BIOGRAPHICAL SKETCH

Kleopa KLEOPA

Name: [*Last, First, Middle Initial(s), Degree(s)*] **Kleopas A. KLEOPA, MD, Ph.D** Personal Webpage: http://www.cing.ac.cy/easyconsole.cfm/id/636	**POSITION TITLE:** Professor, Senior Consultant Neurologist Head of Neurology Clinic E and Neuroscience Laboratory

EDUCATION /TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Wuerzburg, Germany	MD	1987-93	Medicine
University of Wuerzburg, Germany	Ph.D	1994	Neurochemistry
Neurology Clinic, University of Wuerzburg	Postdoctoral	1994-95	Internship in Neurology
Drexel University, Philadelphia		1995-96	Internship in Int. Medicine
Drexel University, Philadelphia		1996-99	Neurology Residency
University of Pennsylvania Medical Center		1999-01	Neuromuscular/EMG Fellowship

A. ACADEMIC AND PROFESSIONAL POSITIONS

POSITIONS HELD

1/2015-: Coordinator, Neuroscience Postgraduate Program, Cyprus School of Molecular Medicine
2/12-: Professor, Cyprus School of Molecular Medicine
11/07-: Head of Neurology Clinic E and Neuroscience Laboratory, Cyprus Institute of Neurology and Genetics
9/2002-: Senior Consultant Neurologist, Cyprus Institute of Neurology and Genetics
7/01-8/02: Clinical Instructor of Neurology, University of Pennsylvania Medical Center
7/00-8/02: Postdoctoral Research Fellowship, National Multiple Sclerosis Society: "Connexin32 mutations and central demyelination", University of Pennsylvania Medical Center
9/00-6/01: Patient Oriented Research Training Program, University of Pennsylvania, Clinical Research Center
1-6/1999: Chief Resident in Neurology, Drexel (MCP-Hahnemann) University, Philadelphia

ADVISORY-ADMINISTRATIVE DUTIES

2000- Ad Hoc Reviewer for scientific journals (Muscle and Nerve, Journal of Neurology, Brain, BioMed Central Neurology, Biotechnology Journal, Journal of Inherited Metabolic Disease, Neuron Glia Biology, Acta Myologica, Journal of the Peripheral Nervous System, Journal of Neuroscience, PLoS Genetics, Acta Neuropathologica, PLoS ONE, Journal Neuropathology Experimental Neurology, Neurobiology of Disease, Neuromolecular Medicine)

2004- Reviewer for Research Funding Organizations (National Multiple Sclerosis Society, USA, The Wellcome Trust, UK; Association Française contre les Myopathies-AFM; National Research Agency, France; European Leukodystrophy Association, ELA), Life Sciences Panel/European Commission Horizon2020: 2014-2015 Marie-Skłodowska-Curie Actions and Personalized Medicine 2016.

2014-	Member of the External Evaluation Committee for the promotion of Academic staff at the University of Crete, University of Athens, University of Thessaly, University of Patras, and University of Thessaloniki, Greece
	External Referee for the Academic promotion at the Department of Neurology, University of Pennsylvania Medical Center, Philadelphia, USA
	External referee for Academic promotion, San Rafaelle Scientific Institute, Milan, Italy
2015-	Member of PhD Exam committees at the University of Cyprus (1), at the University of Crete (1), and at the Cyprus School of Molecular Medicine (5)
	Member of MSc Exam committees at the Cyprus School of Molecular Medicine (8)
2015-	Member of the Academic Committee and the School Council, Cyprus School of Molecular Medicine
2006-09	President of the Cyprus Bioethics Review Committee for Biomedical Research
2015-19	Member, Cyprus National Bioethics Committee
2006	Scientific Advisor, Cyprus Myasthenia Gravis Association
2002-15	Editorial Consultant, American College of Physicians, Physician's Information and Education Resource (PIER): Carpal Tunnel Syndrome module

B. RESEARCH INTERESTS

The main contribution of Prof. Kleopa's research has been the elucidation of the mechanisms causing various neurological disorders using novel experimental models, with main focus on inherited neuropathy and leukodystrophy. Furthermore, he has pioneered world-wide in the last 7 years the cell-targeted gene therapy approach to treat demyelinating neurological diseases. A central objective of his research has been the investigation of the cellular and molecular mechanisms that lead to the manifestation of chronic or transient encephalopathy in patients with inherited mutations in the gap junction protein connexin32 (Cx32), causing X-linked Charcot-Marie-Tooth Disease (CMT1X). Through a series of publications, he has clarified the repertoire of Schwann cell and oligodendroglial gap junction protein expression, their anatomic and functional relationship and possible interactions in health and disease. He showed that Cx32 mutations cause loss of function in CNS and PNS.

Based on these results he has developed gene therapy approaches to replace connexin genes specifically in myelinating glial cells. He has pioneered gene therapy methods using both lentiviral and AAV vectors for cell-targeted expression based on cell-specific promoters. Importantly, in a ground-breaking work, his team has recently demonstrated that the clinically translatable approach of lumbar intrathecal viral vector delivery can lead to widespread expression of the delivered genes throughout the peripheral nervous system.

A further line of research in Dr. Kleopa's lab has been the study of glial connexin pathology in acquired demyelination, examining multiple sclerosis postmortem human brain samples as well as experimental encephalomyelitis (EAE) mouse models. He has shown for the first time world-wide widespread glial connexin pathology with loss of gap junctions in oligodendrocytes in white and gray matter lesions as well as in normal appearing brain with associated astrogliosis and disconnection of astrocytes from oligodendrocytes. These changes correlate with inflammation and disease progression.

He has also contributed to several other important research findings including the cellular and molecular mechanisms in autoimmune encephalopathies and neuromyotonia, as well as in chemotherapy-induced neurotoxicity. He has also participated in research into therapeutic, epidemiological, immunological and genetic aspects of myasthenia gravis, motor neuron disease, and other neuromuscular and neurological disorders.

C. SELECTED PEER-REVIEWED PUBLICATIONS *(max 10) (in chronological order).*

(*from a total of 80 full papers, 16 book chapters, 85 oral or poster presentations; cumulative impact factor:>300; more than 3,800 citations in total to date, H-index=29*)
http://scholar.google.com/citations?user=uqquFR4AAAAJ&hl=en
http://www.ncbi.nlm.nih.gov/pubmed/?term=kleopa

1. Georgiou E, Sidiropoulou K, Richter J, Papaneophytou C, Sargiannidou I, Kagiava A, von Jonquieres G, Christodoulou C, Klugmann M, **Kleopa KA**. Gene therapy targeting oligodendrocytes provides therapeutic benefit in a leukodystrophy model. *Brain*. 2017 Jan 18. pii: aww351. doi: 10.1093/brain/aww351
2. Kagiava A, Sargiannidou I, Theophilidis G, Karaiskos C, Richter J, Bashiardes S, Schiza N, Nearchou M, Christodoulou C, Scherer SS**, Kleopa KA** (2016). Intrathecal gene therapy rescues a model of demyelinating peripheral neuropathy. *Proc Natl Acad Sci U S A,* 113 (17):e2421-9
3. Kyriakoudi S, Sargiannidou I, Kagiava A, Olympiou M, **Kleopa** KA (2017) Golgi-retained Cx32 mutants interfere with gene addition therapy for CMT1X. *Hum Mol Genet*. 2017 26(9):1622-163
4. Olympiou M, Sargiannidou I, Markoullis K, Karaiskos C, Kagiava A, Kyriakoudi S, Abrams CK, **Kleopa KA** (2016). Systemic inflammation disrupts oligodendrocyte gap junctions and induces ER stress in a model of CNS manifestations of X-linked Charcot-Marie-Tooth disease. *Acta Neuropathol Commun*. 2016 Sep 1;4(1):95. doi: 10.1186/s40478-016-0369-5.
5. Sargiannidou I, Kagiava A, Bashiardes S, Richter J, Christodoulou C, Scherer SS, **Kleopa KA** (2015) Intraneural GJB1 gene delivery improves nerve pathology in a model of CMT1X. *Ann Neurol*. 78:303-316.
6. Kagiava A, Theophilidis G, Sargiannidou I, Kyriacou K, **Kleopa KA** (2015). Oxaliplatin-induced neurotoxicity is mediated through gap junction channels and hemichannels and can be prevented by octanol. *Neuropharmacology*, 97:289-305.
7. Schiza N., Sargiannidou I., Kagiava A., Karaiskos C., Nearchou M., **Kleopa KA** (2015) Transgenic replacement of Cx32 in gap junction defiecient oligodendrocytes rescues the phenotype of a hypomyelinating leukodystrophy model, *Hum Mol Genet*, 24: 2049-64.
8. Markoullis K, Sargiannidou I, Gardner C, Hadjisavvas A, Reynolds R, **Kleopa KA** (2012) Disruption of oligodendrocyte gap junctions in experimental autoimmune encephalomyelitis. *Glia*, 60:1053-66.
9. Markoullis K, * Sargiannidou I, * Schiza N, Hadjisavvas A, Roncaroli F, Reynolds R, **Kleopa KA** (2012) Gap junction pathology in multiple sclerosis lesions and in normal appearing white matter. *Acta Neuropathol*, 123:873-86.
10. Sargiannidou I, Vavlitou N, Aristodemou S, Hadjisavvas A, Kyriacou K, Scherer SS, **Kleopa KA** (2009). Connexin32 mutations cause loss of function in Schwann cells and oligodendrocytes leading to PNS and CNS myelination defects. *J Neurosci*, 29:4748-4761.