BIOGRAPHICAL SKETCH

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NAME Fon, Edward A.	
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing,*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Université de Montréal	MD	1989	Medicine
McGill University	FRCP(C)	1994	Neurology Residency
McGill University		1995	Neurogenetics Fellowship
University of California, San Francisco (UCSF)		1999	Postdoctoral training

A. Personal statement

I am a neurologist-scientist at the Montreal Neurological Institute-Hospital (The Neuro) specializing in movement disorders and a Professor in the Department of Neurology and Neurosurgery at McGill University. I am the Director of the FRQS Quebec Parkinson Network (http://rpq-qpn.ca/en/) and the Scientific Director of The Neuro. I was trained at the *Université de Montréal*, McGill University and the University of California, San Francisco (UCSF). My research focuses on the molecular and cellular events leading to Parkinson's disease (PD). My laboratory has made contributions to understanding the function and cell biology of PD genes and in understanding how defects in these genes lead to PD. In particular, we have focused on understanding the function of Parkin, PINK1, α-synuclein, GBA, LRRK2, TMEM175 and DJ-1. We have established the infrastructure at The Neuro to study these genes and pathways in human patient-derived induced pluripotent stem cells (iPSCs), which we differentiate into neurons, glia and 3D brain organoids. We are currently using these iPSC systems to establish a pipeline to better understand the role of *lesser-studied* PD genes, identified in recent genome-wide association studies (GWAS), in PD pathogenesis. In addition, I helped establish the Tanenbaum Open Science Institute (TOSI) at The Neuro (https://www.mcgill.ca/neuro/open-science) and oversee its platforms including the Clinical Biological Imaging and Genetic repository (C-BIGr; https://www.mcgill.ca/c-bigneuro/) and iPSC/CRISPR Early Drug Discovery Unit (EDDU; https://www.mcgill.ca/neuro/open-science/open-science-platforms/eddu).

B. Positions and Honors

Positions and Employment

2018-pres Co-Director, Canadian Open Parkinson Network (C-OPN)
2015-pres Scientific Director, Montreal Neurological Institute
2015-pres Associate Chair, Neuroscience, Department of Neurology & Neurosurgery, McGill
2014-pres Professor, Department of Neurology & Neurosurgery, McGill University
2014-pres Director, FRQS Quebec Parkinson Network
2013-2015 Director of Clinical & Translational Research, Montreal Neurological Institute
2008-pres Director, McGill National Parkinson Foundation (NPF) Center of Excellence
2007-2014 Associate Professor with tenure, Department of Neurology & Neurosurgery, McGill
1999-2007 Assistant Professor, Department of Neurology & Neurosurgery, McGill
1995-1999 Clinical Instructor and Attending neurologist, Department of Neurology, UCSF

Professional Activities (selected)

2021-pres	Organizing committee – Dopamine 2022 meeting
2017	MRC quinquennial review Protein Phosphorylation and Ubiquitylation Unit, U. of Dundee
2016-pres	Consulting Editor, *Journal of Clinical Investigation Insight*
2016	NIH Morris K. Udall Centers Reviews Study section (RFA-NS-16-02)
2015-2017	Associate Editor, *Autophagy*
2014-pres	Michael J. Fox Foundation – multiple Programs (LRRK2/iPD, Alpha-Synuclein and GBA)
2014-pres	Editorial Board, *NPG Parkinson's Disease*
2014-2016	Associate Editor, *Canadian Journal of Neurological Sciences*
2011-pres	CIHR – College of Reviewers and multiple panels (Foundation, Project, NSB)
2010-2013	FRQ-S - Chercheurs Boursiers Senior Awards Panel
2009-2015	Parkinson's Society of Canada – Chair, Scientific Advisory Board
2009-2014	Editorial Board, *Journal of Biological Chemistry*

Honors and Awards (selected)

2019-pres	Canada Research Chair (Tier 1) in Parkinson's disease
2015-pres	Elected Member, American Society for Clinical Investigation (ASCI)
2011-2015	FRQ-S Chercheur National
2008-2011	FRSQ Chercheur-Boursier (Senior)
2007-2012	MNI Killam Scholar
2005-2008	EJLB Foundation Scholar
2003	Prix de Jeune Chercheur Blaise Pascal de l'Ecole Normale Supérieure, France
2003-2006	CIHR Clinician-Scientist Award (Phase II - Renewal)
1994	Chief Neurology Resident, Montreal Neurological Institute, McGill University

C. Contributions to Science

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1Xg6ydqKp3KcVm/bibliography/public/

Google Scholar page: https://scholar.google.ca/citations?user=Bnu46lcAAAAJ&hl=en

Mechanism of Parkin and PINK1 activation (Trainees I supervised indicated by *).

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2. Trempe J-F*[#], Sauvé[#], V, Grenier K*, Seirafi, M, Tang MY*, Ménade M, Krett J*, Wong K, Kozlov G, Nagar B, **Fon EA[§]**, Gehring K[§]. Structure of parkin reveals mechanism of ubiquitin ligase activation. ***Science***. 2013; 340(6139):1451-5. [#]Co-first authors; [§]co-corresponding authors.
3. Koyano F, Okatsu K, Kosako H, Tamura Y, Go E, Kimura M, Kimura Y, Tsuchiya H, Yoshihara H, Hirokawa T, Endo T, **Fon EA**, Trempe JF, Saeki Y, Tanaka K, Matsuda N. Ubiquitin is phosphorylated by PINK1 to activate parkin. ***Nature.*** 2014; 510(7503):162-6
4. Tang MY*, Vranas M, Krahn A*, Pundlik S*, Trempe JF, **Fon EA**. Structure-guided mutagenesis reveals a hierarchical mechanism of Parkin activation. ***Nat. Commun.*** 2017; 8:14697. doi: 10.1038/ncomms14697
5. Yi W*, MacDougall EJ*, Tang MY*, Krahn AI*, Gan-Or Z, Trempe JF, **Fon EA**. The Landscape of Parkin Variants Reveals Pathogenic Mechanisms and Therapeutic Targets in Parkinson's Disease. ***Hum Mol Genet***. 2019 28(17):2811-2825

6. Rasool S, Veyron S, Soya N, Eldeeb M*, Lukacs GL, **Fon EA**, Trempe JF. Structure of PINK1 reveals autophosphorylation dimer and provides insights into binding to the TOM complex. ***bioRxiv*** 2021. doi: https://doi.org/10.1101/2021.08.05.455304

7. Sauvé V, Sung G, MacDougall E*, Kozlov G, Saran A, Fakih R, **Fon EA**, Gehring K. Structural basis for feed forward control in the PINK1/parkin pathway. ***bioRxiv*** 2021. doi:https://doi.org/10.1101/2021.08.05.455304

Role of Parkin and PINK1 in membrane trafficking

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2. McLelland GL*, Soubannier V, Chen CX*, McBride HM, **Fon EA**. Parkin and PINK1 Function in a Vesicular Trafficking Pathway Regulating Mitochondrial Quality Control. ***EMBO J.*** 2014; 33:282-95

3. Sugiura A, McLelland GL*, **Fon EA**, McBride HM. A new Pathway for Mitochondrial Quality Control: Mitochondrial Derived Vesicles. ***EMBO J***. 2014; 33(19):2142-2156

4. McLelland GL*, Lee SA*, McBride HM, **Fon EA**. Syntaxin-17 delivers PINK1/parkin-dependent mitochondrial vesicles to the endolysosomal system. ***J. Cell Biol.*** 2016; 214(3):275-91

5. McLelland GL*, Goiran T*, Yi W*, Dorval G, Chen CX, Lauinger ND*, Krahn AI*, Valimehr S, Rakovic A, Rouiller I, Durcan TM, Trempe JF, **Fon EA**. Mfn2 ubiquitination by PINK1/parkin gates the p97-dependent release of ER from mitochondria to drive mitophagy. ***Elife***. 2018; 7. pii: e32866.

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7. Vranas M, Lu Y, Rasool S, Croteau N, Krett JD*, Sauvé V, Gehring K, **Fon EA**, Durcan TM, Trempe JF. Selective localization of Mfn2 near PINK1 enable its preferential ubiquitination by Parkin on mitochondria. ***bioRxiv*** 2021.08.25.457684; doi: https://doi.org/10.1101/2021.08.25.457684

Function of Parkin interacting proteins

1. Kalia SK, Lee S, Liu L, Crocker SJ, Thorarinsdottir TE*, Smith PD, Glover JR, **Fon EA**, Park DS, Lozano AM. BAG5 inhibits parkin and enhances dopaminergic neuron degeneration. ***Neuron*** 2004; 44:931-45

2. Durcan TM*, Kontogiannea M*, Thorarinsdottir T*, Fallon L*, Williams AJ, Djarmati A, Fantaneanu T*, Paulson HL, **Fon EA**. The Machado-Joseph Disease-Associated Mutant form of Ataxin-3 Regulates Parkin Ubiquitination and Stability. ***Hum. Mol. Genet.*** 2011; 20(1):141-54.

3. Durcan TM*, Tang MY*, Pérusse JR, Dashti EA*, Aguileta MA*, McLelland GL*, Gros P*, Shaler TA, Faubert D, Coulombe B, **Fon EA**. USP8 Regulates Mitophagy by Removing K6-linked Ubiquitin Conjugates from Parkin. ***EMBO J***. 2014; 33(21):2473-91

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Function and genetics of other Parkinson's disease genes

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2. Alcalay RN, Mallett V, Vanderperre B*, Tavassoly O*, Dauvilliers Y, Wu RYJ, Ruskey JA, 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**, Dupre N, Rouleau GA, Gan-Or Z. SMPD1 mutations, activity, and α-synuclein accumulation in Parkinson's disease. ***Mov Disord.*** 2019 34(4):526-535

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knockdown peptide and evaluation of its efficacy in Parkinson's disease models. ***Commun Biol.*** *2021* 4(1):232. PMID: 33608634

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Using patient iPSCs to model brain diseases and clinical contributions

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