, axon regeneration weeks 6-9, and sensory cell regeneration weeks 10-14). At the completion of each of the first two topics you will design a short experiment plan relevant to the topic we just completed.

Preprint Presentation (15%): During the last week of class students will present a preprint of their choosing on neuronal regeneration.

Final Exam(20%): You will have a final exam during the finals period designed to test your mastery of the course learning outcomes. Please note this will be an in person exam so plan your end of the semester travel accordingly.

Final grades will be determined by the following scale:

|  |  |  |  |
| --- | --- | --- | --- |
| **Grade** | **Percentage** | **Grade** | **Percentage** |
| A | 93.0 to 100 | C | 73.0 to 76.9 |
| A- | 90.0 to 92.9 | C- | 70.0 to 72.9 |
| B+ | 87.0 to 89.9 | D+ | 67.0 to 69.9 |
| B | 83.0 to 86.9 | D | 63.0 to 66.9 |
| B- | 80.0 to 82.9 | D- | 60.0 to 62.9 |
| C+ | 77.0 to 79.9 | F | 0.0 to 59.9 |

**Please note that out of fairness for all students, final grades will not be bumped or rounded up or down.**

**Academic Integrity and AI Usage:**

All students are expected to abide by the Student Code of Conduct including policies around academic integrity. Please be sure to review the Student Code of Conduct at the following link (<https://conduct.lafayette.edu/student-handbook/student-code-of-conduct/>). Related to not submitting work that was generated by someone else as your own you should not submit work generated by a generative AI program and present it as your own in this course. I will further discuss the usage of AI technologies as it pertains to individual assignments when they are assigned. If you have any questions on when collaboration is allowed or what sources you are allowed to use please contact me.

**The Importance of an Inclusive Classroom**

I would like to create a learning environment for my students that supports a diversity of thoughts, perspectives and experiences, and honors your identities (including race, gender, class, sexuality, religion, ability, etc.) To help accomplish this:

* If you have a name and/or set of pronouns that differ from those that appear in the class roster, please let me know. Additionally, please let me know if I am mispronouncing your name.
* If you feel like your performance in the class is being impacted by your experiences outside of class, please don't hesitate to come and talk with me. If you do not feel comfortable discussing the issue directly with me, I encourage you to seek out another, more comfortable avenue to address the issue. You may want to consider contacting your class dean (<https://advising.lafayette.edu/class-deans/>) or the counseling center (<https://counselingcenter.lafayette.edu/>).
* If any of our class meetings or assignments conflict with your religious events please let me know during the first two weeks of the semester so we can make arrangements for you.
* If you have suggestions to improve the effectiveness of the course for you personally or other students or student groups please let me know.
* I (like many people) am still in the process of learning about diverse perspectives and identities. If something was said in class (by anyone) that made you feel uncomfortable, please talk to me about it.

**Resources for Student Support**

There are a number of resources available to support your learning at Lafayette. The following link (<https://citls.lafayette.edu/student-academic-support/>) provides information on available offices and programs for academic support. Additionally, the Counseling Center (<https://counselingcenter.lafayette.edu/>) is available to provide counseling and educational programs to help you achieve your academic, social and personal development goals.

Lastly, if you do not have the financial resources to purchase needed course supplies for other courses (like textbooks, access to online modules, calculators, etc) the college has a new fund where you can supply for small grants to help cover these expenses: <https://lafayettec.az1.qualtrics.com/jfe/form/SV_85PLHSVphVGRdmC> .

**Disability statement:**

In compliance with Lafayette College policy and equal access laws, I am available to discuss appropriate academic accommodations that you may require as a student with a disability. Requests for academic accommodations should be made during the first two weeks of the semester if possible, so arrangements can be made. Students must register with the Office of the Dean of Advising and Co-Curricular Programs for disability verification and for determination of reasonable academic accommodations. You can find more information about the accomodations process at the following link (<https://hub.lafayette.edu/disability-services/>)

**Proper Usage of Course Materials**

At Lafayette College, all course materials are proprietary and for class purposes only. This includes posted worksheets, assignments, and other course items. Reposting such materials or distributing them through any means is prohibited. If you have any questions about proper usage of course materials please ask me.

**Compliance statement:**

The student work in this course is in full compliance with the federal definition of a four-credit hour course. Please see the Registrar’s Office web site (<https://registrar.lafayette.edu/wp-content/uploads/sites/193/2013/04/Federal-Credit-Hour-Policy-Web-Statement.doc>) for the full policy and practice statement.

**Course Schedule**

Please note the schedule of covered material may change as the course progresses.

|  |  |  |  |
| --- | --- | --- | --- |
| Week | Days | Topic | Readings |
| 1 | 1/231/25 | The scientific method and neurodevelopment  |  |
| 2 | 1/302/1 | Tissue regeneration – Regeneration patterning | Gurley et al., 2008 |
| 3 | 2/62/8 | Tissue regeneration – nerve dependence | Farkas et al., 2016  |
| 4 | 2/132/15 | Tissue regeneration – stem cells | Kragl et al., 2009Wagner et al., 2011 |
| 5 | 2/202/22 | Tissue regeneration – determining factors | Bedelbaeva et al., 2010Hesse RG et al., 2015  |
| 6 | 2/272/29 | Axon regeneration – overview and screens | Zou et al., 2015Kauer et al., 2022  |
| 7 | 3/5-3/7 | Axon regeneration – reaching the target**Virtual Class:** Clinical Trials for Neuroregeneration | Dun et al., 2019 **\*Read entire paper by Tuesday’s class****\*First experiment plan due 3/8** |
| 8 |  | No Class - Spring Break |  |
| 9 | 3/193/21 | Axon regeneration –Intrinsic factors | Hammarlund et al., 2009 Shin et al., 2012  |
| 10 | 3/263/28 | Axon regeneration –Extrinsic factors | Freund et al., 2006 Lee et al., 2010  |
| 11 | 4/24/4 | Hair cell regeneration – Notch signaling | Ma et al., 2008 Mizutari et al., 2013 |
| 12 | 4/94/11 | Hair cell regeneration – genetic modulation of | **\*Second experiment plan due 4/8**Sun et al., 2021 |
| 13 | 4/164/18 | Retinal regeneration - target selection | **\*Preprint you will be presenting due 4/18**D’Orazi et al., 2016Yoshimatsu et al., 2016  |
| 14 | 4/234/25 | Retinal regeneration – epigenetic modification of | Ueki Y et al., 2015 Jorstad et al., 2017  |
| 15 | 4/305/2 | **Student presentations** | None |

**Final exam during finals period**

**Reading list**

Gurley KA, Rink JC, Sánchez Alvarado A (2008) β-catenin defines head versus tail identity during planarian regeneration and homeostasis. *Science* 319: 323 – 327.

Farkas JE, Freitas PD, Bryant DM, Whited JL, Monaghan JR (2016) Neuregulin-1 signaling is essential for nerve-dependent axolotl limb regeneration. *Development* 143:2724-2731.

Wagner DE, Wang IE, Reddien PW (2011) Clonogenic neoblasts are pluripotent adult stem cells that underlie planarian regeneration. *Science* 332: 811 – 816.

Krag M, Knapp D, Nacu E, Khattak S, Maden M, Epperlein HH, Tanaka EM (2009) Cells keep a memory of their tissue origin during axolotl limb regeneration. *Nature* 460: 60-65.

Bedelbaeva K, Synder A, Gourevitch D, Clark L, Zhang XM, Leferovich J, Cheverud JM, Lieberman P, Heber-Katz E (2010) Lack of p21 expression links cell cycle control and appendage regeneration in mice. *PNAS* 13: 5845-5850

Hesse RG, Kouklis GK, Ahituv N, Pomerantz JH (2015) The human ARF tumor suppressor senses blastemal activity and suppresses epimorphic tissue regeneration. *Elife* 4: e97702.

Zou Y, Stagi M, Wang X, Yigitkanli K, Siegel CS, Nakatsu F, Cafferty WBJ, Strittmatter SM (2015) Gene-Silencing Screen for Mammalian Axon Regeneration Identifies Inpp5f (Sac2) as an Endogenous Suppressor of Reapir after Spinal Cord Injury. *J Neurosci* 35: 10429-10439.

Kauer SD, Fink KL, Li EHF, Evans BP, Golan N, Cafferty WBJ (2022) Inositol Polyphosphate-5-Phosphatase K(*Inpp5k)* Enhances Sprouting of Cortiscospinal Tract Axons after CNS Trauma. *J Neurosci* 42: 2190-2204.

Dun X, Carr L, Woodley PK, Barry RW, Drake LK, Mindos T, Roberts SL, Llyod AC, Parkinson DB (2019) Macrophage-Derived Slit3 Controls Cell Migration and Axon Pathfinding in the Peripheral Nerve Bridge. *Cell Reports* 26:P1458-1472.E4

Hammarlund M, Nix P, Hauth L, Jorgensen EM, Bastiani M (2009) Axon regeneration requires a conserved MAP Kinase Pathway. *Science* 323: 802-806.

Shin JE, Cho Y, Beirowski B, Mibrandt J, Cavalli V, DiAntonio A (2012) Dual Leucine Zipper Kinase is Required for Retrograde Injury Signaling and Axonal Regeneration. *Neuron* 74: 1015-1022.

Freund P, Schmidlin E, Wannier T, Bloch J, Mir A, Schwab ME, Rouiller EM (2006) Nogo-A-specific antibody treatment enhances sprouting and functional recovery after cervical lesion in adult primates. *Nat Med* 12: 790 – 792.

Lee JK, Geoffroy, Chan AF, Tolentino KE, Crawford MJ, Leal MA, Kang B, Zhen B (2010) Assessing spinal axon regeneration and sprouting in Nogo-, MAG-, and OMgp-Deficient Mice. *Neuron* 66: 663-670.

Ma EY, Rubel EW, Raible DW (2008) Notch signaling regulates the extent of hair cell regeneration in the zebrafish lateral line. *J Neurosci* 28: 2261-2273.

Mizutari K, Fujioka M, Hosoya M, Brhamhall N, Okano HJ, Okano H, Edge ASB (2013) Notch inhibition induces cochlear hair cell regeneration and recovery of hearing after acoustic trauma. *Neuron* 77: 58-69.

Sun S, Li S, Luo Z, Ren M, He S, Wang G, Liu Z (2021) Dual expression of Atoh1 and Ikzf2 promotes transformation of adult cochlear supporting cells into outer hair cells

D’Orazi FD, Zhao XF, Wong RO, Yoshimatsu T (2016) Mismatch of Synaptic Patterns between Neurons Produced in Regeneration and during Development of the Vertebrate Retina. *Curr Biol* 26: 2268-79.

Yoshimatsu T, D’Orazi FD, Gamlin CR, Suzuki SC, Suli A, Kimmelman D, Raible DW, Wong RO (2016) Presynaptic partner selection during retinal circuit reassembly varies with timing of neuronal regeneration in vivo. *Nat Commun* 7: 10590.

Ueki Y, Wilken MS, Cox KE, Chipman L, Jorstad N, Sternhagen K, Simic M, Ullom K, Nakafuku M, Reh TA (2015) Transgenic expression of the proneural transcription factor Ascl1 in Müller glia stimulates retinal regeneration in young mice. *Proc Natl Acad Sci* 44:1371-13722.

Jorstad NL, Wilken MS, Grimes WN, Wohl SG, VandenBosch LS, Yoshimatsu, Wong RO, Rieke F, Reh TA (2017) Stimulation of functional neuronal regeneration from Müller glia in adult mice. *Nature* 548: 103-107.