

BIOGRAPHICAL SKETCH

NAME: Toborek, Michal

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

POSITION TITLE: Miller Professor of Biochemistry and Molecular Biology and Vice-Chair for Research

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Silesian School of Medicine, Katowice, Poland	M.D.	1985	Medicine
Silesian School of Medicine, Katowice, Poland	Ph.D.	1989	Biochemistry
University of Kentucky, Lexington, KY	Postdoc	1991/95	Vascular Biology

A. Personal Statement

The main research interest in my laboratory is focused on the involvement of the blood-brain barrier (BBB) in the pathomechanisms of cerebrovascular and neurodegenerative disorders. My laboratory is recognized for studies on the integrity and functions of the BBB and was the first to describe dysfunction of brain endothelial cells in response to methamphetamine (METH) and potentiation of the BBB disruption when exposure to METH and HIV proteins is combined. I also have experience in studies on neurotoxicity of opioids. We extensively published on the role of the BBB in HIV-1 trafficking into the brain. To illustrate my expertise in this area, I am a founding member of the International Brain Barriers Society (IBBS) and serve on the Editorial Boards of journals which are dedicated to the BBB research: Fluids and Barriers of the CNS and Tissue Barriers. In addition, I am a Member of the Scientific Council for the International Symposia on Signaling at the Blood-Brain Barriers. I was the chair of the 20th Symposium on Signal Transduction at the Blood-Brain Barriers in Krakow, Poland in 2016, and the chair of the 13th International Conference on Cerebral Vascular Biology (CVB 2019) in Miami, Florida in 2019. Finally, I served as a Secretary for the Nervous System Delivery Focus Group, the Controlled Release Society, and was recognized as an Expertscape World Expert in the Blood-Brain Barrier for being in the top 0.1% of scholars writing about in the BBB over the past 10 years.

Throughout my carrier, 38 postdoctoral scholars received training in my laboratory, including 16 who obtained faculty positions in the US or abroad. In addition, I mentored 29 graduate students, including 14 PhD students and 15 MS students, and numerous (more than 40) undergraduate students. I am proud that many of my students received prestigious fellowships and have continued on to distinguished research careers in academia, industry and government. In 2011, I received the Mentor Recognition Award, and in 2025 Faculty Mentor of the Year Award upon being nominated by PhD students and Postdoctoral Scholars. I have been a faculty/mentor on several training grants, including several currently active.

I have a long-term interest in neurovirology, pericyte biology, blood-brain barrier, and HIV infection that can be illustrated by the following recent citations.

Osborne et al., Post-Stroke Hippocampal Neurogenesis is Impaired by Microvascular Dysfunction and PI3K Signaling in Cerebral Amyloid Angiopathy. Cell Reports 43, 114848, 2024.

Sun et al., Microvascular dysfunction, mitochondrial reprogramming, and inflammasome activation as critical regulators of ischemic stroke severity induced by chronic exposure to prescription opioids. J Neurosci 45, e0614242024, 2025.

Ngo et al., Sigma-1 Receptor Signaling: A Potential Therapeutic Approach for Ischemic Stroke. J Cereb Blood Flow Metab 44(12):1430-1440.

Naranjo et al., AKT Signaling Modulates Latent Viral Reservoir Viability in HIV-1-Infected BBB Pericytes. J Biol Chem 300, 105526, 2023.

Torices et al., The NLRP3 inflammasome and gut dysbiosis link HIV-1 infection and ischemic stroke. Trends Neurosci 46, 682-693, 2023, invited review.

Bertrand et al., Targeting the HIV-infected brain to improve ischemic stroke outcome. Nat Commun 10, 2009, 2019.

Bertrand et al., Toborek M. Blood-brain barrier pericytes as a target for HIV-1 infection. Brain 142, 502-511, 2019.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024-present	Associate Dean for Basic Science, University of Miami School of Medicine
2011-present	Professor and Vice-Chair for Research, Department of Biochemistry and Molecular Biology, University of Miami School of Medicine
2011-present	Member, Sylvester Comprehensive Cancer Center, University of Miami School of Medicine
2011-present	Adjunct Professor, Department of Neurosurgery, University of Kentucky Medical Center
2005-2011	Professor, Department of Neurosurgery, University of Kentucky Medical Center
2007-2011	Associate Chair for Research, Department of Neurosurgery, University of Kentucky
2005-2011	Professor, Markey Cancer Center, University of Kentucky Medical Center
2005-2011	Professor, Graduate Center for Nutritional Sciences
2008-2011	Member, Barnstable Brown Kentucky Diabetes & Obesity Center

Selected Honors & Awards:

2025	Faculty Mentor of the Year Award
2025	Recognized as a Highly Ranked Scholar (Lifetime) in the field of Endothelium (Top 0.05% of all scholars worldwide)
2023	Distinguished Services Award. The Society on Neuroimmune Pharmacology
2022	Doctor honoris causa, Medical University of Silesia, Katowice, Poland
2021	University of Miami Dean's Annual Faculty Award for Excellence in Research
2021	Recognized as an Expertscape World Expert in the Blood-Brain Barrier for being in the top 0.1% of scholars publishing about in the Blood-Brain Barrier over the past 10 years.
2020	Nervous System Delivery Focus Group, Secretary; The Controlled Release Society
2018-present	Honorary Member of the Romanian Academy of Medical Sciences
2017-2018	Immediate Past President, SNIP
2016	Doctor honoris causa, University of Physical Education, Katowice, Poland
2016-present	Consultant to the Environmental Protection Agency on cerebrovascular effects of PCBs
2016-2017	President and the member of the Executive Committee, SNIP
2015-present	Member of the Executive Committee, the Society for Personalized Nanomedicine
2014	Wybran Award from the Society of Neuroimmune Pharmacology (SNIP), the highest honor bestowed by SNIP in recognition of the very best scientific contributions that have resulted in the preservation and expansion of the field of Neuroimmune Pharmacology
2013-present	Scientific Council for the International Symposia on Signaling at the Blood-Brain Barriers
2013-2015	Secretary, the Society on Neuroimmune Pharmacology
2011-present	Leonard M. Miller Professor of Biochemistry and Molecular Biology, University of Miami
2011	Mentor Recognition Award; The Center for Clinical and Translational Science
2011-2013	Councilor at-large, the Society on Neuroimmune Pharmacology
2011-2113	Chair, NeuroAIDS and other End-organ Diseases Study Section [NAED]
2003-2011	Wethington Research Awards from the University of Kentucky
2003	Commissioned to the Honorable Order of Kentucky Colonel
1998, 2000	Alexander von Humboldt Research Awards
1996	Excellence in Research Award from the American Heart Association
1996	Anafred N. Halpern Award from the American College of Nutrition

C. Contribution to Science: Over 250 peer reviewed publications, excluding book chapters and abstracts; Hirsh index 60 (Web of Science).

1. Over the years, I established my laboratory as one of the leading research groups studying the BBB in HIV infection. To quote Dr. Gendelman (Chair, Department of Pharmacology and Experimental Neuroscience, Director, Center of Neurodegenerative Disorders, Univ. Nebraska Med Center) from one of his e-mails: "there is not another scientist on the planet (that is planet earth) that knows more about the blood brain barrier in the context of biology, physiology and toxicology than you. This is fact."

My vision is that studies on the mechanisms of BBB disruption can only be a starting point of the BBB research. I believe that the main challenge in the field rests on repairing the BBB in order to protect against processes initiated by the disrupted BBB. Although difficult, modulation of the BBB is possible because the

BBB is not a rigid barrier, but rather a dynamic structure that receives continuous input from the CNS cells and can be modulated by environmental and/or pharmacological factors.

- a. Osborne OM, Daftari M, Naranjo O, Johar AN, Brooks S, Colbert BM, Torices S, Lewis E, Sendaydiego J, Drexler G, Bashti M, Margetts AV, Tuesta LM, Mason C, Bilbao D, Vontell R, Griswold AJ, Dykxhoorn DM, **Toborek M**. Post-Stroke Hippocampal Neurogenesis is Impaired by Microvascular Dysfunction and PI3K Signaling in Cerebral Amyloid Angiopathy. *Cell Reports* 43, 114848, 2024.
 - b. Ngo A, Fattakhov N, **Toborek M**. Sigma-1 Receptor Signaling: A Potential Therapeutic Approach for Ischemic Stroke. *J Cereb Blood Flow Metab* 44, 1430-1440, 2024.
 - c. Torices S, Daire L, Simon S, Mendoza L, Daniels D, Joseph JA, Fattakhov N, Naranjo O, Teglas T, **Toborek M**. The NLRP3 inflammasome and gut dysbiosis as a putative link between HIV-1 infection and ischemic stroke. *Trends Neurosci* 46, 682-693, 2023.
 - d. Schurhoff N, **Toborek M**. Circadian rhythms in the brain and blood-brain barrier and their impact on neurological disorders. *Mol Brain* 16, 5, 2023.
 - e. Naranjo O, Torices S, Clifford P, Daftari M, Osborne O, Fattakhov N, **Toborek M**. Pericyte infection by HIV-1: A fatal attraction. *Retrovirology* 19, 27, 2022.
 - f. Rudd H, **Toborek M**. Pitfalls of Antiretroviral therapy: Current Status and Long-Term CNS Toxicity. *Biomolecules* 12, 894, 2022.
 - g. Naranjo O, Osborne O, Torices S, **Toborek M**. In-vivo targeting of the neurovascular unit: challenges and advancements. *Cell Mol Neurobiol* 42, 2131-2146, 2022.
 - h. Osborne O, Peyravian N, Nair M, Daunert S, **Toborek M**. The paradox of HIV blood-brain barrier penetrance and antiretroviral drug delivery deficiencies. *Trends Neurosci* 43, 695-708, 2020.
 - i. Bertrand L, Méroth F, Tournebize M, Leda A, Sun E, **Toborek M**. Targeting the HIV-infected brain to improve ischemic stroke outcome. *Nat Commun* 10, 2009, 2019.
 - j. Bertrand L, Cho HJ, **Toborek M**. Blood-brain barrier pericytes as a target for HIV-1 infection. *Brain* 142, 502-511, 2019.
2. The vast majority of HIV-infected individuals are treated with anti-retroviral therapy immediately after diagnosis. In addition, anti-retroviral drugs have been proposed for pre-exposure prophylaxis (PrEP) in non-HIV infected individuals who are at ongoing high risk of HIV infection. Thus, potential cerebrovascular toxicity of these medications is an important and emerging problem. Therefore, we expanded our research on HIV to evaluate cerebrovascular impact of anti-retroviral therapy. We benefit in this line of research from a stroke model, which is very well developed in our laboratory.
- a. Fattakhov N, Ngo A, Torices S, Joseph J-A, Okoro A, Moore C, Naranjo O, Becker S, **Toborek M**. Cenicriviroc protects against dysregulation of astrocyte/endothelial cross talk induced by ischemia and HIV-1 via inhibiting the NLRP3 inflammasome and pyroptosis. *Am J Physiol Cell Physiol* 326, C487-C504, 2024.
 - b. Rudd H, **Toborek M**. Pitfalls of Antiretroviral therapy: Current Status and Long-Term CNS Toxicity. *Biomolecules* 12, 894, 2022.
 - c. Surnar B, Shah AS, Park M, Kalathil AA, Kamran MZ, Ramirez Jaime R, **Toborek M**, Nair M, Kolishetti N, Dhar S. Brain-accumulating nanoparticles for assisting astrocytes to reduce human immunodeficiency virus and drug abuse-induced neuroinflammation and oxidative stress. *ACS Nano* 15, 15741-15753, 2021.
 - d. Bertrand L, Méroth F, Tournebize M, Leda A, Sun E, **Toborek M**. Targeting the HIV-infected brain to improve ischemic stroke outcome. *Nat Commun* 10, 2009, 2019.
 - e. Velichkovska M, Surnar B, Nair M, Dhar S, **Toborek M**. Targeted mitochondrial CoQ₁₀ delivery attenuates antiretroviral drug-induced senescence of neural progenitor cells. *Mol Pharm* 16, 724-736, 2019.
 - f. Tomitaka A, Arami H, Raymond A, Yndart A, Kaushik A, Jayant RD, Takemura Y, Cai Y, **Toborek M**, Nair M. Development of magneto-plasmonic nanoparticles for multimodal image-guided therapy to the brain. *Nanoscale* 9, 764-773, 2017.
3. Our work on the mechanisms of disruption of the BBB in the context of drug abuse and HIV infection had highly significant impact on research community. My laboratory was the first to describe in a series of papers in 2001 and 2002 that exposure to methamphetamine (METH) results in dysfunction of brain endothelial cells, oxidative stress, and disruption of the barrier function (Lee et al, *J Neurosci Res* 2001 and 2002; Flora et al., *Neuromolecular Med* 2002 and *Exp Neurol* 2003). At that time, METH was believed to injure almost exclusively monoaminergic nerve terminals. Thus, our pioneering study on cerebrovascular toxicity initiated a new direction in METH research. Since then, the loss of the BBB integrity has been established as one of

the most prominent toxic events associated with METH abuse. Several clinical conditions (e.g., accelerated stroke development) in METH abusers have also been linked to the BBB dysfunction. However, the mechanisms underlying cerebrovascular toxicity of METH and other drugs of abuse are still not fully understood and, even more importantly, there is no therapeutic intervention targeting this event during drug abuse.

- a. Sun E*, Torices S*, Osborne OM, **Toborek M**. Microvascular dysfunction, mitochondrial reprogramming, and inflammasome activation as critical regulators of ischemic stroke severity induced by chronic exposure to prescription opioids. *Contributed equally. *J Neurosci* 45, e0614242024, 2025.
 - b. Fattakhov N, Ngo A, Torices S, Joseph J-A, Okoro A, Moore C, Naranjo O, Becker S, **Toborek M**. Cenicriviroc protects against dysregulation of astrocyte/endothelial cross talk induced by ischemia and HIV-1 via inhibiting the NLRP3 inflammasome and pyroptosis. *I am J Physiol Cell Physiol* 326, C487-C504, 2024
 - c. Peyravian N, Sun E, Dikici E, Deo S, Daunert S, **Toborek M**. Opioid antagonist nanodrugs successfully attenuate severity of ischemic stroke. *Mol Pharm* 19, 2254-2267, 2022.
 - d. Fattakhov N, Torices S, Stangis M, Park M, **Toborek M**. Synergistic impairment of the neurovascular unit by HIV-1 infection and methamphetamine use: implications for HIV-1-associated neurocognitive disorders. *Viruses* 13, 1883, 2021.
 - e. Park MS, Baker W, Cambow D, Gogerty D, Leda AR, Herlihy B, Pavlenko D, **Toborek M**. Methamphetamine enhances HIV-induced aberrant proliferation of neural progenitor cells via the FOXO3-mediated mechanism. *Mol Neurobiol* 58, 5421-5436, 2021.
 - f. Liskiewicz A, Przybyla M, Wojakowska A, Marczak L, Bogus K, Nowacka-Chmielewska M, Liskiewicz D, Malecki A, Barski J, Lewin-Kowalik J, **Toborek M**. Physical activity reduces anxiety and regulates brain fatty acid synthesis. *Mol Brain* 13, 62, 2020.
 - g. Liskiewicz A, Przybyla M, Park MS, Liśkiewicz D, Nowacka-Chmielewska M, Malecki A, Barski J, Lewin-Kowalik J, **Toborek M**. Methamphetamine-associated cognitive decline is attenuated by neutralizing IL1 signaling. *Brain Behav Immun* 80, 247-254, 2019.
 - h. Skowronska M, McDonald M, Velichkovska M, Leda AR, Park M, **Toborek M**. Methamphetamine increases HIV infectivity in neural progenitor cells. *J Biol Chem* 293, 296-311, 2018.
4. A major scientific interest of my laboratory is study in depth the signaling mechanisms of the BBB disruption in neuroinfections. We made several important discoveries in this field.
- a. Naranjo O, Torices S, Clifford PR, Rodriguez T, Osborne OM, Tiburcio D, Fattakhov N, Park MS, Stevenson M, **Toborek M**. AKT Signaling Modulates Latent Viral Reservoir Viability in HIV-1-Infected BBB Pericytes. *J Biol Chem* 300, 105526, 2023.
 - b. András IE, Serrano N, Djuraskovic I, Fattakhov N, Sun E, **Toborek M**. Extracellular vesicle-Serpine-1 affects neural progenitor cell mitochondrial functions and synaptic density: modulation by amyloid beta and HIV-1. *Mol Neurobiol* 60, 6441-6465, 2023.
 - c. Torices S, Teglas T, Naranjo O, Fattakhov N, Frydlova K, Cabrera R, Osborne O, Sun E, Kluttz A, **Toborek M**. Occludin regulates HIV-1 infection of brain pericytes by modulation of the interferon stimulated OAS gene family. *Mol Neurobiol* 60, 4966-4982, 2023.
 - d. Torices S, Cabrera R, Stangis M, Naranjo O, Fattakhov N, Teglas T, Adesse D, Toborek M. Expression of SARS-CoV-2-related receptors in cells of the neurovascular unit: implications for HIV-1 infection. *J Neuroinflammation* 18, 67, 2021.
 - e. Cho H J, Velichkovska M, Schurhoff N, András IE, **Toborek M**. Extracellular vesicles regulate gap junction-mediated intercellular communication and HIV-1 infection of human neural progenitor cells. *Neurobiol Dis* 155, 105388, 2021.
 - f. Torices S, Roberts S, Park MS, Malhotra A, **Toborek M**. Occludin, caveolin-1, and Alix form a multi-protein complex and regulate HIV-1 infection and egress in human brain pericytes. *FASEB J* 34, 16319-16332, 2020.
 - g. András IE, Garcia-Contreras M, Yanick C, Perez P, Sewell B, Durand L, **Toborek M**. Extracellular vesicle-mediated amyloid transfer to neural progenitor cells: implications for RAGE and HIV infection. *Mol Brain* 13, 21, 2020.
 - h. Castro V, Skowronska M, Lombardi J, He J, Seth N, Velichkovska M, **Toborek M**. Occludin regulates glucose uptake and ATP production in pericytes by influencing AMP-activated protein kinase activity. *J Cereb Blood Flow Metab* 38, 317-332, 2018.

5. Since the postdoctoral training, a substantial part of my research focus has been on the cerebrovascular toxicity of environmental pollutants. I published the first study on the impact of polychlorinated biphenyls (PCBs) on the integrity of endothelial barrier. This initial paper resulted in a series of study in which we identified that PCBs can interact with endothelial cells via interactions with specific cellular receptors, such as epidermal growth factor receptor (EGFR), leading to activation of redox-regulated signaling pathways, disruption of the barrier functions and tumor cell trafficking across the endothelium. Since then, the vascular effects of PCBs have been widely recognized. We then extended our research and demonstrated for the first time prometastatic effects of PCBs in animal models and alterations of the gut microbiota by PCBs. Finally, our research on environmental toxicology resulted in a series of studies on ZnO nanoparticles.
- a. Joo SH, Knauer K, Su C, **Toborek M**. Antibiotic resistance in plastisphere. *J Environ Chem Eng* 13, 115217, 2025.
 - b. Peixoto-Rodrigues MC, Neto JRM, Teglás T, **Toborek M**, Soares Quinete N, Hauser-Davis RA, Adesse D. Effects of early-life exposure to PCBs and PFAS on the developing Central Nervous System. *J Hazard Mater* 485, 136832, 2025.
 - c. Teglás T, Marcos AC, Torices S, **Toborek M**. Circadian control of polycyclic aromatic hydrocarbon-induced dysregulation of endothelial tight junctions and mitochondrial bioenergetics. *Sci Total Environ* 952, 175886, 2024.
 - d. Teglás T, Torices S, Taylor M, Coker D, **Toborek M**. Disruption of circadian clock modulates endothelial toxicity of polychlorinated biphenyls. *J Hazard Mater* 545, 131499, 2023.
 - e. Carlson LM, Christensen K, Sagiv S, Rajan P, Klocke C, Lein P, Coffman E, Shaffer RM, Yost E, Arzuaga X, Factor-Litvak P, Sergeev A, **Toborek M**, Bloom MS, Trgovcich J, Jusko T, Robertson L, Meeker J, Keating AF, Blain R, Silva R, Snow S, Lin C, Shipkowski K, Ingle B, Lehmann GM. Systematic evidence map for noncancer health effects of polychlorinated biphenyl mixtures. *Environ Res* 220, 115148, 2023.
 - f. Baek S, Joo SH, Su C, **Toborek M**. Toxicity of ZnO/TiO₂-conjugated carbon-based nanohybrids on the coastal marine alga *Thalassiosira pseudonana*. *Environ Toxicol* 35, 87-96, 2020.
 - g. Baek S, Joo SH, Blackwelder P, Knecht MR, **Toborek M**. Effects of coating materials on antibacterial properties of industrial and sunscreen-derived titanium-dioxide nanoparticles on *Escherichia coli*. *Chemosphere* 208, 196-206, 2018.
 - h. Eum SY, Jaraki D, András IE, **Toborek M**. Lipid rafts regulate PCB153-induced disruption of occludin and brain endothelial barrier function through protein phosphatase 2A and matrix metalloproteinase-2. *Toxicol Appl Pharmacol* 287, 258-266, 2015.
 - i. Choi JJ, Rampersaud E, Daunert S, Abreu MT, **Toborek M**. Exercise attenuates changes in the gut microbiome induced by polychlorinated biphenyls. *Environ Health Perspect* 121, 725-730, 2013.

Complete List of my Published Work: <http://www.ncbi.nlm.nih.gov/pubmed/?term=toborek+m>