PROF. LEONORA BUŻAŃSKA - ORGANISER, CHAIR OF SESSION #1

Director, Head of the Department of Stem Cells Bioengineering
Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland

Leonora Buzanska, Ph.D., D.Sc., is a Professor and the Director of Mossakowski Medical Research Institute Polish Academy of Sciences in Warsaw, Poland, as well as the head of the Department of Stem Cell Bioengineering. She started her scientific carrier at the Faculty of Biology, University of Warsaw, where she obtained both M.Sc. and Ph.D. degrees in biology. After her PostDoc fellowship at University of Aberdeen followed by training in INSERM U.495 – Lab. Biologie-Glia Interactions, Paris, she started to work in the research team of prof. Krystyna Domanska-Janik in MMRI PAS, focusing her scientific intrests on human neural stem cells and their therapeutic applications. Her pioneering achievements included showing for the first time, that cord blood stem cells can cross germ line barriers and attain neuronal features (J Cell Sci. 2002) and establishment of the first stable untransformed neural stem cell line (Stem Cell Dev. 2006). This resulted in one-year internship at State University of New York in Buffalo, followed by an invitation to conduct research in Developmental Neurotoxicity Project in the Institute of the European Commission (Inst. of Health and Consumer Protection, Join Research Centre) in Italy, where she worked for 5 years. She has been the head of Stem Bioengineering Unit in MMRI PAS since 2010 and the Director of MMRI PAS since 2019 . Currently she is a member of the Board of Directors of PAS and several Scientific Boards of Medical and Experimental Biology Research Institutes of PAS, vice-chair of The Committee on Neurobiology PAS and the chair of Biology Division of Warsaw Scientific Society. To date she was Principal Investigator or Co-Investigator of 25 grants from Polish or European funding agencies and currently prof. Buzanska runs with her team in the Department of Stem Cell Bioengineering 3 projects modeling the early brain development with human brain organoids to investigate neurodevelopmental disorders (e.g. schizophrenia and Dravet Syndrom). She is an author of more than 100 scientific original papers and reviews garnering over 2500 citations with h-index 26. She received a range of awards for her scientific achievements, e. g. from the Ministry of Science, Polish Neuroscience Society and Medical Sciences Division of the Polish Academy of Sciences, as well as the European Commission Joint Research Centre's Excellence Award. She was also honored by Chance for the Blind Foundation with the awards of "Idol 25-years" and "Idol 30-years" for the charity and popularization of science.

Current research topics of prof. Buzanska include derivation of brain organoids from human induced pluripotent stem cells (hiPSC) for modeling of neurodevelopmental and neurodegenerative diseases and establishing biomimetic microenvironmental in vitro conditions for derivation of therapeutically competent cell populations for neurological disorders treatment.

PROF. MAREK KRAWCZYK – PATRON, CHAIR OF SESSION #1

Dean of the Medical Division, Polish Academy of Sciences, Warsaw, Poland

Born in 1946. From 1969 to the present, employed at the Department of General, Transplantation and Liver Surgery (formerly the 2nd Surgical Department) at the Medical University of Warsaw. He completed his medical studies in the years 1963–1969 at the Faculty of Medicine of the Medical University of Warsaw. He obtained his doctoral degree in 1975 and his habilitation degree in 1987. He received the academic title of professor in 1995. A specialist in general surgery, clinical transplantology and oncological surgery. European expert in Hepato-Pancreato-Biliary Surgery (FEBS). Professor Krawczyk studied at the Surgical Department of the University of Heidelberg (1978/79), the Surgical Department in Mannheim of the University of Heidelberg (1989/1990), the Surgical Department of the University of Dundee (1991), the Surgical Department of the University of Cambridge (1991), and the Saint Joseph Hospital in Charleroi (1991), in the Surgical Department in Villejuif - University of Paris (1993/1994), in the Surgical Department in Strasbourg (1995) and in the Department of Surgery and Liver Transplantation in Bordeaux (1999).

In the years 1996 - 2002 he was the Vice-Dean, and from 2002 to 2008 the Dean of the 1st Faculty of Medicine. In the years 2008 - 2016 he served as Rector of the Medical University of Warsaw. Honorary member of 8 foreign scientific societies and 5 Polish scientific societies. In the years 2001-2003 he was the President of the Polish Transplantation Society, 2011-2013 the President of the Association of Polish Surgeons, and from 2016 to 2017 he was the President of the European Surgical Association

Professor Krawczyk's main scientific interests include short bowel syndrome, acute pancreatitis, intraoperative liver ultrasound, laparoscopic surgery, biliary reconstruction, liver transplantation from a deceased donor and from a living donor, liver and biliary tract cancers, as well as other gastrointestinal cancers.

He is the author or co-author of 571 works, editor or co-editor of 70 books, and presented 770 papers at congresses. Professor Krawczyk was the supervisor of 13 doctoral theses, supervised 8 habilitations, and 9 of his employees obtained the academic title of professor.

Full member of the Polish Academy of Sciences and active member Polish Academy of Arts and Sciences, full member of the Warsaw Scientific Society, member of the Clinical Sciences Committee of the Polish Academy of Sciences, from January 1, 2023, Dean of the 5th the Medical Division of the Polish Academy of Sciences, honorary fellow of the American College of Surgeons, Chancellor of the Chapter of the Gloria Medicinae Medal.

He was awarded the Commander's Cross of the Order of Polonia Restituta, the Knight's Cross of the Order of Polonia Restituta, and the Officer's Cross of the Order of Polonia Restituta. He also received awards from the Minister of Health and the Minister of Science and Higher Education, Academic Palmes from the Minister of National Education of the Republic of France and many other distinctions. Doctor Honoris Causa of the Jan Kochanowski University in Kielce (2020) and Doctor Honoris Causa of the Jagiellonian University in Kraków (2021).

PROF. MARIA ANNA CIEMERYCH-LITWINIENKO – CHAIR OF SESSION #2

Faculty of Biology, University of Warsaw, Warsaw, Poland

Maria Anna Ciemerych-Litwinienko is a developmental and cell biologist. From the beginning of her career, she was associated with the University of Warsaw, where she obtained both M.Sc. and Ph.D. degrees in biology, under the supervision of prof. Andrzej K. Tarkowski. During her Ph.D., she completed one long-term internships at The University of Manchester and several short-term ones at Institute Jacques Monod in Paris. After completion of Ph.D., MACL, as a visiting fellow, did her research first in Magda Żernicka-Goetz lab at Wellcome/CRC Institute (currently Gurdon Institute)/Cambridge University and then as a postdoctoral fellow with Piotr Siciński at the Dana-Farber Cancer Institute/Harvard Medical School in Boston. After returning to Poland, she worked at Department of Embryology and later on joined the Department of Cytology, a head of which she soon became. She is also a head of the Institute of Development Biology and Biomedical Sciences, Faculty of Biology, University of Warsaw. She also served as a Vice-Dean of the Faculty of Biology at Warsaw University. She is an elected member of the Polish Academy of Arts and Sciences (PAU). During her academic career she received START Fellowship of Foundation for Polish Science, 'Stay with us' POLITYKA Fellowship, and L'Oreal/UNESCO for Woman in Science Fellowship. She is a member of AdademiaNet. She is also an academic teacher involved in many outreach activities, such as taking a part in EuroGCT network. In her research she is focusing on differentiation of stem cells, skeletal muscle regeneration, and finding the way to improve it. In her free time she creates collages.

https://www.academia-net.org/profile/maria-anna-ciemerych-litwinienko/78168

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PROF. DOROTA PIJANOWSKA – CHAIR OF SESSION #2

Nałęcz Institute of Biocybernetics and Biomedical Engineering, Polish Academy of Sciences Warsaw, Poland

Prof. Dorota G. Pijanowska - a graduate of the Warsaw University of Technology, she obtained her PhD and Ph.D. degrees in the discipline of biocybernetics and biomedical engineering. She completed her postdoctoral internship at Twente University, Enschede, the Netherlands. In 2007, she was given the mission of organizing a new Department of Hybrid Analytical Microbiosystems at IBIB PAN, of which she became the head, while also being the head of the Laboratory of Biosensors and Analytical Microsystems. He cooperates with Chang Gung University and Christian Chung Yuan University in Taiwan as well as the University of Florence and FH Aachen, Institute of Nano- and Biotechnologies. Currently she is a Deputy Director for Research of IBBE PAS.

Her scientific research is related to biomedical engineering, in particular with interdisciplinary experimental work in the field of micro- and nanotechnology, used to design bioanalytical tools, i.e. biosensors and microfluidic systems for the determination of selected metabolites, disease markers, among others, neurodegenerative disease markers (amyloid-beta, alpha-synuclein), endogenous immunomodulators (e.g. lactoferrin), as well as drugs, such as anti-inflammatory and cystostatics. At Twente University she was working on the first integrated microdialysis based system for brain research.

Another area of her research is related to genetically modified cells thanks to the introduction of genes encoding enzymes to restore lost cell functions for the needs of a bioartificial organs (e.g. BAL).

She is a corresponding member of the Polish Academy of Sciences, a member of the Council of Scientific Excellence and the Committee of Biocybernetics and Biomedical Engineering of the Polish Academy of Sciences, serving as the chairwoman of the Committee for Basic Research in the 2020-2023 term. He is a member of the European Society for Artificial Organs (ESAO), a founding member of the Polish Society of Biomedical Engineering (PTIB) and the secretary of the Polish Society of Sensor Technology (PTTS). She is the Chairman of the 6th Department of Technical Sciences of the Warsaw Scientific Society.

SPEAKERS - SESSION #1

PROF. LEONORA BUŻAŃSKA
ORGANISER, CHAIR OF SESSION #1

Director, Head of the Department of Stem Cells Bioengineering
Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland

Introduction to "Power of Stem Cells to Model Embryos and Organs"

The advent of induced pluripotent stem cell technology allowed for an unprecedented, profound insight into the earliest events of human origin and early development without ethical controversies. An amazing self-organizing capacity of pluripotent stem cells to build up human embryo as well as 3D tissue architecture of different organs revolutionized the field of developmental biology. The Symposium "Power of Stem Cells to model embryos and organs" will present the recent groundbreaking achievements in the field.

Human brain organoids are a great example of such stem cell technological advancements. This 3D structures resemble the brain architecture and physiology by displaying unique layers of neural progenitors and differentiated neuronal and glial cells and are the only in vitro model of prenatal brain development. Thus, brain organoids hold promise for the discovery of still unidentified mechanistic principles of early human brain development but also dysfunction and disorders. Modeling of neurodevelopmental and neurodegenerative disorders with patient-derived brain organoids enables a personalized approach of translational studies. The integration of microenvironmental bioengineering and microfluidics into brain organoid in vitro system facilitates further technological advancement in building vascularized and immunoreactive models for diagnostic and therapeutic applications.

PROF. MAGDALENA ŻERNICKA-GOETZ

California Institute of Technology (CalTech), Pasadena, CA, USA
University of Cambridge, UK

Magdalena Żernicka-Goetz is a developmental biologists who started her scientific career at Faculty of Biology, University of Warsaw preparing her Ph.D. thesis under the guidance of prof. Andrzej K. Tarkowski. Her work with prof. Chris Graham at Department of Zoology, University of Oxford, was supported by PhD SOROS Foundation Fellowship and postdoctoral training with prof. Martin Evans at University of Cambridge, Wellcome Trust/Cancer Research UK Institute, by EMBO Fellowship. She

established her first laboratory at Wellcome Trust/Cancer Research UK Institute in Cambridge founded by many prestigious fellowships. Currently, she is a Professor of Mammalian Development and Stem Cell Biology, at the Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge, UK, as well as Bren Professor of Biology and Biological Engineering, California Institute of Technology, Caltech, Pasadena, USA.

Since the beginning of her research journey prof. Żernicka-Goetz has set new paths in studies of human embryo post-implantation development in vitro, cell fate specification in mouse and human embryos, and the creation of 3D embryos by combining multiple stem cell types. She always aimed to uncover the fundamental principles and molecular mechanisms that regulate cell identity, pluripotency, and embryo plasticity, size, shape, and self-organization. Her work was published in over 160 research papers (Nature, Cell, Developmental Cell, Nature Cell Biology etc. etc.). She received multiple research grants and was prized with many awards, such as recent ones (2023): Ogawa-Yamanaka Stem Cell Prize for uncovering mechanisms of mammalian embryo development leading to the creation of human embryo models that self-assemble from pluripotent stem cells, Pioneer Award, Frontiers in Stem Cells and Regeneration, Woods Hall, 2023, or European Society of Human Genetics Award. She is also foreign ember of Polish Academy of Sciences, foreign member of Polish Academy of Arts and Sciences, fellow of Academy of Medical Sciences, FMedSci, member of European Molecular Biology Organization. Last but not least Magdalena Żernicka-Goetz is no only extraordinary scientists but also great teacher, mentor, science advocate.

https://zernickagoetzlab.com/

"Modelling development with stem cells: the power of self-organization"

The lecture will take you to the world of the earliest stages of our development, describe a journey of one cell to many to build a complex organism – human - with all its individual organs working together.

PROF. TOMASZ NOWAKOWSKI

University of California San Francisco (UCSF), San Francisco, USA

Dr. Tomasz Nowakowski is an Associate Professor of Neurological Surgery and Anatomy at the University of California, San Francisco (UCSF). He earned his Ph.D. in Biomedical Sciences from The University of Edinburgh, where he also completed his BSc and MSc in Physiology and Life Sciences, respectively. He continued his training with postdoctoral research at UCSF under Arnold Kriegstein.

Dr. Nowakowski's research focuses on cortical and brain development, particularly the gene regulatory networks involved. His work in single-cell genomics and cerebral organoid models has advanced understanding of human brain development. He has received several awards, including the Simons Foundation for Autism Research Bridge to Independence Award and the Vilcek Prize for Creative Promise in Biomedical Sciences.

Active in the scientific community, Dr. Nowakowski plays several active roles in NIH consortia, such as the Brain Initiative Cell Atlas Network, the psychENCODE, and the Scalable and Systematic Neurobiology of Psychiatric and Neurodevelopmental Disorder Risk Genes (SSPsyGene) Consortium. He is a member of the Society for Neuroscience and the International Society for Stem Cell Research.

Dedicated to mentoring, Dr. Nowakowski has guided many graduate students and postdoctoral fellows, helping them secure positions in academia and industry. He is also committed to promoting diversity and inclusion in science through various programs supporting underrepresented groups.

"Developmental strategies of human neural stem cells and their relevance to psychiatric disorders"

Development of the human brain involves many complex processes during prenatal and postnatal life that represent vulnerabilities to genetic mutations underlying human neurodevelopmental disorders. Our goal is to understand developmental mechanisms through which stem cells of the developing brain give rise to the complex cells of the human neocortex. To provide insights into the mechanisms through which genetic mutations found in patients with Autism, we have explored the differentiation of neural stem and progenitor cells using massively parallel lineage tracing and uncovered novel patterns of cell lineage differentiation. Subsequently, we have explored how mutations in genes implicated in Autism interfere with normal development and disrupt protein protein interactions, uncovering an exemplar mutation in FOXP1 that alters interactions with its endogenous transcriptional co-factors and leading to altered trajectory of cortical neurons. Finally, we have used gene expression analysis to identify developing human thalamus as a brain region enriched for expression of high confidence Autism risk genes. By modeling the development of this region using stem cell derived organoids, we revealed unexpected disruptions in the axonogenesis of thalamic neurons as a new candidate phenotype associated with neurodevelopmental disorders.

PROF. ANIRBAN DUTTA

State University of New York (SUNY), Buffalo, NY, USA
University of Birmingham, UK

Dr. Dutta is a biomedical engineer specializing in neuroengineering for precision health, i.e., to develop personalized approaches for diagnosing, monitoring, and treating neurological disorders. He holds a Bachelor of Engineering from Jadavpur University, an M.S. from the University of Florida, a Ph.D. from Case Western Reserve University, and an additional M.S. from Charité – Universitätsmedizin Berlin. His career spans roles at Tata Consultancy Services, Janelia Farm Research Campus (Howard Hughes Medical Institute), and the Rehabilitation Institute of Chicago. He has served as a Humboldt research fellow at University Medicine Göttingen, a starting research scientist at INRIA, France, and a tenure-track Assistant then Associate Professor of Research at the University at Buffalo, USA. He is currently Associate Professor of Quantitative Biomedicine at the University of Birmingham, UK. Dr. Dutta's research currently focuses on neuroengineering for neurodevelopment and ageing research, supported by extensive publications with over 2300 citations. He holds certifications in ISO 13485:2016 and ISO 14971:2019 for Medical Devices.

"Complex systems analysis of neonatal brain and organoids"

The talk will explore applying complex systems analysis to neonatal brains and brain organoids using information theory, emphasizing entropy for optimal information transmission through bioelectricity during neurodevelopment. Bioelectricity is crucial for biological organization and function, from subcellular components to entire cells - discoveries include how calcium and potassium ions generate

bioelectric currents and how proteins like tubulin and actin facilitate intracellular communication. Mitochondria form networks for efficient charge transmission, and cell membrane potential variations impact biological processes. Our own study investigated 1/f neural noise in electrophysiological recordings from neonatal brains and brain organoids, linking it to health and disease (DOI: 10.1038/s41598-020-77929-8). A general dynamical system with stochastic drive and minimal assumptions could generate 1/f-like neural field spectra consistent with in vivo observations. Here, our findings showed that cerebral organoids from Schizophrenia patients exhibited structural changes and altered elasticity, influenced by mitochondrial drugs with postulated changes in the microtubular-actin tensegrity structure for physical reservoir computing (DOI: 10.1109/EMBC48229.2022.9871376).

SPEAKERS - SESSION #2

PROF. MARIA ANNA CIEMERYCH-LITWINIENKO

Faculty of Biology, University of Warsaw, Warsaw, Poland

"Stem Cells as a tool to study myogenic differentiation"

Pluripotent stem cells, such as embryonic stem cells (ESCs) or induced pluripotent stem cells (iPSCs), self-renew their population and differentiate into any given tissue that build an organism, including skeletal muscle. Myoblasts derived from pluripotent stem cells hold promise for treating severly injured or disease affected skeletal muscles. So far, many different approaches, such as overexpression of various factors or modified culture conditions were tested, with various efficiency, to induce myogenic differentiation of these cells. Among such factors are miRNAs which we used to improve formation of myoblasts from ESCs.

PROF. NATALIA ROZWADOWSKA

Institute of Human Genetics, Polish Academy of Sciences, Poznań, Poland

Natalia Rozwadowska is a researcher focusing on human genetics and stem cell biology. She obtained her master's degree in biotechnology from Poznan Life Sciences University and her Ph.D. in medical biology from Poznan Medical University. Currently, she serves as the Head of the Molecular Pathology Department at the Institute of Human Genetics PAS and IHG PAS Deputy Director for Development. Her expertise includes in vitro studies supported by functional assays, and preclinical studies on animal models. Her current research interests include the use of induced pluripotent stem cells (iPSCs) for cardiovascular disease modeling wand regenerative therapies approaches. She is involved in multiple projects focusing on cancer genetics and using advanced therapy medicinal products and gene therapy methods for the development of novel approaches for anti-cancer biological drugs. Her scientific achievements have been recognized with several awards, including the FNP START program and the MNiSW Scholarship for Outstanding Young Scientists. She has received twice the prestigious Prime Minister's Award for her doctoral dissertation and habilitation. Additionally, she is passionate about science dissemination. Through her initiatives, the Institute of

Human Genetics PAN annually hosts workshops for nearly a thousand participants. She founded the NGO "Gen-i-już," that aim at promoting human genetics education.

"Advanced tissue models derived from human iPSC for human heart modelling"

Engineered heart tissue (EHT) has revolutionized cardiovascular research by providing a more physiologically relevant model than traditional animal models and induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs). Unlike iPSC-CMs, EHT aims to replicate the architecture of native heart tissue, offering a more accurate representation of human cardiac function. This advancement enables our group to study heart organogenesis, drug responses, and disease mechanisms in a more natural context, thereby enhancing the predictive power of preclinical testing. With EHT, we can say goodbye to the 'one-size-fits-all' approach and embrace a tissue model that beats with the rhythm of human hearts—making our studies both literally and figuratively heart-felt.

PROF. MACIEJ FIGIEL

Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznań, Poland

Professor Maciej Figiel is the Head of the Department of Molecular Neurobiology at ICHB PAN. He is an expert in the fields of neurobiology, polyQ diseases, stem cells, animal models, and organoids. He is the creator of the Ki91 and K150 knock-in model of spinocerebellar ataxia type 3 (SCA3) and has also discovered early phenotypes of Huntington's disease (HD) in stem cells. Currently, he is identifying the mechanisms of neurodegeneration in SCA3/MJD in the early presymptomatic phase in the Ki91 and Ki150 SCA3 model and is also investigating neurodevelopmental mechanisms of HD. Additionally, he is researching therapeutic approaches in both HD and SCA3. In 2016, Maciej Figiel received his habilitation from the Institute of Experimental Biology, M. Nencki PAN, Warsaw, Poland. In 2001, he received his Ph.D. from the Department of Anatomy and Cell Biology, University of Ulm, Germany for discovering the regulation of glutamate transporters controlling synaptic transmission. He has received various awards and distinctions, including a Scholarship from 1997 to 2001 at DFG Graduiertenkolleg Biomolekulare Medizin, University of Ulm, Germany, and a Scholarship from 2007 to 2010 at POL-POSTDOC III, Institute of Molecular Biology and Biotechnology, Adam Mickiewicz University in Poznań.

"Modelling neurodevelopmental pathogenesis of Huntington Disease with human iPSC lines and brain organoids"

Huntington's disease (HD) is a polyglutamine neurodegenerative disease involving pathogenesis within the striatum and cerebral cortex and a neurodevelopmental component, particularly in juvenile HD form (JOHD). We developed a new model, dorso-ventral forebrain fused organoids, to investigate neurodevelopment in Huntington's Disease (HD). Fused brain organoids mimic the affected brain regions in HD and exhibit significant growth and altered gene expression compared to control organoids, suggesting that cells in HD brains represent specific phenotypes that favor increased proliferation over differentiation. We have identified the upregulation of specific markers of several affected cell types in the HD organoids and embryonic mouse brains of an HD model. Additionally, we observed an increase in a specific population of cells occurring in the blood-brain barrier (BBB) in the HD models, which is not present in control organoids and embryos. The

upregulation of the BBB markers in mouse embryos and blood serum suggests its potential significance in HD pathogenesis. Furthermore, identifying the BBB biomarkers in blood serum and the increased BBB cell population in HD models may facilitate early detection and monitoring of HD. These findings could accelerate the development of novel HD therapies targeting the specific brain populations in HD brain.

VALERY ZAYAT, PhD

Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland

Valery Zayat, Ph.D. is an Adiunct at the Mossakowski Medical Research Institute in Warsaw, Poland, specializing in biomedical sciences. With a deep-seated interest in stem cell research, neurogenesis, and organoid models, Dr. Zayat has made significant contributions to the understanding of embryonic development and genomics. His work primarily focuses on the development of 3D models for early neurogenesis and brain organoids.

Dr. Zayat earned his PhD in Biomedical Sciences from the M. Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw, with his research concentrating on the role of Hax-1 protein in the post-transcriptional regulation and degradation of mRNA.

His previous positions also include a postdoc at The Institute For Medical Research-Israel-Canada at The Hebrew University-Hadassah Medical School in Jerusalem, where he was part of a team focusing on stem cell reprogramming during early embryonic development.

"Generation of Human iPSC Lines and Ventral Forebrain Organoids to Model Dravet Syndrome"

Dravet Syndrome (DS) represents a significant challenge in neurodevelopmental disorders, characterized by severe epilepsy and high mortality rates. This talk delves into groundbreaking research utilizing human induced pluripotent stem cells (iPSCs) to generate ventral forebrain organoids, simulating the complex neural environments of DS. By recapitulating the *SCN1A* genetic mutations in iPSCs, we have developed a model that not only illuminates the pathophysiological mechanisms behind DS but also offers a testbed for potential therapeutic interventions. Key findings from our study include insights into the impairment of GABAergic neurons and mitochondrial dysfunction, which could be pivotal in devising targeted treatments for DS. This session aims to provide a comprehensive overview of how iPSC-derived organoid models can revolutionize our understanding and treatment strategies for DS, illustrating the synergy between cellular biology, genetic engineering, and biotechnological innovation in tackling complex health challenges.

MICHALINA WĘŻYK, PhD

Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland

Michalina Wężyk, Ph.D. is an assistant professor at the Mossakowski Medical Research Institute in Warsaw, Poland, specializing in neurodegenerative medical science. Being deeply interested in research on the molecular basis of neurodegeneration in Alzheimer's disease using models derived from induced pluripotent stem cells (iPSC), in particular brain organoids. Dr. Wężyk has made

significant contributions to the understanding of DNA damage stress response (DDR) underlying Alzheimer's disease pathogenesis. Her work primarily focuses on search for pre-symptomatic trigger of neurodegeneration, focused at DDR and synaptic deficits in iPSC neuronal models. Her previous work revealed BRCA1 protein as key player underlying AD origins.

Dr. Wężyk earned her PhD in Neurobiochemical Sciences at Nencki Institute of Experimental Biology in Warsaw, by the work demonstrating gene expression regulation of pathological secretion of catecholamines, focusing at calcium dysregulation of secretory machinery. Currently Dr. Wężyk is using her calcium, secretory and DDR know-how in the research on synaptic dysfunction in AD.

"Modeling of pre-symptomatic synaptic disorders in Alzheimer's disease with cortical organoids"

The emergence of a model of neurons and brain organoids derived from induced pluripotent stem cells (iPSCs) provides a groundbreaking platform for studying the complex mechanisms of neurodegeneration in Alzheimer's disease (AD).

Three-dimensional cortical organoids represent key features of the development and organization of the human brain. Using iPSC technology and miniaturized brain-like structures, we explore cellular and molecular mechanisms underlying the synaptic deficits occurring at the earliest stages of AD pathology. We are focusing on the targets related to exocytotic events and post-synaptic changes preselected based on spectrometry mass results from AD patients. Using the iPSC-derived neuronal model of AD we are targeting early dysregulation of critical synaptic proteins, disrupted neurotransmitter release mechanisms, and altered calcium signaling pathways. Our team deals with the investigation of the role of neuronal pentraxins and key elements of the SNARE complex in synaptic deficiency in an in vitro brain model of AD. We are currently deciphering if some of the analyzed phenomena are pre-symptomatic or occurring following the beta-amyloid pathology. All of this contributes to the breakdown of synaptic communication and plasticity in the AD phenotype of cortical organoids and neurons in 2D cultures.

Taken together, iPSC-derived cortical organoids represent a pioneering tool to study synaptic deficiency in the context of Alzheimer's disease. This model not only summarizes key aspects of AD-associated synaptic disorders but also offers a unique opportunity to dissect the underlying molecular mechanisms as well as look for potential therapeutic agents already at the basic science research stage.

PROF. MICHAŁ STACHOWIAK

State University of New York (SUNY), Buffalo, NY, USA

Michal K. Stachowiak received the M.Sc. degree from Nicolaus Copernicus University, Torun, Poland, in 1973, and the Ph.D. degree in neurosciences from the Academy of Medicine, Gdansk, Poland, in 1980. He is currently a Professor with the Departments of Pathology and Anatomical Sciences, Biomedical Engineering, Neuroscience Program, Genetics, Genomics, and Bioinformatics Program, the Director of the Molecular and Structural Neurobiology and Gene Therapy Program, Stem Cells

Engraftment and In Vivo Analysis Facility with the State University of New York, Buffalo, USA. His studies revealed new global genome controlling mechanism Integrative Nuclear Fibroblast growth factor receptor 1 (FGFR1) Signaling (INFS) and a new theory of ontogeny that describes how coordinate gene programs are constructed and executed during development. Since its discovery, targeting the INFS has been investigated in several laboratories for cancer therapy.

Stachowiak has made seminal discoveries and developed innovative concepts to significantly influence our perception of the genome - its function, structure and regulation. He advanced Genome Archipelago model and theory of the Systems Genome as the principles underwriting development, developmental diseases and different types of cancer. He has integrated human brain organoids, genome, and new optogenomic research (light control of genome functions) to explore new therapies. In particular he has focused on malformations in neuro-developmental disorders such as schizophrenia. Dr. Stachowiak research has been supported by NIH, NSF, and foundation grants. Dr. Stachowiak is a Fulbright Distinguished Professor and the Chair of Medical Sciences.

"Systems and organoid approach to model schizophrenia"

The growing size of the genome throughout evolution requires mechanisms to coordinate the expression of genes at different loci, thereby counteracting dyscoordination and a rise in entropy. As progenitor cells differentiate into neurons, the activities of many genes change; these changes are maintained within a narrow range, referred to as genome homeostasis. The process involves synchronization of the entire expressed genome and is distorted in neurodevelopmental diseases such as schizophrenia. The coordinated gene activity networks are formed by altering sets of genes and comprise recurring coordination modules. The gene activity networks are governed by entropy-controlling action of nuclear FGFR1 and influencing the genome topology. Dysregulation of the pan-ontogenic Integrative Nuclear FGFR1 signaling (INFS) is observed also in cancer and may underly the global gene deprograming. In conclusion, studies bring to the forefront concept of the systems genome and the need for new therapeutic strategies.

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