Michalina Wężyk, PhD

ACADEMIC EXPERIENCE

2015.11.01 – present **- assistant professor** at Laboratory of Neurogenetics, Department of Neurodegenerative Disorders of CNS, Mossakowski Medical Research Centre, PAS, Warsaw

2017.07.01 – 2020.04.27 - postdoctoral fellow at Laboratory of Molecular and Cellular Neurobiology (Jaworski Lab), International Institute of Molecular and Cell Biology in Warsaw

2013.03.01 – 2014.05.31 postdoctoral type position, assistant professor at Laboratory of Neurogenetics, Department of Neurodegenerative Disorders of CNS, Mossakowski Medical Research Centre, PAS, Warsaw

2015.05.15 – 2015.09.18 visiting postdoctoral researcher at Reprogramming and Disease Modeling Laboratory head by Dr. Anna Falk at Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

2012.09.15 – 2013.02.28 postdoctoral fellowship from French Embassy in Poland and from the AXA Research Fund grant, at the Laboratory of Development and Plasticity of the Postnatal Brain - Neuroobese International Associated Laboratory, Jean-Pierre Aubert Research Center, Inserm U837, University of Lille 2, Lille, France

2012.07.01 – 2012.09.01 – **postdoctoral research assistant position** at Department of Biochemistry, Laboratory of Biochemistry of Lipids at Nencki Institute of Experimental Biology, PAS, Warsaw, Poland

2007.10.01 – 2012.05.31 - **junior researcher / PhD student** at Department of Biochemistry, Laboratory of Biochemistry of Lipids at Nencki Institute of Experimental Biology, PAS, Warsaw, Poland

MATERNITY LEAVES / CARRIER BREAKS

2018.04.29-2019.05.09 PIERWSZA PRZERWA MACIERZYŃSKA

2020.04.27-2022.02.28 DRUGA PRZERWA MACIERZYŃSKA

2023.01.01-2023.08.31 TRZECIA PRZERWA MACIERZYŃSKA

EDUCATION

2012.06.29 **PhD degree in biochemistry**, **specialization**: **neurobiochemistry and molecular biology**, Nencki Institute of Experimental Biology, PAS, *supervisor*: prof. dr hab. Slawomir Pikula

***PhD thesis**: "The role of Plasma Membrane Ca^{2+}-ATPases in the process of catecholamine secretion by tumour chromaffin cells (PC12 cell line)"; date of defense: 2012.05.31*

2007 – 2012 **PhD studies**, Department of Biochemistry, Laboratory of Biochemistry of Lipids, Nencki Institute of Experimental Biology, PAS

2007.05.30 **MSc degree in biology**, **specialization: animal biology**, Clinic of Immunology, Transplantology and Internal Diseases, Medical University of Warsaw, *supervisor*: prof. dr hab. n. med. Leszek Paczek

***Msc thesis**: "Evaluation of pathological process in human liver based on gene expression analysis of collagen IV and TGF-β1 with quantitative analysis of collagen IV concentration and collagenase activity measurement", date of defense: 2017.05.30*

2002 – 2007 **MSc Studies**, Warsaw University of Life Sciences, Warsaw, Poland

FELLOWSHIPS AND AWARDS

September 2012 – March 2013 AXA Research Fund Scholarship, Laboratory of Development and Plasticity of the Postnatal Brain, University of Lille 2, Lille, France

September 2012 – December 2012 Bourse de Séjour de Recherche from French Embassy, Laboratory of Development and Plasticity of the Postnatal Brain, University of Lille 2, Lille, France

SUPERVISION OF GRADUATE STUDENTS

2015 – 2016 2 Bachelor Students

Faculty of Biology, Warsaw University, Warsaw, Poland

Faculty of Neurobiology, Jagiellonian University, Cracow, Poland

NUMBER OF COWORKERS

2 people close cooperation per 7 people in total in the Lab

ORGANISATION OF SCIENTIFIC MEETINGS

4 November 2016 Polish-French scientific Conference "Alzheimer's disease and neurodegenerative disorders: what challenges for tomorrow?", organizing committee: Michalina Wężyk, Antonin Borgnon and Sebastien Reymond, Warsaw, Poland

MAJOR COLLABORATIONS

Prof. Christophe Mulle - University of Bordeaux, Prof. Ann Brinkmalm - Univeristy of Gothenburg, Dr. Matthijs Verhage - CNCR/Vrije Universiteit of Amsterdam and Dr. Gabor Tamas - University of Szeged in frames of JPco-fuND2 international project no. 2021/03/Y/NZ5/00112, entitled "Pre-symptomatic synaptic disorders in Alzheimer's disease", financed by the EU Joint Program - Neurodegenerative Disease Research (EU JPND), through the National Science Center.

Dr. Anna Falk, Alzheimer's disease iPSCs-based modelling, Department of Neuroscience, Karolinska Institutet, Sweden

Prof. Haruhisa Inoue, Alzheimer's disease iPSCs-based model, Center for iPS Cell Research and Application, Kyoto University, Japan

Prof. Urszula Wojda, Alzheimer's disease molecular phenotyping, Laboratory Of Preclinical Testing Of Higher Standard, Nencki Institute, Poland

Prof. Jacek Jaworski, disease modelling, electrophysiology and calcium imaging, International Institute of Molecular and Cell Biology in Warsaw, Poland

Dr. Krzysztof Ginalski and Dr. Magdalena Skrzypczak, next generation sequencing, transcriptomic, RNA-seq, Laboratory of Bioinformatics and Systems Biology, Centre of New Technologies, Poland

Dr. Tomasz Wójtowicz – Nencki Institute, Warsaw. Poland, expertise in electrophysiology

LECTURES / SEMINARS (selected)

23 March 2017	Title: " Presenilin 1 and BRCA: participation in pathology in Alzheimer's disease?", team work: "Causal mutations in the patient's genome - how to find and examine? Biology and chemistry approach.". *Invited seminar* at "Scientific Thursdays" at the Science Center of Biological and Chemical Sciences at the University of Warsaw, Poland
31 January 2017	Title: "Breakthrough in BRCA1-driven cell death in familial Alzheimer's disease", *invited seminar* at Biogen inc. Warsaw, Poland
4 November 2016	Title: "DNA damage response in Alzheimer's disease", Polish-French scientific Conference "Alzheimer's disease and neurodegenerative disorders: what challenges for tomorrow?", *conference lecture*, Warsaw, Poland
19 March 2016	Title: "How and why to make a neuron from skin?", *popular science seminar*, "Week of the brain" science festival, Warsaw, Poland
19 November 2015	Title: "From genetics and transcriptomics to pathomechanisms in Alzheimer's disease", *popular science seminar*, Biologists Scientific Club of the Faculty of Biology of the University of Warsaw, Poland
7 September 2015	Title: "Genetics and transcriptomics of Alzheimer's disease", 12th International Congress of the Polish Neuroscience Society, *conference lecture*, Gdansk, Poland
27 June 2014	Title: "Genetics of dementia", *conference lecture*, Neurological Symposium at Collegium Medicum Jagiellonian University, Cracow, Poland

SCIENTIFIC PROJECTS

JPco-fuND2 international project no. 2021/03/Y/NZ5/00112, entitled "Pre-symptomatic synaptic disorders in Alzheimer's disease", financed by the EU Joint Program - Neurodegenerative Disease Research (EU JPND), through the National Science Center. Project partner in a consortium composed of Prof. Christophe Mulle - University of Bordeaux, Prof. Ann Brinkmalm - Univeristy of Gothenburg, Dr. Matthijs Verhage - CNCR/Vrije Universiteit of Amsterdam and Dr. Gabor Tamas - University of Szeged. **PreSSAD project** aim at addressing presymptomatic synaptic deficits in preclinical AD cohorts to human synaptic biology with the use of innovative human biological samples: 1) iPSCs-derived human neurons with altered expression of presynaptic proteins (e.g. called SNARE proteins) in mouse neocortex, 2) human iPSCs-derived cerebral organoids and 3) organotypic cortical cultures obtained from human surgical resections.

National Centre for Research and Development, **STRATEGMED** programme implemented at Laboratory of Molecular and Cellular Neurobiology (Jaworski Lab), International Institute of Molecular and Cell Biology (IIMCB), Project entitled: Application of novel diagnostic and therapeutical methods in epilepsy and neurodevelopmental abnormalities in children based on the clinical and cellular model of mTOR dependent epilepsy (Funding ~700 000 Eur), **Co-investigator**: fibroblasts reprogramming into iPSCs, iPSCs and NSCs neuronal differentiation, 3D neuronal organoids culture, Ca2+ imaging and electrophysiology of neurons and slices cut from organoids, mentoring and introducing younger co-workers to reprogramming Ca2+ imaging and

electrophysiology

National Science Centre – **SONATA6** (UMO-2013/09/D/NZ3/01348, panel NZ3) (2014.02-2017.02.05, extended till 2017.11.05) from National Center of Science in Poland, project title: „Functional studies of rare genetic variants causally connected with Alzheimer's disease in the Polish population", at Laboratory of Neurogenetics of Department of Neurodegenerative Disorders in Mossakowski Medical Research Centre of PAS in Warsaw; (funding 555 850 PLN), ***principal project investigator***

National Science Centre – **SONATA8** (UMO-G1145-2015/17/D/NZ2/03712 panel NZ2) (2015.02-2018.02) from National Center of Science in Poland, project title: „Searching for novel molecular pathways dysregulated in pathophysiology of amyotrophic lateral sclerosis", at Laboratory of Neurogenetics of Department of Neurodegenerative Disorders in Mossakowski Medical Research Centre of PAS in Warsaw; (funding 630 600 PLN), ***co-investigator – establishment of ALS patients' fibroblasts and transcriptome analyses***

The AXA Research Fund (R1600) PostDoc Campaign (2012-2013), project title: "Role of the tanycytic barrier at the blood-hypothalamus interface during metabolic disorder development", at Development and Plasticity of the Postnatal Brain, Jean-Pierre Aubert Research Center, Inserm U837, Universite Lille 2, France (funding 120 000 EUR*),* ***principal project investigator***

"Bourse de Séjour de Recherche" obtenu de L'Ambassade de France à Varsovie (2012-2013), "Rôle de la barrière hémato-encéphalique des tanycytes au cours du développement des maladies métaboliques" (funding 6552 EUR), ***principal project investigator***

N N401 533340 (2010-2011) from National Center of Science in Poland, project title: "Participation of Plasma Membrane Ca^{2+}-ATPases isoforms in catecholamine secretion from adrenal medulla chromaffin cell" coordinated by prof. Slawomir Pikula, at Department of Biochemistry, Laboratory of Biochemistry of Lipids, Nencki Institute of Experimental Biology, Polish Academy of Sciences (funding 50 000 PLN), ***principal project investigator***

BIOINFORMATIC PROJECTS

BioProject PRJNA382346 - RNA sequencing data from PSEN1 familial Alzheimer's disease patients and controls, Sequence Read Archive NCBI database

BioProject PRJNA494073 - RNA sequencing data from SOD1 and C9ORF72r Amyotrophic Lateral Sclerosis patients and controls, Sequence Read Archive NCBI database

BioProject SUB2571439 - RNA sequencing data from FTD-PGRN patients, publication in progress

TECHNICAL SKILLS

Bioinformatic data analysis of RNA sequencing data: experience working in LINUX environment with the programs STAR 2.0.1, TopHat v.2.0.11, Bowtie v.1.0.1; Cufflinks v2.2.1, R-Bioconductor packages and libraries (DESeq, EgdeR, Cummerbund, GAGE and Pathview), Partek Genomics Suite software™v.6.6, Partek Pathway™, and Ingenuity Pathway Analysis software. **Molecular biology methods**: immunoprecipitation chromatin, real-time qPCR (ABI PRISM®7900, ABI PRISM®7500, StepOnePlus Applied Biosystems), gene silencing (siRNA, antisense oligonucleotides), plasmid constructs, cloning, sequencing (ABI Genetic Analyzer 3130). **Microscopic imaging methods**: immunocytochemical staining, co-localization, FRET, FRAP, confocal and fluorescence microscopy (Leica, Zeiss**), microscopic calcium imaging with Fluo-4**. **Biochemical methods**: RP-HPLC, **spectrofluorimetrical measurements of $[Ca^{2+}]_c$,** protein biochemistry techniques (co-immunoprecipitation, Western blotting, methylation, phosphorylation studies). **Flow cytometry**: flow cytometry and sorting (FACSCalibur™, FACSAria III cell sorter Bencton Dickinson). **Electrophysiological whole-cell patch clamp recordings** with Axopatch 200A (Axon Instruments). **Cell culture**: stable cell lines (tumour cell lines),

primary cell lines (ependymal glial cells, astrocytes, neurons from mice and rats, and human fibroblasts from Alzheimer's disease patients and healthy donors), induced pluripotent stem cells, neuroepithelial stem cells, iPSC-derived neurons. **Animals research**: animals perfusion, brain microdissection (mice, rats) with subcutaneous and intraperitoneal injections, intracranial intraventricular sterotaxie, genotyping of animals, mouse brain sectioning using a cryostat (Leica Biosystems) and microtome (Leica vibratone ™ Series; VT1000 P). **Graphic data reprocessing**: CorelDRAW Graphics, ImageJ. **Statistics**: SPSS Statistics, Origin Pro 8.0

LANGUAGES

Polish (native), English (advanced), French (advanced)

PUBLICATIONS

Wezyk M*, Berdyński M, Skrzypczak M, Ginalski K, Zboch M, Winkel I, Żekanowski C Rare A360T mutation alters GSK3β(Ser9) binding in the cytosolic loop of presenilin 1, influencing β-catenin nuclear localization and pro-death gene expression in Alzheimer's disease case. Accepted manuscript: ijms-2680242 **IJMS: section *Molecular Neurobiology* 2023**; *corresponding author

Koscielny A, Liszewska E, Machnicka K, **Wezyk M**, Kotulska K, Jaworski J. mTOR controls endoplasmic reticulum-Golgi apparatus trafficking of VSVg in specific cell types. **Cell Mol Biol Lett. 2021** May 18;26(1):18. doi: 10.1186/s11658-021-00262-z. PMID: 34006213; PMCID: PMC8130434.

Kieroń M, Żekanowski C, Falk A, **Wężyk M***. Oxidative DNA Damage Signalling in Neural Stem Cells in Alzheimer's Disease. ***Oxidative Medicine and Cellular Longevity***. **2019** Nov 13. doi:10.1155/2019/2149812 ***corresponding author***

Wezyk M*, Szybinska A, Wojsiat J, Szczerba M, Day K, Ronnholm H, Kele M, Berdynski M, Peplonska B, Fichna JP, Ilkowski J, Styczynska M, Barczak A, Zboch M , Filipek-Gliszczynska A, Bojakowski K, Skrzypczak M, Ginalski K,Kabza M, Makalowska I, Barcikowska-Kotowicz M, Wojda U, Falk A, Zekanowski C. Overactive BRCA1 Affects Presenilin 1 in Induced Pluripotent Stem Cell-Derived Neurons in Alzheimers Disease. ***Journal of Alzheimers disease.*** **2018**; 62 (1) doi:10.3233/JAD-170830, ***corresponding author***

Wężyk M*, Spólnicka M, Pośpiech E, Pepłońska B, Zbieć-Piekarska R, Ilkowski J, Styczyńska M, Barczak A, Zboch M, Filipek A, Skrzypczak M, Ginalski K, Kabza M, Makałowska I, Barcikowska M, Branicki W, Żekanowski C. TRIM59 and KLF14 hypermethylation might contribute to cell death signaling in early-onset Alzheimer's disease patients. ***Oxidative Medicine and Cellular Longevity***. Feb 5, **2018**, ***corresponding author***

Wezyk M*, Zekanowski C. Role of BRCA1 in neuronal death related to Alzheimer's Disease. ***ACS Chemical Neuroscience.*** **Review upon invitation.** March **2018**, ***corresponding author***

Walerych D, Zyla L, **Wezyk M**, Gaweda-Walerych K, and Zylicz A. Wild-type p53 oligomerizes more efficiently than p53 hot-spot mutants and overcomes mutant p53 gain-of-function via a "dominant-positive" mechanism. *Oncotarget Journal*. February, **2018**

Gaweda-Walerych K, Sitek EJ, Narożańska E, **Wezyk M**, Brockhuis B, Zekanowski C, Sławek Functional characterization of a novel progranulin mutation in a patient with progressive nonfluent aphasia". J. Neurobiol Aging. 2018 Dec;72:186.e9-186.e12. doi: 10.1016/j.neurobiolaging.2018.06.033. Epub 2018 Jul 2.

Spólnicka M, Pośpiech E, Pepłońska B, Zbieć-Piekarska R, Makowska Ż, Pięta A, Karłowska-Pik J, Ziemkiewicz B, **Wężyk M**, Gasperowicz P, Bednarczuk T, Barcikowska M, Żekanowski C, Płoski R, Branicki W. DNA methylation in ELOVL2 and C1orf132 correctly predicted chronological age of individuals from three disease groups. *Int J Legal Med.* 2018 Jan;132(1):1-11. doi: 10.1007/s00414-017-1636-0. Epub **2017** Jul 19.

Dziewulska D, Sulejczak D, **Wezyk M**. What factors determine phenotype of cerebral autosomal dominant arteriopathy with subcortical infarcts and

leukoencephalopathy (CADASIL)? Considerations in the context of a novel pathogenic R110C mutation in the NOTCH3 gene. *Folia Neuropathol*. **2017**;55(4):295-300.

Wężyk M*, Szybińska, Szczerba M, Wojsiat J, Berdyński M, Pepłońska B, Fichna J, Ilkowski J, Styczyńska M, Zboch M, Filipek A, Skrzypczak M, Ginalski K, Kabza M, Makałowska I, Wojda U, Barcikowska M, Żekanowski C "DNA damage response in Alzheimer's disease", *Folia Neuropathologica* **2016** vol**.** 4, p427. DOI10.5114/fn.2016.648 ***corresponding author**

Domitrz I[#], **Kosiorek M[#]*,** Zekanowski C, Kaminska A. Genetic studies of Polish migraine patients: screening for causative mutations in four migraine-associated genes. *Human Genomics*, **2016** Jan 8;10(1):3. doi: 10.1186/s40246-015-0057-8, **[#]first author** and ***corresponding author**

Wezyk M*, Kabza M, Skrzypczak M, Ginalski K, Makałowska I, Barcikowska M, Żekanowski C. "Genetics and transcriptomics of Alzheimer's disease", *Acta Neurobiol. Exp.* Vol. 75 No. 2, **2015**, ***corresponding author**

Kosiorek M*, Podszywalow-Bartnicka P, Zylinska L, Pikula S*. NFAT1 and NFAT3 Cooperate with HDAC4 during Regulation of Alternative Splicing of PMCA Isoforms in PC12 Cells. PLoS One. **2014** Jun 6;9(6):e99118, ***corresponding author**

Kosiorek M*, Zylinska L, Zablocki K, Pikula S*. Calcineurin/NFAT Signaling Represses Genes Vamp1 and Vamp2 via PMCA-Dependent Mechanism during Dopamine Secretion by Pheochromocytoma Cells. Plos One, **2014** 25;9:e92176, ***corresponding author**

Kosiorek M, Podszywalow-Bartnicka P, Zylinska L, Zablocki K, Pikula S. Interaction of plasma membrane Ca^{2+}-ATPase isoform 4 with calcineurin A: Implications for catecholamine secretion by PC12 cells, Biochemical and Biophysical Research Com. 411:235-240, **2011**

Boczek T, Kozaczuk A, Ferenc B, **Kosiorek M**, Pikula S, Zylinska L. Gene expression pattern in PC12 cells with reduced PMCA2 or PMCA3 isoform: selective up-regulation of calmodulin and neuromodulin, Molecular and Cellular Biochemistry, 360:89-102, **2012**

PUBLICATIONS – *IN PROGRESS*

Berdynski M, Wezyk M*, Anders P, Kuzma M, Zekanowski C. Transcriptomic profiling of SOD1 - ALS families reveals RNA U6 small nuclear 2 trait. in preparation, equal first authors*

Gaweda-Walerych K, Wezyk M, Zekanowski C. Transcriptomic profiling of PGRN in FTD patients families following inhibition of the mitochondrial complex I. in preparation

BOOK CHAPTERS (Selected)

Wężyk M* and Zekanowski C (**2017**), "Presenilins interactome in Alzheimer's disease and pathological aging", Book Chapter in "Senescence" , InTechOpen, ISBN 978-953-51-5316-0, ***corresponding author**

CONFERENCES (Selected)

K. Gaweda-Walerych; D. Dymkowska; M. Frontczak-Baniewicz; M. Gewartowska; E. Sitek; E. Narozanska; **M. Wezyk;** M. Mandecka; C. Zekanowski; J. Slawek; M. Barcikowska; K. Zablocki; Characterization of mitochondrial phenotype in fibroblasts from Fronto-Temporal Lobar Degeneration (FTLD) patients with mutations in progranulin gene (PGRN), the 14th International Conference on Alzheimer's and Parkinson's Diseases, 26-31.03.2019, Lisbon, Portugal,

Katarzyna Marta Zoltowska, Joanna Wojsiat, Angelika Więckowska, Mykola Zdioruk, Kinga Gazda, Tomasz Węgierski, **Michalina Maria Wężyk**, Urszula Wojda. Alzheimer's disease-causing gain-of-function mutations in presenilin 1 lead to cell cycle arrest and senescence induction.– Gordon Research Conference - Neurobiology of Brain Disorders, Castelldefels, 5-10 sierpnia, 2018.

Katarzyna Marta Zoltowska, Joanna Wojsiat, Angelika Więckowska, Mykola Zdioruk, Kinga Gazda, Tomasz Węgierski, **Michalina Maria Wężyk**, Urszula Wojda. Alzheimer's disease presenilin1 mutants upregulate ATM/p53/p21 cascade causing G2 cell cycle arrest and senescence onset. Advances in Alzheimer's and Parkinson's Therapies - AAT-AD/PD Meeting (joint meeting between the International Geneva/Springfield Symposium on Advances in Alzheimer Therapy (AAT) and International AD/PD, Turyn, 15-18 marca, 2018. Sesja A2.c, Abstrakt nr 39

Szczerba M, Żekanowski C, **Wężyk M*** „The studies on the role of BRCA1 in Alzheimer's disease using patient-derived neurons". "FENS - 8th Conference of Lithuanian Neuroscience Association", Dec 9-10, **2016**, Vilnus, Lithuania, ***corresponding author**

Wężyk M*, Szybińska, Szczerba M, Wojsiat J, Berdyński M, Pepłońska B, Fichna J, Ilkowski J, Styczyńska M, Zboch M, Filipek A, Skrzypczak M, Ginalski K, Kabza M, Makałowska I, Wojda U, Barcikowska M, Żekanowski C "DNA damage response in Alzheimer's disease", Polish-French scientific Conference "Alzheimer's disease and neurodegenerative disorders: challenges for tomorrow?", Nov 4, **2016**, ***corresponding author**

Szczerba M, Rönnholm H, Kele M, Falk A, Żekanowski C, **Kosiorek M***. Neural differentiation of neural epithelial stem cells derived from Alzheimer's disease patient pluripotent stem cells. Neuronus Neuroscience Forum, Apr 22-24, **2016**, Krakow, ***corresponding author**

Kosiorek M*, Szybińska A, Berdyński M, Pepłońska B, Fichna J, Ilkowski J, Styczyńska M, Zboch M, Filipek A, Skrzypczak M, Ginalski K, Kabza M, Makałowska I, Barcikowska M, Żekanowski C. Whole transcriptome profiling of familial early-onset Alzheimer's disease (EOAD) patients points to cell cycle abnormalities. Molecular Neurodeneration, Welcome Genome Trust Conference, 2015.11.29-12.04 Cambridge, UK, ***corresponding author**

Kosiorek M*, Kabza M, Skrzypczak M, Ginalski K, Makałowska I, Barcikowska M, Żekanowski C. Genetics and transcriptomics of Alzheimer's disease, 12th International Congress of the Polish Neuroscience Society, 6-8 September **2015** in Gdansk, ***corresponding author**

Kosiorek M*, International Society for Stem Cell Research Conference, 24-27 June **2015**, Stockholm, Sweden

Kosiorek M*, Berdyński M, Zielke K, Barczak A, Narożańska E, Pfeffer A, Mandecka M, Filipek-Gliszczyńska A, Gabryelewicz T, Barciszewska M, Zekanowski C. Mutations of PGRN, MAPT and C90RF72 genes causing FTD in the Polish population. World Congress of Neurology, Sep 21-26 **2013**, Vienna, Austria, ***presenting author**

I hereby agree for processing the following personal information strictly for recruitment purposes in accordance with the regulation regarding the protection data passed on the following date: 29.08.97r. Dz. U. nr 133 poz. 883.