

Program in Neurodegeneration and Neuroprotection: The Kynurenone System



Szeged

**University of Szeged and
Biological Research Center of the
Hungarian Academy of Sciences**

**Szeged
Hungary
2010**

Departments of the Program

Biological Research Center of the Hungarian Academy of Sciences
Institute of Biophysics

University of Szeged

Department of Inorganic and Analytical Chemistry
Department of Neurology
Department of Physical Chemistry and Materials Science
Department of Physiology, Anatomy and Neuroscience
Institute of Pharmaceutical Chemistry
Institute of Surgical Research
Department of Medical Microbiology and Immunology

Program Coordinator:

Professor László Vécsei

Program Secretaries:

Zsuzsanna Bohár M.Sc., Ph.D. Student
Dénes Zádori M.D., Ph.D. Student

PREFACE

Several lines of evidence have linked excitotoxic cell death to the pathogenesis of both acute and chronic neurological disorders. In mammals, the vast majority of dietary tryptophan is metabolized via the kynurenine pathway. Kynurenic acid was detected in the canine urine as early as 1853 (Liebig, 1853). No particular biological function was assigned to it until 1982 when its neuroinhibitory properties were discovered in neurophysiological experiments. The role of kynurenine metabolites in many disorders of the central nervous system (infections, dementia, epilepsy, migraine, ischaemia, traumatic brain injury, multiple sclerosis, Parkinson's disease, Huntington's disease and other neurodegenerative and psychiatric disorders) has been hypothesized. Furthermore, the availability of new compounds that selectively target specific receptors and individual enzymes of the kynurenine pathway has led to novel neuropharmacological concepts and provided new opportunities for therapeutic intervention. The aim of this publication is to stimulate further collaboration in the field of kynurenine research between different departments of University of Szeged.

Professor László Vécsei
Program Coordinator

Szeged, July 2010

**Biological Research
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Institute of Biophysics



ISTVÁN A. KRIZBAI

Research Associate Professor

- 1983-90 Medical student, University of Medicine and Pharmacy, Marosvásárhely, Romania and Semmelweis Medical University, Budapest, Hungary
- 1990 Diploma in medicine with a degree of "summa cum laude"
- 1990-1993 Research fellowship of the Hungarian Academy of Sciences at the Laboratory of Molecular Neurobiology, Institute of Biophysics, BRC, Szeged, Hungary Supervisor: Prof. Dr. Ferenc Joó
- 1993-1996 Research assistant, Laboratory of Molecular Neurobiology, Institute of Biophysics, BRC, Szeged, Hungary
- 1994 Volkswagen Fellowship, Zentrum Anatomie, Georg August Universität, Göttingen, Germany (6 months)
- 1995-2000 Visiting scientist, Zentrum Anatomie, Georg August Universität, Göttingen, Germany (2 years)
- 1996 PhD in neurobiology with a degree of "summa cum laude"
- 1996-2000 Research assistant professor Laboratory of Molecular Neurobiology, Institute of Biophysics, BRC, Szeged, Hungary
- 1998-2001 Visiting scientist, Institut für Molekularbiologie, Österreichische Akademie der Wissenschaften, Salzburg, Austria (2.5 years)
- 2001- Research associate professor, Institute of Biophysics, BRC, Szeged, Hungary

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Major Research Interest

Molecular mechanisms regulating the blood brain barrier under physiological and pathological conditions

Selected Recent Publications

- I. Wilhelm, P. Nagyősi, A.E. Farkas, P.O. Couraud, I.A. Romero, B. Weksler, C. Fazakas, N.T.K. Dung, H. Bauer, H.C. Bauer, I.A. Krizbai. Hyperosmotic stress induces Axl activation and cleavage in cerebral endothelial cells. *J Neurochem.* 107:116-26. (2008)
- I. Wilhelm, A.E. Farkas, P. Nagyősi, G. Váró, Z. Bálint, G.A. Végh, P.O. Couraud, I.A. Romero, B. Weksler, I.A. Krizbai. Regulation of Cerebral Endothelial Cell Morphology by Extracellular Calcium. *Phys.Med.Biol.* 52:6261-74. (2007)
- A. Farkas, E. Szatmari, A. Orbok, I. Wilhelm, K. Wejksza, P. Hutamekalin, H. Bauer, HC. Bauer, A. Traweger and I.A. Krizbai. Hyperosmotic Mannitol Induces Src-Kinase-Dependent Phosphorylation Of Beta-Catenin In Cerebral Endothelial Cells. *J. Neurosci. Res.* 80:855-61. (2005)
- I.A. Krizbai, H. Bauer, N. Bresgen, P.M. Eckl, A. Farkas, E. Szatmári, A. Traweger, K. Wejksza and Hans-Christian Bauer. Effect of oxidative stress on the junctional proteins of cultured cerebral endothelial cells. *Cell. Mol. Neurobiol.* 25:129-139. (2005)
- A. Traweger, R. Fuchs, I.A. Krizbai, T.M. Weiger, H.C. Bauer, H. Bauer: The tight junction protein ZO-2 localizes to the nucleus and interacts with the hnRNP protein SAF-B. *J Biol Chem.* 278:2692-700. (2003)

IMOLA WILHELM

Research Fellow

- 1997-2003 Medical student, University of Medicine and Pharmacy, Tg. Mures, Romania
- 2003 Diploma in medicine, University of Medicine and Pharmacy, Tg Mures, Romania
- 2003-2004 ITC fellow, Biological Research Center, Szeged, Hungary
- 2004-2007 PhD student, Biological Research Center, Szeged, Hungary
- 2007- 2009 Research assistant, Biological Research Center, Szeged, Hungary
- 2007 Visiting scientist, Department of Physiology, Biophysics and Neuroscience, Cinvestav, Mexico City (2 months)
- 2009 PhD in Theoretical Medical Sciences, University of Szeged, Szeged, Hungary
- 2009 Research fellow, Biological Research Center, Szeged, Hungary



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Major Research Interest

Molecular mechanisms regulating the blood-brain barrier under physiological and pathological conditions

Selected Recent Publications

Wilhelm I, Nagyörszi P, Farkas AE, Couraud PO, Romero IA, Weksler B, Fazakas C, Dung NT, Bottka S, Bauer H, Bauer HC, Krizbai IA. Hyperosmotic stress induces Axl activation and cleavage in cerebral endothelial cells. *J Neurochem*. 2008, 107:116-26.

Wilhelm I, Farkas AE, Nagyörszi P, Váró G, Bálint Z, Végh GA, Couraud PO, Romero IA, Weksler B, Krizbai IA. Regulation of cerebral endothelial cell morphology by extracellular calcium. *Phys Med Biol*. 2007, 52:6261-74.

Vajda S, Bartha K, Wilhelm I, Krizbai IA, Ádám-Vizi V. Identification of protease-activated receptor-4 (PAR-4) in puromycin-purified brain capillary endothelial cells cultured on Matrigel. *Neurochem Int*. 2008, 52:1234-9.

Bálint Z, Krizbai IA, Wilhelm I, Farkas AE, Párducz A, Szegletes Z, Váró G. Changes induced by hyperosmotic mannitol in cerebral endothelial cells: an atomic force microscopic study. *Eur Biophys J*. 2007, 36:113-20.

Farkas A, Szatmari E, Orbók A, Wilhelm I, Wejksza K, Nagyörszi P, Hutamekalin P, Bauer H, Bauer HC, Traweger A, Krizbai IA. Hyperosmotic mannitol induces Src kinase-dependent phosphorylation of beta-catenin in cerebral endothelial cells. *J Neurosci Res*. 2005, 80:855-61.

Department of Inorganic and Analytical Chemistry



ANTAL PÉTER

Professor of Chemistry

- □1964-1969: Chemist, M.Sc. József Attila University, Szeged
- □1969-1973: Ph.D, József Attila University, Szeged
- □1973: Guest Scientist, University of Kiev, Ukraina
- □1983 Guest Scientist, University of Merseburg, Germany
- □1984: Candidate of Science
- □1987: Guest Scientist, University of Odessa, Ukraina
- □1990: Guest Scientist, University of Regensburg, Germany
- □1994: Guest Scientist, University of Udine, Italy
- □1996: Guest Scientist, University of Udine, Italy
- □2000: Guest Scientist, University of Brno,
- □1991-2006: Guest Scientist, Vrije Universiteit Brussels, Belgium, thirteen study tours (together 4.5 years)
- □2003: Doctor Habil
- □2004: Doctor of Science

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Major Research Interest

Method developments for chiral separation of amino acids and other pharmacologically important analytes. Chiral chromatography.

Investigation of stability of peptides towards enzymatic degradation.

Selected Recent Publications

A. Keresztes, M. Szőcs, A. Borics, K.E. Kövér, E. Forró, F. Fülöp, Cs. Tömböly, A. Péter, A. Páhi, G. Fábián, M. Murányi., G. Tóth: New Endomorphin Analogues with Alicyclic β -Amino acids: Influence on bioactive conformation and pharmacological profile J. Med. Chem., 51, 4270-4279 (2008)

I. Ilisz, G. Fodor, R. Berkecz, R. Iványi, L. Szente, A. Péter : Enantioseparation of β -substituted tryptophane analogs with modified cyclodextrins by capillary zone electrophoresis Journal of Chromatography A 1216 (2009) 3360-3365

I. Ilisz, Z. Pataj, A. Péter: Chiral HPLC separation of amino acid enantiomers and epimers of small, biologically important peptides Mini Reviews in Medicinal Chemistry 10 (2010) 287-298

Z. Pataj, I. Ilisz, R. Berkecz, E. Forró, F. Fülöp, A. Péter: Comparison of Separation performances of amylose- and cellulose-based stationary phases in the high-performance liquid chromatographic enantioseparation of stereoisomers of β -lactams Chirality 22 (2010) 120-128

I. Ilisz, Z. Pataj, R. Berkecz, A. Misicka, D. Tymecka, F. Fülöp, H. J. Choi, M.H. Hyun, A. Péter: High performance liquid chromatographic enantioseparation of β 2-amino acids using a long tethered (+)-(18-crown-6)-2,3,11,12-tetracarboxylic acid-based chiral stationary phase Journal of Chromatography A 1217 (2010) 1075-1082

ISTVÁN ILISZ

Assistant Professor of Chemistry

- 1989-1994: Chemist, MSc. József Attila University, Szeged
- 1993-1994: Teacher of Chemistry, MSc. József Attila University, Szeged
- 1993: Tempus Scholarship, University of Ghent, Belgium
- 1994-1996: Environmental Specialist, József Attila University, Szeged
- 1998: Guest Scientist, University of Ghent, Belgium
- 1999. PhD
- 2010: Doctor Habil



Major Research Interest

Separation sciences, environmental analysis. Method developments for chiral separation of amino acids and other pharmacologically important analytes. Chiral chromatography.

Selected Recent Publications

I. Ilisz, R. Berkecz, A. Péter: Retention mechanism of high-performance liquid chromatographic enantioseparation on macrocyclic glycopeptide-based chiral stationary phases Journal of Chromatography A 1216 (2009) 1845-1860

I. Ilisz, G. Fodor, R. Berkecz, R. Iványi, L. Szente, A. Péter: Enantioseparation of β -substituted tryptophane analogs with modified cyclodextrins by capillary zone electrophoresis Journal of Chromatography A 1216 (2009) 3360-3365

I. Ilisz, Z. Pataj, A. Aranyi, A. Péter: Chiral HPLC separation of amino acid enantiomers and epimers of small, biologically important peptides Mini Reviews in Medicinal Chemistry 10 (2010) 287-298

Z. Pataj, I. Ilisz, R. Berkecz, E. Forró, F. Fülöp, A. Péter: Comparison of Separation performances of amylose- and cellulose-based stationary phases in the high-performance liquid chromatographic enantioseparation of stereoisomers of β -lactams Chirality 22 (2010) 120-128

I. Ilisz, Z. Pataj, R. Berkecz, A. Misicka, D. Tymecka, F. Fülöp, H. J. Choi, M.H. Hyun, A. Péter: High performance liquid chromatographic enantioseparation of β 2-amino acids using a long tethered (+)-(18-crown-6)-2,3,11,12-tetracarboxylic acid-based chiral stationary phase Journal of Chromatography A 1217 (2010) 1075-1082

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Department of Neurology



LÁSZLÓ VÉCSEI

Professor and Director of Neurology

- 1979 MD, Medical University of Szeged, Hungary
- 1984 Board examination in chemical pathology
- 1987 Board examination in clinical neurology
- 1987-1989 Research fellow in neuroscience, University of Lund, Sweden (Ph.D., University of Lund)
- 1989-1990 Research fellow in experimental neurology, Harvard Medical School, Massachusetts General Hospital, Boston, USA
- 1993-Professor and Head of Neurology, University of Szeged
- 2001-2007 Corresponding Member of Hungarian Academy of Sciences
- 2007-Ordinary Member of Hungarian Academy of Sciences
- 2010-Dean of the Medical Faculty

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Major Research Interests

Neurodegeneration and neurorprotection: the role of the kynureneine system
Headache
Multiple sclerosis
Extrapyramidal disorders

Selected Recent Publications

- Vámos E, Fejes A, Koch J, Tajti J, Fülop F, Toldi J, Párdutz A, Vécsei L. Kynureneate Derivative Attenuates the Nitroglycerin-Induced CamKIIalpha and CGRP Expression Changes. *Headache*. 2010 May;50(5):834-43.
- Zádori D, Klivényi P, Vámos E, Fülop F, Toldi J, Vécsei L. Kynurenines in chronic neurodegenerative disorders: future therapeutic strategies. *J Neural Transm*. 2009 Nov;116(11):1403-9.
- Vámos E, Párdutz A, Varga H, Bohár Z, Tajti J, Fülop F, Toldi J, Vécsei L. L-kynurenone combined with probenecid and the novel synthetic kynurenic acid derivative attenuate nitroglycerin-induced nNOS in the rat caudal trigeminal nucleus. *Neuropharmacology*. 2009 Sep;57(4):425-9.
- Vamos E, Pardutz A, Klivenyi P, Toldi J, Vecsei L. The role of kynurenines in disorders of the central nervous system: possibilities for neuroprotection. *J Neurol Sci*. 2009 Aug 15;283(1-2):21-7.
- Sas K, Robotka H, Rózsa E, Agoston M, Szénási G, Gigler G, Marosi M, Kis Z, Farkas T, Vécsei L, Toldi J. Kynurenone diminishes the ischemia-induced histological and electrophysiological deficits in the rat hippocampus. *Neurobiol Dis*. 2008 Nov;32(2):302-8.
- Rajda C, Bergquist J, Vécsei L. Kynurenines, redox disturbances and neurodegeneration in multiple sclerosis. *J Neural Transm Suppl*. 2007;(72):323-9.
- Sas K, Robotka H, Toldi J, Vécsei L. Mitochondria, metabolic disturbances, oxidative stress and the kynureneine system, with focus on neurodegenerative disorders. *J Neurol Sci*. 2007 Jun 15;257(1-2):221-39.
- Gigler G, Szénási G, Simó A, Lévy G, Hársing LG Jr, Sas K, Vécsei L, Toldi J. Neuroprotective effect of L-kynurenone sulfate administered before focal cerebral ischemia in mice and global cerebral ischemia in gerbils. *Eur J Pharmacol*. 2007 Jun 14;564(1-3):116-22.
- Knyihár-Csílik E, Toldi J, Krisztin-Péva B, Chadaide Z, Németh H, Fenyo R, Vécsei L. Prevention of electrical stimulation-induced increase of c-fos immunoreaction in the caudal trigeminal nucleus by kynurenone combined with probenecid. *Neurosci Lett*. 2007 May 17;418(2):122-6. E
- Németh H, Toldi J, Vécsei L. Kynurenines, Parkinson's disease and other neurodegenerative disorders: preclinical and clinical studies. *J Neural Transm Suppl*. 2006;(70):285-304.
- Knyihár-Csílik E, Toldi J, Mihály A, Krisztin-Péva B, Chadaide Z, Németh H, Fenyo R, Vécsei L. Kynurenone in combination with probenecid mitigates the stimulation-induced increase of c-fos immunoreactivity of the rat caudal trigeminal nucleus in an experimental migraine model. *J Neural Transm*. 2007;114(4):417-21.
- Vecsei, L.(ed): Kynurenines in the Brain: from Experiments to Clinics. NOVA, New York, 2005.

ZSUZSANNA BOHÁR

Biologist, PhD student

- 2004-2009 biology student, Faculty of Natural Science and Informatics, University of Szeged
- 2009-present PhD student Department of Neurology, University of Szeged



Research interests

Migraine pathomechanism, experimental modells of migraine and pain.

Trigeminal ganglion stimulation as migraine modell

Selected recent publications

Varga H, Pardutz A, Vamos E, Bohar Z, Bago F, Tajti J, Bari F, Vecsei L. Selective inhibition of cyclooxygenase-2 attenuates nitroglycerin-induced calmodulin-dependent protein kinase II alpha in rat trigeminal nucleus caudalis. *Neurosci Lett*. Feb 20;451(2):170-3. 2009

Vámos E, Párdutz A, Varga H, Bohár Z, Tajti J, Fülöp F, Toldi J, Vécseli L. L-kynurenone combined with probenecid and the novel synthetic kynurenic acid derivative attenuate nitroglycerin-induced nNOS in the rat caudal trigeminal nucleus. *Neuropharmacology*. Sep;57(4):425-9. 2009

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ANNAMARIA FEJES

Biologist, Ph.D. student

- 2000-2006: Biologist, Faculty of Natural Science, University of Szeged, Hungary
- Since 2008: Ph.D. student, Department of Neurology, Faculty of Medicine, University of Szeged, Hungary

Major research interest:

Pathomechanism of migraine

Examination of effect of kynurenic acid analogues on the trigeminal activation in several experimental animal models
Research of novel therapeutic opportunities in migraine

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Selected recent publications:

Eniko Vamos, Arpad Pardutz, Annamaria Fejes, Janos Tajti, Jozsef Toldi, Laszlo Vecsei (2009) Modulatory effects of probenecid on the nitroglycerin-induced changes in the rat caudal trigeminal nucleus. *Eur J Pharmacol* 621(1-3):33-7.

Eniko Vamos, Annamaria Fejes, Julia Koch, Janos Tajti, Ferenc Fulop, Jozsef Toldi, Arpad Pardutz and Laszlo Vecsei (2009) Kynurene Derivative Attenuates the Nitroglycerin-Induced CamKIIalpha and CGRP Expression Changes. *Headache in press*

Annamaria Fejes, Arpad Pardutz, Jozsef Toldi and Laszlo Vecsei (2010) Kynurenone metabolites and migraine: experimental studies and therapeutic perspectives. *Curr Neuropharmacol* in press

PÉTER KLIVÉNYI

Associate Professor of Neurology

- 1993 MD (Summa Cum Laude), Albert Szent-Györgyi University Medical School, Szeged, Hungary (85/1993)
- 1993-1994 Intern, Department of Anesthesiology and Intensive Care Unit, Albert Szent-Györgyi University Medical School, Szeged
- 1994-1999 Resident, Department of Neurology, Albert Szent-Györgyi University Medical School, Szeged, Hungary
- 1997-1998 Research fellow, Neurochemistry Laboratory, Neurology Service, Massachusetts General Hospital, Harvard Medical School, Boston, USA
- 1999 Board exam Neurology
- 1999-2003 Instructor, Department of Neurology, University of Szeged, Szeged, Hungary
- 2000 PhD, University of Szeged
- 2001-2002. Postdoctoral research fellow, Department of Neurology and Neuroscience, Weill Medical College of Cornell University, New York, USA
- 2004-2007 Assistant Professor, Department of Neurology, University of Szeged, Szeged, Hungary
- 2006 Med. habil. University of Szeged
- 2007- Associate Professor Department of Neurology, University of Szeged



Research interests

Clinical neurology, neuropharmacology, free radicals, oxidative stress, excitotoxicity, neurodegeneration, pathomechanism of neurological disorders.

Selected recent publications

Klivenyi P, Kekesi KA, Hartai Z, Juhasz G, Vecsei L. Effects of mitochondrial toxins on the brain amino acid concentrations. *Neurochem Res*. Nov;30(11):1421-7 2005

Klivenyi P, Siwek D, Gardian G, Yang L, Starkov A, Cleren C, Ferrante RJ, Kowall NW, Abeliovich A, Beal MF. Mice lacking alpha-synuclein are resistant to mitochondrial toxins. *Neurobiol Dis*. Mar;21(3):541-8. 2006

Oláh J, Klivényi P, Gardián G, Vécsei L, Orosz F, Kovacs GG, Westerhoff HV, Ovádi J. Increased glucose metabolism and ATP level in brain tissue of Huntington's disease transgenic mice. *FEBS J*. Oct;275(19):4740-55. 2008

Klivényi, P., Zádori, D., Fülöp, F., Toldi, J., Vécsei, L.: Neuroprotective effects of kynurenic acid analog in a transgenic mouse model of Huntington's disease. *Movement Disorders* 24:S1:TU-108 2009.

Vamos E, Voros K, Zaduri D, Vecsei L, Klivenyi P. Neuroprotective effects of probenecid in a transgenic animal model of Huntington's disease. *J Neural Transm*. Sep;116(9):1079-86. 2009

Klivenyi P, Vecsei L. Novel therapeutic strategies in Parkinson's disease. *Eur J Clin Pharmacol*. Feb;66(2):119-25. 2010

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ÁRPÁD PÁRDUTZ

Assistant Professor of Neurology

- 1997 Doctor of Medicine, University of Szeged
- 1997- Clinical doctor, Department of Neurology, University of Szeged
- 1999-2009 Guest scientist under the supervision of Prof. Jean Schoenen, University of Liege, Department of Neuroanatomy (several visits with a total duration of ~2 years)
- 2002 Trained Neurologist
- 2002- Associate Professor, Department of Neurology, University of Szeged
- 2004- PhD degree
- 2007- Assistant Professor, Department of Neurology, University of Szeged

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Major Research Interests

Molecular and cellular basis of pain processing
Modulation of trigeminal activation in animal models of migraine
The role of gonadal steroids in the modulation of trigeminal pain

Selected publications:

Pardutz A., Krizbai I., Multon S., Vecsei L., Schoenen J., Systemic nitroglycerin increases nNOS levels in rat trigeminal nucleus caudalis, *Neuroreport*. 2000 Sep 28;11(14):3071-5.

Pardutz A., Multon S., Malgrange B., Parducz A., Vecsei L., Schoenen J., Effect of systemic nitroglycerin on CGRP- and 5-HT- afferents to rat caudal spinal trigeminal nucleus and its modulation by estrogen, *Eur J Neurosci*. 2002 Jun;15(11):1803-9.

Multon S., Pardutz A., Mosen J., Hua MT., Defays C., Honda SI., Harada N., Bohotin C., Franzen R., Schoenen J., Lack of estrogens increases pain in the the trigeminal formalin model: a behavioural and immunocytochemical study of transgenic ArKO mice, *Pain* 2005 Mar;114(1-2):257-65.

Pardutz A., Hoyk Zs., Varga H., Vecsei L., Schoenen J., Estrogen-modulated increase of calmodulin dependent protein kinase II (CamKII) in rat spinal trigeminal nucleus after systemic nitroglycerin, *Cephalgia* 2007 Jan;27(1):46-53.

Vamos E, Pardutz A, Varga H, Bohar Z, Tajti J, Fulop F, Toldi J, Vecsei L. l-kynurenone combined with probenecid and the novel synthetic kynurenic acid derivative attenuate nitroglycerin-induced nNOS in the rat caudal trigeminal nucleus. *Neuropharmacology*. 2009 Sep;57(4):425-9.

IMOLA PLANGÁR

PhD student – biologist

- 2008 University of Szeged, Faculty of Natural Science, Department of Biology
- 2008-present PhD student in the frame of the „Clinical neuroscience” program

Major Research Interests

pain and pathomechanism of migraine (electrical stimulation of trigeminal ganglion)

the field of neurodegeneration and neuroprotection,
role of different compounds in the spontaneous locomotor activity
and the effects of them on survival in a transgenic mouse model of Huntington's disease and toxin model of Parkinson's disease



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Selected Recent Publications

Cox-2 inhibitor attenuates NO-induced nNOS in rat caudal trigeminal nucleus.

Varga H, Pardutz A, Vamos E, Plangar I, Egyud E, Tajti J, Bari F, Vecsei L.: Headache 47:1319-25 (2007)

Effects of carnosine in a transgenic mouse model of Huntington's disease

Plangár I., Zádori D, Klivényi P, Vécsei L.:
16th International Student Congress of Medical Sciences,
Groningen, The Netherlands, Book of Abstracts P:103 (2009)

Effect of silymarin on the neurotoxicity of MPTP.

Plangár I, Zádori D, Klivényi P, Vécsei L.:
LXXIII. Annual Meeting of the Hungarian Physiological Society,
Szeged, Hungary FÉK/26 (2009)

The role of the kynurenine pathway in neurodegeneration and neuroprotection.

Plangár I, Zádori D, Klivényi P, Fülöp F, Toldi J and Vécsei L.: In: S.J. Baloyannis (editor). 7th International Congress on the Improvement of the Quality of Life on Dementia, Parkinson's Disease, Epilepsy, MS and Muscular Disorders and Neuroethics. Medimond S.r.l., Bologna, 2009.



KATALIN SAS

Assistant Professor of Neurology

- 1985 – M.D. Faculty of Medicine at Albert Szent-Györgyi Medical University of Szeged.
- 1985-1989: Department of Neurology and Psychiatry of the Albert Szent-Györgyi Medical University of Szeged, Psychiatric Unit: Resident later Assistant Professor in psychiatry. 1989: Board examination in psychiatry.
- 1993 - Psychotherapist - degree
- 1990 - Department of Neurology of the Albert Szent-Györgyi Medical University of Szeged. Resident later Assistant Professor in neurology. 1992: Board examination in neurology.
- 2002 - "Stroke specialist" - degree
- 2008 - Ph.D. "Potential role of glutamate neurotransmission in the pathogenesis of ischemic brain damage and of depression. Effects of L-kynurenone on survival of hippocampal neurons and on the corticocerebral blood flow in ischemic animal models."

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Major Research Interests

Stroke, cerebral excitotoxicity, neurodegeneration

Selected Publications

- Sas K., Csete K., Váradi P., Vécsei L., Papp J. Gy.: Az idegrendszeri excitotoxinok patológiai és klinikai jelentősége. I. Rész. A glutamátreceptorok. *Lege Artis Medicinae* 8(6): 406-421, 1998.
- Sas K., Csete K., Váradi P., Vécsei L., Papp J. Gy.: Az idegrendszeri excitotoxinok patológiai és klinikai jelentősége. II. rész. Az ischaemia celluláris következményei. A krónikus neurodegeneráció, a befolyásolás lehetőségei. *Lege Artis Medicinae* 8(6): 406-421, 1998
- Sas K., Csete K., Vécsei L., Papp J. Gy.: Effect of systemic administration of L-kynurenone on corticocerebral blood flow under normal and ischemic conditions of the brain in conscious rabbits. *J. Cardiovasc. Pharmacol.* 42(3): 403-408, 2003
- Sas K., Sztriha L., Fazekas A., Vécsei L.: A depresszió neurobiológiája – Endogén depresszió. *Agyérbekötések* 12(1): 16-26, 2006
- Gigler G., Szénási G., Simó A., Lévay Gy., Hárssing L.G. Jr, Sas K., Vécsei L., Toldi J.: Neuroprotective Effect of L-Kynurenone Sulfate Administered Before Focal Cerebral Ischemia in Mice and Global Cerebral Ischemia in Gerbils. *Eur J Pharmacol.* 564(1-3):116-22, 2007
- Sas K., Robotka H., Toldi J. and Vécsei L.: Mitochondria, metabolic disturbances, oxidative stress and the kynurenone system, with focus on neurodegenerative disorders. *J Neurol Sci.* 257:221-239, 2007
- Sas K., Csete K., Vezekényi Z., Sztriha L., Vécsei L., Papp JGy.: Effects of citalopram and fluoxetine on the corticocerebral blood flow in conscious rabbits. *Acta Physiologica Hungarica* 94(3):167-177, 2007
- Robotka H., Sas K., Agoston M., Rózsa E., Szénási G., Gigler G., Vécsei L., Toldi J.: Neuroprotection achieved in the ischaemic rat cortex with l-kynurenone sulphate. *Life Sci.* 23;82(17-18):915-9. 2008
- Rozsa E., Robotka H., Nagy D., Farkas T., Sas K., Vecsei L., Toldi J. The pentylentetrazole-induced activity in the hippocampus can be inhibited by the conversion of L-kynurenone to kynurenic acid: an in vitro study. *Brain Res Bull.* 76(5):474-9. 2008

JÁNOS TAJTI

Associate Professor of Neurology

- 1983 Graduation (Medicine, "summa cum laude"), University of Szeged, Hungary
- 1983-85 Assistant, Department of Anatomy, University of Szeged
- 1985-89 Resident, Department of Neurology, University of Szeged
- 1989 Board examination in neurology, University of Budapest
- 1989-91 Post-doctoral Fellow, Department of Neurology, Baylor College of Medicine, Houston, Tx, USA
- 1989-95 Consultant neurologist, Department of Neurology, University of Szeged
- 1994 Ph.D., University of Szeged
- 1995-2001 Assistant Professor of Clinical Neurology, Department of Neurology, University of Szeged
- 1997-98 Guest Scientist, Department of Internal Medicine, Division of Experimental Vascular Research, University of Lund, Sweden
- 1999 Habilitation (Neurology), University of Szeged
- 2001- Associate Professor of Clinical Neurology, Department of Neurology, University of Szeged



Major Research Interests

The complex pathomechanism of primary headaches and novel strategies for the therapy of these diseases.

Chronic pain syndromes and the pathomechanism of neurodegenerative disorders.

Selected Recent Publications

Tajti, J., Uddman, R., Möller, S., Sundler, F., Edvinsson, L. Messenger molecules and receptor mRNA in the human trigeminal ganglion. *J. of Autonomic Nervous System* 76:176-183, 1999.

Tajti, J., Uddman, R., Edvinsson, L. Neuropeptide messengers in the migraine generator region of the human brainstem. *Cephalgia* 21:96-101, 2001.

Kuris, A., Xu, C.B., Zhou, M.F., Tajti, J., Uddman, R., Edvinsson, L. Enhanced expression of CGRP in rat trigeminal ganglion neurons during cell and organ culture. *Brain Research* 1173:6-13, 2007.

Zidverc-Trajkovic, J., Stanimirovic, D., Obrenovic, R., Tajti, J., Vécsei, L., Gardi, J., Németh, J., Mijajlovic, M., Sternic, N., Jankovic, L. Calcitonin gene-related peptide levels in saliva of patients with burning mouth syndrome. *J. Oral Pathology and Medicine* 38:29-33, 2009.

Vámos, E., Párdutz, Á., Varga, H., Bohár, Zs., Tajti, J., Fülöp, F., Toldi, J., Vécsei, L. L-kynurenone combined with probenecid and the novel synthetic kynurenic acid derivative attenuate nitroglycerin-induced nNOS in the rat caudal trigeminal nucleus. *Neuropharmacology* 57:425-429, 2009.

Vámos, E., Fejes, A., Koch, J., Tajti, J., Fülöp, F., Toldi, J., Párdutz, Á., Vécsei, L. Kynureneate derivative attenuates the nitroglycerin-induced CamKIIα and CGRP expression changes. *Headache* 50:834-843, 2010.

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BERNADETT TUKA

Biologist – Ph. D. Student

- 2004-2009 biologist student at Faculty of Science and Informatics, University of Szeged. Research interests: Electrophysiological investigation of antiepileptogenic and anticonvulsant effects of new potential drugs on the 4-aminopyridine epilepsy model *in vivo*
- 2009- Ph.D. student at Department of Neurology, Faculty of Medicine, University of Szeged (Cooperation with Department of Physiology, Anatomy and Neuroscience, Faculty of Science and Informatics University of Szeged; sponsored by Gedeon Richter Pharmaceutical Company)

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Major Research Interests

Neuroscience of migraine: Role of pituitary adenylate cyclase-activating polypeptide (PACAP) in the trigeminovascular system in migraine model of rat and genetically modified mouse
Background of neurodegenerative disorders: Change of expression of mitochondrial proteins in transgenic model of Huntington's disease correlation with ages
Excytotoxins and neuroprotection: Association of kynurenone- and hormonal system

Publications

J. Tajti, Á. Párdutz, E. Vámos, B. Tuka, A. Kuris, Zs. Bohár, A. Fejes, J. Toldi, L. Vécsei : Migraine is a neuronal disease Journal of Neural Transmission 2010 (in press)

Zita Gajda, Anikó Martók, Bernadett Tuka, György Kéri, Magdolna Szente: Electrophysiological investigation of antiepileptogenic and anticonvulsant effects of 16463 on the 4-aminopyridine epilepsy model *in vivo*. (IBRO-2008-Poster)

Adrienn Markovics, Katalin Sándor, Éva Szőke, Viktória Kormos, Balázs Gaszner, Dóra Reglödi, Akemichi Baba, János Tajti, László Vécsei, Bernadett Tuka, Árpád Párdutz, Annamária Fejes, Zsuzsanna Bohár, János Szolcsányi, Zsuzsanna Helyes: Role of pituitary adenylate cyclase-activating polypeptide (PACAP) in the nitriglycerin-induced migraine model of the mouse. (IBRO-2010-Poster)

DÉNES ZÁDORI

M.D. – Ph.D. student

- 2007 Doctor of general medicine, University of Szeged
- 2007 English-Hungarian medical translator and interpreter, University of Szeged
- 2007 – present PhD student, Department of Neurology, University of Szeged

Major Research Interests

Neuroscience

Pathomechanism of chronic neurodegenerative disorders

Preclinical and clinical research on neurodegeneration and

Neuroprotection

Neurochemistry



Selected Recent Publications

Fülöp F., Szatmári I., Vámos E., Zádori D., Toldi J., Vécsei L. Synthesis, Transformations and Pharmaceutical Applications of Kynurenic Acid Derivatives. *Curr. Med. Chem.* 2009 16(36): 4828-4842.

Zádori D., Geisz A., Vámos E., Vécsei L., Klivényi P. Valproate ameliorates the survival and the motor performance in a transgenic mouse model of Huntington's disease. *Pharmacol. Biochem. Behav.* 2009 Nov; 94(1):148-153.

Zádori D., Klivényi P., Vámos E., Fülöp F., Toldi J., Vécsei L. Kynurenines in chronic neurodegenerative disorders: future therapeutic strategies. *J. Neural Transm.* 2009 Nov; 116(11):1403-1409.

Hunya A., Földi I., Szegedi V., Soós K., Zarándi M., Szabó A., Zádori D., Penke B., Datki ZL. Differences between normal and alpha-synuclein overexpressing SH-SY5Y neuroblastoma cells after Abeta(1-42) and NAC treatment. *Brain Res. Bull.* 2008 Mar 28;75(5):648-654.

Datki Z., Papp R., Zádori D., Soós K., Fülöp L., Juhász A., Laskay G., Hetényi C., Mihalik E., Zarándi M., Penke B. In vitro model of neurotoxicity of Abeta 1-42 and neuroprotection by a pentapeptide: irreversible events during the first hour. *Neurobiol Dis.* 2004 Dec;17(3):507-515.

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IMRE DÉKÁNY

Head of the Department of Physical Chemistry and Materials Science

- 1965-70. Graduation Chemistry, JATE University Szeged,
- 1970-1990 Department of Colloid Chemistry Research Assistant, Assistant Professor, Associate Professor
- 1989. Doctor of Science, D.Sc.D. Hung.Acad.Sci.
- 1989-present Full Professor and Head of the Department of Colloid Chemistry, now the Department of Physical Chemistry and Materials Science
- 2001-2007 Corresponding member of Hung. Acad. Sci.
- 2007 Full member of Hung. Acad. Sci

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Fellowships:

- 1977-78 DAAD fellowship, LMU, Inst f. Anorganische Chemie Universität München
- 1986-87 Humboldt fellowship, LMU, Inst f. Anorganische Chemie Universität München
- 1991 Forschungszentrum Jülich GmbH, Inst. f. Angew. Phys. Chem.
- 1994 Syracuse University, N.Y. USA, Department of Chemistry
- 1995 Humboldt fellowship, LMU, Inst. f. Anorganische Chemie Universität München
- 1998 Canon Foundation fellowship, Japan
- 1999 Humboldt fellowship, TU München, Inst. für. Technische Chemie

Research Interests

- Preparation and characterization of nanoparticles
- Colloid chemistry, interfacial phenomena
- Structure of solid/liquid interfaces, adsorption, wetting
- thermodynamics of interfaces

Selected Recent Publications

Szabo T, Tombacz E, Illes E, Dekany I Enhanced acidity and pH-dependent surface charge characterization of successively oxidized graphite oxides. CARBON 44: 537-545 2006

Hornok V, Dekany I. Synthesis and stabilization of Prussian blue nanoparticles and application for sensors. JOURNAL OF COLLOID AND INTERFACE SCIENCE 309(1):176-82 2007

Pal E, Hornok V, Oszko A, Dekany I Hydrothermal synthesis of prism-like and flower-like ZnO and indium-doped ZnO structures COLLOIDS AND SURFACES A-PHYSICOCHEMICAL AND ENGINEERING ASPECTS 340(1-3) 1-9 2009

Sebok D, Janovak L, Dekany I Optical, structural and adsorption properties of zinc peroxide/hydrogel nanohybrid films APPLIED SURFACE SCIENCE 256 (17) 5349-5354 2010

**Department of
Physiology, Anatomy
and Neuroscience**



JÓZSEF TOLDI

Professor of Physiology

- 1976 M.Sc. In Biology and Chemistry
- 1978 Doctor univ. degree in Physiology and Anatomy
- 1985 postgraduate student (Sussex University, Brighton, UK)
- 1986 Ph.D. degree (University of Szeged)
- 1985-1986 Department of Anatomy, Georg August Universitat, Göttingen, Germany.
- 1988 Department of Anatomy, Georg August Universitat, Göttingen, Germany.
- 1991-1996 Vice-Dean of the Faculty of Sciences, József Attila University, Szeged
- 1990, 1991 Guest professor (Department of Neurology, The Mount Sinai Medical School, New York, USA)
- 1995 D.Sc. (Hungarian Academy of Sciences)
- 1995 Habilitation (Physiology, Neurophysiology)
- 1996-present Head, Department of Physiology, Anatomy and Neuroscience
- 2009 Guest researcher, University of Kyushu, Fukuoka

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Major Research Interest

Neuroplasticity, Neurodegeneration, Neuroprotection
Mechanism of pathophysiological processes with focus on
neuroprotection with kynurenines
Glutamate scavenging as a tool for neuroprotection

Selected Recent Publication

Marosi M, Nagy D, Farkas T, Kis Z, Rózsa E, Robotka H, Fülöp F, Vécsei L, Toldi J. A novel kynurenic acid analogue: a comparison with kynurenic acid. An in vitro electrophysiological study. *J Neural Transm.* 2010, 117(2):183-8.

Nagy D, Marosi M, Kis Z, Farkas T, Rakos G, Vecsei L, Teichberg VI, Toldi J. Oxaloacetate decreases the infarct size and attenuates the reduction in evoked responses after photothrombotic focal ischemia in the rat cortex. *Cell Mol Neurobiol.* 2009, 29(6-7):827-35.

Sas K, Robotka H, Rózsa E, Agoston M, Szénási G, Gigler G, Marosi M, Kis Z, Farkas T, Vécsei L, Toldi J. Kynurenone diminishes the ischemia-induced histological and electrophysiological deficits in the rat hippocampus. *Neurobiol Dis.* 2008, 32(2):302-8.

TAMÁS FARKAS

Assistant Professor of Physiology

- 1994-1998 PhD student, Attila József University, Szeged
- 1996–1997 guest scientist, Georg-August-Universitat, Göttingen, Germany
- 1998-1999 postdoc fellow, Attila József University, Dept. of Comp. Physiol, Szeged
- 1999-2000 assistant lecturer, University of Szeged, Dept. of Comp. Physiol, Szeged
- 2000 guest scientist, Georg-August-Universitat, Göttingen, Germany
- 2000-2005 senior lecturer, University of Szeged, Dept. of Comp. Physiol, Szeged
- 2006 guest scientist, Karolinska Institutet, Stockholm, Sweden
- 2005- associate professor, University of Szeged, Dept. of Physiology, Anatomy and Neuroscience, Szeged

Major Research Interest

Neuroplasticity, neurodegeneration and neuroprotection in the CNS

Selected Recent Publication

Marosi M, Fuzik J, Nagy D, Rákos G, Kis Z, Vécsei L, Toldi J, Ruban-Matuzani A, Teichberg VI, Farkas T. Oxaloacetate restores the long-term potentiation impaired in rat hippocampus CA1 region by 2-vessel occlusion. *Eur J Pharmacol.* 2009; 604(1-3):51-7. Sas

K, Robotka H, Rózsa E, Agoston M, Szénási G, Gigler G, Marosi M, Kis Z, Farkas T, Vécsei L, Toldi J. Kynurenone diminishes the ischemia-induced histological and electrophysiological deficits in the rat hippocampus. *Neurobiol Dis.* 2008; 32(2):302-8.

Rozsa E, Robotka H, Nagy D, Farkas T, Sas K, Vecsei L, Toldi J. The pentylenetetrazole-induced activity in the hippocampus can be inhibited by the conversion of L-kynurenone to kynurenic acid: an in vitro study. *Brain Res Bull.* 2008; 76(5):474-9.

Füvesi J, Somlai C, Németh H, Varga H, Kis Z, Farkas T, Károly N, Dobcsay M, Penke Z, Penke B, Vécsei L, Toldi J. Comparative study on the effects of kynurenic acid and glucosamine-kynurenic acid. *Pharmacol Biochem Behav.* 2004; 77(1):95-102.

Marosi M, Nagy D, Farkas T, Kis Z, Rózsa E, Robotka H, Fülöp F, Vécsei L, Toldi J. A novel kynurenic acid analogue: a comparison with kynurenic acid. An in vitro electrophysiological study. *J Neural Transm.* 2010; 117(2):183-8.



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JÁNOS FUZIK

Biologist - PhD student

- 1998-2002 SZTE Ságvari Endre grammar school, Szeged
- University of Szeged - biologist (M.Sc.)
- (PhD) Department of Physiology, Anatomy and Neuroscience; University of Szeged

Major Research Interest

Synaptic plasticity, neurodegeneration and neuroprotection in the CNS

Selected Recent Publication

Marosi M, Fuzik J, Nagy D, Rákos G, Kis Z, Vécsei L, Toldi J, Ruban-Matuzani A, Teichberg VI, Farkas T. Oxaloacetate restores the long-term potentiation impaired in rat hippocampus CA1 region by 2-vessel occlusion. Eur J Pharmacol. 2009 Feb 14;604(1-3):51-7.

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LEVENTE GELLÉRT

Biologist - PhD Student

- 2002-2008. student, University of Szeged
- 2008- PhD student, Department of Physiology Anatomy and Neuroscience, University of Szeged
- 2009 Guest scientist, University of Kyushu, Fukuoka

Major Research Interest

Histological and behavioral studies in the field of global cerebral ischaemia and neuro-psychiatric disorders



Selected Recent Publication

Conference abstract:

Gellért L., Göblös A., Sárközi K., Kis Zs., Toldi J (2010)
Neuroprotective effect of the novel kynurene analogue SZR-72
in the four-vessel occlusion model in rats. International IBRO
Workshop, Pécs.

Scientific paper under submission:

„Neuroprotection with a new kynurenic acid analogue in the four-vessel occlusion stroke model”

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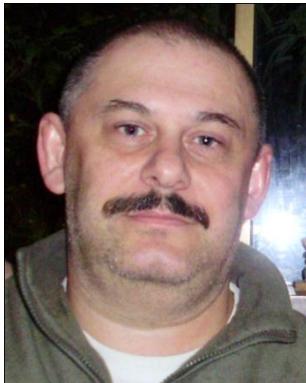
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ZSOLT KIS

Biologist - Senior Lecturer

- 1985-1989 Gyula Juhász Teacher Training School (BSc)
- 1989-1992 Attila József University of Sciences (MSc)
- 1998-2001 Attila József University of Sciences (PhD)
- 1999 Guest scientist, Institute of Anatomy, Georg August University, Göttingen
- 2000 Guest scientist, Institute of Anatomy, Georg August University, Göttingen
- 2006 Guest scientist, Institute of Neurobiology, Slovak Academy of Sciences, Kosice
- 2010 Guest scientist, University of Kyushu, Fukuoka

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Major Research Interest

Neuroplasticity and neuroprotection in the CNS

Selected Recent Publication

Marosi M, Nagy D, Farkas T, Kis Z, Rózsa E, Robotka H, Fülöp F, Vécsei L, Toldi J. A novel kynurenic acid analogue: a comparison with kynurenic acid. An in vitro electrophysiological study. *J Neural Transm.* 2010 Feb;117(2):183-8.

Nagy D, Marosi M, Kis Z, Farkas T, Rakos G, Vecsei L, Teichberg VI, Toldi J. Oxaloacetate decreases the infarct size and attenuates the reduction in evoked responses after photothrombotic focal ischemia in the rat cortex. *Cell Mol Neurobiol.* 2009 Sep;29(6-7):827-35..

Marosi M, Fuzik J, Nagy D, Rákós G, Kis Z, Vécsei L, Toldi J, Ruban-Matuzani A, Teichberg VI, Farkas T. Oxaloacetate restores the long-term potentiation impaired in rat hippocampus CA1 region by 2-vessel occlusion. *Eur J Pharmacol.* 2009 Feb 14;604(1-3):51-7

Sas K, Robotka H, Rózsa E, Agoston M, Szénási G, Gigler G, Marosi M, Kis Z, Farkas T, Vécsei L, Toldi J. Kynurenone diminishes the ischemia-induced histological and electrophysiological deficits in the rat hippocampus. *Neurobiol Dis.* 2008 Nov;32(2):302-8.

Rákós G, Kis Z, Nagy D, Lür G, Farkas T, Hortobágyi T, Vécsei L, Toldi J. Evans Blue fluorescence permits the rapid visualization of non-intact cells in the perilesional rim of cold-injured rat brain. *Acta Neurobiol Exp (Wars).* 2007;67(2):149-54.

MÁTÉ MAROSI

Biologist - Postdoctoral Fellow

- 1995-2001 Szent István Grammar School, Budapest
- University of Szeged - biologist (M.Sc.)
- 2006-2010 (PhD) Department of Physiology, Anatomy and Neuroscience; University of Szeged
- 2010 Guest scientist, Mario Negri Institute for Pharmacological Research, Italy Milan

Major Research Interest

Neuroplasticity, neurodegeneration and neuroprotection in the CNS



Selected Recent Publication

Marosi M, Nagy D, Farkas T, Kis Z, Rózsa E, Robotka H, Fülöp F, Vécsei L, Toldi J. A novel kynurenic acid analogue: a comparison with kynurenic acid. An in vitro electrophysiological study. *J Neural Transm.* 2010 Feb;117(2):183-8

Nagy D, Marosi M, Kis Z, Farkas T, Rakos G, Vecsei L, Teichberg VI, Toldi J. Oxaloacetate decreases the infarct size and attenuates the reduction in evoked responses after photothrombotic focal ischemia in the rat cortex. *Cell Mol Neurobiol.* 2009 Sep;29(6-7):827-35.

Marosi M, Fuzik J, Nagy D, Rákós G, Kis Z, Vécsei L, Toldi J, Ruban-Matuzani A, Teichberg VI, Farkas T. Oxaloacetate restores the long-term potentiation impaired in rat hippocampus CA1 region by 2-vessel occlusion. *Eur J Pharmacol.* 2009 Feb 14;604(1-3):51-7.

Sas K, Robotka H, Rózsa E, Agoston M, Szénási G, Gigler G, Marosi M, Kis Z, Farkas T, Vécsei L, Toldi J. Kynurenone diminishes the ischemia-induced histological and electrophysiological deficits in the rat hippocampus. *Neurobiol Dis.* 2008 Nov;32(2):302-8.

Nemeth H, Robotka H, Kis Z, Rozsa E, Janaky T, Somlai C, Marosi M, Farkas T, Toldi J, Vecsei L. Kynurenone administered together with probenecid markedly inhibits pentylenetetrazol-induced seizures. An electrophysiological and behavioural study. *Neuropharmacology* 47 (2004) 916–925.

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DÁVID NAGY

Biologist - PhD Student

- 2007 - PhD student – Department of Physiology,
- Anatomy and Neuroscience; University of Szeged
- Supervisor: Dr Tamás Farkas, Dr Kis Zsolt
- 2002-2007 University of Szeged – biologist (MSc)
- 1998-2002 Földes Ferenc Grammar School, Miskolc

Major Research Interest

Neuroplasticity and neuroprotection in the CNS

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Marosi M, Nagy D, Farkas T, Kis Z, Rózsa E, Robotka H, Fülöp F, Vécsei L, Toldi J. A novel kynurenic acid analogue: a comparison with kynurenic acid. An in vitro electrophysiological study. *J Neural Transm.* 2010 Feb;117(2):183-8.

Nagy D, Marosi M, Kis Z, Farkas T, Rakos G, Vecsei L, Teichberg VI, Toldi J. Oxaloacetate decreases the infarct size and attenuates the reduction in evoked responses after photothrombotic focal ischemia in the rat cortex. *Cell Mol Neurobiol.* 2009 Sep;29(6-7):827-35..

Marosi M, Fuzik J, Nagy D, Rákós G, Kis Z, Vécsei L, Toldi J, Ruban-Matuzani A, Teichberg VI, Farkas T. Oxaloacetate restores the long-term potentiation impaired in rat hippocampus CA1 region by 2-vessel occlusion. *Eur J Pharmacol.* 2009 Feb 14;604(1-3):51-7..

Rozsa E; Robotka H; Nagy D; Farkas T; Sas K; Vecsei L; Toldi J. The pentylenetetrazole-induced activity in the hippocampus can be inhibited by the conversion of L-kynurenine to kynurenic acid. An in vitro study. *Brain Research Bulletin* 2007; 76 (2008) 474–479.

Rákós G, Kis Z, Nagy D, Lür G, Farkas T, Hortobágyi T, Vécsei L, Toldi J. Evans Blue fluorescence permits the rapid visualization of non-intact cells in the perilesional rim of cold-injured rat brain. *Acta Neurobiol Exp (Wars).* 2007;67(2):149-54.

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Professor of Organic and Pharmaceutical Chemistry

- Ph.D.: Organic chemistry, József Attila University, Szeged, 1978
- D.Sc.: Organic chemistry, Hungarian Academy of Sciences, Budapest, 1990
- Corresponding Member of Hungarian Academy of Sciences, 2007
- 1979-1991: Teaching appointments (assistant, lecturer, reader) at the Institute of Pharmaceutical Chemistry, Albert Szent-Györgyi Medical University
- 1991-present: Full professor, Institute of Pharmaceutical Chemistry, Albert Szent-Györgyi Medical University
- 1998-present: Head of Institute of Pharmaceutical Chemistry, Albert Szent-Györgyi Medical University (From January 2000 Institute of Pharmaceutical Chemistry, University of Szeged)
- 2006-present: Dean of Faculty of Pharmacy

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Major research interest

Synthesis and stereochemistry of saturated heterocycles, nitrogen bridgehead compounds, cycloalkane-fused 1,3-heterocycles, ring-chain tautomerism, tetrahydroisoquinoline-fused 1,3-heterocycles, synthesis of potential drugs, enantioselective reactions, α -amino acids, enzyme reactions, combinatorial chemistry, drug discovery research.

Publications: 460 research publications; 18 review articles. Independent citations: ~3000, 18 drug patents

Selected Recent Publications

- I. M. Mándity, E. Wéber, T. A. Martinek, G. Olajos, G. K. Tóth, E. Vass, F. Fülöp:
Design of peptidic foldamer helices: a stereochemical patterning approach
Angew. Chem. Int. Ed., 48, 2171-2175 (2009)
- Á. Balázs, A. Hetényi, Z. Szakonyi, R. Sillanpää, F. Fülöp:
Solvent Enhanced Diastereo- and Regioselectivity in the Pd(II)-Catalyzed Synthesis
of Six- and Eight-Membered Heterocycles via cis-Aminopalladation
Chem. Eur. J., 15, 7376-7381 (2009)
- D. Zádori, P. Klivényi, E. Vámos, F. Fülöp, J. Toldi, L. Vécsei, L.:
Kynurenines in chronic neurodegenerative disorders: future therapeutic strategies
J. Neural Transm., 116, 1403-1409 (2009)
- K. A. Davis, S. E. Samson, L. Kiss, F. Fülöp, A. K. Grover
Functional linkage of Na⁺-Ca²⁺-exchanger to sarco/endoplasmic reticulum Ca²⁺-
pump in coronary artery: comparison of smooth muscle and endothelial cells
J. Cell. Mol. Med., 13, 1775-1783 (2009)
- E. Vámos, A. Fejes, J. Koch, J. Tajti, F. Fülöp, J. Toldi, Á. Párdutz, L. Vécsei:
Kynurene derivative attenuates the nitroglycerin-induced CamKIIα and CGRP
expression changes
Headache, 50, 834-843 (2010)
- E. Forró, F. Fülöp:
New enzymatic two-step cascade reaction for the preparation of a key intermediate
for the Taxol side-chain.
Eur. J. Org. Chem., 3074-3079 (2010)

ISTVÁN SZATMÁRI

Research Assistant

- 1998 Graduation (Chemistry-Physic), University of Cluj-Napoca
- 2000 (3 months, DAAD grant), 2001 (4 months, DFG grant)
Guest PhD Student, Faculty of Structure Analysis and NMR spectroscopy, University of Potsdam, Germany
- 2004 PhD, Institute of Pharmaceutical Chemistry, University of Szeged
- 2004-present Research Assistant, Institute of Pharmaceutical Chemistry, University of Szeged
- 2006 (3 months, DFG grant) Guest Scientist, Faculty of Structure Analysis and NMR spectroscopy, University of Potsdam, Germany



Major Research Interests

Synthesis, transformations and conformational analysis of naphthalene-condensed heterocycles

Synthesis of chiral ligands and their applications in different modelreactions

Synthesis and transformations of kynurenic acid analogs

Selected Recent Publications

Szatmári, I.; Martinek, T. A.; Lázár, L.; Fülöp, F. Substituent effects in the ring-chain tautomerism of 1,3-diaryl-2,3-dihydro-1H-naphth[1,2-e][1,3]oxazines. *Tetrahedron* 2003, 59, 2877-2884.

Szatmári, I.; Martinek, T. A.; Lázár, L.; Koch, A.; Kleinpeter, E.; Neuvonen, K.; Fülöp, F. Stereoelectronic effect in the ring-chain tautomerism of 1,3-diaryl-2,3-dihydro-1H-naphth[1,2-e][1,3]oxazines and 3-alkyl-1-aryl-2,3-dihydro-1H-naphth[1,2-e][1,3]oxazines. *J. Org. Chem.* 2004, 69, 3645-3653.

Szatmári, I.; Sillanpää, R.; Fülöp, F. Microwave-assisted, highly enantioselective addition of diethylzinc to aromatic aldehydes catalysed by chiral aminonaphthols *Tetrahedron: Asymmetry* 2008, 19, 612-617.

Knyihár-Csillik, E.; Mihály, A.; Krisztin-Peva, B.; Robotka, H.; Szatmári, I.; Fülöp, F.; Toldi, J.; Csillik, B.; Vécsei, L. The kynurene analog SZR-72 prevents the nitroglycerol-induced increase of c-fos immunoreactivity in the rat caudal trigeminal nucleus: Comparative studies of the effects of SZR-72 and kynurenic acid *Neuroscience Research* 2008, 61, 429-432..

Fülöp, F.; Szatmári, I.; Vámos, E.; Zádori, D.; Toldi, J.; Vécs, L. Syntheses, Transformations and Pharmaceutical Applications of Kynurenic Acid Derivatives *Curr. Med. Chem.* 2009, 16, 4828-4842.

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Institute of Surgical Research



MIHÁLY BOROS

Professor of Institute of Surgical Research

- 1983-1987: City Hospital, Hódmezővásárhely, Surgical Department, general surgeon
- 1996: Habilitation (Dr. Habil., University of Szeged)
- 1988-1997: Szent-Györgyi Albert Medical University, Institute of Experimental Surgery, Szeged, Circulation Research Laboratory, associate professor
- 1992-1994: Osaka, Japan, National Cardiovascular Center Research Institute (Science and Technology Agency (STA) Fellowship)
- 1995-1996: München, Germany, LMU, Institute für Chirurgische Forschung (Alexander von Humboldt Fellowship)
- 1997: Associate Professor, Acting Director
- 1998- : University of Szeged, School of Medicine, Institute of Surgical Research, professor, head of department
- 2003: D.Sc. (Doctorate of the Hungarian Academy of Sciences)
- 2003-2005: Secretary General, European Society for Surgical Research (President 2005-2006)

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Major Research Interests

experimental surgery
microcirculation
circulation research
vasoregulation, vasoactive mediators
sepsis,
ischaemia-reperfusion syndromes
shock

Selected Recent Publications

Ghyczy M, Torday C, Kaszaki J, Szabó A, Czobél M, Boros M. Hypoxia-induced generation of methane in mitochondria and eukaryotic cells: an alternative approach to methanogenesis. *Cell Physiol Biochem.* 2008; 21(1-3):251-258.

Varga G, Érces D, Fazekas B, Fülop M, Kovács T, Kaszaki J, Fülop F, Vécsei L, Boros M: N-Methyl-D-aspartate receptor antagonism decreases motility and inflammatory activation in the early phase of acute experimental colitis in the rat. *Neurogastroenterol Motil.* 2010; 22(2): 217-25.

Kaszaki J, Paláthy Z, Erczes D, Rácz A, Torday C, Varga G, Vécsei L, Boros M. Kynurenic acid inhibits intestinal hypermotility and xanthine oxidase activity during experimental colon obstruction in dogs. *Neurogastroenterol Motil.* 2008 20(1): 53-62.

Varga R, Török L, Szabó A, Kovács F, Keresztes M, Varga G, Kaszaki J, Boros M. Effects of colloid solutions on ischemia-reperfusion-induced periosteal microcirculatory and inflammatory reactions: comparison of dextran, gelatin, and hydroxyethyl starch. *Crit Care Med* 2008; 36(10):2828-2837.

Erös G, Ibrahim S, Siebert N, Boros M, Vollmar B: Oral phosphatidylcholine pretreatment alleviates the signs of experimental rheumatoid arthritis. *Arthritis Research & Therapy* 2009, 11:R43

Hartmann P, Szabó A, Erös G, Gurabi D, Horváth G, Németh I, Ghyczy M, Boros M. Anti-inflammatory effects of phosphatidylcholine in neutrophil leukocyte-dependent acute arthritis in rats. *Eur J Pharmacol* 2009; 622(1-3):58-64.

DÁNIEL ÉRCES

M.D. - Ph.D. Student of Institute of Surgical Research

- 2006 English-Hungarian Medical Translator
- 2007 Medical Doctor
- 2007- present Ph.D. Student

Major Research Interests

experimental surgery
microcirculation
circulation research
vasoregulation, vasoactive mediators
sepsis
ischaemia-reperfusion syndromes
shock



Selected Recent Publications

Varga G, Érces D, Fazekas B, Fülöp M, Kovács T, Kaszaki J, Fülöp F, Vécsei L, Boros M: N-Methyl-D-aspartate receptor antagonism decreases motility and inflammatory activation in the early phase of acute experimental colitis in the rat. *Neurogastroenterol Motil.* 2010; 22(2): 217-25.

Kaszaki J, Paláthy Z, Érces D, Rácz A, Torday C, Varga G, Vécsei L, Boros M. Kynurenic acid inhibits intestinal hypermotility and xanthine oxidase activity during experimental colon obstruction in dogs. *Neurogastroenterol Motil.* 2008; 20(1): 53-62.

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BORBÁLA FAZEKAS

M.D. - PhD Student

- 2005 Course in Basic microsurgical techniques, University of Szeged, Institute of Surgical Research
- 2005-2008 Enrolled in a study on NMDA receptor antagonism in an experimental colitis model
- 2007 Graduation (English-Hungarian Medical Translator), University of Szeged
- 2008 Graduation (Medicine), University of Szeged
- 2008 – present PhD Student, University of Szeged, Institute of Surgical Research

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Major Research Interests

experimental surgery
microcirculation
circulation research
ischaemia-reperfusion syndromes
free radical research

Selected Recent Publications

Varga G, Érces D, Fazekas B, Fülöp M, Kovács T, Kaszaki J, Fülöp F, Vécsei L, Boros M: N-Methyl-D-aspartate receptor antagonism decreases motility and inflammatory activation in the early phase of acute experimental colitis in the rat. *Neurogastroenterol Motil.* 2010; 22(2): 217-25.

JÓZSEF KASZAKI

Associate Professor of Institute of Surgical Research

- 1982-1998: assistant professor at the Institute of Surgical Research, Szent-Györgyi Albert Medical University, Szeged, Hungary;
- 1990: Dr. univ degree at the Institute of Experimental Surgery of the Szent-Györgyi Albert Medical University;
- 1998: Ph. D. Szent-Györgyi Albert Medical University
- 1999-2006: senior assistant professor at the Institute of Surgical Research, University of Szeged
- 2001-2004: György Békésy Postdoctorial Scholarship
- 2005: Habilitation (Dr. Habil., University of Szeged)
- 2006 - associate professor at the Institute of Surgical Research, University of Szeged



Major Research Interests

experimental surgery
microcirculation
circulation research
vasoregulation, vasoactive mediators
sepsis,
ischaemia-reperfusion syndromes
shock

Selected Recent Publications

Varga G, Érces D, Fazekas B, Fülöp M, Kovács T, Kaszaki J, Fülöp F, Vécsei L, Boros M: N-Methyl-D-aspartate receptor antagonism decreases motility and inflammatory activation in the early phase of acute experimental colitis in the rat. *Neurogastroenterol Motil.* 2010; 22(2): 217-25.

Czóbel M, Kaszaki J, Molnár G, Nagy S, Boros M: Nonspecific inhibition of nitric oxide synthesis evokes endothelin-dependent increases in myocardial contractility. *Nitric Oxide Biol Chem* 2009; 21: 201-209.

Kaszaki J, Palásthy Z, Erczes D, Rácz A, Torday C, Varga G, Vécsei L, Boros M. Kynurenic acid inhibits intestinal hypermotility and xanthine oxidase activity during experimental colon obstruction in dogs. *Neurogastroenterol Motil.* 2008 20(1): 53-62.

Ghyczy M, Torday C, Kaszaki J, Szabó A, Czóbel M, Boros M. Hypoxia-induced generation of methane in mitochondria and eukaryotic cells: an alternative approach to methanogenesis. *Cell Physiol Biochem.* 2008; 21(1-3):251-258.

Varga R, Török L, Szabó A, Kovács F, Keresztes M, Varga G, Kaszaki J, Boros M. Effects of colloid solutions on ischemia-reperfusion-induced periosteal microcirculatory and inflammatory reactions: comparison of dextran, gelatin, and hydroxyethyl starch. *Crit Care Med* 2008; 36(10):2828-2837.

Kaszaki J, Wolfárd A, Szalay L, Boros M: Pathophysiology of ischemia-reperfusion injury. *Transplant Proc* 2006; 38: 826-828.

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GABRIELLA VARGA

Biologist - Institute of Surgical Research

- 1994-: Szent-Györgyi Albert Medical University, Institute of Experimental Surgery, Szeged, Immunological Research Laboratory, biologist
- 2005- : University of Szeged, School of Medicine, Institute of Surgical Research, Circulation Research Laboratory, biologist

Major Research Interests

experimental surgery
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circulation research
vasoregulation, vasoactive mediators
ischaemia-reperfusion syndromes

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Selected Recent Publications

Varga G, Érces D, Fazekas B, Fülöp M, Kovács T, Kaszaki J, Fülöp F, Vécsei L, Boros M: N-Methyl-D-aspartate receptor antagonism decreases motility and inflammatory activation in the early phase of acute experimental colitis in the rat. *Neurogastroenterol Motil.* 2010; 22(2): 217-25.

Erős G., Varga G., Váradi R., Czóbel M., Kaszaki J., Ghyczy M., Boros M.: Anti-inflammatory action of a phosphatidylcholine, phosphatidylethanolamine and N-acyl phosphatidylethanolamine-enriched diet in carrageenan-induced pleurisy. *Eur. J. Surg. Res.*: 42(1):40-48, 2009. IF: 1,327

Kaszaki J, Palásthy Z, Erczes D, Rácz A, Torday C, Varga G, Vécsei L, Boros M. Kynurenic acid inhibits intestinal hypermotility and xanthine oxidase activity during experimental colon obstruction in dogs. *Neurogastroenterol Motil.* 2008 20(1): 53-62.

Varga R, Török L, Szabó A, Kovács F, Keresztes M, Varga G, Kaszaki J, Boros M. Effects of colloid solutions on ischemia-reperfusion-induced periosteal microcirculatory and inflammatory reactions: comparison of dextran, gelatin, and hydroxyethyl starch. *Crit Care Med* 2008; 36(10):2828-2837.

Medical Microbiology and Immunology



YVETTE MÁNDI

Professor and Head of Medical Microbiology and Immunology

- 1971 Graduation (Medicine) Medical University of Szeged
- 1971-2000 Department of Medical Microbiology
- Lecturer, Assistant Professor, Docent
- 1987 Ph.D. of Medical Sciences
- 1996 Habilitation (Medical Microbiology)
- 1997. D.Sc.
- 2000 Professor
- 2001- present Head of the Department

Fellowships

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Major Research Interest

1. The role of innate immune response in multifactorial diseases with focus on defensins and cytokines
2. Genetic polymorphisms in gastrointestinal and neurological diseases

Selected Recent Publications:

Hofner, P., Balog, A., Gyulai, Z., Farkas, G., Rakonczay, Z., Takács, T., Mándi, Y.: Polymorphism in the IL-8 gene, but not in the TLR4 gene, increases the severity of acute pancreatitis. *Pancreatology* 6: 542-548, 2006.

Hofner, P., Gyulai, Zs., F. Kiss, Zs., Tiszai, A., Tiszlavicz, L., Tóth, G., Szőke, D., Molnár, B., Lonovics, J., Tulassay, Zs., Mándi, Y.: Genetic polymorphisms of NOD1 and IL-8, but not polymorphisms of TLR4 genes, are associated with Helicobacter pylori-induced duodenal ulcer and gastritis. *Helicobacter* 12: 124-131, 2007.

Kocsis, Á.K., Lakatos, P.L., Somogyvári, F., Fuszek, P., Papp, J., Fischer, S., Szamosi, T., Lakatos, L., Kovács, Á., Hofner, P., Mándi, Y.: Association of beta-defensin 1 single nucleotide polymorphisms with Crohn's disease. *Scand. J. Gastroenterol.* 43: 299-307, 2008.

Kocsis Á.K., Szabolcs A., Hofner P., Takács T., Farkas G., Boda K., Mándi Y.: Plasma concentrations of high-mobility group box protein 1, soluble receptor fpr advanced glycation end-products and circulating DNA in patients with acute pancreatitis. *Pancreatology* 9:383-91 2009;

Tiszlavicz Z, Gyulai Z, Bencsik K, Szolnoki Z, Kocsis AK, Somogyvári F, Vécsei L, Mándi Y. RAGE gene polymorphisms in patients with multiple sclerosis. *J Mol Neurosci.* 39:360-363. 2009;

Tiszlavicz Z, Somogyvári F, Kocsis AK, Szolnoki Z, Sztriha LK, Kis Z, Vécsei L, Mándi Y. Relevance of the genetic polymorphism of NOD1 in Chlamydia pneumoniae seropositive stroke patients. *Eur J Neurol.* 11:1224-92009

ZOLTÁN LÁSZLÓ TISZLAVICZ

M.D. - PhD student

- 2008 Graduation (Medicine) University of Szeged

Fellowship

Department of Molecular and Cell Biology, Boston University,
Boston, MA, USA (2009)

Major research interest

1. The role of innate immune response in multifactorial diseases with focus on defensins and cytokines
2. Genetic polymorphisms in gastrointestinal and neurological diseases

Publications

Tiszlavicz Z, Szabolcs A, Takács T, Farkas Gy, Kovács-Nagy R, Szántai E, Sasvári-Székely M, Mándi Y. : Relevance of genetic polymorphisms of beta - defensins in severe acute pancreatitis [Pancreatology in press]

Tiszlavicz Z, Gyulai Z, Bencsik K, Szolnoki Z, Kocsis AK, Somogyvári F, Vécsei L, Mándi Y. : RAGE gene polymorphisms in patients with multiple sclerosis. J Mol Neurosci. 39(3):360-5. 2009;

Tiszlavicz Z, Somogyvári F, Kocsis AK, Szolnoki Z, Sztriha LK, Kis Z, Vécsei L, Mándi Y.: Relevance of the genetic polymorphism of NOD1 in Chlamydia pneumoniae seropositive stroke patients. Eur J Neurol.;16(11):1224-9. 2009;

Kocsis AK, Ocsovszky I, Tiszlavicz L, Tiszlavicz Z, Mándi Y.: Helicobacter pylori induces the release of alpha-defensin by human granulocytes. Inflamm Res. 58(5):241-7. 2009;

Kocsis AK, Kiss ZF, Tiszlavicz L, Tiszlavicz Z, Mándi Y. : Potential role of human beta-defensin 1 in Helicobacter pylori-induced gastritis. Scand J Gastroenterol. 44(3):289-95. 2009;



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Tryptophane

Tryptophane dioxygenase
Indoleamine 2,3-dioxygenase



Formyl-kynurenone

Formamidase



**L-kynurenone
(L-KYN)**

*Kynurenine
aminotransferase*

**Kynurenic acid
(KYNA)**

Kynureninase

kynurenone 3-hydroxylase

Anthranilic acid

**3-hydroxykynurenone
(3-HK)**

*Kynurenine
aminotransferase*

Xanthurenic acid

Kynureninase

3-hydroxyanthranilic acid

*3-hydroxyanthranilic acid
oxygenase*



**Quinolinic acid
(QUIN)**

*Quinolinic acid
phosphoribosyl-
transferase*



NAD⁺