

## NEUR502-Basic and Clinical Aspects of Neuroimmunology

**Instructors:** Course coordinators: (by appointment, office hours)

***Ji Zhang, M.D, Ph.D***

***Associate professor***

The Alan Edwards Center for Research on Pain  
Genome Building, Suite 3200C  
McGill University  
514-398-7203, x00036  
[Ji.Zhang@mcgill.ca](mailto:Ji.Zhang@mcgill.ca)

***Jo Anne Stratton, PhD***

***Assistant professor***

Montreal Neurological Institute  
Neuroimmunology Unit, Room NW109  
McGill University  
514-224-2558  
[jo.stratton@mcgill.ca](mailto:jo.stratton@mcgill.ca)

Guest lecturers: see course schedule

**Term of implementation:** Winter (2022)

**Credits:** 3 credits

**Location:** ***This course will be online/delivered remotely.*** In the situation that the Covid-19 pandemic has subsided, and if given permission by the Faculty of Medicine, this course might hold formal Face-to-Face classes. If so, these will be held in the Genome building (740, Dr Penfield), room 3001

**Time:** Tuesday 1:00pm-4:00pm (Montreal time)

**Pre-requisites:** At least one course from Immunology (MIMM 214 or MIMM 314 or MIMM414 or PHGY 313) and one course from Neuroscience (NSCI200 or NSCI210 or PHGY209 or NEUR310 or ANAT 321 or ANAT 323 or PHGY 314) are pre-requisites, or permission of instructor

**Note:** -Graduate students working on the topic of neuroinflammation are also eligible  
-A cap of 15 students applies

### **Brief course description (from course calendar)**

The role of inflammation in physiological function of the nervous system, as well as in a broad range of neurological diseases where inflammation can act as a contributing factor to the development of pathology or promote recovery, including fundamentals of neuroimmunology to molecular/cellular aspects of neuroinflammation underlying the pathology seen in clinical conditions.

### **Learning outcomes**

Upon completion of this course, students will be

- Introduced to the field of Neuroimmunology
- Exposed to the basic and clinical aspects of neuroinflammation
- Able to integrate and appraise the most updated knowledge of the involvement of inflammation in various neurological disorders
- Able to develop critical thinking and judgement on research outcomes
- Expected to have enhanced oral/written communication skills
- Able to design a neuroinflammation-related research project under the format of mock grant writing

### **Instructional Methods:**

The course will consist of 1 session of introduction, 12 sessions of lectures with or without paper discussion, 3 grant workshops. In each lecture/paper discussion session, a lecture on the selected topic will be given by the instructor during the first 60 minutes. During the second part of the session (2

hours), students will make presentations on assigned reading materials. 1-2 students will be assigned as "presenters" for each class. The "presenters" will be required to prepare a power point presentation including a general introduction, figures/tables and a conclusion, and lead a discussion of the paper, with all students participating in the discussion. Students will be required to read, present assigned research papers, and participate in discussion on a weekly basis (when there is a paper discussion session). A review paper on the relevant topic will also be provided for background reading if needed (optional).

**Required course materials:**

Research articles for each session are listed in the course syllabus and uploaded in myCourses

**Evaluation:**

There is no exam for this course; however, the evaluation process is as follow:

- Presentation, discussion and ability to critically analyse information will be assessed in each class (5% per each session). 12 sessions of lecture/paper discussion will made up 60%, then be converted to 50% of the total grade. Students’ performance on paper presentation/discussion will be communicated for the first 6 graded sessions after the session on Feb 15<sup>th</sup>.

In an effective presentation/discussion, you should try to answer the following questions:

- What are the authors trying to demonstrate?
- What questions are they asking?
- Why is this question worth asking?
- What methods did they use to answer the question?
- What did they find?
- Did they succeed in answering their question?
- Where do they go from here?
- 

Evaluation when there is lecture/paper discussion:

<b>Preparation (1 point)</b>	<b>Presentation: (2 points)</b>	<b>Discussion: (2 points)</b>
Students are required to read research article/s, send one question on the research article the day before the class (before 5pm) to the presenters on that week for in class discussion. Presenters will incorporate questions into the powerpoint on the appropriate slide, and send a summary of the questions to the course coordinators.	All students will be evaluated on their understanding and interpretation of the article. Presenting students will be evaluated on the introduction of the topic and the ability to lead the discussion. Non-presenting students will be evaluated on readiness/clarity to describe figures/tables in the research articles.	All students will be evaluated on their active participation in the discussion (raise questions and comments); the insight and critical thinking displayed during the lecture and the paper discussion

- In cases where there is no paper presentation/discussion, the lecture discussion counts for 5%
- Mock grant writing and oral presentations will count for 50% of the grade.

- The grant will be prepared and presented as a team grant (~3 students/grant). The team will be assigned by the course directors after the add/drop deadline (Jan 18<sup>th</sup>).
- Three grant preparation workshops:
  - **Grant workshop I (Jan 25<sup>th</sup>) (5%)-Brainstorming and preparation of letter of intent (LOI).** 90 min group discussion + 30 min summary presentation of your LOI (one slide/team) to the group. A one page LOI /team should be submitted one week after the workshop I (Feb 1<sup>st</sup>) including group members names, PI/project title (if grad student).
  - **Grant workshop II (Feb 22<sup>nd</sup>) (5%): Team discussion and revision:** 2 days before the workshop, each member of the team will send a 2 page-draft of the rationale and experimental design of their specific aim to their team members. During the workshop, each member presents their parts and seeks for comments and suggestions from the peers. 90 min group discussion + 30 min summary presentation of your proposal (in progression version) (three slides/team) to the group.
  - **Grant workshop III (March 22<sup>nd</sup>) (10%): Peer Review:** To facilitate discussion during this workshop, each team should send a one page-summary reflecting what they are going to present, two days before the workshop to the group. At the workshop, each team will give an oral presentation of their proposed grant, including background, objectives, justification, experimental design etc. All students will act as reviewers to provide comments and suggestions. Constructive feedback could entail pointing out “*novelty*”: the significance and the impact of the project; and “*feasibility*”; refinement of hypothesis, refocusing ideas or concepts, appropriate choice of experimental approach, appropriate controls, statistical analysis methods *etc.* At the end of the in-class discussion, all students need to submit a short written feedback summarizing the strengthes, the weaknesses and suggestions for their peers’ grants.

**The objective of the three workshops are:** 1) to provide opportunities to learn and help each other to improve grants; 2) to stimulate critical thinking; 3) to provide opportunity to strengthen oral communication skills; 4) to experience the grant review process; 5) It is expected that feedback from this workshop is incorporated into final oral and written assigment. Detailed guidelines of grant writing will be provided during the first class.

The final grant will be shared with peers by oral presentation at the last class. In addition, a written version will be submitted several days after the last class (April 18<sup>th</sup>) (25%). Late submission of team grants will have a penalty: 5/25 points per day up to 5 days. The grant will not be reviewed by the instructors if it is not submitted within 5 days post-deadline.

Grant workshop (20%)			Grant writing (25%)	Teamwork (5%) (Evaluated by team members)
I (5%)	II (5%)	III (10%)		
Team discussion and generation of LOI	Team discussion on each specific aim	-Oral presentations (5) Clarity Synthesis Logic -In-class discussion and written	Summary: 5 Final written version: 20	-Thoughtful and respectful contribution to teamwork; -Share responsibilities with team

		comments (5) Critical thinking Helpful and constructive feedback		members; -Meet deadlines
--	--	--	--	-----------------------------

**McGill Policy Statements:**

**Language of Submission:**

In accord with McGill University's Charter of Students' Rights, students in this course have the right to submit in English or in French any written work that is to be graded. This does not apply to courses in which acquiring proficiency in a language is one of the objectives. (Approved by Senate on 21 January 2009 - see also the section in this document on Assignments and Evaluation.)

**Academic Integrity:**

McGill University values academic integrity. Therefore, all students must understand the meaning and consequences of cheating, plagiarism and other academic offences under the Code of Student Conduct and Disciplinary Procedures" (see [www.mcgill.ca/students/srr/honest/](http://www.mcgill.ca/students/srr/honest/) for more information). (Approved by Senate on 29 January 2003)

**Overview of course schedule:**

Week	Topic	Assessment (% of the final grades)	Lecturer
Jan 11th	Course introduction, Grant writing/reviewing Clinical Aspects of Neuroinflammation in Multiple Sclerosis	N/A  5%	Ji Zhang Jack Antel
Jan 18th	Neuroinflammation in depression and suicide	5%	Reza Rahimian
Jan 25th	Microbiota and neurological disorders <i>Grant workshop I: Group brainstorming/LOI</i>	5% 5%	Irah King Ji Zhang/Jo Anne Stratton
Feb 1st	The neurovascular unit in Alzheimer's disease and dementia	5%	Edith Hamel
Feb 8th	Astrocytes as key components of the brain metastatic microenvironment	5%	Peter Siegel
Feb 15th	Gut Brain Axis in Parkinson's disease	5%	Samantha Gruenheid
Feb 22nd	Cerebral Spinal Fluid & Brain Barrier Cells: Immune cell gateways <i>Grant workshop II: internal discussion/revision</i>	5% 5%	Jo Anne Stratton Ji Zhang/Jo Anne Stratton
Reading week (February 28 <sup>th</sup> -March 4 <sup>th</sup> )			
Mar 8th	Brain Imaging & Neuroinflammation	5%	David Rudko
Mar 15th	Inflammation and circadian rhythms Gut	5%	Nicolas Cermakian
Mar 22nd	<i>Grant workshop III: Peer review</i>	10%	Ji Zhang/Jo Anne Stratton
Mar 29th	Monogenic diseases and immunity	5%	Roberta La Piana
Apr 5th	Neuroinflammation in chronic pain	5%	Ji Zhang
Apr 12th	Perinatal infection and brain lesions <i>Final grant sharing by oral presentation</i>	5%	Guillaume Sebire Ji Zhang/Jo Anne Stratton
Due date (April 18 <sup>th</sup> 8pm) for final submission of mock grant (25%)			

**Course content:**

🔗 **January 11<sup>th</sup>: Course Introduction, Grant writing (Ji Zhang)**

🔗 **January 11<sup>th</sup>: Clinical Aspects of Neuronflammation in Multiple Sclerosis (Jack Antel)**

**Review article:** Progressive multiple sclerosis. Ontaneda D, Fox RJ. *Curr Opin Neurol.* 2015 Jun; 28(3): 237-43

🔗 **January 18<sup>th</sup>: Neuroinflammation in depression and suicide: evidence from animal models and postmortem investigations (Reza Rahimian)**

**Review article:** Microglia emerge as central players in brain disease. Salter MW, Stevens B. *Nat Med.* 2017 Sep 8;23(9):1018-1027. doi: 10.1038/nm.4397

**Research Article:** Distinct non-inflammatory signature of microglia in post-mortem brain tissue of patients with major depressive disorder. Gijsje J L J Snijders, Marjolein A M Sneeboer, Alba Fernández-Andreu, Evan Udine, Psychiatric donor program of the Netherlands Brain Bank (NBB-Psy); Marco P Boks, Paul R Ormel, Amber Berdenis van Berlekom, Hans C van Mierlo, Chotima Böttcher, Josef Priller, Towfique Raj, Elly M Hol, René S Kahn, Lot D de Witte *Mol Psychiatry*, 2021 Jul;26(7):3336-3349. doi: 10.1038/s41380-020-00896-z.

🔗 **January 25<sup>th</sup>: Microbiota and neurological disorders (Irah King)**

**Review article:** The gut microbiota-brain axis in behaviour and brain disorders. Morais LH, et al. *Nat Rev Microbiol.* 2020. PMID: 33093662 Review

🔗 **February 1<sup>st</sup>: The neurovascular unit in Alzheimer's disease and dementia (Edith Hamel)**

**Review article:** Cerebral blood flow regulation and neurovascular dysfunction in Alzheimer disease. Kisler K, Nelson AR, Montagne A, Zlokovic BV. *Nat Rev Neurosci.* 2017 Jul;18 (7):419-434.

**Research Article:** Cerebrovascular pathology during the progression of experimental Alzheimer's disease. Giannoni P, Arango-Lievano M, Neves ID, Rousset MC, Baranger K, Rivera S, Jeanneteau F, Claeysen S, Marchi N. *Neurobiol Dis.* 2016 Apr;88:107-17.

🔗 **February 8<sup>th</sup>: Astrocytes as key components of the brain metastatic microenvironment (Peter Siegel)**

**Review article:** 1) The Potential of Astrocytes as Immune Modulators in Brain Tumors. Priego N, Valiente M. *Front Immunol.* 2019 Jun 11;10:1314. doi: 10.3389/fimmu.2019.01314. eCollection 2019. PMID: 31244853

2) Reactive Astrocytes in Brain Metastasis. Wasilewski D, Priego N, Fustero-Torre C, Valiente M. *Front Oncol.* 2017 Dec 11;7:298. doi: 10.3389/fonc.2017.00298. eCollection 2017. PMID: 293128

**Research Article:** STAT3 labels a subpopulation of reactive astrocytes required for brain metastasis. Priego N, Zhu L, Monteiro C, Mulders M, Wasilewski D, Bindeman W, Doglio L, Martínez L, Martínez-Saez E, Ramón Y Cajal S, Megías D, Hernández-Encinas E, Blanco-Aparicio C, Martínez L, Zarzuela E, Muñoz J, Fustero-Torre C, Piñeiro-Yáñez E, Hernández-Laín A, Bertero L, Poli V, Sanchez-Martinez M, Menendez JA, Soffietti R, Bosch-Barrera J, Valiente M. *Nat Med.* 2018 Jul;24(7):1024-1035. doi: 10.1038/s41591-018-0044-4. Epub 2018 Jun 11. PMID: 29892069

🔗 **February 15<sup>th</sup>: Gut Brain Axis in Parkinson's disease (Samantha Gruenheid)**

**Review article:** Brain-gut-microbiota axis in Parkinson's disease. Mulak A, et al. *World J Gastroenterol.* 2015. PMID: 26457021

**Research Article:** Intestinal infection triggers Parkinson's disease-like symptoms in Pink1<sup>-/-</sup> mice. Diana Matheoud, Tyler Cannon, Aurore Voisin, Anna-Maija Penttinen, Lauriane Ramet, Ahmed M Fahmy, Charles Ducrot, Annie Laplante, Marie-Josée Bourque, Lei Zhu, Romain Cayrol, Armelle Le

Campion, Heidi M McBride, Samantha Gruenheid, Louis-Eric Trudeau, Michel Desjardins Nature 2019 Jul;571(7766):565-569

🔗 **February 22<sup>nd</sup>: Cerebral Spinal Fluid & Brain Barrier Cells: Immune cell gateways (Jo Anne Stratton)**

**Review article:** Surface-in pathology in multiple sclerosis: a new view on pathogenesis?

Matteo Pardini, J William L Brown, Roberta Magliozzi, Richard Reynolds, Declan T Chard. Brain, Volume 144, Issue 6, June 2021, Pages 1646–1654. <https://academic.oup.com/brain/article-abstract/144/6/1646/6238675?redirectedFrom=fulltext>

🔗 **March 8<sup>th</sup>: Brain Imaging and neuroinflammation (David Rudko)**

**Review article:** Ultra-high-field MR imaging in multiple sclerosis. Filippi M<sup>1</sup>, Evangelou N, Kangarlu A, Inglese M, Mainero C, Horsfield MA, Rocca MA. J Neurol Neurosurg Psychiatry. 2014 Jan;85(1):60-6.

**Research Article:** The topography of demyelination and neurodegeneration in the multiple sclerosis brain. Haider L, Zrzavy T, Hametner S, Höftberger R, Bagnato F, Grabner G, Trattinig S, Pfeifenbring S, Brück W, Lassmann H. Brain. 2016 Mar;139(Pt 3):807-15.

🔗 **March 15<sup>th</sup>: Inflammation and circadian rhythms (Nicolas Cermakian)**

**Review article:** Circadian clocks and inflammation: reciprocal regulation and shared mediators. Cermakian N, Westfall S, Kiessling S. Arch Immunol Ther Exp (Warsz). 2014 Aug;62(4):303-18

**Research Article:** Circadian clock protein Rev-erba regulates neuroinflammation. Griffin P, Dimitry JM, Sheehan PW, Lananna BV, Guo C, Robinette ML, Hayes ME, Cedeño MR, Nadarajah CJ, Ezerskiy LA, Colonna M, Zhang J, Bauer AQ, Burris TP, Musiek ES. Proc Natl Acad Sci U S A. 2019 Mar 12;116(11):5102-5107. doi: 10.1073/pnas.1812405116. Epub 2019 Feb 21.

🔗 **March 29<sup>th</sup>: Monogenic diseases and immunity (Roberta La Piana)**

**Review article** Rare phenotypes in the understanding of autoimmunity.” Zeissig Y, Britt-Sabina P, Franke A, Blumberg RS, Zeissig S. Immunol Cell Biol. 2016 Nov;94(10):943-948. doi: 10.1038/icc.2016.76

**Research Article:** Homozygous Mutations in CSF1R Cause a Pediatric-Onset Leukoencephalopathy and Can Result in Congenital Absence of Microglia” Oosterhof N, Chang IJ, Karimiani EG, Kuil LE, Jensen DM, Daza R, Young E, Astle L, van der Linde HC, Shivaram GM, Demmers J, Latimer CS, Keene CD, Loter E, Maroofian R, van Ham TJ, Hevner RF, Bennett JT. Am J Hum Genet. 2019 May 2;104(5):936-947. doi: 10.1016/j.ajhg.2019.03.010.

🔗 **April 5<sup>th</sup>: Neuroinflammation in chronic pain (Ji Zhang)**

**Review article:** Pain regulation by non-neuronal cells and inflammation Ji RR, Chamesian A, Zhang YQ. Science. 2016 Nov 4;354(6312):572-577.

**Research Article:** Passive transfer of fibromyalgia symptoms from patients to mice. Goebel A, Krock E, Gentry C, Israel MR, Jurczak A, Urbina CM, Sandor K, Vastani N, Maurer M, Cuhadar U, Sensi S, Nomura Y, Menezes J, Baharpoor A, Brieskorn L, Sandström A, Tour J, Kadetoff D, Haglund L, Kosek E, Bevan S, Svensson CI, Andersson DA. J Clin Invest. 2021 Jul 1;131(13):e144201. doi: 10.1172/JCI144201.

🔗 **April 12<sup>th</sup>: Perinatal infection and brain lesions (Guillaume Sebire)**

**Review article:** The Role of Immune Factors in Shaping Fetal Neurodevelopment Alice Lu-Culligan, Akiko Iwasaki *Annu Rev Cell Dev Biol.* 2020 Oct 6;36:441-468. doi: 10.1146/annurev-cellbio-021120-033518. Epub 2020 Jul 28