BIOGRAPHICAL SKETCH

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NAME: Jean-François Trempe

eRA COMMONS USER NAME (credential, e.g., agency login): n.a.

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
McGill University, Montreal, Quebec, Canada	BSc	06/2000	Biochemistry
McGill University, Montreal, Quebec, Canada	MSc	02/2003	Biochemistry
University of Oxford, United Kingdom	DPhil	01/2007	Biochemistry
McGill University, Montreal, Quebec, Canada	Postdoc	08/2010	Biochemistry
Montreal Neurological Institute, Montreal, Quebec, Canada	Postdoc	07/2012	Neuroscience

A. Personal Statement

Jean-Francois Trempe obtained his doctorate degree from the University of Oxford in 2007. After postdoctoral training at McGill and the Montreal Neurological Institute, he obtained a Faculty position at McGill in 2013. His goal is to elucidate the function of proteins implicated in Parkinson's disease (PD) through 3D structure determination and proteomics studies, as well as design small molecules to modulate their activities. He held a Tier 2 Canada Research Chair in Structural Pharmacology and has received the *New Investigator Award* from Parkinson Canada in 2014. He has published a total of 81 articles during his career (H-index 37, 6444 citations), mostly on the topics of ubiquitin and neurodegenerative diseases. His most important contributions to date are the structure determination of Parkin, which revealed the mechanism of auto-inhibition of this important PD target, as well as the elucidation of the mechanism of PINK1 kinase activation.

B. Positions and Honors

Positions

2012-2013 Research Associate, Montreal Neurological Institute, McGill University
2013-2019 Assistant Professor, McGill University, Department of Pharmacology & Therapeutics
2019-now Associate Professor (tenured), McGill University, Department of Pharmacology & Therapeutics
2020-now Director, Proteomics & Molecular Analysis Platform, Research Institute of the McGill University Health Center

Honors & Fellowships

2000-2002 NSERC Scholarship for Graduate Studies.
2002-2006 Wellcome Trust Studentship for Structural Biology (Oxford)
2007-2009 Richard H. Tomlinson postdoctoral fellowship (McGill University)
2007-2010 Canadian Institute of Health Research (CIHR) postdoctoral fellowship
2010-2012 Parkinson Canada, Basic Research Fellowship (postdoctoral)
2014-2016 Parkinson Canada, New Investigator Award
2014-2024 Canada Research Chair in Structural Pharmacology (Tier 2, not renewable)

Committees, membership

2015-now Member of the Michael J. Fox Foundation Parkin Consortium group
2016-now Scientific Advisory Committee, Parkinson Canada
2016-now Reviewer, NSERC Discovery Grants, CFI LOF
2018-now Executive committee member, *Centre de Recherche en Biologie Structurale* (CRBS)
2019-now Chair of the Outreach Committee, CRBS
2019-now Evaluation committees, FRQNT, FRQS (Junior 2)
2023-now Graduate training committee, Dept of Pharmacology & Therapeutics
2024-now Evaluation committee, CIHR Project grants

Current consulting and Industrial activities

-Biogen Inc, collaborator
-Structural Genomics Consortium (SGC) Scientist, NeuroSGC site at McGill University

C. Contributions to science (see www.trempelab.org for complete list)

Publications in last 5 years
*Indicates equal contributions to work #Indicates corresponding authors Trempe trainees underlined

1. Sauvé V, Stefan E, Croteau N, Goiran T, Fakih R, Bansal N, Hadzipasic A, Fang J, Fon EA, Hirst WD, Silvian LF#, **Trempe JF**, Gehring K# (2024) Activation of Parkin by a molecular glue. ***Nature Communications***, 15: 7707. PMID 39300082
2. Cummer R, Grosjean F, Bolteau R, Vasegh SE, Veyron S, Keogh L, **Trempe JF**, Castagner B# (2024) Structure-Activity Relationship of Inositol Thiophosphate Analogs as Allosteric Activators of *Clostridioides difficile* Toxin B. ***Journal of Medicinal Chemistry***, doi: 10.1021/acs.jmedchem.4c01408. PMID 39254660
3. Saran A, Kim HM, Manning I, Hancock MA, Schmitz C, Madej M, Potempa J, Sola M, **Trempe JF**, Zhu Y, Davey ME, Zeytuni N# (2024) Unveiling the molecular mechanisms of the type IX secretion system's response regulator: Structural and functional insights. ***PNAS Nexus***, 3(8):pgae316. PMID 39139265
4. Penalva YCM, Paschkowsky S, Recinto SJ, Duchesne A, Hammond T, Spiegler P, Jansen G, Levet C, Charron F, Freeman M, McKinney RA, **Trempe JF**, Munter LM# (2024) Eta-secretase-like processing of the amyloid precursor protein (APP) by the rhomboid protease RHBDL4. ***Journal of Biological Chemistry***, 300(8):107541. PMID 38992438
5. Rasool S*, Shomali T*, Truong L, Croteau N, Veyron S, Bustillos BA, Springer W, Fiesel FC, **Trempe JF**# (2024) Identification and structural characterization of small molecule inhibitors of PINK1. ***Scientific Reports,*** 14(1):7739. PMID 38565869
6. Eldeeb MA*, Bayne AN*, Fallahi A, Goiran T, MacDougall EJ, Soumbasis A, Zorca CE, Tabah JJ, Thomas RA, Karpilovsky N, Mathur M, Durcan TM, **Trempe JF**#, Fon EA# (2024) TOM20 gates PINK1 activity and mediates its tethering of the TOM and TIM23 translocases upon mitochondrial stress. ***Proceedings of the National Academy of Sciences U.S.A.*** 121:e2313540121 PMID 38416681
7. Yu E, Larivière R, Thomas RA, Liu L, Senkevich K, Rahayel S, **Trempe JF**, Fon EA, Gan-Or Z# (2023) Machine learning nominates the inositol pathway and novel genes in Parkinson's disease. ***Brain,*** Oct 6:awad345. PMID 37804111
8. Senkevich K, Beletskaia M, Dworkind A, Yu E, Ahmad J, Ruskey JA, Asayesh F, Spiegelman D, Fahn S, Waters C, Monchi O, Dauvilliers Y, Dupré N, Greenbaum L, Hassin-Baer S, Nagornov I, Tyurin A, Miliukhina I, Timofeeva A, Emelyanov A, **Trempe JF**, Zakharova E, Alcalay RN, Pchelina S, Gan-Or Z# (2023) Association of Rare Variants in ARSA with Parkinson's Disease. ***Movement Disorders (IF: 8.7)***, doi:10.1002/mds.29521. PMID 37381728
9. **Trempe JF**#, Gehring K# (2023) Structural mechanisms of mitochondrial quality control mediated by PINK1 and parkin. ***Journal of Molecular Biology***, 12:168090. PMID 37054910
10. Bayne AN*, Dong J*, Amiri S, Farhan SMK#, **Trempe JF**# (2023) MTSviewer: a database to visualize mitochondrial targeting sequences, cleavage sites, and mutations on protein structures. ***PLoS One***, 18: e0284541. PMID 37093842

11. Stevens MU*, Croteau N*, Eldeeb MA*, Antico O, Zeng ZW, Toth R, Durcan TM, Springer W, Fon EA#, Muqit MMK#, **Trempe JF**# (2023) Structure-based design and characterization of Parkin activating mutations. ***Life Science Alliance,*** e202201419. PMID 36941054
12. Khan SM*, Martin RD*, Bayne AN, Pétrin D, Bourque K, Jones-Tabah J, Bouazza C, Blaney J, Lau J, Martins-Cannavino K, Gora S, Zhang A, MacKinnon S, Trieu P, Clarke PBS, **Trempe JF**, Tanny JC#, Hébert TE# (2023) Gβγ subunits colocalize with RNA polymerase II and regulate transcription in cardiac fibroblasts. ***Journal of Biological Chemistry***, 299:103064. PMID 36841480
13. Senkevich K, Zorca CE, Dworkind A, Rudakou U, Somerville E, Yu E, Ermolaev A, Nikanorova D, Ahmad J, Ruskey JA, Asayesh F, Spiegelman D, Fahn S, Waters C, Monchi O, Dauvilliers Y, Dupré N, Greenbaum L, Hassin-Baer S, Grenn FP, Chiang MSR, Sardi SP, Vanderperre B, Blauwendraat C, **Trempe JF**, Fon EA, Durcan TM, Alcalay RN, Gan-Or Z# (2022) GALC variants affect galactosyl-ceramidase enzymatic activity and risk of Parkinson's disease. ***Brain***, 146:1859-1872. PMID 36370000
14. Varghaei P, Estiar MA, Ashtiani S, Veyron S, Mufti K, Leveille E, Yu E, Spiegelman D, Rioux MF, Yoon G, Tarnopolsky M, Boycott KM, Dupre N, Suchowersky O, **Trempe JF**, Rouleau GA, Gan-Or Z# (2022) Genetic, structural and clinical analysis of spastic paraplegia 4. ***Parkinsonism Related Disorders***, 98:62-69. PMID 35487127
15. Maruszczak KK, Jung M, Rasool S, **Trempe JF**, Rapaport D# (2022) The role of the individual TOM subunits in the association of PINK1 with depolarized mitochondria. ***Journal of Molecular Medicine***, 100:747-762. PMID 35391620
16. Dong J*, Duchesne A*, Bayne AN*, Mohamed NV, Yi W, Mathur M, Chen CXQ, You Z, Abdian N, Taylor L, Fon EA, Durcan TM, **Trempe JF**# (2022) An approach to measuring protein turnover in human induced pluripotent stem cell organoids by mass spectrometry. ***Methods***, 203:17-27. PMID 35331912
17. Vranas M*, Lu Y*, Rasool S, Croteau N, Krett JD, Sauvé V, Gehring K, Fon EA, Durcan TM, **Trempe JF**# (2022) Selective localization of Mfn2 near PINK1 enable its preferential ubiquitination by Parkin on mitochondria. ***Open Biology***, 12:210255. PMID 35042405
18. Rasool S, Veyron S, Soya N, Eldeeb M, Lukacs G, Fon EA, **Trempe JF**# (2022). Mechanism of PINK1 activation by autophosphorylation and insights into assembly on the TOM complex. ***Molecular Cell***, 82:1-16. PMID 34875213
19. Sosero YL, Yu E, Estiar MA, Krohn L, Mufti K, Rudakou U, Ruskey JA, Asayesh F, Laurent SB, Spiegelman D, **Trempe JF**, Quinnell TG, Oscroft N, Arnulf I, Montplaisir JY, Gagnon JF, Desautels A, Dauvilliers Y, Gigli GL, Valente M, Janes F, Bernardini A, Sonka K, Kemlink D, Oertel W, Janzen A, Plazzi G, Antelmi E, Biscarini F, Figorilli M, Puligheddu M, Mollenhauer B, Trenkwalder C, Sixel-Döring F, Cochen De Cock V, Monaca CC, Heidbreder A, Ferini-Strambi L, Dijkstra F, Viaene M, Abril B, Boeve BF, Postuma RB, Rouleau GA, Ibrahim A, Stefani A, Högl B, Hu MTM, Gan-Or Z# (2022) Rare PSAP Variants and Possible Interaction with GBA in REM Sleep Behavior Disorder. ***Journal of Parkinson's Disease***. 12(1):333-340, PMID 34690151
20. Shi F, Aloufi N, Traboulsi H, **Trempe JF**, Eidelman DH, Baglole CJ# (2021) Endogenous regulation of the Akt pathway by the aryl hydrocarbon receptor (AhR) in lung fibroblasts. ***Scientific Reports***, 11:23189. PMID 34848742
21. Torrealba-Acosta G, Yu E, Lobo-Prada T, Ruíz-Martínez J, Gorostidi-Pagola A, Gan-Or Z, Carazo-Céspedes K, **Trempe JF**, Mata IF, Fornaguera-Trías J# (2021) Clinical and Genetic Analysis of Costa Rican Patients With Parkinson's Disease. ***Frontiers in Neurology***, 12:656342. PMID 34421783
22. Varghaei P, Yoon G, Estiar MA, Veyron S, Leveille E, Dupré N, **Trempe JF**, Rouleau GA, Gan-Or Z# (2021) GCH1 mutations in hereditary spastic paraplegia. ***Clinical Genetics***, 100:51-58. PMID 33713342
23. Khan N*, Pelletier D*, McAlear TS, Croteau N, Veyron S, Bayne AN, Black C, Ichikawa M, Khalifa AAZ, Chaaban S, Kurinov I, Kurinov I, Brouhard G, Bechstedt S, Bui KH, **Trempe JF**# (2021) Crystal structure of human PACRG in complex with MEIG1 reveals roles in axoneme formation and tubulin binding. ***Structure***, 29: 572-586. PMID 33529594
24. Mufti K, Yu E, Rudakou U, Krohn L, Ruskey JA, Asayesh F, Laurent SB, Spiegelman D, Arnulf I, Hu MTM, Montplaisir JY, Gagnon JF, Desautels A, Dauvilliers Y, Gigli GL, Valente M, Janes F, Bernardini A, Högl B, Stefani A, Holzknecht E, Sonka K, Kemlink D, Oertel W, Janzen A, Plazzi G, Antelmi E, Figorilli M, Puligheddu M, Mollenhauer B, Trenkwalder C, Sixel-Döring F, Cochen De Cock V, Monaca CC, Heidbreder A, Ferini-Strambi L, Dijkstra F, Viaene M, Abril B, Boeve BF, **Trempe JF**, Rouleau GA, Postuma RB, Gan-Or Z# (2021) Novel Associations of BST1 and LAMP3 With REM Sleep Behavior Disorder. ***Neurology***, 96:1402-1412. PMID 33397775

25. Robert RF, Bayne AN, Goiran T, Lévesque D, Boisvert F-M, **Trempe JF**, Fon EA[#] (2021) Proteomic profiling of mitochondrial-derived vesicles in brain reveals enrichment of respiratory complex sub-assemblies and small TIM chaperones. ***Journal of Proteome Research***, 20: 506-517
26. Eldeeb MA, Bayne AN, **Trempe JF**, Fon EA[#] (2020) Fine-tuning TOM-mitochondrial import via ubiquitin. ***Trends in Cell Biology***, 30: 425-427. PMID 32345464
27. Khalifa A, Ichikawa M, Dai D, Black C, Peri K, McAlear TS, Kubo S, Veyron S, Yang SK, Vargas J, **Trempe JF**, Bechstedt S, Bui KH[#] (2019) The inner junction complex of the cilia is an interaction hub that involves tubulin post-translational modifications. ***Elife***, e52760. PMID 31951202
28. Semmler S, Gagné M, Garg P, Pickles SR, Baudouin C, Hamon-Keromen E, Destroismaisons L, Khalfallah Y, Chaineau M, Caron E, Bayne AN, **Trempe JF**, Cashman NR, Star AT, Haqqani AS, Durcan TM, Meiering EM, Robertson J, Grandvaux N, Plotkin SS, McBride HM, Vande Velde C[#] (2019) The E3 ubiquitin ligase TRAF6 is a novel interacting protein of amyotrophic lateral sclerosis-linked misfolded SOD1. ***Journal of Biological Chemistry,*** 295, 3808-3825. PMID 32029478
29. Estiar MA, Léveillé E, Spiegelman D, Dupré N, **Trempe JF**, Rouleau GA, Gan-Or Z[#] (2020) Clinical and genetic analysis of ATP13A2 in hereditary spastic paraplegia expands the phenotype. ***Molecular Genetics Genomic Medecine,*** pii: e1052. doi: 10.1002/mgg3.1052. PMID 31944623
30. Krohn L, Öztürk TN, Vanderperre B, Ouled Amar Bencheikh B, Ruskey JA, Laurent SB, Spiegelman D, Postuma RB, Arnulf I, Hu MTM, Dauvilliers Y, Högl B, Stefani A, Monaca CC, Plazzi G, Antelmi E, Ferini-Strambi L, Heidbreder A, Rudakou U, Cochen De Cock V, Young P, Wolf P, Oliva P, Zhang XK, Greenbaum L, Liong C, Gagnon JF, Desautels A, Hassin-Baer S, Montplaisir JY, Dupré N, Rouleau GA, Fon EA, **Trempe JF**, Lamoureux G, Alcalay RN, Gan-Or Z[#] (2020) Genetic, Structural, and Functional Evidence Link TMEM175 to Synucleinopathies. ***Annals of Neurology***, 87: 139-153. PMID 31658403
31. Léveillé E, Estiar MA, Krohn L, Spiegelman D, Dionne-Laporte A, Tarnopolsky M, Boycott KM, Yoon G, Suchowersky O, Dupré N, **Trempe JF**, Rouleau GA, Gan-Or Z[#] (2019) SPTAN1 mutations cause autosomal recessive hereditary spastic paraplegia. ***Journal of Human Genetics,*** 64: 1145-1151. PMID 31515523
32. Fava VM, Xu YZ, Lettre G, Thuc NV, Orlova M, Thai VH, Croteau N, Eldeeb MA, MacDougall EJ, Cambri G, Tao S, Lahiri R, Adams L, Fon EA, **Trempe JF**, Cobat A, Alcaïs A, Abe L, Schurr E[#] (2019) Pleiotropic effects for Parkin and LRRK2 in leprosy type-1 reactions and Parkinson's Disease. ***Proceedings of the National Academy of Sciences U.S.A.***, 116:15616-15624. PMID 31308240
33. Bayne AN, **Trempe JF**[#] (2019) Mechanisms of PINK1, ubiquitin and Parkin interactions in mitochondrial quality control and beyond. ***Cellular and Molecular Life Sciences***, 76: 4589-4611. PMID 31254044
34. Svoboda M, Konvalinka J, **Trempe JF**, Šašková KG[#] (2019). The yeast proteases Ddi1 and Wss1 are both involved in the DNA replication stress response. ***DNA Repair (Amst)***, 80: 40-51. PMID 31276951
35. Alcalay RN, Mallett V, Vanderperre, B, Tavassoly O, Dauvilliers Y, Leblond CS, Ambalavanan A, Laurent SB, Spiegelman D, Dionne-Laporte A, Liong C, Levy OA, Fahn S, Waters C, Kuo SH, Chung WK, Ford B, Marder KS, Kang UJ, Hassin-Baer S, Greenbaum L, **Trempe JF**, Wolf P, Oliva P, Zhang XK, Clark LN, Langlois M, Dion PA, Fon EA, Dupré N, Rouleau GA, Gan-Or Z[#] (2019) SMPD1 mutations, activity and α-synuclein accumulation in Parkinson's disease. ***Movement Disorders***, 34: 526-535. PMID 30788890
36. Yi W, MacDougall EJ, Tang MY, Krahn AI, Gan-Or Z, **Trempe JF**, Fon EA[#] (2019) The landscape of Parkin variants reveals pathogenic mechanisms and therapeutic targets in Parkinson's disease. ***Human Molecular Genetics***, pii: ddz080. PMID 30994895
37. Laughlin TG, Bayne AN, **Trempe JF**, Savage DF, Davies KM[#]. (2019) Structure of NDH, the complex I-like molecule of oxygenic photosynthesis. ***Nature***, 566: 411-414. PMID 30742075
38. **Trempe JF**[#], Gehring K[#] (2018) Small-angle X-ray scattering for the study of proteins in the ubiquitin pathway. In: Mayor & Kleiger (eds) *The Ubiquitin Proteasome System*, ***Methods in Molecular Biology***. 1844: 197-208. PMID 30242711
39. Rasool S, **Trempe JF**[#] (2018) New insights into the structure of PINK1 and the mechanism of ubiquitin phosphorylation. ***Critical Reviews in Biochemistry and Molecular Biology***. 21: 1-20. PMID 30238821
40. Sauvé V*, Sung G*, Soya N, Kozlov G, Blaimschein N, Miotto LS, **Trempe JF**[#], Lukacs GL, Gehring K[#] (2018). Mechanism of parkin activation by phosphorylation. ***Nature Structural and Molecular Biology***. 25: 623-630. PMID 29967542
41. Ménade M*, Kozlov G*, **Trempe JF***, Pande H, Shenker S, Wickremasinghe S, Dicaire M-J, Li X, Brais B, McPherson PS, Gehring K[#] (2018) Structures of Ubl and Hsp90-like domains of sacsin provide insight into pathological mutations. ***Journal of Biological Chemistry***. 293: 12832-42. PMID 29945973

42. McLelland G-L, Yi W, Dorval G, Chen CX, Lauinger ND, Valimehr S, Rakovic A, Rouiller I, Durcan TM, **Trempe JF**, Fon EA[#] (2018) Mfn2 ubiquitination by PINK1/parkin gates the p97-dependent release of ER from mitochondria to drive mitophagy. ***Elife***, 7:e32866. PMID 29676259
43. Rasool S, Soya N*, Truong L*, Croteau N, Lukacs G, **Trempe JF**[#] (2018) PINK1 autophosphorylation is required for ubiquitin recognition. ***EMBO Reports***, 19: e44981. PMID 29475881

Selected publications, 2005 to 2017

1. Tang MY*, Vranas M*, Krahn AI, Pundlik S, **Trempe JF**[#], Fon EA[#] (2017) Structure-guided mutagenesis reveals a hierarchical mechanism of Parkin activation. ***Nature Communications***, 8:14697. PMID 28276439
2. Sauvé V*, Lilov A*, Seirafi M*, Vranas MM, Rasool S, Kozlov G, Sprules T, Wang J, **Trempe JF**[#], Gehring K[#] (2015) A Ubl/ubiquitin switch in the activation of Parkin. ***EMBO Journal***, e201592237. PMID 26254305
3. **Trempe JF***, Sauvé V*, Grenier K, Seirafi M, Tang MY, Ménade M, Al-Abdul-Wahid S, Krett J, Wong K, Kozlov G, Nagar B, Fon EA[#], Gehring K[#] (2013) Structure of parkin reveals mechanisms for ubiquitin ligase activation. ***Science***, 340: 1451-1455. PMID 23661642
4. **Trempe JF**[#], Fon EA[#] (2013) Structure and function of Parkin, PINK1 and DJ-1, the three musketeers of neuroprotection. ***Frontiers in Neurology***, 4: 38. PMID 23626584
5. **Trempe JF**[#] (2011) Reading the ubiquitin postal code. ***Current Opinion in Structural Biology***, 21: 792-801. PMID 22036065
6. **Trempe JF***, Chen CXQ*, Grenier K, Camacho EM, Kozlov G, McPherson PS, Gehring K[#], Fon EA[#] (2009) SH3 domains from a subset of BAR-proteins define a novel Ubl-binding domain and implicate parkin in synaptic ubiquitination. ***Molecular Cell,*** 36: 1034-1047. PMID 20064468
7. **Trempe JF**, Brown NR, Lowe ED, Gordon C, Campbell ID, Noble MEM, Endicott JA[#] (2005) Mechanism of Lys48-linked polyubiquitin chain recognition by the Mud1 UBA domain. ***EMBO Journal*** 24: 3178-3189. PMID 16138082

D. Additional Information: Research Support

Current Operating Support

NSERC – Discovery grant
Title: Structure-guided investigation of the mechanisms linking protein import, substrate processing, and respiration in mitochondria
Principal Investigator: Jean-François Trempe
Funding: April 2022 - Mar 2027, $200,000 CDN

CIHR – Project Scheme
Title: Structural studies and development of chemical probes for PINK1, a mitochondrial ubiquitin kinase implicated in Parkinson's disease.
Principal Investigator: Jean-François Trempe; Co-applicant/collaborator: Nicolas Moitessier, Edward Fon
Funding: Apr 2023 - Mar 2028, $967,725 CDN

CIHR – Project Scheme
Title: Molecular Tools that Block Maturation of the Nuclear Lamin A, Leading to Decrease in Proliferation and Metastasis of Pancreatic Ductal Adenocarcinoma and Colorectal Cancer.
Principal Investigator: Youla Tsantrizos; Co-applicants: Jean-François Trempe, Michael Sebag
Funding: Sep 2022 - Aug 2027, $1,071,000 CDN (10% to JFT)

Michael J. Fox Foundation – Target Optimization Program

Title: Structure and mechanism of PINK1-TOM supercomplex formation (renewal).
Lead Principal Investigators: Mohamed Eldeeb, Edward Fon, Jean-François Trempe
Dec 2023 - Nov 2025 $387,090 USD