

BIOGRAPHICAL SKETCH

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NAME: **Elisa GREGGIO**

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POSITION TITLE: **Associate Professor of Physiology**

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
University of Padova	BS/MS	2001	Molecular Biology
University of Padova	PhD	2005	Molecular Physiology and Structural Biology
National Institute on Aging	Postdoc	2009	Neuroscience

A. Personal Statement

In 2005 I obtained my PhD in Molecular Physiology at University of Padova in collaboration with the National Institute of Health (Bethesda, USA) in Mark Cookson's laboratory, which I joined for my postdoctoral training until 2009, when I returned to University of Padova with a Brain Gain Assistant Professorship. Since 2014, I am Associate Professor at the University of Padova and Coordinator of the Physiology, Genetic and Behavior Unit. My research is centered around the understanding of the molecular mechanisms leading to neurodegeneration in Parkinson's disease and related disorders. My major contribution in the field has been the characterization of the pathobiology of LRRK2 at molecular, cellular and organismal level. I was the first to establish the role of LRRK2 kinase activity in neurodegeneration (Greggio et al., 2006), setting the stage for prolific research on LRRK2 inhibitors as Parkinson's therapeutics. Thanks to the support from Michael J Fox and Telethon grants, my team discovered the protective nature of PAK6 against LRRK2-linked PD, disclosed novel roles of LRRK2 at the presynaptic compartment and contributed to the understanding of LRRK2 in neuroinflammation. My group also investigates the pathobiology of SPG11/spatacsin, a protein mutated in a familiar form of Hereditary Spastic Paraplegia with parkinsonism and of the lysosomal enzyme GBA1, whose mutations confer risk for Parkinson.

I participated to several collaborative projects bringing unique expertise in PD biology and coordinated six international grants. I was invited to present my work 26 times as seminars (notably at Oxford University and UCL), lectures at symposia and conference talks. I organized two Biochemical Society Focused meetings on LRRK2 (2016 and 2018). I published 72 papers with 3896 / 5419 citations (Scopus / Google Scholar), h-index of 32 / 39 (Scopus / Google Scholar) and i10-index of 59 (Google Scholar).

B. Positions and Honors**Professional experiences**

2014-present	Associate Professor of Physiology, Department of Biology, University of Padua, Italy
2009-2014	Assistant Professor, Department of Biology, University of Padua, Italy
2005-2009	Postdoctoral research fellow, Laboratory of Neurogenetics, NIA, NIH, Bethesda, MD, USA
2002-2005	Graduate student in Molecular Physiology and Structural Biology, University of Padua, Italy

Honors and awards

2015	“Milla Baldo Ceolin” Award, selected woman researcher of the year at the University of Padova, Italy
2009	Nathan W. Shock Award, NIA, NIH, USA
2009	“Paolo Guidetti” Award, University of Modena, Italy
2009	Brain Gain (Rientro dei Cervelli) award, Italy
2008	Juan de la Cierva research fellowship, University of Valencia, Spain (declined for overlap with Brain Gain fellowship), Spain
2006	NIH-FARE - Fellowship Award for Research Excellence, NIH, USA
2005-2009	NIH visiting fellowship award, NIH, USA
2004	Aldo Gini fellowship award, University of Padova, Italy

Memberships

2006-present	Member of the Society for Neuroscience
2011-present	Member Italian Society of Physiology
2015-present	Member ISN (International Society for Neurochemistry)
2011-present	Editorial board member: PLoS ONE
2015-present	Editorial board member: Journal of Neurochemistry

C. Contributions to Science

Selected peer-reviewed publications

For a full list of 72 published papers since 2005, see: <https://www.ncbi.nlm.nih.gov/pubmed/?term=greggio+e>

1. **Greggio E**, Bergantino E, Carter D, Ahmad R, Costin GE, Hearing VJ, Clarimon J, Singleton A, Eerola J, Hellström O, Tienari PJ, Miller DW, Beilina A, Bubacco L, Cookson MR, (2005) “Tyrosinase exacerbates dopamine toxicity but is not genetically associated with Parkinson’s disease” *J Neurochem* **93**(1): 246-56.
2. **Greggio E**, Jain S, Kingsbury A, Bandopadhyay R, Lewis P, Kaganovich A, van der Brug MP, Beilina A, Blackinton J, Thomas KJ, Ahmad R, Miller DW, Kesavapany S, Singleton A, Lees A, Harvey RJ, Harvey K, Cookson MR. (2006) “Kinase activity is required for the toxic effects of mutant LRRK2/dardarin” *Neurobiol Dis.* **23**(2): 329-41.
3. **Greggio E**, Lewis PA, van der Brug MP, Ahmad R, Kaganovich A, Ding J, Beilina A, Baker AK, Cookson MR (2007) “Mutations in the LRRK2/dardarin associated with Parkinson disease are more toxic than the equivalent mutations in the homologous kinase LRRK1” *J Neurochem*, **102** (1): 93–102.
4. Deng J, Lewis PA, **Greggio E**, Sluch E, Beilina A, Cookson MR (2008) “Structure of the ROC domain from the Parkinson's disease associated Leucine-rich repeat kinase 2 reveals a novel dimeric GTPase” *Proc Natl Acad Sci U S A*, 105(5): 1499-150.
5. **Greggio E**, Zambrano I, Kaganovich A, Beilina A, Taymans JM, Daniëls V, Lewis P, Jain S, Ding J, Syed A, Thomas KJ, Baekelandt V and Cookson MR (2008) “The Parkinson’s disease associated leucine-rich repeat kinase 2 (LRRK2) is a dimer that undergoes intra-molecular autophosphorylation” *J Biol Chem*, 283(24): 16906-14.
6. **Greggio E** and Cookson MR, “Leucine Rich Repeat Kinase 2 mutations and Parkinson’s disease: three questions”, *ASN Neuro*, 2009, doi:10.1042/AN20090007
7. **Greggio E**, Taymans JM, Zhen EY, Ryder J, Vancraenenbroeck R, Beilina A, Sun P, Deng J, Jaffe H, Baekelandt V, Merchant K, Cookson MR, (2009) “The Parkinson's disease kinase LRRK2 autophosphorylates its GTPase domain at multiple sites” *Biochem Biophys Res Commun* 389(3):449-54.
8. **Greggio E**, Bisaglia M, Civiero L, Bubacco L (2011) “Leucine-rich repeat kinase-2 and alpha-synuclein: intersecting pathways in the pathogenesis of Parkinson’s disease?” *Mol Neurodegen* 6(1):6.
9. **Greggio E**, Civiero L, Bisaglia M, Bubacco L, (2012) “Parkinson's disease and immune system: is the culprit LRRKking in the periphery?” *J Neuroinflammation*, 9(1):94.
10. Civiero L, Vancraenenbroeck R, Belluzzi E, Beilina A, Lobbstaël E, Reyniers L, Gao F, Micetic I, De Maeyer M, Bubacco L, Baekelandt V, Cookson MR, **Greggio E***, Taymans JM* (2012) Biochemical characterization of highly purified Leucine-rich repeat kinases 1 and 2 demonstrates formation of homodimers *PLoS One*, 7(8):e43472
11. Beilina A, Rudenko I, Kaganovich A, Civiero L, *et al.*, **Greggio E**, Cookson MR (2014) Unbiased screen for interactors of Leucine-rich repeat kinase 2 supports a common pathway for sporadic and familial Parkinson’s disease, *Proc Natl Acad Sci U S A*. 10.1073/pnas.1318306111.
12. Civiero L, Cirnaru MD, Beilina A, Rodella U, Russo I, Belluzzi E, Lobbstaël E, Reyniers L, Hondhamuni G, Lewis PA, Van den Haute C, Baekelandt V, Bandopadhyay R, Bubacco L, Piccoli G, Cookson MR, Taymans JM, **Greggio**

- E. Leucine-rich repeat kinase 2 interacts with p21-activated kinase 6 to control neurite complexity in mammalian brain. *J Neurochem*. 2015 Sep 16. doi: 10.1111/jnc.13369
13. Belluzzi E, Gonnelli A, Cirnaru MD, Marte A, Plotegher N, Russo I, Civiero L, Cogo S, Carrion MP, Franchin C, Arrigoni G, Beltramini M, Bubacco L, Onofri F, Piccoli G, **Greggio E**. LRRK2 phosphorylates pre-synaptic N-ethylmaleimide sensitive fusion (NSF) protein enhancing its ATPase activity and SNARE complex disassembling rate. *Mol Neurodegener*. 2016 Jan 13;11(1):1.
 14. Russo I, Berti G, Plotegher N, Bernardo G, Filograna R, Bubacco L, **Greggio E**. Leucine-rich repeat kinase 2 positively regulates inflammation and down-regulates NF- κ B p50 signaling in cultured microglia cells. *J Neuroinflammation*. 2015 Dec 9;12(1):230.
 15. Civiero L, Cogo S, Kiekens A, Morganti C, Tessari I, Lobbestael E, Baekelandt V, Taymans JM, Chartier-Harlin MC, Franchin C, Arrigoni G, Lewis PA, Piccoli G, Bubacco L, Cookson MR, Pinton P, **Greggio E**. PAK6 Phosphorylates 14-3-3 γ to Regulate Steady State Phosphorylation of LRRK2. *Front Mol Neurosci*. 2017 Dec 14;10:417. doi: 10.3389/fnmol.2017.00417. eCollection 2017.
 16. Madero-Pérez J, Fdez E, Fernández B, Lara Ordóñez AJ, Blanca Ramírez M, Gómez-Suaga P, Waschbüsch D, Lobbestael E, Baekelandt V, Nairn AC, Ruiz-Martínez J, Aiastrui A, López de Munain A, Lis P, Comptaer T, Taymans JM, Chartier-Harlin MC, Beilina A, Gonnelli A, Cookson MR, **Greggio E**, Hilfiker S. Parkinson disease-associated mutations in LRRK2 cause centrosomal defects via Rab8a phosphorylation. *Mol Neurodegener*. 2018 Jan 23;13(1):3.
 17. Russo I, Di Benedetto G, Kaganovich A, Ding J, Mercatelli D, Morari M, Cookson MR, Bubacco L, **Greggio E**. Leucine-rich repeat kinase 2 controls protein kinase A activation state through phosphodiesterase 4. *J Neuroinflammation*. 2018;15(1):297.
 18. Russo I, Kaganovich A, Ding J, Landeck N, Mamais A, Varanita T, Biosa A, Tessari I, Bubacco L, **Greggio E**, Cookson MR. Transcriptome analysis of LRRK2 knock-out microglia cells reveals alterations of inflammatory- and oxidative stress-related pathways upon treatment with α -synuclein fibrils. *Neurobiol Dis*. 2019 Sep;129:67-78. doi: 10.1016/j.nbd.2019.05.012. Epub 2019 May 15.
 19. Marte A, Russo I, Rebosio C, Valente P, Belluzzi E, Pischedda F, Montani C, Lavarello C, Petretto A, Fedele E, Baldelli P, Benfenati F, Piccoli G, **Greggio E**, Onofri F. Leucine-rich repeat kinase 2 phosphorylation on synapsin I regulates glutamate release at pre-synaptic sites. *J Neurochem*. 2019 Aug;150(3):264-281. doi: 10.1111/jnc.14778.
 20. Cogo S, Manzoni C, Lewis PA, **Greggio E**. Leucine-rich repeat kinase 2 and lysosomal dyshomeostasis in Parkinson disease. *J Neurochem*. 2020 Feb;152(3):273-283. doi: 10.1111/jnc.14908. Epub 2019 Nov 24.
 21. Filippini A, Mutti V, Faustini G, Longhena F, Ramazzina I, Rizzi F, Kaganovich A, Roosen DA, Landeck N, Duffy M, Tessari I, Bono F, Fiorentini C, Greggio E, Bubacco L, Bellucci A, Missale M, Cookson MR, Gennarelli M, Russo I. Extracellular clusterin limits the uptake of α -synuclein fibrils by murine and human astrocytes. *Glia*. 2021 Mar;69(3):681-696. doi: 10.1002/glia.23920. Epub 2020 Oct 12.
 22. Iannotta L, Biosa A, Kluss JH, Tombesi G, Kaganovich A, Cogo S, Plotegher N, Civiero L, Lobbestael E, Baekelandt V, Cookson MR, Greggio E. Divergent Effects of G2019S and R1441C LRRK2 Mutations on LRRK2 and Rab10 Phosphorylations in Mouse Tissues. *Cells*. 2020 Oct 22;9(11):2344. doi: 10.3390/cells9112344.
 23. Pischedda F, Cirnaru MD, Ponzoni L, Sandre M, Biosa A, Carrion MP, Marin O, Morari M, Pan L, **Greggio E**, Bandopadhyay R, Sala M, Piccoli G. LRRK2 G2019S kinase activity triggers neurotoxic NSF aggregation. *Brain*. 2021 Apr 20;awab073. doi: 10.1093/brain/awab073.
 24. Cogo S, Tomkings J, Vavouraki N, Forcellato F, Franchin C, Tessari I, Arrigoni G, Cendrin L, Manzoni C, Civiero L, Lewis PA, **Greggio E** PKA-mediated phosphorylation of SPG11/spatacsin regulates binding with a subset of 14-3-3 proteins. *BiorXiv*. doi: <https://doi.org/10.1101/2020.09.09.289009>

D. Additional Information: Research Support and/or Scholastic Performance

Over the past 11 years, I obtained funding from national and international agencies (Italian Ministry of Research, University of Padova, Telethon Foundation, Cariplo Foundation, Cariparo Foundation, Michael J Fox Foundation) raising more than 3 million euros. In addition, I trained 8 post-doctoral fellows (with two of them currently holding an Assistant Professorship), 4 PhD students and >20 master students in Biosciences. I am Faculty Member of the PhD School in Biosciences (Dept of Biology, University of Padova, since 2015); Coordinator, Erasmus program for BSc in Biotechnology (Dept of Biology, University of Padova, since 2017); Coordinator of teaching activities in Physiology (since 2019); elected member of the Steering Scientific Committee for Biological Sciences (University of Padova, since 2020); Coordinator of Physiology, Genetics and Behavior Unit (Dept of Biology, University of Padova, since 2020).