

MILESTONES

From acetylcholinesterase of motor end plates to the chemoanatomy of the thalamic reticular nucleus: celebrating the 80th birthday of Professor Bertalan Csillik

András Mihály

Department of Anatomy, Faculty of Medicine, University of Szeged, Szeged, Hungary

It was 86 years ago, when the Szeged Department of Anatomy was established in the building at Kossuth Lajos Avenue No. 40. First director-professors of the Department were: Dr. Leo Davida, Dr. Jenő Davida, Dr. Ferenc Kiss, Dr. Albert Gellért. The fifth professor of the Szeged Department of Anatomy, Bertalan Csillik celebrated his 80th birthday in November 2007. We organized a scientific meeting in the Faculty of Medicine, to celebrate him. Previously, when he was 75, we also greeted him with scientific lectures. The past 5 years brought development in the Department of Anatomy, and this development (new colleagues, PhD achievements) has been witnessed by Professor Csillik. He was really glad, seeing that neurohistochemistry (nowadays mainly immunohistochemistry) is still a decisive held in the Department, and the scientific results based on this methodology are excellent, and publishable in good international journals, all over the world. One of his famous mottos was: "publish or perish". He was living according to this motto, and always stimulated his colleagues to publish the scientific results. The number of his publications is almost 300, amongst them 5 books, and 15 university handouts (all of them very popular amongst the students). He stimulated a number of talented young scientists (e.g.: Ferenc Joó, Péter Kása, Elizabeth Knyihár, Lajos Tóth and the author of this paper), who grew up in the Szeged Anatomy Department and became internationally acknowledged researchers and university teachers. He was chairman of the Department for 25 years, and during this quarter of a century he reshaped the Anatomy Institute, reshaped the way of anatomy teaching and renewed the research conducted there. His main scientific discoveries were as follows:

The exact description of acetylcholinesterase activity and localization in motor endplates - including the developmental aspects.

The detailed neuroanatomical description of the localization of fluoride-resistant acid phosphatase (FRAP) in the dorsal horn of the spinal cord and the spinal trigeminal nucleus.

The plasticity of the primary nociceptive neuron following peripheral nerve transection: transganglionic degenerative atrophy (TDA), which is a transient disconnection of the synapses in the dorsal horn, followed by complete structural and functional restitution, *i.e.* regeneration in the central nervous system (CNS). The TDA and the following CNS regeneration are entirely new discoveries, listed in the Encyclopedia of Neuroscience.

The exact chemoanatomy and morphology of large calyciform nerve endings in the thalamic reticular nucleus - this is a discovery of the past ten years, as indicated in the publication list.

We tried to summarize (it was not easy) the decisive events of the 58 years' long scientific carrier of Professor Csillik

January 2, 1949. Enters the Anatomy Department as a student instructor (demonstrator). Preparation of human anatomy specimens for the Anatomy Museum. First steps in histotechnology and histochemistry.

1951. Sabbatical at Prof. J. Szentágothai's Department of Anatomy; learning histotechnology of silver impregnation of the nervous system and the methods for detection of axon degeneration.

1954. Diploma (MD), becomes a general practitioner and gets a position (teaching and research assistant) in the Department of Anatomy of the Szeged Medical University.

1954. First paper on the acetylcholinesterase reaction of motor end plates (presented on the Annual Meeting of the Hungarian Physiological Society).

1957: Sabbatical at Prof. G. Romhányi's Department of Pathology (Pécs): learning the basics of polarization microscopical analysis. Assistant Professor at the Szeged Department of Anatomy.

1958. First paper on degeneration and regeneration of the acetylcholinesterase-active subneural apparatus of the motor end plate, together with simultaneous protargol (silver) impregnation of nerve fibers (Acta Neurovegetativa).

1959. First papers on the submicroscopic organization of

Accepted Oct 12, 2007

Corresponding author. E-mail: mihaly@anatomy.szote.u-szeged.hu



The staff of the Department of Anatomy in 1969, one year after the promotion of Professor Csillik, as the chairman of the Institute.



Professor Csillik, the emeritus professor of the Anatomy Department in 2004, together with the staff of the Institute, under the chairmanship of Professor András Mihály.

the post-synaptic membrane in the neuromuscular junction and structural demonstration of its molecular alterations in the course of impulse transmission (Nature, Ann. Histochem., J. Cell Biol.).

1961. Sabbatical at the Department of Anatomy, Soha, Bulgaria, in the laboratory of Prof. D. Kadanoff, who was the discoverer of numerous (encapsulated) sensory nerve endings.

1962. PhD ("Candidate") of Medical Sciences (Hungarian Academy of Sciences, Budapest).

1962-1963. Sabbatical at the Department of Pharmacology of University of Pennsylvania, Philadelphia, PA, USA, on invitation by Prof. G. B. Koelle, inventor of the acetylthiocholine method for the histochemical detection of acetylcholinesterase.

1964. Associate Professor in the Department of Anatomy, of Yale University, New Haven, USA, Szeged.

1964. Sabbatical at the Department of Anatomy, Université de Liege, Belgium, on invitation by Prof. M. A. Gerebtzoff, discoverer of fluoride-resistant acid phosphatase.

1965. Publication of the book "The Post-Synaptic Membrane". (Second edition: 1967).

1966. Electron microscopic demonstration of acetylcholinesterase activity in motor end plates (Acta Histochemica).

1968. DSc degree (Doctor of the Hungarian Academy of Sciences, Budapest).

1968. Professor and Chairman of the Anatomy Department, Szeged.

1969-1970. Discovery of the approach of localizing of various enzymes involved in impulse transmission, by locating their specific enzyme inhibitors (with E. Knyihâr: Nature, J. Histochem. Cytochem.).

1972-1973. Sabbatical at the Neuroscience Research Program, Boston, MA, USA, in the laboratory of F.O. Schmitt, discoverer of the laminated structure of the myelin sheath.

1975-1978. Discovery of the law of transganglionic degenerative atrophy and regenerative proliferation: biodynamic plasticity of central terminals of sensory neurons, resulting from the blockade of axoplasmic transport of nerve growth factor in the peripheral sensory nerve (with E. Knyihâr, in Exp. Brain Res., Z. mikr-anat. Forsch., Experientia, Progr. Neurobiol., Res. Comm. Chem. Path. Pharm.).

1977-1978. Sabbatical at the Department of Neurobiology, Harvard Medical School, Boston, MA, USA, on invitation by Prof. Pasko Rakic, discoverer of the leading role of radial glia in the migration of neuroblasts. Discovery of transient synapses in the developing spinal cord (Science).

1981. Discovery of the role of fluoride resistant acid phosphatase (FRAP) in nociception (Progr. Histochem. Cytochem.).

1982. Discovery of chronic pain treatment via transganglionic degenerative atrophy evoked by transcutaneous iontophoresis of *Vinca* alkaloids, with E. Knyihar and A. Szücs

(Neurosci. Lett., J. Neurosci. Res., J. Comp. Neurol., Acta Neurol. Scand., Histochemistry, Recent Results in Cancer Research, Cell Tiss. Res., etc...).

1985. Starting lectures and practicaís of Anatomy, Histology and Embryology in English language at the Albert Szent-Györgyi University Medical School.

1982- 1992. Successful treatment with *Vinca* iontophoresis of 923 chronic pain patients in the Pain Clinic of the Albert Szent-Györgyi University Medical School.

1983- 1993. Discovery of the role of calcium channels in the neuromuscular junction (Histochemistry, J. Himforsch., Ann. New York Acad. Sci. USA, Intemat. Rev. Cytology, etc...).

1992-1995. Fogarty Senior Fellow, commissioned by the National Institute of Health, USA, in the Dept. Neurobiology

of Yale University, New Haven, USA.

1993. Retirement as Chairman of the Anatomy Department; appointment as Professor of Anatomy at the Harvard University Medical School, Boston, MA, USA and simultaneous promotion to the post of Project Director in the Bay Zoltán Institute of Biotechnology, Szeged.

1994-1999. Publication of the results of the research performed at Yale University, USA.

1999. Returning to the Department of Anatomy as a teaching Emeritus Professor, and giving regular anatomy lectures in German language.

2001. Organizing a new research laboratory in the Department of Anatomy, as an Emeritus Professor of Neuroanatomy.

2002. Discovery of large, calyciform parvalbumin-containing axo-somatic synapses in the reticular nucleus of the rat thalamus (Acta Biol. Hung., Acta Physiol. Hung.).

2005. Discovery of coexistence of GABA and calcium-binding proteins in large, calyciform presynaptic complexes in the reticular nucleus of the rat thalamus (J. Chem. Neuroanatomy, Neuroreport).

2006-2007. Discovery of neogenesis of oncomodulin-immunoreactive regenerating axons in parvalbumin-knockout, young adult animals (Acta Physiol. Hung., IBRO-Congress), in collaboration with Prof. Schwaller, Fribourg, Switzerland.

At present, Professor Csillik is an active member of the teaching- and research staff of the Anatomy Department. He is giving lectures in German, and works on his own scientific project in connection with the thalamic reticular nucleus. We, young and elderly members of the Anatomy Institute, wish him a good health and success in his work, for the benefit of the Department and Szeged University.

Publications of Professor Bertalan Csillik in the past ten years (1998-2007)

Csillik B., Rakic P, Knyihâr-Csillik E.: Peptidergic innervation and the nicotinic acetylcholine receptor in the primate

- basal nucleus. *Eur. J. Neurosci.* 10: 573-85 (1998)
- Csillik B.: István Apáthy and neurofibrils. *Orv. Hetil.* 139:1917-9(1998)
- Csillik B., Nemcsók J., Boncz I., Knyihár-Csillik E.: Nitric oxide synthase and the acetylcholine receptor in the prefrontal cortex: metasyntaptic organization of the brain. *Neurobiology* 6: 383-404 (1998)
- Knyihár-Csillik E., Vécsei L., Goldman-Rakic PS, Csillik B.: Columnar organization of nitric synthase (NOS) in the prefrontal cortex of primates. *Neurobiology* 7: 479-80 (1999)
- Knyihár-Csillik E., Rakic P., Csillik B.: Development of glomerular synaptic complexes and immunohistochemical differentiation in the superficial dorsal horn of the embryonic primate spinal cord. *Anat. Embryol.* 199: 125-128 (1999)
- Knyihár-Csillik E., Rakic P., Csillik B.: Illusive transience of parvalbumin expression during embryonic development of the primate spinal cord. *Int. J. Dev. Neuroscience.* 17: 79-97 (1999)
- Csillik B., Nemcsók J., Chase B., Csillik A. E., Knyihár-Csillik E.: Infraterminal spreading and extrajunctional expression of nicotinic acetylcholine receptors in denervated rat skeletal muscle. *Exp. Brain. Res.* 125: 426-434 (1999)
- Knyihár-Csillik E., Boncz I., Sárosi G., Nemcsók J., Csillik B.: Parabrachial origin of calcitonin gene-related peptide-immunoreactive axons innervating Meynert's basal nucleus. *Exp. Neurol.* 157: 268-76 (1999)
- Csillik B., Knyihár-Csillik E.: Degeneration. In: *Encyclopedia of Neuroscience* (Adelman G., Smith B.H., editors). Elsevier, 1999, pp 523-528 (könyvfejezet)
- Csillik B., Fazekas J, Nemcsók J, Knyihár-Csillik E.: Effect of the pesticide Deltamethrin on the Mauthner cells of Lake Balaton fish. *Neurotoxicology* 21: 343-52 (2000)
- Csillik B., Kálmán, J., Boncz, I., Knyihár, E., Janka, Z.: Nociception, the c-jun system and the Nerve Growth Factor. *Annals of Anatomy, Suppl.* 183: 35 (2001)
- Csillik, AE., Csillik, B., Okuno, E., Vécsei, L., Knyihár, E.: Kynurenine aminotransferase and NMDA receptors in the subplate. *Annals of Anatomy, Suppl.* 183: 34-35 (2001)
- Knyihár-Csillik, E., Tajti, J., Chadaide, Z., Csillik, B., Vécsei, L.: Functional immunohistochemistry of neuropeptides and nitric oxide synthase in the nerve fibers of the supratentorial dura mater in an experimental migraine model. *Microsc. Res. Tech.* 53: 193-211 (2001)
- Samsam, M., Covenas, R., Csillik, B., Ahangari, R., Yajeva, J., Riquelme, R., Narvaez, JA., Tramu, G.: Depletion of substance P, neurokinin A and calcitonin gene-related peptide from the contralateral and ipsilateral caudal trigeminal nucleus following unilateral electrical stimulation of the trigeminal ganglion: a possible neurophysiological and neuroanatomical link to generalized head pain. *J. Chem. Neuroanat.* 31: 161-169 (2001)
- Behrends, S., Knyihár-Csillik, E., Kempfert, J., Scholz, H., Csillik, B., Vécsei, L.: Glyceryl trinitrate treatment up-regulates soluble guanylyl cyclase in rat dura mater. *Neuroreport* 12: 3993-3996 (2001)
- Csillik, AE., Knyihár, E., Okuno, E., Csillik Bertalan, Vécsei, L.: Expression of kynurenine aminotransferase in the subplate of the rat: its possible role in the regulation of programmed cell death. *Cereb. Cortex.* 12: 1193-1201 (2002)
- Csillik Bertalan, Pálfi, A., Gulya, K., Mihály András, Knyihár-Csillik, E.: Somato-dendritic synapses in the nucleus reticularis thalami of the rat. *Acta Biol. Hung.* 53: 33-41. (2002)
- Csillik Bertalan, Pálfi, A., Gulya, K., Samsam, M., Mihály András, Vécsei, L., Knyihár-Csillik, E.: Parvalbumin immunoreactive large presynaptic complexes in the reticular nucleus of the rat. *Acta Physiol Hung.* 89: 12 (2002)
- Csillik Bertalan.: A nociceptio strukturális vonatkozásai. *Fájdalom-Pain.* 3: 4-13 (2002)
- Csillik, AE., Knyihár, E., Okuno, E., Krisztin-Péva Beáta, Csillik Bertalan, Vécsei, L.: Effect of 3-nitropropionic acid on kynurenine aminotransferase in the rat brain. *Exp. Neurol.* 177: 233-244 (2002)
- Bertalan Csillik, Z. Janka, I. Boncz, J. Kálmán, András Mihály, L. Vécsei, E. Knyihár: Molecular plasticity of primary nociceptive neurons: relations of the NGF-c-jun system to neurotomy and chronic pain. *Ann. Anat.* 185: 303-314 (2003)
- Andrea Czigler, M. Samsam, Á. Pálfi, K. Gulya, András Mihály, L. Vécsei, E. Knyihár-Csillik, Csillik, B.: Large calcyform presynaptic complexes in the reticular nucleus of the rat thalamus expressing parvalbumin immunoreactivity. *Clinical Neuroscience/Idegy. Szle;* 56 (2) (2003)
- Csillik, B., Mihály, A., Knyihár-Csillik, E.: Cytochemi-

- cal correlates of the sleep-wake interface: concerted expression of brain-derived nitric oxide synthase (bNOS) and the nicotinic acetylcholine receptor (nAChR) in a columnoid organization of the primate prefrontal cortex. *Ann. Anat.* 186: 217-21 (2004)
- Knyihár-Csillik E., Chadaide Z., Okuno E., Krisztin-Péva B., Toldi J., Varga Cs., Molnár A., Csillik B., Vécsei L.: Kynurenine aminotransferase in the supratentorial dura mater of the rat: effect of stimulation of the trigeminal ganglion. *Exp. Neurol.* 186: 242-47 (2004)
- Knyihár-Csillik E., Csillik B., Pakáski M., Krisztin-Péva B., Dobó E., Okuno E., Vécsei L.: Decreased expression of kynurenine aminotransferase-I (KAT-I) in the substantia nigra of mice after 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) treatment. *Neuroscience* 126: 899-914 (2004)
- Csillik, B., Mihály, A., Gulya, K., Samsam, M.: Parvalbumin-immunoreactive calyciform presynaptic complexes in the thalamic reticular nucleus. *Ann. Anat. Suppl.* 186: 40 (2004)
- Csillik, B., Rakic, P., Sáry, G., Vécsei, L., Knyihár-Csillik, E.: Cholinergic amplification and calcitonin gene-related peptide in the maintenance of Meynert's basal nucleus. *Clinical Neuroscience (Ideggyógyászati szemle)* 57: 324 (2004)
- Csillik, B., Chadaide, Z., Samsam, M., Knyihár-Csillik, E.: Calcium binding proteins in the reticular nucleus of the thalamus. *Acta Physiol. Hung.* 91: 283-84 (2004)
- Knyihár-Csillik E, Chadaide Z, Mihály András, Krisztin-Péva Beáta, Csillik Bertalan: Effect of electrical stimulation of the reticular nucleus of the rat thalamus upon c-fos immunoreactivity in the retrosplenial cortex. *Ann. Anat.* 187: 245-9 (2005)
- Csillik Bertalan, Mihály András, Krisztin-Péva Beáta, Chadaide Z, Samsam M, Knyihár-Csillik E, Fenyő Róbert: GABAergic parvalbumin-immunoreactive large calyciform presynaptic complexes in the reticular nucleus of the rat thalamus. *J Chem. Neuroanat.* 30: 17-26 (2005)
- Csillik Bertalan, Mihály András, Krisztin-Péva Beáta, Fenyő Róbert, Knyihár-Csillik, E.: Calcium-binding proteins in GABAergic calyciform synapses of the reticular nucleus. *Neuroreport* 17: 575-578 (2006)
- Knyihár, E., Csillik Bertalan: Plasticity of nociception: recent advances in function-oriented structural pain research. *Clinical Neuroscience* 59: 87-97 (2006)
- Csillik Bertalan, Fenyő Róbert, Mihály András, Chadaide, Z., Vécsei, L., Schwaller, B., Knyihár-Csillik, E.: Functional structure of GABAergic large calyciform synapses in the reticular nucleus of the thalamus. *Acta. Physiol. Hung.* 93: 163-164 (2006)
- Knyihár-Csillik E, Vécsei L, Mihály A, Fenyő R, Farkas I, Krisztin-Péva B, Csillik B.: Effect of vinpocetine on retrograde axoplasmic transport. *Ann. Anat.* 189: 39-45 (2007).