

PUBLICATIONS

Articles in Peer-Reviewed Journals (* Denotes trainees that Dr. Fon supervised)

1. Eldeeb MA*, Fahlman RP, Esmalili M, **Fon EA**. Formylation of Eukaryotic Cytoplasmic Proteins: Linking Stress to Degradation. *Trends Biochem, Sci*. 2019 doi.org/10.1016/j.tibs.2018.12.008
2. Rudakou U, Ouled Amar Bencheikh B, Ruskey JA, Krohn L, Laurent SB, Spiegelman D, Liang C, Fahn S, Waters C, Monchi O, **Fon EA**, Dauvilliers Y, Alcalay RN, Dupré N, Gan-Or Z. Common and rare GCH1 variants are associated with Parkinson's disease. *Neurobiol Aging*. 2019 Jan;73:231.e1-231.e6. doi: 10.1016/j.neurobiolaging.2018.09.008. Epub 2018 Sep 15
3. McLelland GL*, **Fon EA**. MFN2 retrotranslocation boosts mitophagy by uncoupling mitochondria from the ER. *Autophagy*. 2018 doi: 10.1080/15548627.2018.1505154
4. McLelland GL*, **Fon EA**. Principles of mitochondrial vesicle transport. *Curr. Opin. Physiol*. 2018; 3:25–33; <https://doi.org/10.1016/j.cophys.2018.02.005>
5. Ouled Amar Bencheikh B, Leveille E, Ruskey JA, Spiegelman D, Liang C, **Fon EA**, Rouleau GA, Dauvilliers Y, Dupre N, Alcalay RN, Gan-Or Z. Sequencing of the GBA coactivator, Saposin C, in Parkinson disease. *Neurobiol Aging*. 2018 pii: S0197-4580(18)30239-2. doi: 10.1016/j.neurobiolaging.2018.06.034
6. Ruskey JA, Zhou S, Santiago R, Franche LA, Alam A, Roncière L, Spiegelman D, **Fon EA**, Trempe JF, Kalia LV, Postuma RB, Dupre N, Rivard GE, Assouline S, Amato D, Gan-Or Z. The GBA p.Trp378Gly mutation is a probable French-Canadian founder mutation causing Gaucher disease and synucleinopathies. *Clin Genet*. 2018 doi: 10.1111/cge.13405
7. Bell S, Maussion G, Jefri M, Peng H, Theroux JF, Silveira H, Soubannier V, Wu H, Hu P, Galat E, Torres-Platas SG, Boudreau-Pinsonneault C, O'Leary LA, Galat V, Turecki G, Durcan TM, **Fon EA**, Mechawar N, Ernst C. Disruption of GRIN2B Impairs Differentiation in Human Neurons. *Stem Cell Reports*. 2018 pii: S2213-6711(18)30236-4. doi: 10.1016/j.stemcr.2018.05.018.
8. Li J, Ruskey JA, Arnulf I, Dauvilliers Y, Hu MTM, Högl B, Leblond CS, Zhou S, Ambalavanan A, Ross JP, Bourassa CV, Spiegelman D, Laurent SB, Stefani A, Charley Monaca C, Cochen De Cock V, Boivin M, Ferini-Strambi L, Plazzi G, Antelmi E, Young P, Heidebreder A, Labbe C, Ferman TJ, Dion PA, Fan D, Desautels A, Gagnon JF, Dupré N, **Fon EA**, Montplaisir JY, Boeve BF, Postuma RB, Rouleau GA, Ross OA and Gan-Or Z. Full sequencing and haplotype analysis of MAPT in Parkinson disease and REM sleep behavior disorder. *Mov. Disord*. 2018; doi: 10.1002/mds.27385
9. 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. doi: 10.7554/eLife.32866.
10. Mohtashami S, He Q, Ruskey JA, Zhou S, Dion PA, Allen RP, Earley CJ, **Fon EA**, Xiong L, Dupré N, Dauvilliers Y, Rouleau GA, Gan-Or Z. TOX3 Variants Are Involved in Restless Legs Syndrome and Parkinson's Disease with Opposite Effects. *J Mol Neurosci*. 2018; 64(3):341-345. doi: 10.1007/s12031-018-1031-4
 11. Ross JP, Mohtashami S, Leveille E, Johnson AM, Xiong L, Dion PA, **Fon E**, Dauvilliers Y, Dupré N, Rouleau GA, Gan-Or Z. Association study of essential tremor genetic loci in Parkinson's disease. *Neurobiol Aging*. 2018; pii: S0197-4580(18)30001-0. doi: 10.1016/j.neurobiolaging.2018.01.001
 12. Manecka DL*, Vanderperre B*, **Fon EA**, Durcan TM. The Neuroprotective Role of Protein Quality Control in Halting the Development of Alpha-Synuclein Pathology. *Front Mol Neurosci*. 2017;10:311. doi: 10.3389/fnmol.2017.00311
 13. 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
 14. Rodriguez L, Mohamed NV, Desjardins A, Lippé R, **Fon EA**, Leclerc N. Rab7A regulates Tau secretion. *J. Neurochem*. 2017; 141(4):592-605
 15. Das S et al. Cyberinfrastructure for Open Science at the Montreal Neurological Institute. *Front. Neuroinform*. 2017; 10:53. doi: 10.3389/fninf.2016.00053
 16. Roberts RF*, **Fon EA**. Presenting mitochondrial antigens: PINK1, Parkin and MDVs steal the show. *Cell Res*. 2016; 26(11):1180-1181
 17. Roberts RF*, Tang MY*, **Fon EA**, Durcan TM. Defending the mitochondria: The pathways of mitophagy and mitochondrial-derived vesicles. *Int J Biochem Cell Biol*. 2016; 79:427-436
 18. Munoz DP, **Fon EA**, Chen R. A New Collaboration Between the Canadian Association for Neuroscience and CJNS. *Can J Neurol Sci*. 2016;43(1):2. doi: 10.1017/cjn.2015.362
 19. Klionsky DJ et al. Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy*. 2016; 12(1):1-222
 20. 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
 21. Schreij AM, **Fon EA**, McPherson PS. Endocytic membrane trafficking and neurodegenerative disease. *Cell Mol Life Sci*. 2016; 73(8):1529-45

22. Durcan TM*, **Fon EA**. The three P's of Mitophagy: PARKIN, PINK1 and Post-Translational Modifications. *Genes Dev.* 2015; 29(10):989-999.
23. Ryan BJ, Hoek S, **Fon EA**, Wade-Martins R. Mitochondrial dysfunction and mitophagy in Parkinson's: from familial to sporadic disease. *Trends Biochem Sci.* 2015; 40(4):200-210
24. Edwards AM et al. SGC Open Source Target-Discovery Partnership. Preclinical target validation using patient-derived cells. *Nat Rev Drug Discov.* 2015; 14(3):149-50
25. Durcan TM*, **Fon EA**. USP8 and PARK2/parkin-mediated mitophagy. *Autophagy.* 2015; 11(2):428-9
26. Aguilera MA*, Korac J, Durcan TM*, Trempe JF*, Haber M*, Gehring K, Elsasser S, Waidmann O, **Fon EA**, Husnjak K. The E3 Ubiquitin ligase parkin is recruited to the 26S proteasome via the proteasomal ubiquitin receptor Rpn13. *J Biol Chem.* 2015; 290(12):7492-505. doi: 10.1074/jbc.M114.614925
27. Bertolin G, Jacoupy M, Traver S, Ferrando-Miguel R, Saint Georges T, Grenier K*, Ardila-Osorio H, Muriel MP, Takahashi H, Lees AJ, Gautier C, Guedin D, Coge F, **Fon EA**, Brice A, Corti O. Parkin maintains mitochondrial levels of the protective Parkinson's disease-related enzyme 17- β hydroxysteroid dehydrogenase type 10. *Cell Death Differ.* 2015; 22(10):1563-76. doi: 10.1038/cdd.2014.224
28. Schreij AMA*, Chaineau M, Ruan W, Lin S, Barker, PA, **Fon EA**[§], McPherson PS[§]. LRRK2 localizes to endosomes and interacts with clathrin-light chains to limit Rac1 activation. *EMBO Rep.* 2015; 16(1):79-86. [§]co-corresponding authors
29. Grenier K*, Kontogiannina M*, **Fon EA**. Short mitochondrial ARF triggers Parkin/PINK1-dependent mitophagy in neurons. *J. Biol. Chem.* 2014; 289(43):29519-30
30. Durcan TM*, Tang MY*, Pérusse JR, Dashti EA*, Aguilera 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
31. 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
32. 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

33. 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(4):282-95
34. Bertolin G, Ferrando-Miguel R, Jacoupy M, Traver S, Grenier K*, Greene AW*, Dauphin A, Waharte F, Bayot A, Salamero J, Lombès A, Bulteau AL, **Fon EA**, Brice A, Corti O. The TOMM machinery is a molecular switch in PINK1 and PARK2/PARKIN-dependent mitochondrial clearance. *Autophagy*. 2013; 9(11):1801-17
35. Grenier K*, McLelland GL*, **Fon EA**. Parkin- and PINK1-Dependent Mitophagy in Neurons: Will the Real Pathway Please Stand Up? *Front Neurol*. 2013; 4:100. doi: 10.3389/fneur.2013.00100
36. 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.
37. Durcan TM*, **Fon EA**. Ataxin-3 and its E3 partners: Implications for Machado-Joseph disease. *Front. Neur*. 2013; 4:46. doi: 10.3389/fneur.2013.00046
38. Trempe JF*, **Fon EA**. Structure and function of parkin, PINK1 and DJ-1, the three musketeers of neuroprotection. *Front. Neur*. 2013; 4:38. doi: 10.3389/fneur.2013.00038
39. Ruan W*, Unsain N, Desbarats J, **Fon EA**[§], Barker PA[§]. Wengen, the Sole Tumour Necrosis Factor Receptor in Drosophila, Collaborates with Moesin to Control Photoreceptor Axon Targeting During Development. *PLoS One* 2013; 8(3): e60091. doi: 10.1371/journal.pone.0060091. [§]co-corresponding authors
40. Daoud H, Noreau A, Rochefort D, Paquin-Lanthier G, Gauthier MT, Provencher P, Pourcher E, Dupré N, Chouinard S, Jodoin N, Soland V, **Fon EA**, Dion PA, Rouleau GA. Investigation of C9orf72 repeat expansions in Parkinson's disease. *Neurobiol Aging*. 2013; 34(6): 1710.e7-9. doi: 10.1016/j.neurobiolaging.2012.11.025
41. Klionsky DJ et al. Guidelines for the use and interpretation of assays for monitoring autophagy. *Autophagy*. 2012; 8(4):445-544
42. Greene AW*, Grenier K*, Aguilera MA*, Muise S*, Farazi R, Haque ME, McBride HM, Park DS, **Fon EA**. Mitochondrial Processing Peptidase Regulates PINK1 Processing, Import and Parkin Recruitment. *EMBO Rep*. 2012; 13(4):378-85

43. Soubannier V, McLelland GL*, Zunino R, Braschi E, Rippstein P, **Fon EA**, McBride HM. A novel vesicular transport pathway shuttles cargo from mitochondria to lysosomes. *Curr. Biol.* 2012; 22(2):135-41
44. Durcan TM*, Kontogiannea M*, Bedard N, Wing SS, **Fon EA**. Ataxin-3 deubiquitination is coupled to parkin ubiquitination via the E2 ubiquitin-conjugating enzyme. *J. Biol. Chem.* 2012; 287(1):531-41
45. Grimes D, Gordon J, Snelgrove B, Lim-Carter I, **Fon E**, Martin W, Wieler M, Suchowersky O, Rajput A, Lafontaine AL, Stoessl J, Moro E, Schoffer K, Miyasaki J, Hobson D, Mahmoudi M, Fox S, Postuma R, Kumar H, Jog M; Canadian Neurological Sciences Federation. Canadian Guidelines on Parkinson's Disease. *Can J Neurol Sci.* 2012 ;39 (4 Suppl 4):S1-30
46. Durcan TM*, **Fon EA**. Mutant ataxin-3 promotes the autophagic degradation of parkin. *Autophagy.* 2011; 7(2):233-4
47. 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.
48. Irrcher I, Aleyasin H, Seifert EL, Hewitt SJ, Chhabra S, Phillips M, Lutz AK, Rousseaux MW, Bevilacqua L, Jahani-Asl A, Callaghan S, Maclaurin JG, Winklhofer KF, Rizzu P, Rippstein P, Kim RH, Chen CX*, **Fon EA**, Slack RS, Harper ME, McBride HM, Mak TW, Park DS. Loss of the Parkinson's Disease-linked gene DJ-1 perturbs mitochondrial dynamics. *Hum. Mol. Genet.* 2010; 19(19):3734-46
49. Théard D, Labarrade F, Partisani M, Milanini J, Sakagami H, **Fon EA**, Wood SA, Franco M, Luton F. USP9x-mediated deubiquitination of EFA6 regulates de novo tight junction assembly. *EMBO J.* 2010;29(9):1499-509
50. Bouvier D, Tremblay ME, Riad M, Corera AT*, Gingras D, Horn KE, Fotouhi M, Girard M, Murai KK, Kennedy TE, McPherson PS, Pasquale EB, **Fon EA**, Doucet G. EphA4 is localized in synaptic and clathrin-coated vesicles in adult mouse brain. *J. Neurochem.* 2010; 113(1):153-65
51. Trempe JF, Chen CXQ*, Grenier K*, Camacho EM, Kozlov G, McPherson PS, Gehring K, **Fon EA**. SH3 Domains from a Subset of BAR-Proteins Define a Novel Ubl-Binding Domain and Implicate Parkin in Synaptic Ubiquitination. *Mol. Cell* 2009; 36(6):1034-47
52. Corera AT*, Doucet G, **Fon EA**. Long-Term Potentiation in Isolated Dendritic Spines. *PLoS ONE.* 2009; 4(6): e6021. doi:10.1371/journal.pone.0006021
53. Scanlon TC, Gottlieb B, Durcan TM*, **Fon EA**, Beitel LK, Trifiro MA. Isolation of human

- proteasomes and putative proteasome-interacting proteins using a novel affinity chromatography method. *Exp. Cell Res.* 2009; 315(2):176-89.
54. Bouvier D, Corera AT*, Tremblay ME, Riad M, Chagnon M, Murai KK, Pasquale EB, **Fon EA**, Doucet G. Presynaptic and postsynaptic localization of EphA4 and EphB2 in adult mouse forebrain. *J. Neurochem.* 2008; 106(2):682-95
55. Cookson MR, Dauer W, Dawson TM, **Fon EA**, Guo M, Shen J. The roles of kinases in familial Parkinson's disease. *J. Neurosci.* 2007; 27(44):11865-8. *CIHR Operating Grant #MOP-62714*
56. Kaiser P, **Fon EA**. Keystone Meeting on Ubiquitin and Signaling: Expanding Horizons at Big Sky. *EMBO Rep.* 2007; 8(9):817-22. *CIHR Operating Grant #MOP-62714*
57. Joch M*, Ase AR, Chen X*, MacDonald PA*, Kontogiannia M, Corera AT*, Brice A, Séguéla P, **Fon EA**. Parkin-Mediated Monoubiquitination of the PDZ Protein PICK1 Regulates ASIC Channel Activity. *Mol. Biol. Cell.* 2007; 18(8):3105-18.
58. Zhou L, Martinez SJ, Haber M, Jones EV, Bouvier D, Doucet G, Corera AT, Fon EA, Zisch AH, Murai KK. EphA4 signaling regulates phospholipase Cgamma1 activation, cofilin membrane association, and dendritic spine morphology. *J. Neurosci.* 2007; 27(19):5127-38.
59. Fallon L*, Bélanger CML*, Corera AT*, Kontogiannia M, Regan-Klapisz E, Moreau F, Voortman J, Haber M*, Rouleau G*, Thorarinsdottir TE*, Brice A, van Bergen en Henegouwen P, **Fon EA**. A Regulated Interaction with the UIM-protein Eps15 Implicates Parkin in EGF Receptor Trafficking and PI(3)K-Akt Signalling. *Nature Cell Biology.* 2006; 8(8):834-42. *CIHR Operating Grant #MOP-62714 & Michael J. Fox Foundation.*
60. Regan-Klapisz E, Sorokina I, Voortman J, de Keizer P, Roover RC, Verheesen P, Urbé S, Fallon L*, **Fon EA**, Verkleij A, Benmerah A, van Bergen en Henegouwen PMP. Ubiquitin recruits Eps15 into Ubiquitin-rich cytoplasmic aggregates via UIM-UBL interaction. *J. Cell Sci.* 2005; 118(19):4437-50. *CIHR Operating Grant #MOP-62714.*
61. Croft BG*, Fortin G, Corera AT*, Beaudet A, Edwards RH, Trudeau LE, **Fon EA**. Normal biogenesis and cycling of synaptic vesicles in dopamine neurons of VMAT2 knockout mice. *Mol. Biol. Cell* 2005; 16(1):306-15. *CIHR Operating Grant #MOP-4245.*
62. 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(6):931-45. *CIHR Operating Grant #MOP-62714.*
63. Fallon L*, Moreau F, Croft BG*, Labib N*, Gu WJ, **Fon EA**. Parkin and CASK/LIN-2 associate via a PDZ-mediated interaction and are co-localized in lipid rafts and postsynaptic densities in brain. *J Biol Chem.* 2002; 277(1):486-91. *Parkinson's Society of Canada Grant.*

64. Larsen KE, **Fon EA**, Hastings TG, Edwards RH, and Sulzer D. Methamphetamine-induced degeneration of dopaminergic neurons involves autophagy and upregulation of dopamine synthesis. *J. Neurosci.* 2002; 22(20):8951-60
65. Alvarez C, Vitalis T, **Fon EA**, Hanoun N, Hamon M, Seif I, Edwards RH, Gaspar P, Cases O. Effects of genetic depletion of monoamines on somatosensory cortical development. *Neurosci.* 2002; 115(3):753-64
66. **Fon EA**, Edwards RH. Molecular Mechanism of Neurotransmitter Release. *Muscle & Nerve* 2001; 24:581-601.
67. Reimer RJ, **Fon EA**, Edwards, RH. Vesicular Neurotransmitter Transport and the Presynaptic Regulation of Quantal Size. *Curr Opin Neurobiol* 1998; 8:405-412
68. Carmant L, Decarie JC, **Fon EA**, Shevell MI. Transient visual symptoms as the initial manifestation of childhood adrenoleukodystrophy. *Pediatr Neurol.* 1998 Jul; 19:62-64
69. **Fon EA**, Pothos, EN, Sun B-C, Killeen N, Sulzer D, Edwards RH. Vesicular Transport Regulates Monoamine Storage and Release but Is Not Essential for Amphetamine Action. *Neuron* 1997; 19:1271-1283
70. Lafreniere RG, Kibar Z, Rochefort D, Han F-Y, **Fon EA**, Dube M-P, Kang X, Baird S, Korneluk R, Andermann E, Rommens J, Rouleau GA. Genomic structure of the GT334 (EHOC-1) gene mapping to 21q22.3. *Gene* 1997;198:313-321
71. Song H-J, Ming G-L, **Fon E**, Bellochio E, Edwards RH, Poo M-M. Expression of a putative vesicular acetylcholine transporter facilitates quantal transmitter packaging. *Neuron* 1997; 18:815-826
72. Joobar R, Rouleau G, **Fon EA**, Lal S, Palmour R, Bloom D, Labelle A, Benkelfat C. Apolipoprotein E genotype in schizophrenia. *Am J Med Genet* 1996; 67: 235
73. Lafreniere RG, Rochefort DL, Kibar Z, **Fon EA**, Han F-Y, Cochius J, Kang X, Baird S, Korneluk RG, Andermann E, Rommens JM, Rouleau GA. Isolation and characterization of GT335, a novel human gene conserved in E. coli and mapping to 21q22.3. *Genomics* 1996; 38:264-272
74. **Fon EA**, Sarrazin J, Meunier C, Alarcia J, Shevell MI, Leboyer M, Rouleau GA. Analysis of the Adenylosuccinate Lyase (ADSL) gene in Infantile autism. *Am J Med Genet* 1995;60:554-557
75. **Fon EA**, Mackey A, Côté R, Wolfsan C, McIlraith D, Leclerc J, Bourque F. Hemostatic markers in acute transient cerebral ischemia. *Stroke* 1994;25:282-286
76. **Fon EA**, Demczuk S, Delattre O, Thomas G, Rouleau GA. Mapping of the human adenylosuccinate lyase gene to chromosome 22q13.1-q13.2. *Cytogenet Cell Genet* 1993;64:201-203

77. Ingelfinger JR, Zuo WM, **Fon EA**, Ellison KE, Dzau VJ. In situ hybridization evidence for angiotensinogen messenger RNA in the rat proximal tubule. An hypothesis for the intrarenal renin angiotensin system. *J Clin Invest* 1990;85:417-423
78. Anand-Srivastava MB, Thibault G, Sola C, **Fon EA**, Ballak M, Charbonneau C, Haile-Meskel H, Garcia R, Genest J, Cantin M. Atrial natriuretic factor in Purkinje fibers of rabbit heart. *Hypertension* 1989;13:789-798

Book Chapters

1. McLelland GL* and **Fon EA**. A Get-Together to Tear it Apart: The Mitochondrion Meets the Cellular Turnover Machinery. In "The Functions, Disease-Related Dysfunctions, and Therapeutic Targeting of Neuronal Mitochondria". *Wiley Series on Neuropharmacology* Edited by J. Marie Hardwick, Valentin K. Gribkoff, Elizabeth A. Jonas. Wiley & Sons, 2015
2. Duquette A* and **Fon EA**. Novel Functions of Parkin. In "The Ubiquitin Proteasome System In Nervous System: From Physiology To Pathology - 2008 update". Edited by Mario Di Napoli, M.D. and Cezary Wojcik, M.D., Ph.D., D.Sc.