



Rzeczpospolita
Polska



NARODOWE CENTRUM NAUKI

artiQ

ARTIQ

ARTIQ - AI Centres of Excellence

Application for a Host Institution

Institution	National Centre for Research and Development, National Science Centre
Project Joint National Project:	ARTIQ – AI Centres of Excellence
Deadline for the submission of applications	8th of April-11th of May 2021

I. HOST INSTITUTION DATA

Identification data of the Host Institution

Name (full)	Nencki Institute of Experimental Biology of the Polish Academy of Sciences
Name (short)	Nencki Institute
Name of the main organisational unit (where applicable)	Polish Academy of Sciences
Address of the registered office	
Street	L. Pasteur
Building No.	3
Office No.	-
Postal code	02-093
City/district	Warsaw
Post office	Warsaw
Municipality	Warsaw

County	Poland
Province	Mazovia
Correspondence address (if different than the address of the registered office)	
Street	
Building No.	
Office No.	
Postal code	
City/district	
Post office	
Municipality	
County	
Province	
EPUAP [Electronic Platform for Public Administration Services] mailbox	ePUAP: /InstytutNenckiego/SkrytkaESP
Legal form	state organizational units/ scientific Institute of the Polish Academy of Sciences
The person appointed for contact with NCBR and with the potential Leader/Project Manager	
First name	Bożena
Last name	Kamińska
Position	Professor
Phone number	48 22 5892209
E-mail address	b.kaminska@nencki.edu.pl
The person authorised to represent the applicant	
First name	Agnieszka
Last name	Dobrzyń
Function/Position	Director of the Institute

II. CAPACITY OF THE HOST INSTITUTION TO PERFORM THE PROJECT

1. Description of major research achievements in the scope of implementation of R&D projects, as well as the commercialisation of deliverables of such projects regarding artificial intelligence for the last 5 years prior to or in the year of the application along with a list of the most important publications and patents of the applicant (max. 1 A4 page).
- **Establishment of the Nencki Genomics Portal** (2012) - The Nencki Genomics Portal is a platform of integrated computational tools and databases for the analysis of transcription regulation. The functionality of the portal is available from the level of a web browser via the Galaxy server (<http://bco.ibb.waw.pl/bio-info/nencki-genomics-portal>). The analysis layer is in the form of SOAP / WSDL webservices, integrated with each other in the form of streams running on the Taverna server. The portal's data layer contains the Genomic Database and the Expression Database, used to store user input and analysis results. Publications using the Nencki Genomics Portal: *Krystkowiak et al. Database (Oxford). 2013: bat069. doi: 10.1093 / database / bat069*; *Ellert-Miklaszewska et al. Glia. 2013 Jul; 61 (7): 1178-90. doi: 10.1002 / glia.22510*; *Kulesza et al. Lab Investig. 2019, 99 (11): 1607-1621 doi: 10.1038 / s41374-019-0288-8*; *Glia. 2019; 67 (12): 2312-2328. doi: 10.1002 / glia.23686*. The obtained results became the basis for the following patents: "Compositions for treating glioma" (2012, PCT/IB2012/056533); patents granted: in Europe, patent no. 2780363, validated in CH, DE, FR, UK, IT, SE; in Japan, Patent No. 6,426,001; in US Patent No. 9,453,050; application "Compositions for treating glioma", submitted on November 27, 2019, in international mode PCT/IL2019 /051298 and project: **PBS GLIATOR**: New, comprehensive and highly specific therapy of gliomas (NCBR).
 - Machine learning and an innovative single-class logistic regression machine learning algorithm were applied to extract sets of transcriptomic and epigenetic traits of "stemness = pluripotency". The use of stemness indicators for TCGA data from 33 types of tumors allowed for the identification of new targets and potential targeted anticancer therapies (*Malta TM, Sokolov A, Gentles AJ, Burzykowski T, Poisson L, Weinstein JN, Kamińska B, et al. Cell 2018; 173 (2): 338-354.e15, doi: 10.1016 / j.cell.2018.03.034*; *Kijewska et al. Oncotarget. 2017; 8 (10): 16340-16355. Doi: 10.18632 / oncotarget.14092*).
 - **Establishment of the TEAM-TECH Core** Facility financed by the Foundation for Polish Science. Biobank of 300 glioblastoma samples a digital repository of genomic and transcriptomic data were created. A panel of 700 cancer and epigenetic related genes was developed to facilitate molecular classification and therapy prediction for brain tumors. This will enable the precise diagnosis of genetic changes, the assessment of the tumor malignancy and the prediction of tumor response to therapy .
 - Implemented translational projects: NCN SYMFONIA3: Atlas of regulatory areas specific for the human brain - a new tool for discovering pathways causing selected brain diseases; NCBR STRATEGMED2: DIMUNO Development of new therapies based on the stimulation of the anti-cancer activity of the immune system; NCBR Strategmed1: EPITHERON - Epigenetic therapies in oncology; STRATEGMED3: EPISTOP: Application of new methods of diagnosis and treatment of epilepsy and neurodevelopmental disorders in children based on the clinical and cellular model of epilepsy depending on the mTOR pathway; NCBR STRATEGMED3 GLIOMED - Diagnostics of gliomas based on the circulating tumor DNA.

2. A list of 5 research and development projects within national and international competitions in the area of artificial intelligence and implemented within the last 5 years prior to or in the year of the application (title, manager, source of financing, amount of financing) (max. 1 A4 page).
- **STRATEGMED3: EPIMARKER:** Application of new methods of diagnosis and treatment of epilepsy and neurodevelopmental disorders in children based on the clinical and cellular model of epilepsy depending on the mTOR pathway; tasks 4,6 cooperation with the industrial partner ELMIKO, National Center for Research and Development (NCBR), 2018-2021, Head: Bozena Kaminska, PLN 1,917,500
 - **STRATEGMED3 GLIOMED:** Diagnostics of gliomas based on the circulating tumor DNA, tasks 6 and 8, cooperation with Cyfronet AGH, NCBR, 2018-2020, Head: Kaminska, PLN 1,917,500
 - **TEAM-TECH Core Facility:** NGS platform for comprehensive diagnostics and personalized therapy in neuro-oncology, Foundation for Polish Science, 2018-2021, Head: Bozena Kaminska, PLN 2,444,840
 - **ERA-NET-NEURON/18/2018:** Microglial control of synaptic function in stress response and vulnerability to depression. The project aims at the integration of transcriptomic and proteomic data from microglia of depressed mice to model human disease. NCBR, 2018-2021, Head: Bozena Kaminska, PLN 1,092,575
 - **Dioscuri Center of Scientific Excellence** for Evolutionary and Functional Genomics of astrocytes. Program initiated by the Max Planck Society, managed jointly with the Polish National Science Center, co-financed by the Polish Ministry of Science and Higher Education (MNiSW) and the German Federal Ministry of Education and Research (BMBF); Head: Aleksandra Pękowska, 2019-2024, PLN 6,825,000
 - **BRAINCITY - Center of Excellence in Research on Neural Plasticity and Brain Diseases** International Research Agenda financed by the Foundation for Polish Science (<https://braincity.nencki.gov.pl/#home>). The strategic partner is the European Molecular Biology Laboratory (EMBL). The goal of BRAINCITY is to understand neural plasticity and to develop new diagnostic and therapeutic approaches targeting neurological diseases (eg, epilepsy, schizophrenia, addictions, depression and autism). Newly formed teams are using advanced computational methods to analyze electrophysiological data and super-resolution imaging. BrainCity is based on 5 teams and modern laboratories, which cooperate with the neurological and psychiatric clinics of the Medical University of Warsaw, the Institute of Psychiatry and Neurology in Warsaw and the Children's Center in Międzyzylesie. Cooperation with biotechnology and pharmaceutical companies, such as Celon Pharma and OncoArendi Therapeutics, ensures a smooth transfer of research results to clinics. Head: Leszek Kaczmarek, Ewelina Knapska, 2018-2024, PLN 35,000,000.

3. Available research equipment, apparatus/infrastructure and intangible assets held in the context of implementation of a project regarding artificial intelligence (max. 1 A4 page).
- **NEBI - National Centre for Advanced Analysis of Biological and Biomedical Imaging** - a state-of-the-art platform for multidimensional imaging of biological processes necessary for proper functioning of the organism and its dysfunctions underlying civilization diseases. NEBI has an advanced IT infrastructure for data collection and processing and the creation of an integrated computing platform. Unique computer programs are developed for the analysis of large data sets from gene sequencing and transcriptomics, cell phenotyping and imaging of metabolic processes, cells, tissues and whole organisms. Selected equipment: apparatus for high-throughput assessment of mouse behavior combined with *in vivo* imaging of brain activity; magnetic resonance imaging, two confocal microscopes, high throughput confocal microplate microscope; super-resolution microscope, holographic (3D) microscope, *in vivo* bioluminescence imaging device, 5-laser cell sorter; 5-laser Spectral Cytometer; numerous specialized laboratories of molecular biology, biochemistry and neurobiology using numerous specialized software for large-scale analyzes. The project ensures full complementarity of research and enables platform users to implement both static and dynamic scenarios on the external HPC/HTC supercomputing infrastructure in Poland and Europe (access to the PL-Grid infrastructure and the new PRACE-LAB infrastructure).
 - **Neurobiology Center** - Equipment: Novaseq6000 and HiSeq Illumina 1500 sequencers with 3 servers with 180 TB capacity; 2 sets of instruments for isolation and analysis of nucleic acids (TAPESTATION, Bioanalyzer), laser microdissection system, Controller Chromium 10X single cell library preparation and transcriptome analysis workstation. NGS sequencing protocols were developed for various applications: RNAseq, miRNAseq, ATACseq, scRNAseq, targeted, exome and whole-genome DNA sequencing, circulating tumor DNA sequencing.
 - Existing unique bioinformatics resources: **Nencki Genomics Portal** - integrated IT tools and genomic and transcriptomic databases. **NGS platform** – a diagnostic platform for molecular analysis of brain tumors (<https://ngs.nencki.edu.pl/>).
 - Unique software developed at the Nencki Institute: dendritic spike morphology analysis software based Monte Carlo simulations (Ruszczycki et al. BMC Bioinformatics. 2012, 13:213. doi: 10.1186/1471-2105-13-213); software combining 3D-EMISH and 3-D chromatin imaging (Trzaskoma et al. Nat Commun. 2020, 11(1):2120. doi: 10.1038/s41467-020-15987-2).
 - Unique repository developed at the Nencki Institute: unprocessed and computationally compiled data on DNA methylation, transcription, chromatin openness, histone modifications (H3K4me3, H3K27ac, H3K27me3) from 32 glioma patients (<http://regulomics.mimuw.edu.pl/GliomaAtlas/>) (Stepniak et al. Nat Commun. in print; BioRX <https://doi.org/10.1101/867861>). Datasets on single cell RNAseq from immune cells from gliomas (Ochocka et al. Nat Commun **12**, 1151 (2021). <https://doi.org/10.1038/s41467-021-21407-w>).

4. Facilities or incentives to establish an AI Centre of Excellence in the entity (max. 1 A4 page).

The Nencki Institute is one of Poland's top-ranking centers in basic and translational research. Our modern research infrastructure enables us to acquire unique biological data on a large scale, including information about entire genomes and transcriptomes, three-dimensional chromatin and cellular structures, and physiological activity profiles. The Genomic, MRI, and Imaging Microscopy facilities provide high-quality services for research groups. It enables researchers to use large-scale, unbiased technologies as a part of their research. Profound changes in gene expression profiles and the activity of signaling pathways underlie human diseases from cancer to neurodegenerative, lifestyle and civilization diseases. Therefore, identifying the mechanisms leading to aberrant cell activity is crucial for developing new clinical strategies. However, the complex etiology of human diseases combined with the intricacy of the functional interactions between genomes and environment renders this task difficult. The answer will be to adopt a holistic approach to jointly represent the biochemical and biophysical processes occurring in the cells in normal and pathological settings. Hence, the integration of transcriptomics, and epigenomics including the information on chromatin three-dimensional structure, will allow us to build more realistic models of cellular states and create a dynamic picture of molecular processes driving pathological states. Currently, computational approaches towards large and multivariate data integration are not sophisticated. Hence, the salient biological information remains hidden, buried in noise introduced by inadequacies of cross-platform data integration. **Therefore, there is an urgent need to create new computational tools and statistical approaches to jointly analyze and model data across analytical platforms.** Due to its robustness and power, artificial intelligence (AI) and machine learning approaches are the future of the analysis of the collected genomic, biochemical and physiological data. Hence, we propose to organize the AI center devoted to the development of AI tools to combine multiple 'omics' data generated at the Nencki Institute with high content microscopy to create an interactive, three-dimensional image of the cellular nucleome/cells. Alongside, using the AI we will decorticate publicly available genomic, transcriptomic, epigenetic, 3-dimensional chromatin structure data from disease condition, including brain tumors and brain metastases, and create more realistic models of cell states in pathological contexts. This systematic approach will likely allow us to find new diagnostic markers, which will be potentially critical for the future design of personalized therapies in oncology. We will develop and implement virtual and augmented reality analysis techniques for intuitive and straightforward data visualization and interpretation. Our aim is to build easily transferable data packages and tools that we will disseminate to other institutions and to clinicians. This will allow to address the pressing need to bridge the gap between fundamental science and clinical practice. Our Institute's infrastructure provides optimal environment for running challenging computational experiments and simulations (data streaming & pipelines). We access high performance parallel computing resources including cloud (ICHB PAN, PSNC) and clusters within the PRACE-LAB and PL-Grid infrastructure in Poland; we currently build an edge computing cluster (a branch of the institute in Mikołajki). We have already established multiple computational routines to automatically process imaging data, and next generation sequencing data and extract biologically significant information.

5. Other information concerning internationalisation of the entity, foreign scientists employed in this institution, availability of seminars in English, etc. (max. 1 A4 page).

The internationalization of the Nencki Institute is evidenced by the implementation of such projects as:

- **Bio4Med** (EU Horizon 2020 MSCA COFUND) - international, interdisciplinary and cross-sectoral PhD studies aimed at understanding molecular mechanisms of civilization diseases. 22 PhD projects were led by 22 leading research groups of the Nencki Institute collaborating with Partners from 22 leading scientific institutions from the EU, Switzerland, Japan, Canada, USA and Ukraine.

- **DIOSCURI** (two Centers of Excellence jointly organized by the Polish National Science Center and the German Max Planck Society). The DIOSCURI International Advisory Board consists of: Prof. Joachim Sauer (Humboldt-Universität), Prof. Sir Leszek Borysiewicz (University of Cambridge), Prof. Rainer Blatt (Universität Innsbruck), Prof. Ralph Bock (Max Planck Institute), Prof. Eberhard Bodenschatz (Max Planck Institute), Prof. Stefanie Dehnen (Universität Marburg), Prof. Eva Holtgrewe-Stukenbrock (Universität zu Kiel), Prof. Ulman Lindenberger (Max Planck Institute), Prof. Eero Tarasti (University of Helsinki), Prof. Magdalena Waligórska-Huhle (Universität Bremen) and Prof. Maciej Żylicz (FNP).

- **FOIE GRAS** and **ECMED (Initial Training Networks)** under EU Horizon 2020), as well as **EXTRABRAIN**, **nEUROinflammation** and **NAMASEN** (Innovative Training Networks under the EU FP7).

- **BRAINCITY: Center of Excellence for Neural Plasticity and Brain Disorders** – an International Research Agenda funded by the Foundation for Polish Science (2018-2024), with the European Molecular Biology Laboratory (EMBL) as the strategic partner. The aim of BRAINCITY is to understand the mechanisms and develop new diagnostic and therapeutic methods targeting neurological diseases. BRAINCITY consists of 5 modern scientific laboratories that cooperate with neurological and psychiatric clinics of Warsaw Medical University, Institute of Psychiatry and Neurology in Warsaw and Children's Memorial Health Institute in Międzylesie. Cooperation with biotechnology and pharmaceutical companies, such as Celon Pharma and OncoArendi Therapeutics, ensures the potential translation of research results into applications for patients. The BRAINCITY International Scientific Committee consists of: Dr. Cornelius Gross (EMBL Rome), Prof. Marta Miączyńska (International Institute of Molecular and Cell Biology), Prof. Camilla Bellone (University of Geneva), Prof. Jakub Gołąb (Medical University of Warsaw), Katarzyna Kotulska-Jóźwiak (Children's Memorial Health Institute), Dr. Kyung-Min Noh (EMBL Heidelberg), Prof. Sir Michael Owen (Cardiff University), Prof. Giuseppe Testa (University of Milan) and Dr. Maciej Wiczorek (Celon Pharma SA).

- In 2019, the Nencki Institute of the Polish Academy of Sciences hosted the official opening of the **SPARK-POLAND** program, a part of the global SPARK-GLOBAL 'translational scientists without borders' initiative. The Director of SPARK POLAND is Prof. Agnieszka Dobrzym (Director of the Nencki Institute), the Manager - Dorota Gierej-Czerkies, PhD. SPARK POLAND Advisory Board consists of: Prof. Craig Garner, Dr. Liliane Brunner Halbach, Prof. Franz Theuring and Prof. Maciej Żylicz.

Currently, the Nencki Institute employs 18 scientists from 11 countries. The Institute seminars and lectures at the PhD school are conducted in English. Also, seminars in the laboratories are conducted in English, depending on the internationalization of the participants.

6. Other significant information confirming the experience and resources of the institution (max. 1 A4 page).

The Nencki Institute of Experimental Biology of the Polish Academy of Sciences is currently the largest non-university biological research centre in Poland (**scientific category A+**). Currently, the Institute employs over 350 people and educates over 160 PhD students from 9 countries. Over 160 scientists conduct their research here working collaboratively across disciplines. A high number of publications in prestigious journals from the JCR list (ca. 140/year) attests to the great research potential of the Institute's staff. The Institute is dedicated to understanding the fundamental biology underlying health and disease. Our work is helping to understand why disease develops and to translate discoveries into new ways to prevent, diagnose and treat illnesses such as cancer, heart disease, diabetes, stroke, aging, infections and neurodegenerative diseases. In addition to basic biological research, the Institute provides expertise in translational research, including preclinical studies. The Institute is open to cooperation with industrial entities aimed at introducing new products into the pharmaceutical, biomedical and biotechnological markets.

The Institute conducts interdisciplinary world-class research in the field of high-resolution and high-throughput imaging. The accumulation of equipment base and scientific expertise in the area of bioimaging enabled the Institute to obtain the status of the **Polish Euro-BioImaging Node** and to offer advanced techniques of structural and functional imaging of biological material to users, also outside the Institute. In addition, the Nencki Institute has extensive experience in the construction and management of national research infrastructure, as exemplified by its participation in the key OPIE project - Centre for Preclinical Research and Technology (CePT), which was the largest biomedical and biotechnological project in Central and Eastern Europe and, at the same time, the largest investment in science in Poland. As part of this project, the Neurobiology Centre was established at the Nencki Institute on newly built space, which successfully functions as a complex of open environmental laboratories. We interact with scientific units from all over the world. Currently, the staff of the Nencki Institute carry out over 60 research works in scientific cooperation with research units from 25 countries, participating in almost 30 scientific consortia and 8 scientific networks. We are currently implementing 5 projects within Horizon 2020 program (including two ERC Starting Grants), over 170 projects financed from NCBiR, NCN, MNiSW and FNP funds (among others, a grant for establishing an International Research Agenda - Centre of Excellence for Neuronal Plasticity and Brain Disorders BRAINCITY), two DIOSCURI Centres of Excellence, and a prestigious grant within the Human Frontier Science Program.

The institute has a group of researchers interested in applying artificial intelligence to the analysis of complex and large data sets. The new leader will be provided with a friendly and creative environment to exchange ideas and experiences. The institute offers excellent opportunities for outstanding scientists from different disciplines and at all career stages to develop themselves and their research. This dynamic career structure and the associated staff turnover will allow the introduction of fresh knowledge and ideas to drive the development and renewal of our scientific programmes.