BIOGRAPHICAL SKETCH

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NAME: **MARIA XILOURI**

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

POSITION TITLE: **Investigator C' (Assistant Professor level)**, Center of Clinical, Experimental Surgery & Translational Research, Biomedical Research Foundation of the Academy of Athens, Greece

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 Athens Greece	B.S.	09/1999	Biological Sciences
University of Athens, Greece	Ph.D.	04/2007	Biological Sciences
Biomedical Research Foundation of Athens, Greece	Postdoctoral	03/2015	Basic Neurosciences

A. Personal Statement

The main focus of my research is to illuminate processes underlying the pathogenesis of most neurodegenerative disorders, with an emphasis on diseases related to the accumulation of the neuronal protein alpha-synuclein, such as Parkinson's disease (PD) and multiple system atrophy (MSA). The cellular pathways investigated relate to protein misfolding and aggregation, which may lead to impairment of protein degradation systems (with an emphasis on the role of the autophagy-lysosome pathway, ALP) and eventually to neuronal demise. Beyond clearance, we are also targeting the release (occurring partly via small nanovesicles called exosomes), uptake and seeding of alpha-synuclein in neurons and oligodendrocytes, in an attempt to scrutinize whether similar or different protein strains cause PD- and MSA-like pathology, respectively. In the context of MSA in particular, we are investigating the interplay between alpha-synuclein with the oligodendroglial phosphoprotein TPPP/p25α, a protein that we have recently identified as a key culprit mediating the spread of alpha-synuclein pathology in MSA-like experimental models (Mavroeidi et al, 2019; 2022). Our approach encompasses a variety of cellular (cell lines, primary cultures, iPSC-derived neurons or oligodendrocytes and 3D organoids) and animal models of both PD and MSA coupled with state-of-the art technologies. Major findings are being validated in human PD and MSA post-mortem brain material, whereas biological fluids, such as CSF and blood plasma and serum serve as a pool to identify novel disease biomarkers. Collectively, our research aims to may provide further insights into the mechanisms underlying disease initiation and progression. Once such mechanisms are understood, they can be harnessed in order to provide meaningful disease-modifying therapies.

B. Positions and Honors

POSITIONS / EMPLOYMENT

2000-2002 **Research assistant in Histopathology Department**, I.D.C.A. Hygeia (Harvard Medical) Hospital, Athens, Greece

2004 – 2006 **Research Assistant/PhD Student,** Dept. of Biology, University of Athens, Greece

2006– 2014 **Post-doctoral Research Associate**, Division of Basic Neurosciences, Foundation for Biomedical Research of the Academy of Athens (BRFAA), Greece

2010-2011 **Visiting Scientist,** Brain Repair and Imaging in Neural Systems (BRAINS) Unit, BMC D11, Lund University, Sweden (Total Period: 3 months)

2015-2020 **Investigator D' (Lecturer level)**, Center of Clinical, Experimental Surgery & Translational Research, Biomedical Research Foundation of the Academy of Athens, Greece

2020-present **Investigator C' (Assistant Professor level)**, Center of Clinical, Experimental Surgery & Translational Research, Biomedical Research Foundation of the Academy of Athens, Greece

AWARDS / HONORS

1998 - 1999 EPEAEK Scholarship, Department of Biology, University of Athens, Athens, Greece

2002 – 2005 Postgraduate Studentship, ΠΕΝΕΔ 2002-2005, National and Kapodistrian University of Athens, Greece

2008 Travel grant Scholarship Wellcome Trust Advanced Courses, Molecular Neurology and Neuropathology**,** Hinxton, Cambridge UK

2009 FEBS Youth Travel Fund for participation in the EMBO Conference, Autophagy, Cell Physiology and Pathology, Monte Verita, Ascona, Switzerland

2009-2010 Postdoctoral Research Fellowship, States Scholarship Foundation for the project entitled: "*Investigation of wild-type and mutant alpha-synuclein degradation and effects in primary neuronal cultures-Correlation with Parkinson's disease*"

2011 Travel Award from the International Society of Neurochemistry, ISN ESN Meeting, Athens 2011

2012 Best Post-Doctoral Research Fellow Achievement Award from the Biomedical Research Institution of the Academy of Athens (10 year award)

2015 Travel Award from the International Parkinson and Movement Disorders Society**, "**Alpha-Synuclein: The Gateway to Parkinsonism" Course, Innsbruck, Austria

2015 Best Poster Award from the International Parkinson and Movement Disorders Society**, "**Alpha-Synuclein: The Gateway to Parkinsonism" Course, Innsbruck, Austria

2022 "*Fotis Kafatos*" Award of Excellence in Biology from the Panhellenic Union of Biosciences (to Mavroeidi P as the first author and Xilouri M as the corresponding author) for the original reseach paper entitled "*Autophagy mediates the clearance of oligodendroglial SNCA/alpha-synuclein and TPPP/p25A in multiple system atrophy models*", published at the high Impact factor journal «Autophagy», Athens, Greece.

2025 Oral presentation selection for the work entitled "Inducing Chaperone-Mediated Autophagy as a Means to Counteract alpha-Synuclein Pathology in Non-Human Primates", Synuclein 2025 Meeting, Cambridge, UK.

C. Contributions to Science

My research is mostly focused on alpha-synuclein neurobiology, a protein strongly implicated in PD pathogenesis. During my post-doctoral studies, I have identified the selective proteolytic pathway of Chaperone-Mediated Autophagy (CMA) as a major route for alpha-synuclein degradation in neuronal systems [Vogiatzi T, *J Biol Chem*; 283 (35): 23542-56, (2008)], publication that has received more than 450 citations and has been supplemented by an addendum to the prestigious Autophagy journal (Xilouri M*, Autophagy;* Oct;4(7):917-9, 2008). We have also found that the CMA pathway is a target for the toxic effects of aberrant alpha-synuclein on lysosomal pathways [Xilouri M, *Plos ONE*; 4(5):e5515, 2009)]. This publication, with more than 250 citations, was featured in the News' section of the Alzheimer's disease Forum website, under the name "*Do Chaperones Need Protection From α-Synuclein*?", two weeks after the article was published in the PLoS ONE Journal (June 2009). Moreover, the same article was commented on the Lab Times magazine under the name *"Defeating the Shakes", Synuclein degradation and Parkinson's disease in Athens* (May 2009). Most importantly, we have shown that boosting CMA function represents a fruitful therapeutic strategy to counteract alpha-synuclein pathology, both in neuronal systems and in the rodent dopaminergic system [Xilouri M, *Brain*, 136; (Pt7):2130-2146, (2013)], article that was again commented in the Autophagy journal

(Xilouri M, Autophagy 9(12): 2166-8, 2013]. More recently, we have uncovered the importance of the proper CMA function in the living brain, reporting that inhibition of CMA function specifically in the rat substantia nigra, the area mainly affected in PD, induces widespread dopaminergic degeneration (Xilouri M, Autophagy, Nov;12(11): 2230-2247, 2016). As an independent investigator, I got particularly interested in investigating the mechanisms underlying alpha-synuclein pathological accumulation within oligodendrocytes of MSA patients, the origin of which still remains perplexing. Towards this direction, we demonstrated for the first time that endogenous oligodendroglial alpha-synuclein, however minute in amount at baseline, is a major component of insoluble, highly aggregated, pathological assemblies and that the oligodendroglial phosphoprotein TPPP/p25α accelerates the recruitment of the endogenous alpha-synuclein and the generation of such aberrant species. Hence, we proposed that the endogenous alpha-synuclein and TPPP/p25α form a dangerous dynamic duo that predisposes oligodendrocytes to accumulate intracellular alpha-synuclein aggregates reminiscent of the oligodendroglial inclusions detected in MSA brains (Mavroeidi et al, Acta Neuropathol, 138(3): 415-441, 2019). More recently, we identified the autophagy-lysosome pathway as the main route responsible for the clearance of both alpha-synuclein and TPPP/p25α in oligodendrocytes, both under physiological and MSA-like conditions Fascinatingly, augmentation of CMA or macroautophagy accelerated the removal of the engendered pathological alpha-synuclein and TPPP/p25α aggregates, further suggesting that autophagy targeting may represent a successful approach in the context of MSA (Mavroeidi et al, Autophagy, Jan 9;1-30, 2022).

D. Teaching and training activities

(A) Undergraduate Courses taught

March-Aug 2011: Lecturer in Physiology, Charokopeio University of Athens, Greece
May 2023-present: Instructor at the American College of Greece, Athens, Greece

(B) Graduate Courses taught (1-2 lectures / year, Topic: Neurobiology)

2011-present: MSc Application of Biology in Medicine, Department of Biology, National and Kapodistrian University of Athens
2011-present: MSc Molecular and Applied Physiology, Medical School, National and Kapodistrian University of Athens
2017-present: Athens International MSc program Master's Programme in Neurosciences, Medical School, National and Kapodistrian University of Athens
2018-present: MSc Clinical Biochemistry – Molecular Diagnostics, Department of Biology, National and Kapodistrian University of Athens.
2019-present: International MSc Molecular Biomedicine, National and Kapodistrian University of Athens and "Alexander Fleming Institute"

E. Professional Memberships and Review Activities

2022 – present Associate Editor for Frontiers in Dementia
2021 – present Associate Editor for Frontiers in Neuroscience, section Neurodegeneration
2021 – present Editorial Board Member of the IJMS Section "*Molecular Neurobiology*"
2021 – present Guest Editor for the Special Issue "*Recent Advances in α-Synuclein Neurobiology in Health and Disease*". Biomolecules journal
2017 – present Reviewer editor in Frontiers in Molecular Neuroscience Journal and Frontiers in Neuroscience Journal.
2021 Grant Evaluator for Tyrolean Science Fund & the National Science Centre Poland
2020 Grant Evaluator for the Michael J Fox Foundation (Target Advancement Program) and the Cure Parkinson's Trust
2008 Grant Evaluator for the Parkinson's Disease Society (PDS) Innovation Grants UK and Parkinson's UK Grants (PDUK)
2008 – present Reviewer in peer reviewed journals (*including*): Acta Neuropathologica Communications, Aging, Aging Cell, Autophagy, Behavioral Brain Research, Brain, Brain and Behavior, eNeuro, Experimental Neurology, Frontiers in Molecular Neuroscience, Frontiers in Neuroscience, IJMS, iSCIENCE, Human Molecular Genetics, Journal of Neuroscience, Journal of Biological Chemistry, Journal of Neurochemistry, Molecular Neurobiology, Neurobiology of Aging, Neurobiology of Disease, Neurochemistry International,

Neuropharmacology, Neurotoxicity Research, NPJ Parkinson's disease, PLoS One, Scientific Reports, Translational Neurodegeneration
2020 – present Member of the MSA study group (MDS)
2015 – present International Parkinson and Movement Disorders Society (MDS)
2011 – present International Society of Neurochemistry (ISN)
2006 – present Hellenic Association of Biochemistry and Molecular Biology (FENS member)
2004 – present Hellenic Society for Neuroscience (Member of IBRO and FENS)
2003 – present Hellenic Society for Biological Sciences

Selected peer-review publications (emphasis on more recent work and related to the ASAP proposal) in peer-reviewed journals, selected from 57

Overall Metrics
(Google Scholar/Scopus): 20,341/10,588
***h*-index (Google Scholar/Scopus) : 33/29**

1. Karamanakos PN, Fouka M, Aretha D, Panteli ES, Panopoulos I, Kletsas D, Goussia A, Papoudou-Bai A, Zacharioudaki A, Trafalis DT, Orfanakos K, Marselos M, **Xilouri M**, Papalois A. (2026) Effects of disulfiram and copper in combination with temozolomide on survival, tumor size and autophagy markers in a F98 rat glioma model. ***International Journal of Molecular Sciences***, 27(4), 1966.
2. Fouka M, Tsakogias I, Giallinaki E, Stavropoulos A, Volbracht C, De Muynck L, Moechars D, Melki R, Tofaris GK, Stefanis L, **Xilouri M**. (2025) *In vivo* validation of novel non-invasive PHP.eB AAVs as a potential therapeutic approach for alpha-Synucleinopathies. ***Acta Neuropathol Commun.*** Sep 29;13(1):207. doi: 10.1186/s40478-025-02121-w.
3. Darricau M, Kulifaj V, Arotcarena ML. Li Q, Katsinelos T, McEwan WA, **Xilouri M**, Dehay B, Bezard E. & Planche V. (2025) Additive effect of distant Lewy bodies and tau seeds injections on nigral degeneration in macaques. ***NPJ Parkinson's disease*** **11**, 75 https://doi.org/10.1038/s41531-025-00938-9.
4. Benedikt F, Geraets JA, Strohäker T,…**Xilouri M**, Zweckstetter M, Schröder GF (2022) Quaternary structure of patient-homogenate amplified α-synuclein fibrils modulates seeding of endogenous α-synuclein, ***Commun Biol*** 5, 1040. https://doi.org/10.1038/s42003-022-03948-y
5. Antoniou N, Prodromidou K, Kouroupi G,… **Xilouri M**. …Matsas R. (2022) High content screening and proteomic analysis identify a kinase inhibitor that rescues pathological phenotypes in a patient-derived model of Parkinson's disease NPJ Parkinson's disease. 8 (1):15. doi: 10.1038/s41531-022-00278-y.
6. Polissidis A, Koronaiou E, Nikolopoulou G, ...**Xilouri M**, Vekrellis K, Stefanis L. (2022) A double-hit in vivo model of GBA viral microRNA-mediated downregulation and human alpha-synuclein overexpression demonstrates nigrostriatal degeneration. Neurobiology of Disease, 163:105612. doi: 10.1016/j.nbd.2022.105612.
7. Mavroeidi P, Arvanitaki F, Vetsi M, Becker S, Vlachakis D, Jensen PH, Stefanis L, **Xilouri M**. (2022) Autophagy mediates the clearance of oligodendroglial SNCA/alpha-synuclein and TPPP/p25A in multiple system atrophy models. Autophagy. Jan 9;1-30. doi: 10.1080/15548627.2021.2016256.
8. Mavroeidi P, **Xilouri M**. (2021) Neurons and glia interplay in a-synucleinopathies. ***International Journal of Molecular Sciences,*** 22(9), 4994.
9. Polissidis A, Koronaiou M,....**Xilouri M**, Stefanis L. (2021) Psychosis-Like Behavior and Hyperdopaminergic Dysregulation in Human a-Synuclein BAC Transgenic Rats. ***Movement Disorders.*** 36(3);716-728.
10. Fouka M, Mavroeidi P, Tsaka G, **Xilouri M**. (2020) In Search of Effective Treatments Targeting a-Synuclein Toxicity in Synucleinopathies: Pros and Cons. ***Frontiers in Cell and Developmental Biology,*** 8, 559791.
11. Divolis D, Stavropoulos A, Manioudaki M, Apostolidou A, Doulou A, Gavriil A, Dafnis I, Chroni A, Mummery C, **Xilouri M,** Sideras P, (2019) Activation of both transforming growth factor-b and bone morphogenetic protein signaling pathways upon traumatic brain injury restrains pro-inflammatory and boosts tissue reparatory responses of reactive astrocytes and microglia. ***Brain Communications*** Oct 21;1(1):fcz028, doi: 10.1093/braincomms/fcz028. eCollection 2019.
12. Mavroeidi P, Arvanitaki F, Karakitsou AK, Vetsi M, Kloukina I, Zweckstetter M, Giller K, Becker S, Sorrentino ZA, Giasson BI, Jensen PH, Stefanis L, **Xilouri M**. (2019) Endogenous oligodendroglial alpha-synuclein and TPPP/p25α orchestrate alpha-synuclein pathology in experimental multiple system atrophy models. ***Acta Neuropathol.*** Sep;138(3):415-441. doi: 10.1007/s00401-019-02014-y.

13. Papagiannakis N, **Xilouri M**, Koros C, Simitsi AM, Stamelou M, Maniati M, Stefanis L. (2019) Autophagy dysfunction in peripheral blood mononuclear cells of Parkinson's disease patients. ***Neurosci Lett.*** Apr 4;704:112-115.
14. Elkouris M, Kouroupi G, Vourvoukelis A, Papagiannakis N, Kaltezioti V, Matsas R, Stefanis L, **Xilouri M**, Politis PK. (2019) Long Non-coding RNAs Associated With Neurodegeneration-Linked Genes Are Reduced in Parkinson's Disease Patients. ***Front Cell Neurosci.*** Feb 22;13:58.
15. Brekk OR, Makridakis M, Mavroeidi P, Vlahou A, **Xilouri M**, Stefanis L. (2019) Impairment of chaperone-mediated autophagy affects neuronal homeostasis through altered expression of DJ-1 and CRMP-2 proteins. ***Mol Cell Neurosci.*** Mar;95:1-12.
16. Xilouri M, Brekk OR, Polissidis A, .. Stefanis L (2016) Impairment of chaperone-mediated autophagy induces dopaminergic neurodegeneration in rats**.** ***Autophagy;*** Nov; 12(11): 2230-2247.
17. Xilouri M, Stefanis L (2016) Chaperone mediated autophagy in aging: Starve to prosper. ***Ageing Res Rev;*** Dec; 32:13-21.
18. Xilouri M, Brekk OR, Stefanis L. Autophagy and Alpha-Synuclein: Relevance to Parkinson's Disease and Related Synucleopathies (2016) ***Movement disorders : official journal of the Movement Disorder Society***; Feb;31(2): 178-92.
19. Papagiannakis N, **Xilouri M,** Koros C, Stamelou M, Antonelou R, Maniati M, Papadimitriou D, Moraitou M, Michelakakis H, Stefanis L. (2015) Lysosomal alterations in peripheral blood mononuclear cells of Parkinson's disease patients. ***Movement disorders: official journal of the Movement Disorder Society***; 30:1830-4.
20. Xilouri M, Stefanis L. (2015) Chaperone mediated autophagy to the rescue: A new-fangled target for the treatment of neurodegenerative diseases. ***Molecular and cellular neurosciences***; 66:29-36.
21. Xilouri M, Brekk OR, Kirik D, Stefanis L (2013) LAMP2A as a therapeutic target in Parkinson disease. ***Autophagy;*** 9(12): 2166-8.
22. Xilouri M, Brekk OR, Landeck N, Pitychoutis PM, Papasilekas T, Papadopoulou-Daifoti Z, Kirik D, Stefanis L (2013) Boosting chaperone-mediated autophagy *in vivo* mitigates a-synuclein-induced neurodegeneration. ***Brain***; 136; (Pt7):2130-2146.

D. Existing Funding

- Funding Source: *Defeat MSA Canada / Vaincre l'atrophie multisystématisée (AMS) Canada*; Role: lead PI; **Title: *Untangling the role of extracellular vesicles in MSA pathogenesis utilizing human iPSC-derived oligodendrocytes and 3D brain organoids***; 37,000 $, 03/2026-03/2027. Abstract: *Aim of the current proposal is to uncover the role of extracellular vesicles in human MSA using iPSC-derived oligodendrocytes and 3D organoids*. PE: 10% per year, non-salaried.
- Funding Source: Multiple System Atrophy Trust (UK) (Grant ID 2024/MSAT_MX01); Role: lead PI; **Title: *Targeting the Role of Autophagy-lysosome pathway in Human MSA***; 50,000 £/year, 09/2024-08/2027. Abstract: *Aim of the current proposal is to uncover the role of the autophagy-lysosome pathway in in human MSA using peripheral biological material (serum, plasma, exosomes, PBMCs) and 3D organoids*. PE: 10% per year, non-salaried.
- Funding Source: Target Advancement Program of the Michael J Fox Foundation (USA) (Grant ID MJFF-024029); Role: lead PI; **Title: *Extension to CMA as a Means to Counteract alpha-Synuclein Pathology in Non-Human Primates***; total amount: 180,000 $, 12/2023-12/2025. Abstract: The aim of this project is to investigate whether induction of the CMA pathway may exert beneficial effects in the highest order mammalian synucleinopathy model, the non-human primate. PE: 10% per year, non-salaried.
- Funding Source: Hellenic Foundation for Research and Innovation (HFRI) (Grant ID 3661); Role: lead PI*; "**Dissecting the Mechanisms Underlying Multiple System Atrophy Pathogenesis**"; 200,000 €, 04/2022-09/2025.* Abstract: *Aim of the current proposal is to utilize well-characterized induced pluripotent stem cells (iPSCs) from sporadic MSA patients (and age- and sex-matched controls) and differentiate them into mature oligodendrocytes in an attempt to identify putative factors that may trigger the accumulation of alpha-synuclein selectively in MSA oligodendroglia.* PE: 20% per year, non-salaried.