

CURRICULUM VITÆ

PERSONAL INFORMATION

GRATUZE, Maud

- ORCID: 0000-0002-1552-8815
- Research ID: T-2193-2017

Date of birth: 15th of November 1988

Nationality: French

URL for web site: <https://inp.univ-amu.fr/en/teams/synaptic-degeneration-and-gliosis> or <https://scholar.google.com/citations?user=BcgEJdEAAAAJ&hl=fr&oi=ao>

EDUCATION

- 2013-2017 PhD in Neurosciences, *Université Laval*, Quebec City, Canada; Supervisor: E. Planel
Impact of obesity and type 2 diabetes on tau pathology in Alzheimer's disease
- 2009-2011 Master's degree in Health Biology, *Université Montpellier 2*, Montpellier, France
M1 Supervisor: M. Vignes (IBMM)
Effects of theanine on hippocampal neurons in vitro: measurement of a neuroprotective action and interactions with glutamate receptors
M2 Supervisor: E. M. Lerner-Natoli (IGF)
New therapeutic strategy targeting angiopoietin 1 and 2 for strengthening the blood-brain barrier in drug-resistant epilepsies

CURRENT POSITION

- 2023-present **Tenured research scientist (CRCN) at CNRS - ATIP-Avenir Young group leader**
Institute of Neurophysiopathology - AMU, France;
Role of ApoE4 in the interrelation between microglia, neurons, and astrocytes leading to tau-mediated synaptic degeneration in Alzheimer's disease

PREVIOUS POSITIONS

- 2022 Postdoctoral fellow, *Institute of Neurophysiopathology, Aix-Marseille University*, France
Interrelation between microglia, neurons, and astrocytes leading to tau-mediated synaptic degeneration in Alzheimer's disease.
- 2017-2022 Postdoctoral fellowship, *Washington University School of Medicine in St. Louis*, USA
Role of microglia, TREM2 and ApoE on tau pathology and tau-mediated neurodegeneration
- 2013-2017 PhD Student in Neurosciences; Faculty of Medicine, *Université Laval*, Canada
- 2010-2011 Traineeship at Institut des Biomolécules Max Mousseron, France
- 2010 Traineeship at Institut de Génomique Fonctionnelle, France

GRANTS AND AWARDS

Grants (written and obtained)

- 2024-2025 ANR Tremplin – ERC Starting Grant (T-ERC StG), *INP, Aix-Marseille University*, France
- 2023-2026 ATIP-Avenir program, *INP, Aix-Marseille University*, France
- 2023 Technical boost from A*MIDEX, *INP, Aix-Marseille Université*, France
- 2023-2025 France Alzheimer association research grant, *INP, Aix-Marseille Université*, France
- 2022-2024 MSCA postdoctoral fellowship, *INP, Aix-Marseille University*, France
- 2020-2022 BrightFocus Foundation postdoctoral fellowship, *Washington University*, USA
- 2019-2020 McDonnell Center for Cellular and Molecular Neurobiology Postdoctoral Fellowship, *Washington University*, USA
- 2014-2017 Alzheimer Society of Canada - Biomedical PhD Scholarship Award, *Université Laval*, Canada

Major awards

- 2023 **Tenured CNRS researcher**
- 2021 **30th Anniversary Tau Leadership Award, Rainwater Foundation**

- 2020 Hope Center award at Washington University
 2020 Finalist of the James L. O’Leary Prize for Research in Neuroscience
 2016 Poster presentation award (10th Research meeting in Neuroscience of Laval University)
 2016 Excellence award in Research of the Réseau québécois de recherche sur le vieillissement (RQRV, 1st place)
 2016 Oral presentation award (Annual meeting of Health Research in Laval University)
 2016 Second place of the international competition "my thesis in 180 seconds"
 2016 Personality of the Year award (graduate students associations) of Laval University
 2016 Third place of the national competition "my thesis in 180 seconds"
 2016 First place of the competition "my thesis in 180 seconds" (**Academic** selection)
 2016 First place of the competition "my thesis in 180 seconds" (**Faculty** selection)
 2015 Award for Excellence in Research of RQRV(4th place)
 2015 Excellence award for conference of Association des Chercheuses et Chercheurs Étudiant à la faculté De Médecine de l'Université Laval (ACCEM)
 2014 Poster presentation award (12th RQRV Annual Meeting)
 2014 Poster presentation award (1nd Annual PERFORM Centre Research Conference)

SUPERVISION OF STUDENTS

- 2017-present 2 PhD students and 3 undergraduates, *Washington University School of Medicine, USA*
 2013-2017 1 Master Student and 4 undergraduates, Faculty of Medicine, *Université Laval, Canada*

ORGANISATION OF SCIENTIFIC MEETINGS

- 2015-2017 Co-organizer of the first Pint Of Science event in Canada (**Science Outreach event**, 500 participants/year in Quebec city)
 2017 Co-organizer of the TroubleShooting workshops with ACCEM association (50 participants)

INSTITUTIONAL RESPONSIBILITIES

- 2014-2017 Faculty of Medicine council member, *Université Laval, Canada*
 2014-2017 Member of programs committee (Student representative), *Université Laval, Canada*
 2015-2017 Co-organization committee of the first Day in Health Research, *Université Laval, Canada*
 2015-2017 President of ACCEM (Students association), *Université Laval, Canada*
 2013-2017 Associate Director of Finances of ACCEM, *Université Laval, Canada*

REVIEWING ACTIVITIES

Editorial board

- Neurobiology of disease

Reviewing for international peer-reviewed journals

- Molecular Neurodegeneration
- Brain
- Frontiers in Molecular Neuroscience
- Neurobiology of disease
- Plos One
- Brain research

Reviewing for research funding bodies

- France Alzheimer

MAJOR MEMBERSHIPS OF SCIENTIFIC NETWORKS

- 2016-present Member, Society for Neuroscience, USA
 2013-2017 Member, Canadian Association for Neuroscience, Canada
 2021-present Working Group member of the Proteocure COST Action within the framework of Horizon Europe

MAJOR COLLABORATIONS

- Dr. David M Holtzman, *Washington University in St. Louis, USA*
- Dr. Virginia MY Lee, *University of Pennsylvania, USA*
- Drs. Alison Goate & Anne Schaefer, *Icahn School of Medicine at Mt Sinai, USA*
- Dr. Christopher K. Glass, *University of California, USA*
- Dr. Jonathan Kipnis, *Washington University in St. Louis, USA*

- Dr. Marie Eve Tremblay, *Université Laval*, Canada
- Dr. Marco Colonna, *Washington University in St. Louis*, USA
- Dr. David Blum, *Université de Lille*, France

LANGUAGE SKILLS

Fluency French (mother tongue), English

Basic skills Spanish

OUTREACH AND COMMUNICATION TO THE GENERAL PUBLIC

2015-2017	Co-organization of Pint Of Science events in Canada (Science Outreach event)
10/2010	Invited speaker in radio science outreach programme “Futur simple” on CKRL radio
09/2016	Second place of the international competition "my thesis in 180 seconds"
05/2016	Invited speaker in radio outreach programme “Les années lumière” on Radio-Canada radio
04/2016	Third place of the national competition "my thesis in 180 seconds"
2016	Three videos on different science outreach YouTube channels

SKILLS & ABILITIES

Research skills. Development of a research project, experiments and analysis of results, reflection on research perspectives, writing of scientific article and grant application.

Imaging. *In vivo* BioImaging.

Microscopy. Confocal, fluorescence and light microscopy, Super Resolution microscopy, 3D Imaris structural reconstructions.

Biochemistry. Western blot, immunohistochemistry, (co-)immunoprecipitation, ELISA, DNA / RNA extraction, enzymatic/activity assays, RT-qPCR, AAV generation, proteomic analysis, click chemistry.

Animal manipulation. Handling, feeding, breeding, insulin and glucose tolerance test, injection,

Dissection. Dissection of brain area, various organs (several muscles, pancreas, white and brown fat, liver...), organotypic slices, and cryostat brain slicing.

Cellular biology. Organotypic slices culture; primary neurons microglia and astrocytes culture, BV2 cells, Bone marrow-derived macrophage culture.

Neuronal activity. Microelectrode Array electrophysiology *in vitro*, Calcium Imaging of neurons using Fura-2

Software. Microsoft Excel, Word, PowerPoint, Adobe Photoshop, Adobe illustrator, Inkscape, Canvas, GraphPad Prism, Image Gauge, ImageJ, LAS X, Imaris, Zen-Zeiss, R, Matlab, Metamorph, R & Rstudio (basics)

SCIENTIFIC PRODUCTION

PUBLICATIONS / INVITED CONFERENCES

- 30 publications in international peer-reviewed journals
- 1 book chapter
- 21 oral communications (11 invited)
- h-index=20; 1558 citations (June 13th, 2023, Google Scholar)

Peer-reviewed published articles (#corresponding author - *co-first authors)

1. Drieu A, Du S, Kipnis M, Herz J, Lee C, Jiang H, Manis M, Kipnis J, Holtzman DM and **Gratuze M[#]**. Parenchymal border macrophages regulate tau pathology and tau-mediated neurodegeneration. *Life Sci Alliance*. 2023 Aug 10;6(11):e202302087.
2. Parhizkar S, Gent G, Rensing N, **Gratuze M**, Strout S, Sviben S, Tycksen E, Zhang Q, Erdmann Gilmore P, Sprung R, Malone J, Chen W, Remolina Serrano J, Bao X, Lee C, Wang C, Landsness E, Fitzpatrick J, Wong M, Townsend R, Colonna M, Schmidt RE Holtzman M. Sleep deprivation exacerbates microglial reactivity and A β deposition: TREM2-dependence in wild type mice and a model of amyloidosis. *Sci Transl Med*. 2023 Apr 26;15(693):eade6285.
3. **Gratuze M***, Xiong M*, Wang C*, Xin Bao X, Lee C, Remolina Serrano J, Gonzales ER, Kipnis M, Holtzman DM. Astrocytic APOE4 removal confers cerebrovascular protection despite increased cerebral amyloid angiopathy. *Mol Neurodegener*. 2023 Mar 16;18(1):17.
4. **Gratuze M**, Schlachetzki JCM, D'Oliveira Albanus R, Jain N, Novotny B, Brase L, Rodriguez L, Mansel C, Kipnis M, O'Brien S, Pasillas MP, Lee C, Manis M, Colonna M, Harari O, Glass CK, Ulrich JD, Holtzman DM. TREM2-independent microgliosis promotes tau-mediated neurodegeneration in the presence of ApoE4. *Neuron*. 2022 Nov 4:S0896-6273(22)00955-2.
5. **Gratuze M***, Jiang H*, Wang C, Xiong M, Bao X, Holtzman DM. APOE Antibody Inhibits A β -Associated Tau Seeding and Spreading in a Mouse Model. *Ann Neurol*. 2022 Jun;91(6):847-852.
6. **Gratuze M**, Chen Y, Parhizkar S, Jain N, Strickland MR, Serrano JR, Colonna M, Ulrich JD, Holtzman DM. Activated microglia mitigate A β -associated tau seeding and spreading. *J Exp Med*. 2021 Aug 2 218(8):e20210542.
7. Wang C, Xiong M, **Gratuze M**, Bao X, Shi Y, Andhey PS, Manis M, Schroeder C, Yin Z, Madore C, Butovsky O, Artyomov M, Ulrich JD, Holtzman DM. Selective removal of astrocytic APOE4 strongly protects against tau-mediated neurodegeneration and decreases synaptic phagocytosis by microglia. *Neuron*. 2021 May 19;109(10):1657-1674.e7.
8. **Gratuze M**, Holtzman DM. Targeting pre-synaptic tau accumulation: a new strategy to counteract tau-mediated synaptic loss and memory deficits. *Neuron*. 2021 Mar 3;109(5):741-743
9. Xiong M, Jiang H, Serrano JR, Gonzales ER, Wang C, **Gratuze M**, Hoyle R, Bien-Ly N, Silverman AP, Sullivan PM, Watts RJ, Ulrich JD, Zipfel GJ, Holtzman DM. APOE immunotherapy reduces cerebral amyloid angiopathy and amyloid plaques while improving cerebrovascular function. *Sci Transl Med*. 2021 Feb 17;13(581):eabd7522.
10. **Gratuze M**, Leyns CE, Sauerbeck AD, St-Pierre MK, Xiong M, Kim N, Serrano JR, Tremblay MÈ, Kummer TT, Colonna M, Ulrich JD, Holtzman DM. Impact of TREM2R47H variant on tau pathology-induced gliosis and neurodegeneration. *J Clin Invest*. 2020 Sep 1;130(9):4954-4968.
11. Sauerbeck AD, Gangolli M, Reitz SJ, Salyards MH, Kim SH, Hemingway C, **Gratuze M**, Makkapati T, Kerschensteiner M, Holtzman DM, Brody DL, Kummer TT. SEQUIN Multiscale Imaging of Mammalian Central Synapses Reveals Loss of Synaptic Connectivity Resulting from Diffuse Traumatic Brain Injury. *Neuron*. 2020 Jul 22;107(2):257-273.e5.
12. Guisle I, **Gratuze M**, Petry S, Morin F, Keraudren R, Whittington RA, Hébert SS, Mongrain V, Planel E. Circadian and sleep/wake-dependent variations in tau phosphorylation are driven by temperature. *Sleep*. 2020 Apr 15;43(4):zsz266.

13. **Gratuze M***, Leyns CEG*, Narasimhan S, Jain N, Koscal LJ, Jiang H, Manis M, Colonna M, Lee VMY, Ulrich JD, Holtzman DM. TREM2 function impedes tau seeding in neuritic plaques. *Nat Neurosci.* 2019 Aug;22(8):1217-1222.
14. Muhire G, Iulita MF, Vallerand D, Youwakim J, **Gratuze M**, Petry FR, Planel E, Ferland G, Girouard H. Arterial Stiffness Due to Carotid Calcification Disrupts Cerebral Blood Flow Regulation and Leads to Cognitive Deficits. *J Am Heart Assoc.* 2019 May 7;8(9):e011630
15. **Gratuze M[#]**, Josset N, Petry FR, Pflieger M, Jong LE, Truchetti G, Poitras I, Julien J, Bezeau F, Morin F, Samadi P, Cicchetti F, Bretzner F, Planel E. The toxin MPTP generates similar cognitive and locomotor deficits in hTau and Tau Knock-Out mice. *Brain Res.* 2019 Jan 11 ;1711:106-114.
16. **Gratuze M**, Leyns CEG, Holtzman DM. New insights into the role of TREM2 in Alzheimer's disease. *Mol Neurodegener.* 2018 Dec 20;13(1):66.
17. Joly-Amado A*, **Gratuze M***, Benderradji H, Vieau D, Buée L, Blum D. [Brain insulin signaling and Tau: impact for Alzheimer's disease and Tauopathies]. *Med Sci (Paris).* 2018 Nov;34(11):929-935.
18. Whittington RA, Virág L, **Gratuze M**, Lewkowitz-Shpuntoff H, Cheheltanan M, Petry F, Poitras I, Morin F, Planel E. Administration of the benzodiazepine midazolam increases tau phosphorylation in the mouse brain. *Neurobiol Aging.* 2019 Mar;75:11-24.
19. **Gratuze M***, Joly-Amado A*, Vieau D, Buée L, Blum D. Mutual Relationship between Tau and Central Insulin Signalling: Consequences for AD and Tauopathies? *Neuroendocrinology.* 2018;107(2):181-195.
20. **Gratuze M**, Julien J, Morin F, Marette A, Planel E. Differential effects of voluntary treadmill exercise and caloric restriction on tau pathogenesis in a mouse model of Alzheimer's disease-like tau pathology fed with Western diet. *Prog Neuropsychopharmacol Biol Psychiatry.* 2017 Oct 3;79(Pt B):452-461.
21. **Gratuze M**, Planel E. Regulation of brain insulin signaling: A new function for tau. *J Exp Med.* 2017 Aug 7;214(8):2171-2173.
22. Sebih F, Rousset M, Bellahouel S, Rolland M, de Jesus Ferreira MC, Guiramand J, Cohen-Solal C, Barbanel G, Cens T, Abouazza M, Tassou A, **Gratuze M**, Meusnier C, Charnet P, Vignes M, Rolland V. Characterization of l-Theanine Excitatory Actions on Hippocampal Neurons: Toward the Generation of Novel N-Methyl-d-aspartate Receptor Modulators Based on Its Backbone. *ACS Chem Neurosci.* 2017 Aug 16;8(8):1724-1734.
23. **Gratuze M.**, Julien J., Petry FR., Morin F., Planel E. Insulin deprivation induces PP2A inhibition and Tau hyperphosphorylation in hTau mice, a model of Alzheimer's disease-like tau pathology. *Sci Rep.* 2017 Apr 12;7:46359.
24. **Gratuze M.**, El Khoury N., Julien C., Marcouiller F., Morin F., Calon F., Hébert SS, Marette A., Planel E. Tau hyperphosphorylation in the brain of ob/ob mice is due to hypothermia: importance of thermoregulation in linking diabetes and Alzheimer's disease; *Neurobiology of disease.* 2017 Feb;98:1-8.
25. **Gratuze M.**, Julien J., Morin F., Calon F., Hébert SS, Marette A., Planel E. (2016) High fat, sugar and cholesterol consumption does not impact tau pathogenesis in a mouse model of Alzheimer's disease-like tau pathology; *Neurobiology of Aging.* 2016 Nov;47:71-73.
26. **Gratuze M.**, Cisbani G., Cicchetti F., Planel E. (2016) Is Huntington's disease a tauopathy?; *Brain.* 2016 Apr;139(Pt 4):1014-25.
27. **Gratuze M.***, El Khoury N.*, Petry F., Papon MA., Julien C., Marcouiller F., Morin F., Calon F., Hébert SS, Marette A., Planel E. (2016) Hypothermia mediates age-dependent increase of tau phosphorylation in db/db mice; *Neurobiology of disease.* 2016 Apr;88:55-65.
28. **Gratuze M.**, Noël A., Julien C., Cisbani G., Milot-Rousseau P., Morin F., Dickler M., Goupil C., Bezeau F., Poitras I., Bissonnette S., Whittington R.A., Hébert S.S., Cicchetti F., Parker J.A., Samadi P., Planel E. (2015) Tau hyperphosphorylation and deregulation of calcineurin in mouse models of Huntington's disease; *Hum Mol Genet.* 2015 Jan 1;24(1):86-99.

29. Whittington RA, Virág L, **Gratuze M**, Petry FR, Noël A, Poitras I, Truchetti G, Marcouiller F, Papon MA, El Khoury N, Wong K, Bretteville A, Morin F, Planel E. Dexmedetomidine increases tau phosphorylation under normothermic conditions in vivo and in vitro (2015). *Neurobiol Aging*. 2015 Aug;36(8):2414-28.
30. El Khoury N.B., **Gratuze M.**, Papon M.A., Bretteville A., Planel E. (2014) Insulin dysfunction and Tau pathology; *Front. Cell. Neurosci.*, 2014 Feb 11;8:22.

Book chapter

Gratuze M, Joly-Amado A, Buee L, Vieau D, Blum D. Tau, Diabetes and Insulin. *Adv Exp Med Biol*. 2019;1184:259-287.

Invited speaker (*International)

- 2024 - *Proteomic heterogeneity behind microglia reactivity and neuronal degeneration in AD*. Gordon Conference on the Cell Biology of the Neuron. June 23 - 28, 2024, Waterville Valley, USA *
- 2024 - *TREM2-independent microgliosis promotes tau-mediated neurodegeneration in the presence of ApoE4*. Holtzman symposium. June 13, 2024, Saint Louis, USA *
- 2023 - *Parenchymal border macrophages regulate tau pathology and tau-mediated neurodegeneration*. CALM. November 14-15, 2023, Montpellier, France
- 2023 - *TREM2-independent microgliosis promotes tau-mediated neurodegeneration in the presence of ApoE4*. EuroTau. April 27-28, 2023, Lille, France *
- 2023 - *Can TREM2 deletion counteract the detrimental effect of ApoE4 on tau-mediated neurodegeneration?* AD/PD. March 28- April 1, 2023, Gothenburg, Sweden *
- 2022 - *TREM2-independent microgliosis promotes tau-mediated neurodegeneration in the presence of ApoE4*. ISMND. October 10-12, 2022, Athens, Greece *
- 2022 - *Can TREM2 deletion counteract the detrimental effect of ApoE4 on tau-mediated neurodegeneration?* BIG Symposium. April 25-26, 2022, Saint Louis, USA
- 2022 - *Can TREM2 deletion counteract the detrimental effect of ApoE4 on tau-mediated neurodegeneration?* Knight ADRC seminar. Washington University. March 1st, 2022, St. Louis, USA
- 2021 - *Activated microglia mitigate A β -associated tau seeding and spreading*. CureALZ Research Leadership Group, Zoom meeting *
- 2021 - *Functional and activated microglia are essential to mitigate A β -associated tau seeding and spreading*. Center for Neuroimmunology & Neuroinfectious Diseases Basic Science Meeting. Washington University. Saint Louis, USA
- 2020 - *Impact of TREM2 R47H variant on microgliosis, tau pathology and neurodegeneration in a mouse model of tau pathology*. O'Leary Prize Competition. Washington University, Saint Louis, USA
- 2019 - *Functions of AD-associated TREM2 variant on tau pathology*. Knight ADRC seminar. Washington University, Saint Louis, USA
- 2017 - *Impact of type 2 diabetes and obesity on phosphorylation of tau protein in the db/db and ob/ob mice model : role of hypothermia*; Séminaire JPA RC Université de Lille, Lille, France *
- 2015 - *Huntington's disease: a tauopathy?* 2nd Zing Neurodegeneration Conference. Cancun, Mexico *