Biographical Sketch
Emmanouilidou Evangelia

PRESENT POSITION: Assistant Professor in Biochemistry, Department of Chemistry, National and Kapodistrian University of Athens

EDUCATION

Dept. of Chemistry, University of Athens, Greece	BSc	1998	Chemistry
Dept. of Biochemistry, University of Bristol, UK	MSc	1999	Biochemistry
Dept. of Chemistry, University of Athens, Greece	PhD	2003	Chemistry

POSITIONS AND EMPLOYMENT

01-09/2004	Post Doctoral Research Fellow, Division of Analytical Chemistry, Dept. of Chemistry, University of Athens, Greece.
11/2004 – 3/2018	Post Doctoral Research Fellow, Division of Basic Neurosciences, Foundation for Biomedical Research of the Academy of Athens (BRFAA), Greece.

TEACHING

Undergraduate: Biochemistry I and II. Laboratory practicals for Biochemistry II.

AWARDS

- 1st Novartis Award for Poster Presentation.
  17th Joint Meeting of the British Endocrine Societies, Edinburgh, UK (1998)
- Youth Travel Fund (YTF) Grant for participating in the EMBO-FEBS workshop on "Amyloid formation", Firenze, Italy (2006)
- Travel Grant for participating in the 1st International Meeting on "A-Synuclein in Health and Disease", Lausanne, Switzerland (2008)
- "George Papanikolaou" Award from the University of Athens for the research project: "Cell-derived alpha-synuclein oligomeric species are targeted to, and impair, the 26S proteasome" (2009)
- Travel Award for participating in the 23rd ISN/ESN Biennial Meeting, Athens, Greece (2011)
- Travel Award for an oral presentation in the meeting "Grand Challenges in Parkinson's Disease: Focus in alpha-synuclein", Grand Rapids, Michigan, USA (2015)
- Travel Award for presentation in the meeting "7th ISN Special Neurochemistry Conference on Synaptic function and dysfunction in brain diseases», Coimbra, Potugal (2016)

MEMBERSHIPS

- Hellenic Association of Chemists
- Hellenic Association of Biochemistry and Molecular Biology (Member of FENS)
- Hellenic Society for Neuroscience (Member of IBRO and FENS)
- International Society of Neurochemistry (ISN)

PEER-REVIEWED PUBLICATIONS

1. Pouli A.E., Emmanouilidou E., Zhao C., Wasmeier C., Hutton J.C., and Rutter G.A. (1998) Secretory-granule dynamics visualized *in vivo* with a phogrin-green fluorescent protein chimaera. Biochemical Journal 333: 193-199.

2. Emmanouilidou E., Teschemacher A.G., Pouli A.E., Nicholls L.I., Seward E.P., and Rutter G.A. (1999) Imaging Ca2+ concentration changes at the secretory vesicle surface with a recombinant targeted cameleon. Current Biology 9(16): 915-918.

3. Emmanouilidou E., Ioannou P.C., Christopoulos T.K., and Polizois K. (2003) Determination of prostate specific antigen mRNA in peripheral blood by reverse transcriptase polymerase chain reaction and a simple chemiluminometric hybridization assay in a high-throughput format. Analytical Biochemistry 313: 97-105.

4. Emmanouilidou E., Ioannou P.C., and Christopoulos T.K. (2004) High-throughput chemiluminometric determination of prostate-specific membrane antigen mRNA in peripheral blood by RT-PCR using a synthetic RNA internal standard. Analytical and Bioanalytical Chemistry 380: 90-7.

5. Emmanouilidou E., Tannous B., Ioannou P.C., and Christopoulos T.K. (2005) Duplex RT-PCR and chemiluminometric hybridization assay for combined screening of the mRNAs of prostate-specific antigen and prostate-specific membrane antigen in peripheral blood. Analytica Chimica Acta 531: 193-198.

6. Litos I.K., Emmanouilidou E., Glynou K.M., Laios E., Ioannou P.C., Christopoulos T.K., Kampa M., Castanas E., Gravanis A. (2007) Rapid genotyping of CYP2D6, CYP2C19 and TPMT polymorphisms by primer extension reaction in a dipstick format. Analytical and Bioanalytical Chemistry 389: 1849-1857.

7. Vekrellis K., Xilouri M., Emmanouilidou E., Stefanis L. (2009) Inducible over-expression of wild type alpha-synuclein in human neuronal cells leads to caspase-dependent non-apoptotic death. Journal of Neurochemistry 109: 1348.

8. Emmanouilidou E., Stefanis L., and Vekrellis K. (2010) Cell-produced alpha-synuclein oligomers are targeted to, and impair, the 26S proteasome. Neurobiol Aging 31: 953.

9. Emmanouilidou E., Melachroinou K., Roumeliotis T., Garbis S.D., Ntzouni M., Margaritis L.H., Stefanis L., Vekrellis K. (2010) Cell-produced alpha-synuclein is secreted in a calcium-dependent fashion by exosomes and impacts neuronal survival. J. Neurosci. 30: 6838.

10. Emmanouilidou E., Elenis D., Papasilekas T., Stranjalis G., Gerozissis K., Ioannou P.C., and Vekrellis K. (2011) Assessment of α-synuclein secretion in mouse and human brain parenchyma. PLoS ONE, 6(7): e22225.

11. Vekrellis K, Xilouri M, Emmanouilidou E, Rideout HJ, Stefanis L (2011) Pathological roles of α-synuclein in neurological disorders. Lancet Neurol. 10(11):1015-25.

12. Melachroinou K, Xilouri M, Emmanouilidou E, Masgrau R, Papazafiri P, Stefanis L, and Vekrellis K. (2013) Deregulation of calcium homeostasis mediates secreted α-synuclein-induced neurotoxicity. Neurobiol Aging. 34: 2853.

13. Kapaki E, Paraskevas GP, Emmanouilidou E, and Vekrellis K. (2013) The diagnostic value of CSF α-synuclein in the differential diagnosis of dementia with Lewy bodies vs. normal subjects and patients with Alzheimer's disease. PLoS One, 8(11):e81654.

14. Ouzounoglou E, Kalamatianos D, Emmanouilidou E, Xilouri M, Stefanis L, Vekrellis K, Manolakos ES. (2014) In silico modeling of the effects of alpha-synuclein oligomerization on dopaminergic neuronal homeostasis. BMC Syst Biol. 8:54.

15. Chutna O, Gonçalves S, Villar-Piqué A, Guerreiro P, Marijanovic Z, Mendes T, Ramalho J, Emmanouilidou E, Ventura S, Klucken J, Barral DC, Giorgini F, Vekrellis K, Outeiro TF. (2014) The small GTPase Rab11 co-localizes with α-synuclein in intracellular inclusions and modulates its aggregation, secretion and toxicity. Hum Mol Genet. Aug 4. pii: ddu391.

16. Antonelou RCh, Emmanouilidou E, Gasparinatos G, Velona T, Voumvourakis KI, Stefanis L. (2015) Decreased levels of alpha-synuclein in cerebrospinal fluid of patients with clinically isolated syndrome and multiple sclerosis. J. Neurochem. 134:748-55

17. Emmanouilidou E, Minakaki G, Keramioti MV, Xylaki M, Balafas E, Chrysanthou-Piterou M, Kloukina I, Vekrellis K. (2016) GABA transmission via ATP-dependent K+ channels regulates α-synuclein secretion in mouse striatum. Brain 139:871-90.

18. Fernandes HJR, Hartfield EM, Christian HC, Emmanoulidou E, Zheng Y, Booth H, Bogetofte H, Charmaine Lang, Ryan BJ, S. Sardi P, Badger J, Vowles J, Evetts S, Tofaris GK, Vekrellis K, Talbot K, Hu MT, James W, Cowley SA, Wade-Martins R. (2016) ER stress and autophagic perturbations lead to elevated extracellular α-synuclein in GBA-N370S Parkinson's iPSC-derived dopamine neurons. Stem Cell Reports 6:342-56.

19. Emmanouilidou E, Vekrellis K. (2016) Exocytosis and spreading of normal and aberrant α-synuclein. Brain Pathol., doi: 10.1111/bpa.12373 (review).

20. Constantinides VC, Paraskevas GP, Emmanouilidou E, Petropoulou O, Bougea A, Vekrellis K, Evdokimidis I, Stamboulis E, Kapaki E. (2017) CSF biomarkers β-amyloid, tau proteins and a-synuclein in the differential diagnosis of Parkinson-plus syndromes. J. Neurol. Sci. 382:91-95.

21. Minakaki G, Menges S, Agnes Kittel A, Emmanouilidou E, Schaeffner I, Barkovits K, Bergmann A, Rockenstein E, Adame A, Marxreiter F, Mollenhauer B, Galasko D, Buzás EI, Schlötzer-Schrehardt U, Marcus K, Xiang W, Lie DC, Vekrellis K, Masliah E, Winkler J, Klucken J. (2018) Autophagy inhibition promotes alpha-synuclein release and transfer via extracellular vesicles with a hybrid autophago/exosome-like phenotype. Autophagy 14(1):98-119.

22. Papadopoulos VE, Nikolopoulou G, Antoniadou I, Karachaliou A, Arianoglou G, Emmanouilidou E, Sardi SP, Stefanis L, Vekrellis K (2018) Modulation of β-Glucocerebrosidase Increases α-Synuclein secretion and Exosome release in Mouse Models of Parkinson's Disease. Hum. Mol. Gen. (in press).

CHAPTERS

Vekrellis K, Minakaki G, Emmanouilidou E (2011) Chapter 8: Effects of alpha-synuclein on cellular homeostasis. Etiology and pathophysiology of Parkinson's disease. Rana AQ, ed, (Intech Open Access Publisher) pp 167-192

FUNDED GRANTS

- Rapid Response Innovation Award (2008), Michael J. Fox Foundation, USA
  Role: Principal Investigator, Budget: 75,000 $
  Title: "*In vivo* assessment of alpha-synuclein secretion"
- MJFF Research Grant (2010)
  Role: Principal Investigator
  Michael J. Fox Foundation, USA (150,000 $)
  Title: "Investigation of the mechanisms involved in alpha-synuclein secretion *in vivo*"
- MJFF Research Grant (2012), Supplement of the previous grant
  Role: Principal Investigator
  Michael J. Fox Foundation, USA (150,000 $)
  Title: "Investigation of the mechanisms involved in alpha-synuclein secretion *in vivo*"

RESEARCH INTERESTS

The major focus of my research work involves investigation of the molecular mechanisms of protein secretion and degradation that are of particular importance in neurodegenerative disorders.

More specifically, I am working with α-synuclein, a small, pre-synaptic neuronal protein, which plays a central role in the pathobiology of Parkinson's Disease (PD) and other related neurodegenerative conditions collectively called synucleinopathies. α-Synuclein is genetically and biochemically linked with PD pathogenesis. Importantly, deposition of aggregated forms of α-synuclein in cytoplasmic inclusion bodies (Lewy Bodies) is tightly associated with the neurodegeneration of dopaminergic neurons observed in PD. Under this prism, part of my work is trying to identify which of the oligomeric α-synuclein species impact cell viability and the mechanism through which they confer their detrimental effects using a variety of cellular and animal models. Having in mind that such aberrant conformations primarily burden the intracellular degradation systems, I have extensively studied the interaction of oligomeric and monomeric α-synuclein species with the proteasome, a major degradation machinery of the cell. In fact, my recent studies focus on the investigation of the interaction between free lipids and α-synuclein oligomers, with emphasis on how such an interaction can affect their proteasome-dependent degradation.

Since my early years in research, I became fascinated by the mechanisms involved in the regulatory and non-conventional protein secretion and by the technical advancements developed to follow these events in vitro and

in vivo. Although α-synuclein has been initially thought to be a protein localized exclusively in the cytoplasm of cells, it is now common knowledge that it can be readily released in human and mouse brain parenchyma even though it does not carry a signal peptide. The extracellular form of α-synuclein has been implicated in a cell-to-cell transfer mechanism of disease propagation that ultimately may lead to PD initiation and/or progression. Yet, the normal function of the secreted α-synuclein has not been yet elucidated. However, I, and other researchers in the field, support the notion that the secreted form of the protein is strongly related to its physiological action. Given the importance of extracellular α-synuclein, my work is mostly focused on the elucidation of key players in the secretory pathway of α-synuclein in cellular and animal models. A significant contribution in this field that came through my early work was the discovery that part of cytoplasmic α-synuclein is secreted in association with exosomes, small vesicles of endocytic origin that have been implicated in cell-to-cell communication. Whether exosome-associated α-synuclein also possesses specific biological activity is still under investigation.

Other basic research questions include which receptors are motivated, what kind of molecules could trigger α-synuclein release, and how neurons crosstalk in a certain brain area to accomplish this release. Unraveling the regulatory mechanisms that control α-synuclein release in vivo and see how such mechanisms are modified or become compromised under pathological conditions are two important challenges. Towards this direction, I have established an in vivo brain microdialysis approach coupled with an ultra-sensitive in-house ELISA to monitor and pharmacologically manipulate α-synuclein secretion in the parenchyma of mouse striatum. My future plans include the development of a combinatory approach in the mouse that will couple optogenetics with microdialysis (a novel technique that is called optodialysis) in order to investigate whether the activation of one brain area can trigger the secretion of α-synuclein in a different, inter-connected brain area.

It is my opinion that knowing the physiological function of extracellular α-synuclein and its secretory pathway would answer critical biological questions about the etiology of PD and would possibly uncover novel, yet unsuspected, therapeutic interventions that would aim to restore the normal function of the protein.

Another aspect of my research work covers the development of sensitive and specific assays to evaluate the potential use of certain biomolecules as biomarkers for the diagnosis or staging of human disease. The bioassays provide a useful tool to aid the analysis of a great number of clinical biological samples which is critical in order to assess the utility of the target molecule. Such a translational effort is of fundamental importance in order to combine the experimental results with the clinical unresolved problems.