CURRICULUM VITAE

NAME: RANGACHARI, Manu

POSITION TITLE: Professor, Université Laval

EDUCATION AND TRAINING:

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
McMaster University, Hamilton ON	B.Arts Sc. (Hons)	06/2000	Minor in Biology
University of Toronto, Toronto ON	Ph.D.	07/2007	Immunology
Brigham & Women's Hospital/Harvard Medical School, Boston MA USA	Postdoctoral fellow	04/2013	Neurology

A. Personal Statement

My career research focus has been on better understanding the cellular and molecular mechanisms by which T lymphocytes control autoimmunity. Specifically, we study the immunopathogenesis of multiple sclerosis using experimental autoimmune encephalomyelitis (EAE), a mouse disease that recapitulates many of the immune features of MS. We use "active immunization" approaches, in which genetically susceptible mice are immunized with myelin-derived peptides, as well as "adoptive transfer" models, in which T cells with transgenic specificity for central nervous system antigen are cultured *ex vivo* and introduced into immunologically naïve animals. My team has developed an adoptive transfer mouse model that can recapitulate the relapse/remitting (RR) → secondary progressive (SP) disease course observed in close to half of MS patients. This is important because while the past decade has seen an explosion in the number of therapies available for RRMS, treatment options for progressive forms of the disease remain limited. Notably, male T cells in our model drive an exacerbated chronic phenotype, mirroring clinical observations that men living with MS may advance to progressive disease more rapidly than women. Further, as another key gap in the field is the paucity of biomarkers that can predict the onset or severity of progressive MS, we have recently expanded our focus to identify markers from human biomaterials using transcriptional and machine learning approaches.

As a Senior scholar of the *Fonds de recherche de Québec-Santé* (FRQS), >90% of my time is protected for research and the direct supervision of trainees. Nevertheless, I <u>teach</u> graduate-level courses at Université Laval, as well as at other universities. I am comfortable teaching in both English and French.

B. Academic Positions

1999-2000	Honours undergraduate student, Department of Psychiatry and Behavioural Neurosciences,
	McMaster University. Supervisor: L. T. Young.
2000	Summer research student, C.H. Best Institute, University of Toronto. Supervisor: J. Greenblatt
2000-06	Ph.D. student, Department of Immunology, <i>University of Toronto</i> . Supervisor: J. Penninger
2003-06	Ph.D. student, Institute for Molecular Biotechnology of the Austrian Academy of Sciences,
	Vienna AT. Supervisor: Josef Penninger
2007-13	Postdoctoral fellow, Center for Neurologic Diseases, Brigham & Women's Hospital, Harvard
	Medical School, Boston MA, USA. Supervisor: Vijay K. Kuchroo.
2013-18	Assistant Professor (tenure-track, «sous octroi»), Department of Molecular Medicine, Université
	Laval, Québec QC
2013-	Researcher, Department of Neurosciences, Centre de recherche du CHU de Québec -
	Universitè Laval (Quebec City University Hospital Research Center), Québec QC
2018-19	Associate Professor («sous octroi»), Department of Molecular Medicine, Université Laval
2019-	Associate Professor (tenured, «permanence»), Department of Molecular Medicine, Université
	Laval
2022-	Full Professor, Department of Molecular Medicine, Université Laval

C. Postgraduate Fellowships and Investigator Salary Support Awards

2000	Banting and Best Summer Research Studentship, University of Toronto
2000-01	Ontario-Pasteur Mérieux Graduate Scholarship in Science and Technology, Government of
	Ontario (\$10,000)
2001-03	Postgraduate Scholarship, NSERC (\$18,279/a)
2003-04	Dean's Merit Scholarship, University of Toronto (\$16,000)
2007-10	Postdoctoral Fellowship, MS Society of Canada (\$39,000/a)
2010	Postdoctoral Fellowship, CIHR (\$50,000/a); terminated early to accept TCDA (below)
2011-13	EMD Serono, Canada and endMS Network Transitional Career Development Award (TCDA);
	training component (\$70,000/a)
2014-18	Junior-1 «chercheurs-boursiers», Fonds de recherche du Québec – Santé (FRQS)
2018-22	Junior-2 «chercheurs-boursiers», FRQS
2022-	Senior «chercheurs-boursiers», FRQS
2007-10 2010 2011-13 2014-18 2018-22	Postdoctoral Fellowship, MS Society of Canada (\$39,000/a) Postdoctoral Fellowship, CIHR (\$50,000/a); terminated early to accept TCDA (below) EMD Serono, Canada and endMS Network Transitional Career Development Award (TCDA training component (\$70,000/a) Junior-1 <i>«chercheurs-boursiers»</i> , Fonds de recherche du Québec – Santé (FRQS) Junior-2 <i>«chercheurs-boursiers»</i> , FRQS

CMSF-Josten's Provincial Award for University Entrance (\$500)

D. Recognitions and Honors

1996

1997	Dean's Honour List, McMaster University
1998	Dean's Honour List, McMaster University
1998-2000	Gary Lautens Memorial Scholarship, McMaster University (\$2400)
1999	Dean's Honour List, McMaster University
2000	Graduated summa cum laude, McMaster University
2006	Participant, Roche Symposium for Leading Bioscientists of the Next Decade, Basel CH
2006	First author (Rangachari et al, <i>J Exp Med</i> 2006) of a Faculty of 1000 "Recommended Read"
2006	Author (Loeser et al, J Exp Med 2006) of a Faculty of 1000 "Recommended Read"
2006	Selected Participant, EMBO Course on Flow Cytometry, Berlin DE
2009	Travel Award, FOCIS, San Francisco CA (\$750 US)
2011	Subject of a press release from the MS Society of Canada, announcing receipt of the
	Transitional Career Development Award (24/3/2011)
2011	Travel Award, ECTRIMS, Amsterdam NL (400 euros)
2012	First author publication (Rangachari et al, Nat Med 2012) the subject of a Nature Medicine News
	& Views (Haining <i>Nat Med</i> et al)
2013	Subject of an article in Le Chuchoteur (CHU de Québec) announcing recruitment to Université
	Laval and CHU de Québec (16/5/2013)
2014	Best Poster Prize, MSBOSTON 2014, Boston MA (\$1500 US)
2016	Travel Award, ACTRIMS Progressive MS Forum, New Orleans LA (\$600 US)
2019	Obtained tenure, Université Laval
2022	Senior author publication (Doss et al., <i>Cell Rep</i> 2021) subject of a press release from the Centre de recherche du CHU de Québec – Université Laval
2021	Senior author publication (Doss et al., <i>Cell Rep</i> 2021) subject of news coverage (Noovo
2021	Network, Canada; NVL, <i>«Avance pour la SP»</i> ("Advance for MS"). March 18, 2021
2021	Press release on senior author publication (Doss et al., <i>Cell Rep</i> 2021) tweeted by the Hon.
2021	Patty Hajdu, Minister of Health for Canada.
2022	Senior author publication (Doss et al., Cell Rep 2021) subject of a lay article on the Fonds de
	recherche du Québec website (frg.gouv.ca)
2022	Recognized by the CIHR College of Reviewers as an "Outstanding Reviewer" for the Fall 2021
	CIHR Project Grant Competition
2022	Hosted the Hon. Jean-Yves Duclos, Minister of Health for Canada, on a lab tour, shooting a
	video recognizing "World MS Day" that was publicized on the Minister's Facebook/Twitter feeds
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E. Committees and Participation

Committees

1999-2000	President, Society of Arts and Science Students (SASS), McMaster University
2010-12	Postdoctoral representative, Research Oversight Committee, Brigham & Women's Hospital,
	Boston MA

2015-16	Member, endMS Network Evaluation Advisory Committee, MS Society of Canada
2018	Scientific Merit Evaluation Subcommittee, Animal Protection Committee, Centre de recherche
	du CHU de Québec - Université Laval.
2018-	Chair, Grant Peer Review Committee, Department of Neurosciences, Centre de recherche du
	CHU de Québec - Université Laval.
2019	Faculty Selection Committee, Department of Obstetrics, Gynecology and Reproduction,
	Unviversité Laval
2021-	Member, Data Access Committee, Canadian Progressive MS Cohort (CanProCo)

Conference Chairing and Organization

Local and provincial

2016-17	Poster judge, Cytokines in Inflammation, Ageing, CanCer and Obesity (CIACCO) 2016
2015-	Organizing Committee Member, CIACCO

National

2013 2013 2014	Planning Committee Member, endMS Conference 2013, St. Sauveur QC Abstract Review Committee, endMS Conference 2013, St Sauveur QC Poster judge, Canadian Society of Immunology Annual Meeting, Québec QC
2014	Member, Travel Awards Committee, Canadian Society of Immunology, Winnipeg MB
2016	Selection Committee, endMS SPRINT Programme
2016	Abstract Review Committee, endMS Conference 2016, Toronto ON
2016	Platform Session Chair, "Neuroimmunology", endMS Conference 2016, Toronto ON
2016	Platform Session Chair, "Progressive MS", endMS Conference 2016, Toronto ON
2017	Selection Committee, endMS Summer School, St. John's NL
2019	Plenary session chair, MS Xchange 2019, Montreal QC
2019	Plenary session co-chair, endMS 2019 Conference, Calgary AB
2019-20	Local Organizing Committee Member, Canadian Society of Immunology (CSI) 2020, Hotel
	Cheribourg, QC (canceled due to COVID-19 and rescheduled 2023)
2020	Plenary session chair, MS Xchange 2020 Virtual Conference.
2021	Symposium Co-Chair, CSI 2021 (with N. Mookherjee, U Manitoba), Victoria BC, "Sex effects on
	immune function and disease"
2020-23	Chair, Local Organizing Committee, CSI 2023, Lac-Orford QC
2019-	Scientific Planning Committee Member, MS Xchange, Montréal QC

International

2016	Platform session chair, "New CellsNew Frontiers", FOCIS 2016 Boston MA
2020	Session Chair, Americas Committee for Treatment and Research in MS (ACTRIMS) Forum
	2020, "Cutting-edge developments", West Palm Beach, FL
2020	Session Chair, FASEB Translational Neuroimmunology Virtual Conference; "The Role of the
	Adaptive Immune System in Primary Neurological Diseases".
2020	Panel member, FASEB Translational Neuroimmunology Virtual Conference; "Meet the Experts"
2020-23	Member, Local Organizing Committee, International Society of Neuroimmunology (ISNI),
	Quebec City

Editorial Activities

2014-2016 Co-Handling Editor, Special Topic, *Frontiers in Immunology*, "Lymphocytes in MS & EAE: More than Just a CD4+ World".

Peer Review

Manuscript peer review

2009	Peer reviewer: European Journal of Immunology
2013	Peer reviewer: Mediators of Inflammation, Immunology

2014	Peer reviewer: Multiple Sclerosis Journal, Saudi Medical Journal, Journal of Neurotoxicity Research
2015	Peer reviewer: Mediators of Inflammation, Journal of Neuroimmunology, BMC Neuroscience, Cytokine
2016	Peer reviewer: Immunology, Journal of Visualized Experiments, Frontiers in Immunology, Clinical and Experimental Pharmacology & Physiology, Molecular Vision, Neurological Research, Molecular Pharmaceutics
2017	Peer reviewer: Journal of Immunology, Human Genetics, Brain Behaviour & Immunity, Biomedicine & Pharmacotherapy, Front Immunol
2018	Peer reviewer: Front Immunol, PLOS ONE, European Journal of Immunology, American Journal of Pathology, Brain Behaviour & Immunity, Journal of Immunology, Neuroscience Letters, Journal of Neuroscience Research, Scientific Reports, International Journal of Molecular Sciences.
2019	Peer reviewer: Frontiers in Immunology, Mediators of Inflammation, Journal of Clinical Medicine, Frontiers in Molecular Neuroscience, Progress in Neurobiology, Cytokine, Cells, European Journal of Neurology
2020	Peer reviewer: PLOS ONE, Cells, Neural Regen Res, Brain Behavior & Immunity, J Clin Invest, Front Immunol, J Neuroinflammation, Int Immunopharmacol, Sci Rep, MS and Related Disorders.
2021	Peer reviewer: ImmunoHorizons, MS Journal: Experimental, Translational and Clinical, International Journal of Molecular Sciences, Science Advances, Current Topics in Behavioural Neurosciences (book chapter), J Clin Invest.
2022	Peer reviewer: Neural Regen Res, Mol Immunol, MS and Related Disorders, Molecular Pharmaceutics, Cell Press Community Review (Cell Reports/iScience)
Funding and	organizational peer review
2014-15	Committee Member, FRQS (Fonds de recherche de Québec – Santé) Doctoral Awards Committee FF5-11D (provincial)
2014-15	External Reviewer, William Harvey Translational Research Academy (international)
2016	Peer Review Observer, William Harvey Translational Research Academy (international)
2017-18	External Reviewer, Genes Cells & Molecules Committee, Discovery Grants, Natural Sciences and Engineering Research Council of Canada (NSERC) (<u>national</u>)
2018	Early Career Observer, Systems and Clinical Neurosciences-A Committee, CIHR (national)
2018, 19	Member, Biomedical Operating Grants Review Committee, MS Society of Canada (<u>national</u>)
2019	External reviewer, Clinical & Population Health Grants Review Committee, MS Society of Canada (<u>national</u>)

Reviewer, National Science Centre, Poland (international) 2019

Reviewer, Planning and Dissemination Grants (Winter 2019), CIHR (national) 2019

2019-20 External Reviewer, Genes Cells & Molecules Committee, Discovery Grants, NSERC (national)

Committee Member, FRQS (Fonds de recherche de Québec – Santé) Doctoral Awards 2019-22

Committee FF5-53D (Microbiology and immunology) (provincial)

Invited expert reviewer for internal peer review process, Office of Research Administration, 2021

University of Toronto (national)

Committee Member, Personnel Awards Committee, MS Society of Canada (national) 2013-16, 21

Peer reviewer, Diabetes Fonds Fellowship, Dutch Diabetes Research Foundation (international) 2021

2021 Peer reviewer, Austrian Science Fund (FWF Der Wissenschaftfonds) (international)

Expert external reviewer, Junior Research Professorship recruitment, University of Leuven. 2021 Belgium (international)

Peer reviewer, CIHR Project Grant, Cancer Biology & Therapeutics (CBT) Committee (spring 2021, 22

21, fall 21, spring 22) (national)

2022 Scientific Officer, Biomedical Research Grants Committee, MS Society of Canada (national)

F. Contributions to Research

Peer reviewed Publications (underline indicates corresponding authorship)

Rangachari M, Penninger JM. "Negative regulation of T cell receptor signals." Curr Opin Pharmacol, 2004 Aug

(4): 415-22

Rangachari M, Mauermann N, Marty RR, Dirnhofer S, Kurrer MO, Komnenovic V, Penninger JM, Eriksson U. "T-bet negatively regulates autoimmune myocarditis by suppressing local production of interleukin-17." *J Exp Med*. 2006 Aug 7;203(8):2009-19.

Loeser S, Loser K, Bijker MS, **Rangachari M**, van der Burg SH, Wada T, Beissert S, Melief CJ, Penninger JM. "Spontaneous tumor rejection by cbl-b-deficient T cells." *J Exp Med.* 2007 Apr 16;204(4):879-91.

Joza N, Galindo K, Pospisilik JA, Benit P, **Rangachari M**, Kanitz EE, Nakashima Y, Neely GG, Rustin P, Abrams JM, Kroemer G, Penninger JM. "The molecular archaeology of a mitochondrial death effector: AIF in Drosophila." *Cell Death Differ.* 2008 Jun;15(6):1009-18.

Mengshol JA, Golden-Mason L, Arikawa T, Smith M, Niki T, McWilliams R, Randall JA, McMahan R, Zimmerman MA, **Rangachari M**, Dobrinskikh E, Busson P, Polyak SJ, Hirashima M, Rosen HR. "A crucial role for Kupffer cell-derived galectin-9 in regulation of T cell immunity in hepatitis C infection." *PLoS One*. 2010 Mar 4;5(3):e9504.

Quintana FJ, Jin H, Burns EJ, Nadeau M, Yeste A, Kumar D, **Rangachari M**, Zhu C, Xiao S, Seavitt J, Georgopoulos K, Kuchroo VK. "Aiolos promotes TH17 differentiation by silencing II2 expression." *Nat Immunol*. 2012 Jul 1;13(8):770-7.

Rangachari M, Zhu C, Sakuishi K, Xiao S, Karman J, Chen A, Angin M, Wakeham A, Greenfield EA, Sobel RA, Okada H, McKinnon PJ, Mak TW, Addo MM, Anderson AC, Kuchroo VK. "Bat3 promotes T cell responses and autoimmunity by repressing Tim-3-mediated cell death and exhaustion." *Nat Med.* 2012 Sep;18(9):1394-400.

Wu C, Pot C, Apetoh L, Thalhamer T, Zhu B, Murugaiyan G, Xiao S, Lee Y, **Rangachari M**, Yosef N, Kuchroo VK. "Metallothioneins negatively regulate IL-27-induced type 1 regulatory T-cell differentiation." *Proc Natl Acad Sci U S A*. 2013 May 7;110(19):7802-7.

Rangachari M, Kuchroo VK. "Using EAE to better understand principles of immune function and autoimmune pathology." *J Autoimmun*. 2013 Sep;45:31-9.

Zhu C, Sakuishi K, Xiao S, Sun Z, Zaghouani S, Gu G, Wang C, Tan DJ, Wu C, **Rangachari M**, Pertel T, Jin HT, Ahmed R, Anderson AC, Kuchroo VK. "An IL-27/NFIL3 signalling axis drives Tim-3 and IL-10 expression and T cell dysfunction." *Nat Commun.* 2015 Jan 23;6:6072.

Boivin N, Baillargeon J, Doss PM, Roy AP, <u>Rangachari M</u>. "Interferon-beta suppresses murine Th1 cell function in the absence of antigen-presenting cells" *PLoS One*. 2015 Apr 17;10(4):e0124802.

Ignatius Arokia Doss PM, Roy AP, Wang A, Anderson AC, <u>Rangachari M</u>. "The non-obese diabetic mouse strain as a model with which to study CD8+ T cell function in relapsing and progressive multiple sclerosis." *Front Immunol.* 2015 Oct 22;6:541.

Zhornitsky S, McKay KA, Metz LM, Teunissen CE, <u>Rangachari M</u>. "Cholesterol and markers of cholesterol turnover: relationship with disease outcomes." *Mult Scler Relat Disord*. 2016 Jan;5:53-65.

Rangachari M, Kerfoot SM, Arbour N, Alvarez JI. "Editorial: Lymphocytes in MS and EAE: More Than Just a CD4+ World." *Front Immunol*. 2017 Feb 13;8:133.

Paré A, Mailhot B, Lévesque SA, Juzwik C, Ignatius Arokia Doss PM, Lécuyer MA, Prat A, **Rangachari M**, Fournier A, Lacroix S. "IL-1β enables CNS access to CCR2^{hi} monocytes and the generation of pathogenic cells through GM-CSF released by CNS endothelial cells". *Proc Natl Acad Sci U S A*. 2018 Feb 6;115:E1194-E1203.

Cobos EJ, Nickerson CA, Gao F, Chandran V, Bravo-Caparrós I, González-Cano R, Riva P, Andrews NA, Latremoliere A, Seehus CR, Perazzoli G, Nieto FR, Joller N, Painter MW, Ma CHE, Omura T, Chesler EJ, Geschwind DH, Coppola G, **Rangachari M**, Woolf CJ, Costigan M. "Mechanistic Differences in Neuropathic Pain Modalities Revealed by Correlating Behavior with Global Expression Profiling". *Cell Rep.* 2018 Jan 30:22:1301-1312.

Cronin SJF, Seehus C, Weidinger A, Talbot S, Reissig S, Seifert M, Pierson Y, McNeill E, Longhi MS, Turnes BL, Kreslavsky T, Kogler M, Hoffmann D, Ticevic M, da Luz Scheffer D, Tortola L, Cikes D, Jais A, **Rangachari M**, Rao S, Paolino M, Novatchkova M, Aichinger M, Barrett L, Latremoliere A, Wirnsberger G, Lametschwandtner G, Busslinger M, Zicha S, Latini A, Robson SC, Waisman A, Andrews N, Costigan M, Channon KM, Weiss G, Kozlov AV, Tebbe M, Johnsson K, Woolf CJ, Penninger JM. "The metabolite BH4 controls T cell proliferation in autoimmunity and cancer". *Nature*. 2018 Nov;563:564-568.

St-Amour I, Bosoi CR, Paré I, Ignatius Arokia Doss PM, **Rangachari M**, Hébert SS, Bazin R, Calon F. "Peripheral adaptive immunity of the triple transgenic mouse model of Alzheimer's disease". *J Neuroinflammation*. 2019 Jan 5;16:3.

Crosson T, Roversi K, Balood M, Othman R, Ahmadi M, Wang J-C, Pereira PJ, Tabatabaei M, Couture R, Eichwald T, Latini A, Prediger R, **Rangachari M**, Seehus C, Foster S, Talbot S. "Profiling of how nociceptor neurons detect danger; new and old foes." *J Intern Med.* 2019 Jul 7. 286(3):268-289.

Wang R, Rangachari M, Kuchroo VK. "Tim-3: a co-receptor with diverse roles in T cell exhaustion and tolerance." *Semin Immunol.* 2019 Apr. 42, 101302.

Yeola AP, Ignatius Arokia Doss PM, Baillargeon J, Akbar I, Mailhot B, Balood M, Talbot S, Anderson AC, Lacroix S, **Rangachari M**. "Endogenous T cell receptor rearrangement represses central nervous system autoimmunity in a TcR-transgenic model on the non-obese diabietic background". *Front Immunol*. 2020 Jan 15; 10:3115

Yeola AP, Akbar I, Baillargeon J, Ignatius Arokia Doss PM, Paavilainen VO, <u>Rangachari M</u>. "Protein translocation and retro-translocation across the endoplasmic reticulum are crucial to inflammatory effector CD4+ T cell function". *Cytokine*. 2020 May 129:154944.

Maleki AF, Cisbani G, Laflamme N, Prefontaine P, Plante M-M, Baillargeon J, **Rangachari M**, Gosselin J, Rivest S. "Selective immunomodulatory and neuroprotective effects of a NOD2 receptor agonist on mouse models of multiple sclerosis". *Neurotherapeutics*. 2021 Apr 18(2):889-904

Doss PMIA, Umair M, Baillargeon J Fazazi MR, Fudge N, Akbar I, Yeola AP, Williams JB, Leclercq M, Joly-Beauparlant C, Beauchemin P, Ruda GF, Alpaugh M, Anderson AC, Brennan PE, Droit A, Lassmann H, Moore CS, <u>Rangachari M</u>. "Male sex chromosomal complement exacerbates the pathogenicity of Th17 cells in a chronic model of CNS autoimmunity". *Cell Reports* 2021 Mar 9 34:108833.

Zhu C, Dixon K, Singer M, Xiao S, Zaghouani S, Wang C, Schramm M, Goto K, Christian E, Newcomer K, Rangachari M, Rozenblatt-Rosen O, Mak T, Okada H, Regev A, Xiang G, Zhang H, Kuchroo VK. "Tim-3 adapter protein Bat3 regulates T cell terminal differentiation and exhaustion in an mTORC2-dependent manner". Science Advances 2021 April 30 7(18):eabd2710

Umair M, Fazazi MR, <u>Rangachari M</u>. "Biological sex as a critical variable in CD4+ effector T cell function in preclinical models of multiple sclerosis". *Antioxidants & Redox Signaling* 2022 Jan 4. doi: 10.1089/ars.2021.0202

Doré É, Joly-Beauparlant C, Morozumi S, Mathieu A, Lévesque T, Allaeys I, Duchez A-C, Cloutier N, Leclercq M, Bodein A, Payre C, Martin C, Petit A, Gelb M, **Rangachari M**, Murakami M, Davidovic L, Flamand N, Arita M, Lambeau G, Boilard É. "The interaction of secreted phospholipase A2-IIA with the microbiota alters its lipidome and promotes inflammation". *JCI Insight* 2022 Jan 25;7(2):e152638.

MacDougall M, El-Hajj Sleiman J, Beauchemin P, <u>Rangachari M</u>. "SARS-CoV-2 and multiple sclerosis – potential for disease exacerbation". *Front Immunol*. Published online Apr 22, 2022 doi: 10.3389/fimmu.2022.871276

Other Publications

Rangachari M, Vollmann EH, Eriksson U, Penninger JM. "A novel model for pathogenesis of autoimmune heart failure: the role of dendritic cells." *International Congress Series* 2005 1285: 192-201

Preprints

Doss PMIA, Yeola AP, Mailhot B, Baillargeon J, Grenier P, Lacroix S, Bertrand N, <u>Rangachari M</u>. MOGreactive B cells exacerbate the severity of CD4+ T cell-driven CNS autoimmunity. Posted to biorXiv on August 1, 2019. **doi**: https://doi.org/10.1101/721696

Published Abstracts

Quintana FJ, Jin HL, Burns EJ, Nadeau M, Yeste A, Kumar D, **Rangachari M**, Zhu C, Xiao S, Kuchroo VK. "Aiolos silences II2 expression and promotes Th17 Cell Differentiation." 65th Annual Meeting of the American Academy of Neurology, San Diego CA (2013). *Neurology* 2013 80:S5002.

Rangachari M, Boivin N, Chen A, Zhu C, Kuchroo VK. "Serpine1 is a negative regulator of experimental autoimmune encephalomyelitis". Joint American/European Committees for Research and Treatment of MS Meeting, Boston MA (2014). *MS Journal* 2014 20:234-234.

Rangachari M, Doss PMIA, Anderson AC. "Myelin-specific CD8+ T cells induce progressive-like disease in a novel mouse model of multiple sclerosis." Americas Committee for Research and Treatment of MS Forum, New Orleans LA (2016). *MS Journal* 2014 20:234-234.

Doss, PMIA, Yeola AP, Lassmann H, Anderson AC, **Rangachari M.** "Development of a new chronic model of T cell-driven CNS autoimmunity." Joint American/European Committees for Research and Treatment of MS Meeting, Paris FR (2017). *MS Journal* 2017 23:98-98.

Doss PMIA, Yeola AP, Lassmann H, Anderson AC, **Rangachari M**. "Collaborative Role for Type-17 and CD8+ T Cell Immunity in Relapsing to Secondary Progressive EAE". ACTRIMS Forum 2018. *MS Journal 2018* 24:90-90.

Oral Presentations as principal investigator

2013	"Modulating tissue inflammation and autoimmunity by inducing T cell exhaustion: role of the Tim-3 signaling pathway." <i>Yale School of Medicine</i> , New Haven CT.
2013	"Analysis of gene function in models of CNS autoimmunity using retrovirally mediated gene transfer". Journée du Département de Médecine Moléculaire, <i>Université Laval</i> , Québec QC.
2013	"Analysis of gene function in models of CNS autoimmunity using retrovirally mediated gene transfer". Centre de recherche en infectiologie, Centre de recherche du CHU de Québec, Québec QC.
2014	«Analyse de la fonction des gènes dans les modèles de l'auto-immunité du SNC en utilisant le transfert de gène retroviral.» Axe Neurosciences, Centre de recherche du CHU de Québec, Québec QC.
2014	"Analysis of gene function in models of CNS autoimmunity using retrovirally mediated gene transfer." 3 rd Cytokines in Inflammation, Ageing, CanCer and Obesity (CIACCO) Conference, Sherbrooke QC.
2014	"Molecular and cellular regulation of T cell inflammation in central nervous system autoimmunity." <i>Journée scientifique du Centre de recherche du CHU de Québec</i> , Québec QC.
2014	"Serpine1 is a negative regulator of experimental autoimmune encephalomyelitis." <i>MSBOSTON</i> 2014, <i>Joint ACTRIMS/ECTRIMS Meeting</i> , Boston MA. Platform presentation at closing session to recognize Best Poster Award
2015	"Regulation of CNS inflammation in antigen-specific CD4+ and CD8+ T cell transgenic mice." <i>University of Zurich</i> , Zurich CH
2016	"Immune checkpoint signaling: a potential target in autoimmunity." Department of Microbiology & Immunology, <i>McGill University</i> , Montréal QC.
2016	"Immune checkpoints as master regulators of cancer and autoimmunity." Toronto Bladder Cancer Summit, <i>Mount Sinai Hospital</i> , Toronto ON.

2017 "Immune checkpoint signaling: a potential target in autoimmunity." 2016-2017 Quebec-France MS/ALS Meeting, Université de Montpellier, Montpellier FR. "Three short stories on the adaptive immune system and progressive CNS immunity." Djavad 2018 Mowafaghian Centre for Brain Health. University of British Columbia. Vancouver. BC. "Three short stories on the adaptive immune system and progressive CNS immunity." University 2018 of Sydney, Sydney Australia. 2018 "Male sex, type 17 responses and CD8+ T cells as factors that aggravate secondary progressive CNS autoimmunity." Department of Pharmacology & Physiology, University de Montréal. Montreal QC. 2019 "Three short stories on the adaptive immune system and progressive CNS immunity." Toronto Multiple Sclerosis Group, *University of Toronto*, Toronto ON. 2019 "Three short stories on the adaptive immune system and progressive CNS immunity." University of Alberta, Edmonton AB. 2019 "Three short stories on the adaptive immune system and progressive CNS immunity." Hotchkiss Brain Institute, *University of Calgary*, Calgary AB. "Male sex and Th17 T cells exacerbate disease in a mouse model of progressive multiple 2019 sclerosis." Organization for the Study of Sex Differences 2019, Washington D.C. "Male sex and Th17 T cells exacerbate disease in a mouse model of progressive multiple 2019 sclerosis." Ann Romney Center for Neurologic Diseases, Brigham & Women's Hospital, Harvard Medical School. Boston MA. "Neuroimmunology of MS.", 3rd Americas School of Neuroimmunology, Montreal QC. 2019 2020 "Biological sex as a determinant in inflammatory T cell responses in progressive CNS autoimmunity", Centre de recherche CERVO, Quebec City QC 2020 "Male sex and Th17 cells exacerbate disease in a mouse model of progressive CNS autoimmunity", St. Michael's Hospital, University of Toronto, ON (Scheduled March 2020; postponed due to COVID-19 crisis) "Male sex and Th17 cells exacerbate disease in a mouse model of progressive CNS 2020 autoimmunity", FASEB Translational Neuroimmunology Virtual Conference. "Male Sex Chromosomal Complement Exacerbates the Pathogenicity of Th17 Cells in a Chronic 2021 Model of CNS Autoimmunity", Canadian Society of Immunology Virtual Conference. 2021 "Sex chromosomal complement as a critical regulator of T cell responses in chronic CNS autoimmunity". MS Xchange, Montreal QC "Biological sex as a determinant in inflammatory T cell responses in chronic CNS autoimmunity" 2022 ACTRIMS Forum, West Palm Beach FL 2022 "Severe T cell driven EAE in MOG-specific B cell transgenic mice: possible role for Tph cells". Cytokines in Inflammation, Ageing, CanCer and Obesity (CIACCO), Sherbrooke QC "Biological sex as a determinant in inflammatory T cell responses in chronic CNS autoimmunity" 2022 Cutting-edge advances in MS management, 43rd International Symposium of the Université de Montreal Department of Neurosciences. Montréal QC. Presentations to Industry 2015 "Immunotherapy of multiple sclerosis: from bonch to hadeide " FMD Sarana Canada National

2013	Meeting, Toronto ON.
2015	"T cell negative regulatory receptors: Promising targets for cancer immunotherapy." Boehringer Ingelheim RCV GmBH & Co, Vienna AT.
2017	"Immune biology of MS." Biogen Canada National Meeting, Québec QC.

2019 *«Biologie immunitaire de la sclérose en plaques»* ("Immune Biology of MS"), Biogen RN

meeting, Boucherville QC

2019 "Immune Biology of MS", Biogen Medical Science Liaison meeting, Montreal QC

G. Research Funding

Current Operating Funds

- 2014-22 Discovery Grant, *Natural Sciences and Engineering Research Council of Canada (NSERC)*. "Cellular and molecular mechanisms of inflammatory T cell regulation." \$32,000/a. Principal Applicant.
- 2018-23 Project Grant, CIHR. "Cellular mechanisms regulating the pathogenesis of secondary progressive CNS autoimmunity." \$162,180/a. Principal Applicant (co-applicant A. Droit, Université Laval).
- 2020-23 Discovery Operating Grant, *MS Society of Canada (MSSOC)*. "Sex chromosomes dictate Th17 cell pathogenicity in a mode of progressive CNS autoimmunity". \$114,000/a. <u>Principal Applicant</u>.
- 2019-24 Project Grant, *CIHR*. "Nociceptor neurons control cancer immunosurveillance." \$153,000/a. <u>Coapplicant</u> (Principal Applicant, S. Talbot, Université de Montréal).
- 2021-26 Project Grant, Canadian Institutes of Health Research (CIHR). "Cellular characterization of a novel putative immune biomarker of MS progression" \$180,540/a. Principal Applicant (coapplicant C. Moore, Memorial University of Newfoundland).

Completed Operating Grants

- 2013-16 EMD Serono, Canada and endMS Network Transitional Career Development Award, independent investigator component "Role of the Tim-3 signaling pathway in modulating CNS autoimmunity." \$120,000/a. Principal Applicant.
- 2014-17 Operating Grant, *MSSOC*. "Elucidating the function of the immunoregulatory molecules Bat3 and Serpine1 in CD4+ and CD8+ T cell mediated CNS autoimmunity." \$100,000/a. Principal Applicant.
- 2016-18 Catalyst Grant, Sex as a Variable in Biomedical or Translational Research, *CIHR*. "Investigating sex-specific differences in a T cell-driven mouse model of MS." \$74,976/a. Principal Applicant.
- 2017-20 Operating Grant, *MSSOC*. "Investigating a novel inhibitory signaling mechanism that represses T cell-driven CNS autoimmunity." \$99,984/a. Principal Applicant.
- 2018-20 Catalyst Grant, Sex as a Variable in Biomedical or Translational Research, CIHR "The role of sex in regulating interleukin-17-mediated toxicity in the central nervous system." \$75,000/a. Principal Applicant.

Infrastructure Funds

John R. Evans Leader's Fund, *Canada Foundation for Innovation*. "Creation of a molecular and cellular immunological laboratory to study T cell-mediated pathogenesis of CNS autoimmunity." \$294,405 total. Principal Applicant.

Conference Organization Funds

- 2015-16 Planning and Dissemination Grant, *CIHR*. "CIACCO-2016 (7th annual symposium on Cytokines in Inflammation, Ageing, CanCer and Obesity)." \$10,000. Co-applicant (Principal Applicant: S. Ilangumaran, U. Sherbrooke).
- 2016-17 Planning and Dissemination Grant, *CIHR*. "CIACCO-2017 (8th annual symposium on Cytokines in Inflammation, Ageing, CanCer and Obesity)." \$10,000. Co-applicant (Principal Applicant: S. Ilangumaran, U. Sherbrooke).

Planning and Dissemination Grant, CIHR. "CIACCO-2018 (9th annual symposium on Cytokines in Inflammation, Ageing, CanCer and Obesity)." \$10,000. Co-applicant (Principal Applicant: A. Menendez, U. Sherbrooke).
 Planning and Dissemination Grant, CIHR. "CIACCO-2019 (10th annual symposium on Cytokines in Inflammation, Ageing, CanCer and Obesity)." \$10,000. Co-applicant (Principal Applicant: J. Fritz, McGill U).
 Planning and Dissemination Grant, CIHR. "Sex effects in immune functions and diseases: CSI-2020." \$10,000. Co-applicant (Principal Applicant, S. Ramanathan, U. Sherbrooke).

H. External Contracts

2019-21 Remedy Pharmaceuticals (New York, NY). Evaluating the efficacy of a therapeutic compound in a preclinical model of MS. Direct costs of 89,163 US\$.

I. Teaching and Mentorship

Courses Taught

Université Laval	(graduate level)
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2016-20	«Médécine moléculaire et immunologie» (MMO-7026); autumn, 1 lecture; not offered in 2021.

2015-7, 20- «Principes de neuroimmunologie» (MMO-7010), winter, 1 lecture ; not offered in 2018, 19.

2018- «Neurosciences II» (NRB-7008), winter, 1 lecture

2020, 22- *«Données récentes en neurosciences»* (NRB-8004); winter, 1 lecture; <u>not offered in 2021</u>

2022- «Épigenétique et pathologies associées» (MMO-7004); winter, 1 lecture

Other universities as guest lecturer (undergraduate level)

2021- McMaster University, Hamilton ON. "Cellular and molecular biology" (HTHSCI-1106).

2022- Queen's University, Kingston ON. "Sexual dimorphism in health and disease" (REPD387).

Trainees Mentored

Trainess Mentored		
	Postdoctoral	
	2013-14	Nicolas Boivin, <i>Université Laval.</i> "Analysis of gene and molecular pathway function in T lymphocytes <i>in vitro</i> and <i>in vivo</i> ."
	2014-15	Simon Zhornitsky, <i>University of Calgary</i> . "Cholesterol as a biomarker of MS progression". Mentored as part of the endMS Network Scholar Program for Researchers In Training (SPRINT)
	Ph.D	
	2013-19	Prenitha Mercy Ignatius Arokia Doss, <i>Université Laval</i> . Ph.D. in Microbiology and Immunology. <u>Thesis title</u> : "Molecular pathways in inflammatory T lymphocytes and their role in the pathology of mouse models of autoimmunity." <u>Defended Dec 2019</u> .
	2014-15	Kyla McKay, <i>University of British Columbia</i> . "Cholesterol as a biomarker of MS progression". Mentored as part of the endMS Network Scholar Program for Researchers In Training (SPRINT)
	2015-21	Asmita Yeola, <i>Université Laval</i> , Ph.D. in Molecular Medicine. <u>Thesis title</u> : "TcR transgenic

function". Defended Dec 2021 (thesis submission delayed due to COVID-19).

models to study CNS autoimmunity and the role of the ERAD pathway in regulating T cell

2017-Mohammad Balood, Université de Montréal, Ph.D in Pharmacology. Thesis title: "Nociceptor neurons impair cancer immunosurveillance" (co-supervised; principal supervisor S. Talbot). Irshad Akbar, Université Laval, Ph.D. in Molecular Medicine. Thesis title: "The pathogenic 2019contribution of CD8+ T cells to CNS autoimmunity" 2019-Muhammad Umair, Université Laval, Ph.D. in Molecular Medicine, Thesis title: "Male sex as a regulator of Th17 pathogenicity" 2021-Mohamed Reda Fazazi, Université Laval, Ph.D. in Molecular Medicine. Thesis title: "Epigenetic regulation of T cell function in MS and its animal models" Vahid Safdari, Université Laval, Ph.D. in Molecular Medicine. Thesis title: "Expression and 2022function of putative biomarkers of MS progression" M.Sc. 2020-21 Mohamed Reda Fazazi, Université Laval, M.Sc. in Molecular Medicine. Thesis title: "Epigenetic regulation of T cell function in MS and its animal models". Transferred to Ph.D. program in 2021. Undergraduate 2013 AiLi Wang, McMaster University, Hamilton ON. MS Society of Canada summer internship. "Investigation of the role of Nfe2l2 Pathway in mediating anti-inflammatory results of Interferonbeta treatment". 2014-15 Jean-Sébastien Bérubé, Université Laval, SBM-3002, SBM-3030. « Identification des interactions moléculaires d'une protéine immunorégulatrice » 2015-16 Azucena Gonzalez, Instituto Tecnologico y de Estudios Superiores de Monterrey (Monterrey MX). MITACS Globalink internship and 4th year honors thesis project at ITESM. "Dissecting the molecular regulation of an immunoregulatory pathway in T lymphocytes using mass spectrometry" 2016 Frédérique Parent-Prévost, Université Laval, SBM-3002. « Analyse des cellules T CD4⁺ et CD8⁺ dans un modèle murin de l'EAE par cytométrie en flux » 2017 Émil Grammond, *Université Laval*, BIO-2590 (Internship in biology) 2019 Débora Cortés, University of Brasilia (Brazil). MITACS Globalink internship. "Cellular regulation of secondary progressive CNS autoimmunity" Mohamed Reda Fazazi, Université Laval, SBM-3002, SBM-3030. "Understanding the role of the 2019-20 immune regulator Jarid1C in progressive multiple sclerosis". 2020 Gabrielle Hudon, Université Laval, SBM-3002 « Quels sont les rôles inflammatoires et immunomodulatoires des GPCRs dans l'EAE ?» 2021 Marika Lemire-Rondeau, Université Laval, SBM-3002. «Quel est le rôle du sexe biologique dans la sclérose en plaque progressive?» 2021-Madison Macdougall, Salisbury University (Salisbury MD USA). MITACS Globalink internship.

"COVID-19 as an exacerbating factor in multiple sclerosis"