

**BIOGRAPHICAL SKETCH**

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NAME: András Büki, MD., Ph.D., D.Sc.

eRA COMMONS USER NAME (credential, e.g., agency login): andrbuki

POSITION TITLE: Full Professor and Chair of Neurosurgery

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Medical University of Pécs, Hungary	MD.	1990	general medicine
Medical University of Pécs, Hungary – Board exam		1996	neurosurgery
EANS - European written board exam		1996	neurosurgery
Medical University of Pécs, Hungary	Ph.D.	1999	neurotraumatology
University of Pécs, Hungary – Board exam		2011	oncology
Hungarian Academy of Sciences; Hungary	D.Sc.	2012	neurotraumatology

**A. Personal Statement**

I have been pursuing research activity in the field of neurosciences since 30 years- starting as a student research society member in the field of anatomy, further extending my work in Richmond, VA as a research fellow studying proteolytic processes in traumatic axonal injury and now, conducting studies in the field of biomarker research in the clinical setup. I have entered the field of neurotrauma research in 1996 as a board certified neurosurgeon, thereby taking every effort to participate in translational research activities. In 2005 I was the first to publish that proteolytic processes operant in traumatically damaged axons may serve as biomarkers in injured humans. Since then I have established strong collaboration with authors of the present application materialized in joint projects and publications. I am actually heading the biomarker work-package of the unprecedented research endeavor CENTER TBI funded by the FP-7 project of the European Union. Considering my interest in translational research projects I see a great potential in the present application to achieve a real change in the diagnostics and treatment of the head injured.

**B. Positions and Honors****Positions and Employment**

1990-1992	research associate; Department of Anatomy, Medical University of Pécs, Hungary
1992-1996	resident in neurosurgery; Department of Neurosurgery, Medical University of Pécs, Hungary
1996-1997	assistant professor of neurosurgery; Department of Neurosurgery, Medical University of Pécs, Hungary
1997-1999	research fellow; Department of Anatomy, Medical College of Virginia Commonwealth University, Richmond, Virginia USA
1999-2006	assistant professor of neurosurgery; Department of Neurosurgery, University of Pécs, Hungary
2006-2014	associate professor of neurosurgery; Department of Neurosurgery, University of Pécs, Hungary

2014- full professor of neurosurgery/head of the Department; Department of Neurosurgery, University of Pécs, Hungary

### **Other Experience and Professional Memberships**

1991- Hungarian Anatomical Society  
1995- Hungarian Neurosurgical Society, (secretary:2002-, re-elected:2006, 2010, 2014)  
1995- Hungarian Medical Chamber  
1995- Hungarian Society of Neurosonology  
2000-2010 Hungarian Neurotrauma Society (secretary:2005-2010)  
2002- International Society for Neurochemistry  
2002 „Visiting Professor” – Department of Anatomy and Neurobiology Virginia Commonwealth University, Richmond, VA  
2003- European Association of Neurosurgical Societies – Individual Membership  
2003- National Neurotrauma Society (USA)  
2005- Hungarian Neurooncology Society  
2005 Hungarian College of Neurosurgeons  
2006 „Visiting Professor” – Department of Neurosurgery Virginia Commonwealth University, Richmond, VA  
2007-2011 European Association of Neurosurgical Societies – Training Committee member  
2008 „Visiting Professor” – Department of Anatomy and Neurobiology Virginia Commonwealth University, Richmond, VA  
2011- European Association of Neurosurgical Societies – Treasurer  
2011-2014 International Neurotrauma Society – Vice President  
2014-2016 International Neurotrauma Society – President  
2016 International Neurotrauma Society – Past President  
2016 European Association of Neurosurgical Societies – Neurotrauma Committee - Member  
2016 World Federation of Neurosurgical Societies – Neurotrauma Committee – Member  
2018 „Visiting Professor” – Department of Neurosurgery University of Messina, Italy  
2018 Hungarian Neurosurgical Society - President

### **Honors**

1997-1999 Martin Rodbel Fellowship of the Virginia Commonwealth University and the Hungarian Academy of Sciences  
2000 European Association of Neurosurgical Societies Aesculap Prize  
2000-2003 Bólyai Fellowship of the Hungarian Academy of Sciences  
2001-2004 NIH Fogarty International Research Collaboration Award, (FIRCA)  
2003-2006 Békési Scholarship of the Hungarian Academy of Sciences  
2018 Markusovszky Prize of Szombathely Hospital Research Committee

## **C. Contribution to Science**

### **Research on the pathogenesis of diffuse axonal injury**

Provided the first light microscopic and ultrastructural evidence that calcium-induced, calpain-mediated spectrin proteolysis plays a pivotal role in traumatically induced axonal injury in rodents.

1. **Büki A**, Siman R, Trojanowski JQ, Povlishock JT. The role of calpain-mediated spectrin proteolysis in traumatically induced axonal injury. *J Neuropathol Exp Neurol.* 1999 Apr;58(4):365-75.

First demonstrated that in a “necrotic” model of traumatic axonal injury mitochondrial damage leads to the release of cytochrome c with resultant activation of apoptotic enzyme systems, thereby caspase and calpain interact to cause axonal demise.

1. **Büki A**, Okonkwo DO, Wang KK, Povlishock JT. Cytochrome c release and caspase activation in traumatic axonal injury. *J Neurosci.* 2000 Apr 15;20(8):2825-34.

As a “byproduct” of these studies with Coworkers developed a new fluorescent-electron microscopic double labelling technic.

1. **Büki A**, Walker SA, Stone JR, Povlishock JT. Novel application of tyramide signal amplification (TSA): ultrastructural visualization of double-labeled immunofluorescent axonal profiles. *J Histochem Cytochem.* 2000 Jan;48(1):153-61.

### **Studies conducted to therapeutically influence diffuse axonal injury**

The above observations provided a solid basis for therapeutic investigations where together with coworkers demonstrated that the inhibition of mitochondrial pathology prevents axonal damage. Similarly, demonstrated that a halt of proteolytic processes by the application of therapeutic hypothermia or calpain inhibitors turns into better morphological and functional outcome.

The observations on the beneficial effects of cyclosporine A on mitochondrial pathology initiated further, preclinical and later phase II clinical studies and motivated the NeuroVive Pharmaceutical Company to initiate its trail with a cyclosporine A analogue in myocardial ischemia.

1. Okonkwo DO, **Büki A**, Siman R, Povlishock JT. Cyclosporin A limits calcium-induced axonal damage following traumatic brain injury. *Neuroreport.* 1999 Feb 5;10(2):353-8.
2. **Büki A**, Okonkwo DO, Povlishock JT. Postinjury cyclosporin A administration limits axonal damage and disconnection in traumatic brain injury. *J Neurotrauma.* 1999 Jun;16(6):511-21.
3. **Büki A**, Koizumi H, Povlishock JT. Moderate posttraumatic hypothermia decreases early calpain-mediated proteolysis and concomitant cytoskeletal compromise in traumatic axonal injury. *Exp Neurol.* 1999 Sep;159(1):319-28.
4. **Büki A**, Farkas O, Doczi T, Povlishock JT. Preinjury administration of the calpain inhibitor MDL-28170 attenuates traumatically induced axonal injury. *J Neurotrauma.* 2003 Mar;20(3):261-8.

### **Translational biomarker studies**

First demonstrated that proteolytic processes described in rats are also detectable in head injured humans providing a potential biomarker of traumatic brain injury.

1. Farkas O, Polgár B, Szekeres-Barthó J, Dóczi T, Povlishock JT, **Büki A**. Spectrin breakdown products in the cerebrospinal fluid in severe head injury--preliminary observations. *Acta Neurochir (Wien).* 2005 Aug;147(8):855-61.

With Coworkers in various trials and studies identified and established potential biomarkers and elucidated their prognostic properties.

1. Mondello S, Robicsek SA, Gabrielli A, Brophy GM, Papa L, Tepas J, Robertson C, **Büki A**, Scharf D, Jixiang M, Akinyi L, Muller U, Wang KK, Hayes RL.  $\alpha$ -spectrin breakdown products (SBDPs): diagnosis and outcome in severe traumatic brain injury patients. *J Neurotrauma.* 2010 Jul;27(7):1203-13.
2. Czeiter E, Mondello S, Kovacs N, Sandor J, Gabrielli A, Schmid K, Tortella F, Wang KK, Hayes RL, Barzo P, Ezer E, Doczi T, **Büki A**. Brain injury biomarkers may improve the predictive power of the IMPACT outcome calculator. *J Neurotrauma.* 2012 Jun 10;29(9):1770-8.

### **Critical appraisal of contemporary biomarker studies**

Under the umbrella of the CENTER TBI research project lead the group that provided the first living systematic review on the potential application of biomarkers in traumatic brain injury.

1. Mondello S, Sorinola A, Czeiter E, Vámos Z, Amrein K, Synnot A, Donoghue EL, Sándor J, Wang KKW, Diaz-Arrastia R, Steyerberg EW, Menon D, Maas A, **Buki A**. Blood-Based Protein Biomarkers for the Management of Traumatic Brain Injuries in Adults Presenting with Mild Head Injury to Emergency Departments: A Living Systematic Review and Meta-Analysis. *J Neurotrauma*. (2018, in press).
2. Synnot A, Gruen RL, Menon D, Steyerberg EW, **Buki A**, Peul WC, Elliott JH, Maas A. A New Approach to Evidence Synthesis in Traumatic Brain Injury: A Living Systematic Review. *J Neurotrauma*. (2018, in press).
3. Maegele M, Schöchl H, Menovsky T, Maréchal H, Marklund N, **Buki A**, Stanworth S. Coagulopathy and haemorrhagic progression in traumatic brain injury: advances in mechanisms, diagnosis, and management. *Lancet Neurol*. 2017 Aug;16(8):630-647.

### **Establishment of the Pecs Traumatic Brain Injury Database**

With Coworkers funded and further developed the Pecs Severe Traumatic Brain Injury Database now containing clinical, imaging and biomarker (follow-up) data of over 600 patients in 16 years.

The broader analysis also revealed regional inequalities and insufficiencies of the Hungarian health care system.

1. Sorinola A, **Buki A**, Sandor J, Czeiter E. Effectiveness of Traumatic Brain Injury Management Guideline Introduction in Hungary. *Turk Neurosurg*. 2018;28(3):410-415.
2. Nemes O, Kovacs N, Szujó S, Bodis B, Bajnok L, **Buki A**, Doczi T, Czeiter E, Mezosi E. Can early clinical parameters predict post-traumatic pituitary dysfunction in severe traumatic brain injury? *Acta Neurochir (Wien)*. 2016 Dec;158(12):2347-2353.
3. Nemes O, Kovacs N, Czeiter E, Kenyeres P, Tarjanyi Z, Bajnok L, **Buki A**, Doczi T, Mezosi E. Predictors of post-traumatic pituitary failure during long-term follow-up. *Hormones (Athens)*. 2015 Jul-Sep;14(3):383-91.

**Complete List of Published Work in MyBibliography is under upload, searchable at Hungarian Academy of Sciences webpage at:**

**<https://vm.mtmt.hu/www/index.php#>**

### **D. Research Support**

**EU FP-7 - Grant no: 602150:** PI: Andrew IR Maas, David K Menon; 01/10//2013-31/03//2020

**Title:** Collaborative European NeuroTrauma Effectiveness Research in TBI – CENTER-TBI

**Goal:** The aim of this multicentric, prospective, descriptive project is to re-characterize and redefine traumatic brain injury and its treatment in Europe, in conjunction with Worldwide collaborative studies.

**Role:** Biomarkers WP-leader

**Hungarian National Research, Development and Innovation Office - Grant No. 2017-1.2.1-NKP-2017-**

**00002:** PI: Tamás Freund, Tamás Dóczi; 01/12/2017-30/11/2021

**Title:** Hungarian Brain Research Program 2.0

**Goal:** The goal of this project is to support clinical research in neuroscience where the sub-project specifically focuses on the construction of large patient database to facilitate biomarker research in traumatic brain injury.

**Role:** Sub-PI, project-leader

**Hungarian Economic Development and Innovation Operational Programme - Grant no: GINOP-2.3.2-15-**

**2016-00048:** PI: Péter Hegyi; 01/02/2017-31/01//2021

**Title:** *Életet veSzélyezTető Akut megbetegedések súlYossági és hALálózási mutatólnak jaVítása translációs orvostudományi mEgközelítésben* – STAY ALIVE

**Goal:** The goal of this project is to support clinical research in vascular diseases of the central nervous system where the sub-project specifically focuses on the construction of large patient database to facilitate biomarker research in stroke of various origin.

**Role:** Sub-PI, project-leader

**Hungarian Economic Development and Innovation Operational Programme - Grant no: GINOP- 2.3.3-15-2016-00032:** PI: Tamás Dóczi; 01/01/2017-31/12/2019

**Title:** *Neurorehabilitációs és ember-gép kapcsolat kutatási központ kialakítása a Pécsi Tudományegyetemen*

**Goal:** The aim of this project is to develop a modern/complex neurorehabilitational center in the University of Pécs and investigations with innovative technologies like human-machine interfaces or implementation of robot technology to the rehabilitation of neurological patients.

**Role:** Sub-PI, project-leader

**Hungarian Economic Development and Innovation Operational Programme - Grant no: GINOP- 2.3.3-15-2016-00013:** PI: András Büki; 01/07/2016-30/07/2018

**Title:** *Világszínvonalú neuronavigációs infrastruktúra, K+F és oktatási platform kialakítása Magyarországon*

**Goal:** This governmental grant aims the development of new clinical research infrastructure to serve further research and development purposes. The specific task is to establish/develop intraoperative image guided navigation and 3D printing in spine surgery.

**Role:** PI

**EFOP-3.6.2.-16-2017-00008:** PI: István Ábrahám; 01/07/2017-31/10/2020

**Title:** The role of neuro-inflammation in neurodegeneration: from molecules to clinics

**Goal:** This governmental grant aims to investigate neuroinflammation and neurodegeneration following traumatic brain injury, where the sub-PI focuses on the application of image-guided, navigated transcortical magnetic stimulation in the assessment of late cognitive sequelae of traumatic brain injury in conjunction with biomarker studies.

**Role:** Sub-PI

### **Completed Research Support**

**Hungarian National Development Agency Grant No.: KTIA\_13\_NAP-A-II/8:** PI: Tamás Freund, Tamás Dóczi; 01/12/2013-30/11/2017

**Title:** Hungarian Brain Research Program

**Goal:** This sub-project aimed to characterize biomarkers of traumatic brain injury and their role in outcome prediction.

**Role:** Sub-PI (Clinical Arm, Pecs University)

### **MTA/Hungarian Academy of Sciences - Research Groups Attached to Universities**

MTA-PTE Clinical Neuroscience MR Research Group PI: Tamás Dóczi - membership in the research group: 01/01/2012-30/06/2017

**Goal:** This project aimed at the identification of imaging biomarkers in brain injury of various origin.

**Role:** Sub-PI