

Biosketch

Judith Miklossy MD, PhD, DSc
FRCP (H) in Neurology, Psychiatry & Psychotherapy
FRCP (CH) in Neuropathology

Prevention Alzheimer International *Foundation*
International Alzheimer Research Center
Martigny-Croix CP 16
1921 Switzerland

Tél: [REDACTED]

URLs: www.miklossy.ch
www.preventionalzheimer.org

Centre Médical Vigimed
Consultation de Neurologie
Rue du Léman 12B
1920 Martigny

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Education/ Training

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| 1971 | MD, University Medical School of Debrecen, Hungary with EU & AELE conformity certificate) |
| 1976 | Board certified in Neurology, University of Debrecen, National Board of Specialization, Hungary with EU & AELE conformity certificate |
| 1982 | Board certified in Psychiatry and Psychotherapy, National Institute Neurology & Psychiatry, Budapest, National Board of Specialization, Hungary with EU & AELE conformity certificate. |
| 1995 | Maitre d'Enseignement et de Recherche (MER), CHUV University of Lausanne |
| 1995 | PD (Dr. habil, DSc), University Institute of Neuropathology, CHUV & University of Lausanne, Switzerland |
| 2001-2004 | Invited scientist Molecular biology, Temple University, Philadelphia, P.A., U.S.A. |
| 2005 | PhD, Neurobiology, University of Debrecen, Hungary |
| 2004-2007 | Invited scientist Neurological research, University of British Columbia, Vancouver, Canada, Head of neuropathology in the Kinsmen Laboratory of Neurological Research, The University of British Columbia |
| 2011 | Board certified in Neuropathology (FMH), Federation of Swiss Physicians, Switzerland |

Positions and employments

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| 1967-1971 | Resident as student, Institute of Physiology, University of Debrecen, Hungary |
| 1971-1976 | Resident, Chief-Resident, staff member, neurologist, Institute of Neurology, Psychiatry and Neurosurgery, University of Debrecen (DOTE), Hungary |
| 1977-1982 | Staff member - Instructor, psychiatrist, National Institute of Neurology and Psychiatry, Budapest, Hungary |

- 1982-1995 Staff member – Instructor, neuropathologist, University Medical School of Lausanne, Switzerland
- 1995-2005 Médecin associé, MER and PD, equivalent of Assistant Professor, University Institute of Pathology, CHUV, University Medical School of Lausanne, Switzerland
- 2001-2004 Visiting scientist, neuroscience research in molecular biology, Participation in the introduction of Alzheimer's research, Center for NeuroVirology, Temple University, Philadelphia, PA, USA
- 2004 – 2007 Visiting scientist, Kinsmen Laboratory of Neurological Research, Head of Neuropathology laboratory in the Kinsmen Laboratory of Neurological Sciences (Director. Prof. Patrick L. McGeer) The British Columbia University, Vancouver, BC, Canada
- 2010 - President, then Director of the Prevention Alzheimer International *Foundation*, Martigny-Combe, Switzerland
- 2012- Director of the International Alzheimer Research Center, Martigny-Combe, Switzerland. Neurology consultation on memory and Lyme disease in the Medical Center of Vigimed, Martigny, Switzerland

Awards and Honors

- 1971 - 2nd National prize and 1st university prize of distinction for MD thesis, University Medical School of Debrecen, Hungary
- 1975 - Specialty board Exam and Certificate in Neurology Institute of Neurology, Psychiatry and Neurosurgery, Hungary, with distinction excellent (5/5)
- 1976 Best young researcher award, Institute of Neurology, Psychiatry and Neurosurgery, DOTE, University of Debrecen, Hungary
- 1980 Specialty board Exam and Certificate in Psychiatry and Psychotherapy, National Institute of Neurology and Psychiatry, Budapest, with distinction excellent (5/5)
- 1995 PD and MER degrees – Assistant Professor, University Institute of Pathology, Lausanne, Switzerland
- 2005 - PhD thesis (Summa cum laude), University Medical School of Debrecen, Academy of Sciences, Hungary - Director and supervisor Prof PL McGeer, The University of British Columbia, Vancouver, BC, Canada

Other Experiences and Professional Memberships

- 1971- 2005 Postgraduate and undergraduate teaching of Neurology, Psychiatry and Neuropathology
- 1995 – 2005 Head of research group "Neurodegeneration", University Institute of Pathology, University Medical School of Lausanne, University of Lausanne (CHUV, UNIL), Switzerland
- 2004-2007 Head of Neuropathology laboratory, Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, Canada
- 1996- On the Board of Director Physicians of Swiss Hospitals, Switzerland
- 2005- On the Board of Directors then on the Scientific Advisory Board of the Canadian Lyme Foundation
- 2008- On the Advisory Scientific Board of the Deutsche Borreliose Gesellschaft
- 2012 - On the Scientific Advisory Scientific Board of Lyme Research Allianz
- 2005- 2008 Associate editor of the Journal of Alzheimer Disease (JAD), from 2008 of the International Journal of Alzheimer Disease, and from 2011 of the Acta Neuropathologica Communications.
- Member of several scientific organizations, including Association of Swiss Neuropathologists, Association of Swiss Neurologists, Society of Swiss Pathologists, Society of Neuroscience, Alzheimer's

Association, International Society to Advance Alzheimer Research and Treatment (ISTAART), International Brain Organization (IBRO), Société Académique Vaudoise, International Society of Neurovirology, Swiss Medical Association (FMH).

2014- Member of the foreign body of the Hungarian Academy of Sciences

Research interest

Our research interests include the pathogenesis of Alzheimer's disease (AD) and other neurodegenerative and chronic inflammatory disorders. From 1993 my research focused on the role of bacteria, particularly of spirochetes, in persistent chronic infection, inflammation and amyloidogenesis in AD.

A century ago, Fischer (1907) has been suggested and Alzheimer and his colleagues have been cited his view and discussed the possibility that microorganisms might play a role in senile plaque formation. Additionally, there is an example in the history of medicine that chronic bacterial infection, namely chronic spirochetal infection (*Treponema pallidum*) can cause slowly progressive dementia and reproduce the pathological and biological hallmarks of AD.

Increasing amount of recent data indicate, as we have suggested in 1993, that several types of spirochetes, including *Borrelia burgdorferi* and periodontal pathogen spirochetes are involved in the pathogenesis of AD. Recently, reviewing all data available in the literature a statistically strongly significant association, with a high risk factor was found between spirochetes and AD, fulfilling Hill's criteria in favor of a causal relationship.

Exposure of human and mammalian primary CNS cells and organotypic cultures to spirochetes, showed that similarly to *Treponema pallidum*, *Borrelia burgdorferi* reproduces the pathological and biological hallmarks of AD (increased A β PP, A β and (p)tau levels).

We have identified the first susceptibility gene, the Islet-brain-1 (IB1, encoded by MAPK8IP1), for type 2 diabetes and reported first the presence of local infection and inflammation associated with affected pancreatic islets in type-2 diabetes. Bacterial peptidoglycan, LPS and several bacteria, including spirochetes, *Chlamydia pneumoniae* and *Helicobacter pylori* were found to be associated with amyloid deposition in the affected Langerhans islets.

Now from three decades we are involved in Lyme disease research. We have published the first pathological confirmation of the meningovascular form of chronic or late Lyme neuroborreliosis leading to cerebral vascular infarcts. Together with other authors we contributed to the pathological confirmation of the other major form of chronic Lyme neuroborreliosis, which is identical to the atrophic form of general paresis associated with slowly progressive dementia caused by *Treponema pallidum* in syphilis. We presented evidences on the direct involvement of *Borrelia burgdorferi* in the major tertiary forms of chronic Lyme neuroborreliosis. On invitation we contributed with a chapter on the pathology and biology of dementia in syphilis and Lyme disease in the prestigious Handbook of Clinical Neurology.

We have published observations on the presence of various pleomorphic forms, including the more resistant cystic, granular and L forms of *Borrelia burgdorferi*, in pure *Borrelia* cultures in infected cell cultures and in brains of demented patients with clinically, serologically and pathologically confirmed Lyme neuroborreliosis. We have also shown that *Borrelia burgdorferi* spirochetes cultivated from the brains of these patients are virulent and invade neuronal and glial cells and cause apoptosis.

Recently, reviewing descriptions and illustrations available on the pathology of Lyme neuroborreliosis from the past 30 years, we reported that the major late or chronic forms of neurosyphilis were

pathologically confirmed in Lyme disease as well and *Borrelia burgdorferi* was cultivated from tertiary lesions by various authors. These observations definitely indicate that chronic Lyme disease exists and *Borrelia burgdorferi*, similarly to *Treponema pallidum* plays a direct role in the pathogenesis of the tertiary manifestations of chronic/late Lyme disease.

Publications

Number of publications (articles, book chapters and published abstracts: 238)

Published articles and book chapters: 113 (105 per reviewed)

Mean impact factor: 5.02

Some selected publications

1. Miklossy J, Kuntzer T, Bogousslavsky J, Regli F, Janzer RC. Meningovascular form of neuroborreliosis: Similarities between neuropathological findings in a case of Lyme disease and those occurring in tertiary neurosyphilis. *Acta Neuropathol* 1990;80:568-572.
2. Miklossy J. Alzheimer's disease - A spirochetosis? *Neuroreport*. 1993; 4:841-848
3. Miklossy J, Taddei K, Martins R, Escher G, Kraftsik R, Pillevuit O, Lepori D, Campiche M. Alzheimer disease: curly fibers and tangles in organs other than brain. *J Neuropathol Exp Neurol*. 1999;58:803-814.
4. Waeber G, Delplanque J, Bonny C, Mooser V, Steinmann M, Widmann C, Maillard A, Miklossy J, Dina C, Hani E, Vionnet N, Nicod P, Boutin P, Froguel P. The gene MAPK8IP1, encoding islet-brain-1, is a candidate for type 2 diabetes. *Nature Genetics*, 2000; 24: 291-295. Press release
5. Mooser V, Helbecque N, Miklossy J, Marcovina SM, Nicod P, Amouyel Ph. Interactions between Apolipoprotein E and Apolipoprotein(a) in patients with Late-Onset Alzheimer disease. *Ann Intern Med* 2000;132:533-537.
6. Miklossy J, Khalili K, Gern L, Ericson RL, Darekar P, Bolle L, Hurlimann J, Paster BJ. *Borrelia burgdorferi* persists in the brain in chronic Lyme neuroborreliosis and may be associated with Alzheimer disease. *J Alzheimer's Disease* 2004, 6:1-11.
7. Guo J, Arai T, Miklossy J, and McGeer PL. A-beta and tau form soluble complexes that may promote self aggregation of both into the insoluble forms observed in Alzheimer disease. *P.N.A.S. Proc Natl Acad Sci U S A*. 2006;103:1953-8.
8. Miklossy J, Kis A, Radenovic A, Miller L, Forro L, Martins R, Reiss K, Darbinian N, Darekar P, Mihaly L, Khalili K. Beta-amyloid deposition and Alzheimer's type changes induced by *Borrelia* spirochetes. *Neurobiol Aging* 2006; 27:228-236.
9. Miklossy J. Biology and neuropathology of dementia in syphilis and Lyme disease. In: *Handbook of Clinical Neurology, Dementias, Vol 89 (3rd series)*, Eds: C Duyckaerts, I Litvan, Elsevier, (Edinburgh, London), 2008, Volume 89, Chapter 72, pp. 825-844.
10. Miklossy J, Kasas S, Zurn A, McCall S, Yu S, McGeer PL. Persisting atypical and cystic forms of *Borrelia burgdorferi* and local inflammation in Lyme neuroborreliosis. *J. Neuroinflammation*, 2008,5:40.
11. Miklossy J. Alzheimer's disease - a neurospirochetosis. Analysis of the evidence following Koch's and Hill's criteria. *J Neuroinflammation*. 2011; 8:90, highly cited
12. Miklossy J. Emerging roles of pathogens in Alzheimer disease. *Expert Rev Mol Med*. 2011; 13: e30.