Marceli Nencki was born in 1847 in Boczki near Sieradz in western Poland. He studied medicine in Berlin and obtained the degree of Doctor of Medicine in 1870 for his studies on the oxidation of aromatic compounds. In 1872, he worked as a research assistant at the University of Bern (Switzerland). In 1876, he was appointed Associate Professor and a year later full Professor and Director of the Institute of Medical Chemistry (Medizinisch-Chemisches Institut) at the University of Bern (currently Institut für Biochemie und Molekularbiologie). After 20 years working in Bern, Nencki and the well-known Russian physiologist Ivan P. Pavlov established the Institute of Experimental Medicine, in St. Petersburg, Russia, where he spent the last decade of his life. He died of stomach cancer in 1901 at the age of 54.

Nencki’s scientific interests concentrated, among others, on urea synthesis, chemistry of purines and biological oxidation of aromatic compounds. He was also interested in the structure of proteins, enzymatic processes in the intestine and bacterial biochemistry. One of his key achievements was the demonstration that urea is formed from amino acids, rather than existing in a preformed state on a protein molecule, and that its biosynthesis is accompanied by carbon dioxide fixation. He also demonstrated, together with Pavlov, that the liver is the site of urea synthesis in animals. Another of his key discoveries, in collaboration with Leon Marchlewski, was on the chemical structure of haemoglobin. Leon Marchlewski (1869-1946), who studied the chemical nature of the green plant pigment chlorophyll, initially in the United Kingdom and then at the Jagiellonian University in Cracow (Poland), came across Nencki (who by then was interested in the chemical structure of haemoglobin) by chance through his published work. The two scientists started correspondence and exchanging samples of degradation products of these pigments. The ultimate result of this long-distance collaboration was the discovery of a close chemical relation between haem and chlorophyll. Three letters from Nencki to Marchlewski have recently been acquired by the Institute concerning their collaboration.
BIO-IMAGINE is a strategic project aimed at establishing the Nencki Institute as a leading central European research centre studying the all aspects of the nervous system from molecular to the whole organism using advanced biological imaging techniques. The Institute is the beneficiary of one of only two projects funded in Poland in response to the FP7 Capacities call for proposals FP7-REGPOT-2010 by the European Commission.

TOTAL budget: 3 623 666 EUR
EC Contribution: 2 550 000 EUR

General project objectives
• to foster interactions between the Nencki Institute and leading research partners in Europe
• to expand the scope of technologies and introduce new state-of-the-art imaging equipment at the Institute and broaden its know-how
• to strengthen the competence of the Institute and increase its attractiveness to researchers from other institutions and countries
• to improve the Institute’s position as a regional competence centre and an important node of the Euro-BioImaging (European Biomedical Imaging Infrastructure) initiative in Europe.

Specific project objectives
• to improve the Institute’s human potential and intellectual capacity by recruiting 13 experienced researchers: 11 postdocs, one new group leader and one imaging core facility manager
• to initiate, reinforce and/or consolidate the cooperation, transfer of know-how and research methods between fourteen Nencki research groups and their partners from 14 prominent research institutions in Europe
• to stimulate innovation through implementation of a policy for management of intellectual property and knowledge transfer, through activities and support mechanisms by partnering with and transferring know-how and best practice from European leaders in this area
• to upgrade the highly specialized equipment base by acquiring a confocal system based on the spinning (or Nipkow) disk technology and a Guava easyCyte 8HT Flow Cytometry System, a “desk top” solution. Both systems will be used in joint research by the recruited researchers, in education and training as well as for technology transfer and innovation-type activities
• to promote knowledge exchange and the Institute’s research at the European level by i) organizing workshops, international conferences and satellite sessions to larger meetings as well as ii) supporting attendance at international conferences and workshops for Nencki researchers
• to increase the recognition of the Nencki Institute brand name, to disseminate knowledge and improve awareness of the results of its scientific research among various stakeholder groups through organization of promotional and open education events and use of other promotion channels
• to improve and update the management procedures and the organizational structure of the Institute through effective project management and recommendations from an 11-member Steering Committee comprised of several prominent European scientists and science managers among other stakeholder representatives
• to evaluate the achieved project results and their long term sustainability by an external group of Commission experts working closely with the Steering Committee and the project management team.

BIO-IMAGINE work programme consists of 7 interrelated Work Packages that will enable the applicant to achieve the seven specific project objectives.

The flagship workpackage of the project is WP1 (Increasing Human Potential) and it is its most critical component. During the course of the project 13 experienced researchers will be recruited. Workpackage 2 (Sharing of Know-How and Technologies through Networking) will facilitate scientific exchange with fourteen outstanding research groups at leading research organizations in Europe. Workpackage 3 is designed to stimulate Innovation and Technology Transfer. Results
of this WP should enable designing a TT model as a case study for Poland in the Life Sciences sector. Purchases of research tools and equipment were planned within WP4 (Improvement of Research Capacity). Within WP5 (Conferences and Workshops) various meetings will be organized, all within the general thematic scope of WP1 and 2. WP6 (Promotional Activities and Dissemination of Knowledge) will help to increase the awareness and appreciation of the significance of scientific results and discoveries generated by the Institute researchers among various stakeholder groups (decision makers, funding agencies, students at high school and university levels and the general public). Workpackage 7 (Project Management) will facilitate efficient and effective execution of all other project activities and provide guidance for the Institute to sustain project results and build on its positive impact to fulfil its long-term mission. The Institute achievements in this project will be evaluated by a team of independent experts in WP8 after the completion of all other activities.

Achieving the Project goals would help the Nencki Institute to establish a position of a regional bio-imaging competence centre and to become an active and important node of the Euro-BioImaging initiative in Europe. It will become possible through close partnerships, including twinning with research groups elsewhere in Europe. Through these activities the Institute will become fully integrated in the European Research Area as a whole. The process of unlocking research potential at the Nencki Institute in Warsaw will have a catalytic effect on collaborating research centres within the CePT consortium on the Ochota Research Campus as well as elsewhere in Poland and the neighbouring convergence regions. BIO-IMAGINE can provide the triggering effect for stimulating innovation in life sciences for the Ochota Research Campus and the entire region.
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Mission of the Nencki Institute
The Mission of the Nencki Institute of Experimental Biology is to excel in basic scientific research, maintaining the highest quality of scientific output in terms of created and disseminated knowledge, which can be applied in the context of wider societal needs to improve the quality of life.

The Institute aspires to fulfill its mission by investing in human capital, in modern technologies, and by stressing the importance of effective international collaboration.

Nencki Institute of Yesterday
The Institute was founded in 1918, shortly after the re-establishment of Poland as an independent country. It was based on three pre-existing laboratories affiliated with the Scientific Society of Warsaw (Towarzystwo Naukowe Warszawskie): Laboratory of Neurobiology (1911), Laboratory of Physiology (1913) and Laboratory of General Biology (1918). Formation and development of the Institute was supported in part by a donation of Nadine Sieber-Shumova, a close co-worker of Marceli Nencki from Bern and St. Petersburg.

Over the next two decades the Institute grew to become the leading biological research centre in Poland. The outbreak of World War II interrupted a period of its intensive expansion and achievement of scientific excellence in the field of experimental biology. After the turmoil of the war, during which over a dozen of the Institute’s staff lost their lives, and its premises (including most of its 30,000-volume library) were destroyed, the surviving staff members (professors Jan Dembowski, Jerzy Konorski, Włodzimierz Niemierko, Liliana Lubinińska, Stella Niemierko and Stanisława Dembowska) re-established the Nencki Institute. In 1952, the Institute was incorporated into the newly founded the Polish Academy of Sciences, and the Institute’s director, Prof. Dembowski, became the first President of the Academy. During the period of 1953-55, a newly erected building at 3 Pasteur Street in Warsaw became the final home of the Nencki Institute.

In 1990, the Institute was invited to become a member of the Global Network for Molecular and Cell Biology (MCBN) within UNESCO. Continuously hiring new talented researchers and awarding approximately 15–20 doctoral degrees annually, the Nencki Institute is known for its competitiveness in securing external funding for research projects as well as for the number and quality of its scientific publications. Recent success of its researchers in competitive European Community proposals is demonstrated by the formation of two European Centres of Excellence within the Institute.

Nencki Institute of Today
At the beginning of the 21st century, biology is faced with the enormous task of understanding how the information of the entire genome results in the complex biology of living organisms. Employing over 230 full-time staff (of whom about 140 are research scientists) and training 117 PhD students, who are doing their research in 33 laboratories located in 4 departments (Department of Neurophysiology – 11 laboratories, Department of Molecular and Cellular Neurobiology – 8 laboratories, Department of Biochemistry – 9 laboratories, Department of Cell Biology – 5 laboratories), the Nencki Institute is currently the largest non-university biological research centre in Poland. The Institute is committed to generating, disseminating, and preserving biological knowledge in order to meet contemporary challenges of the Polish society. High quality of externally funded research, excellent publication record, and strong international links place the Nencki Institute among the leading biological institutions of Central and Eastern Europe.
The research goals of the Nencki Institute are to arrive at molecular, cellular and systemic explanations of excitability, movement, development, memory, learning, behaviour, ageing and disease. All those tasks need to be both intellectually satisfying and relevant to problems of human health.

Neurobiology and biochemistry represent two main research areas of the Institute. The Nencki Institute is the only research centre in Poland, in which neurobiology is thoroughly studied from the molecular to the systemic level. Research projects in this field are carried out by teams belonging to the Department of Neurophysiology, Department of Molecular and Cellular Neurobiology and the Department of Biochemistry. For the teams from the two latter departments neural tissue and cells are the principal models, whereas in the Department of Neurophysiology studies are also conducted on rodents, cats, insects and humans. In addition, research in the Department of Biochemistry is focused on structure and functional properties of cytoskeletal and motor proteins, on regulation of contractile processes, on biological membranes, bioenergetics of cellular processes, metabolic regulation, signal transduction, and regulation of gene expression. The Department of Cell Biology and several other laboratories carry out studies on signaling, plasma membrane dynamics, cell growth and differentiation, cell motility, molecular mechanisms of cell excitability, and ion channels of eukaryotic and prokaryotic cells.

The Institute also places a high emphasis on education and training. We actively recruit the best PhD candidates with the highest academic achievements, keen intellectual curiosity, and the desire to excel professionally and personally. Our staff provides them with a rigorous background in scientific concepts, tools, and a hands-on learning environment. The best of the students, after completing PhD studies with honours and a successful external postdoctoral stage, have the opportunity to return to one of our scientific teams as assistant professors, or to form a new team. New laboratories are created at the Institute to facilitate recruitment of the best specialists in research areas that are new and complementary to our current research profile. The Nencki Institute is an equal opportunity employer with full awareness of gender issues in scientific research (women account for approximately 65% of the Institute’s research and administrative staff, including senior level positions).
Scientific Council in the term of 2011–2014

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Leszek Kaczmarek

**Vice-chairmen**
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Andrzej Wróbel

**Secretary**
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Barbara Przewłocka
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Andrzej Tarkowski
Piotr Zielenkiewicz
Structure of the Nencki Institute

The Nencki Institute consists of four Departments subdivided further into laboratories, supporting units, a modern animal house, a library, scientific publications section and administration units.

DEPARTMENT OF BIOCHEMISTRY
Head: Jolanta Maria Rędowicz

8
Laboratory of Lipid Biochemistry
Head: Sławomir Pikuła

10
Laboratory of Bioenergetics and Biomembranes
Head: Jerzy Duszyński

12
Laboratory of Comparative Enzymology
Head: Wojciech Rode

14
Laboratory of the Molecular Basis of Ageing
Head: Ewa Sikora

16
Laboratory of Intracellular Ion Channels
Head: Adam Szewczyk

18
Laboratory of Cellular Metabolism
Head: Krzysztof Zabłocki

20
Laboratory of Cell Signaling and Metabolic Disorders
Head: Agnieszka Dobrzyń

22
Laboratory of Motor Proteins
Head: Andrzej A. Kasprzak

24
Laboratory of the Molecular Basis of Cell Motility
Head: Maria Jolanta Rędowicz

DEPARTMENT OF CELL BIOLOGY
Head: Katarzyna Kwiatkowska

28
Laboratory of Cell Membrane Physiology
Head: Elżbieta Wyroba

30
Laboratory of Transcription Regulation
Head: Bożena Kamińska-Kaczmarek

32
Laboratory of Cell Movement Physiology
Head: Stanisław Fabczak

34
Laboratory of Plasma Membrane Receptors
Head: Andrzej Sobota

36
Laboratory of Signal Transduction
Head: Tomasz Wilanowski
DEPARTMENT OF NEUROPHYSIOLOGY
Head: Andrzej Wróbel

Laboratory of Psychophysiology
Head: Anna Grabowska

Laboratory of Defensive Conditioned Reflexes
Head: Tomasz Werka

Laboratory of the Limbic System
Head: Stefan Kasicki

Laboratory of Ethology
Head: Ewa Joanna Godzińska

Laboratory of the Visual System
Head: Andrzej Wróbel

Laboratory of Neuropsychology
Head: Elżbieta Szeląg

Laboratory of Reinnervation Processes
Head: Julita Czarkowska-Bauch

Inter-institute Laboratory of Neuromuscular Plasticity
Head: Urszula Sławińska

Laboratory of Molecular and Systemic Neuromorphology
Head: Grzegorz Wilczyński

Laboratory of Neuroinformatics
Head: Daniel Wójcik

Laboratory of Preclinical Studies in Neurodegenerative Diseases
Head: Grażyna Niewiadomska

DEPARTMENT OF MOLECULAR AND CELLULAR NEUROBIOLOGY
Head: Małgorzata Kossut

Laboratory of Calcium Binding Proteins
Head: Anna Filipek

Laboratory of Mechanisms of Transport Through Biomembranes
Head: Katarzyna Nałęcz

Laboratory of Neuroplasticity
Head: Magorzata Kossut

Laboratory of the Molecular Basis of Brain Plasticity
Head: Jolanta Skangiel-Kramska

Laboratory of Neurobiology
Head: Leszek Kaczmarek

Laboratory of Developmental and Evolutionary Neurobiology
Head: Krzysztof Turlejski

Laboratory of Epileptogenesis
Head: Katarzyna Łukasiuk

Laboratory of Bioinformatics and Systems Biology
Head: Krzysztof Pawłowski
SUPPORTING UNITS

82 Laboratory of Electron Microscopy
Head: Elżbieta Wyroba

83 Laboratory of Confocal Microscopy
Head: Wanda Kłopocka

84 Laboratory of Cytometry
Head: Katarzyna Piwocka

85 Laboratory of Cell Engineering
Head: Agata Klejman

86 The Animal House
Head: Anna Passini

87 Information Technology Unit
Head: Mirosław Sikora

88 Library
Head: Jan Bienias

89 Publications Office
Head: Krzysztof Turlejski

90 Office of International Relations and Project Management
Head: Marcin Szumowski

EDUCATION

91 PhD Studies
Head: Jolanta Sklangiel-Kramska

ADMINISTRATION UNITS

92 Administration
Head: Anna Jachner-Miśkiewicz

92 Finance and Account
Head: Hanna Michalska

93 Human Resources and Recruitment Office
Head: Urszula Dziewulska

93 Administrative Support:
- Secretary to the Director of the Institute
  Beata Kuźniarska
- Secretary to the Administrative Director
  Elżbieta Stańkiewicz
- Secretary to the Scientific Council
  Agata Siudek
The Department of Biochemistry consists of nine laboratories. The research projects carried out in the Department are focused on molecular regulation of cell fate and physiology under normal and pathological conditions.

We are interested in delineating signaling pathways responsible for cell stress, death and senescence as well as lipid metabolism in normal and pathological conditions. The mechanisms of the protective action of potassium channel openers on cardiac and skeletal muscle mitochondria are also a subject of the studies, as they can have serious application in protecting against heart damage. Projects aimed at novel approaches to old targets in chemotherapy are focused on thymidylate synthase post-translational modifications and capacity to bind RNA and suppress translation. In particular, attention is paid to the role of mitochondria in cellular stress, apoptosis and calcium homeostasis with an emphasis on various calcium-binding proteins. Mammalian annexins, their structure, function and role in human diseases, in which membrane permeability to ions and vesicular transport are affected, are also investigated. The studies on motile systems are mainly focused on structure-function relationships of molecular motors (kinesins and myosins), cytoskeletal and adaptor proteins. Functional interaction of prions with the microtubular system is also studied. The molecular mechanisms of mitotic catastrophe and cellular senescence as a cell fate of cancer cells resistant to apoptosis induced by many factors and demonstrating that curcumin, a natural dye, is a potent inducer of these processes (Head of Laboratory – Ewa Sikora)

Major recent achievements of the laboratories include:

- characteristics of participation of annexins in tissue mineralization, secretion of catecholamines, and transport and storage of cholesterol in Niemann-Pick type C disease (Head of Laboratory – Sławomir Pikula)
- further elucidation of the mechanism of cellular stress and a role of interactions between mitochondria, the plasma membrane and the endoplasmic reticulum under normal and pathological conditions in mammalian cells (Head of Laboratory – Jerzy Duszyński)
- finding of high expression of enzymes involved in thymidylate biosynthesis in developmentally arrested larvae of parasitic (Trichinella spiralis and T. pseudospiralis) and free-living (Caenorhabditis elegans) nematodes, suggesting global cell cycle arrest (Head of Laboratory – Wojciech Rode)
- elucidation of the molecular mechanisms of mitotic catastrophe and cellular senescence as a cell fate of cancer cells resistant to apoptosis induced by many factors and demonstrating that curcumin, a natural dye, is a potent inducer of these processes (Head of Laboratory – Ewa Sikora)
- identification of new potassium channels in the inner mitochondrial membrane (Head of Laboratory – Adam Szewczyk)
- identification of nucleotide receptors participating in the impaired calcium homeostasis in dystrophic mouse myoblasts (Head of Laboratory – Krzysztof Zabłocki)
- establishing the role of stearoyl-CoA desaturase in regulation of cardiac substrate utilization and of muscle insulin sensitivity (Head of Laboratory – Agnieszka Dobrzyń).
- production and purification of a heterodimeric kinesin Ncd, in which each of the subunits can be independently genetically manipulated (Head of Laboratory – Andrzej Kasprzak).
- characterization of the effects of prion protein on microtubule formation and proteomic analysis of Ruk/CIN85 binding-partners and functional implications of translocation of myosin VI into the nucleus (Head of Laboratory – Maria Jolanta Rędowicz)

The field of expertise of members of the Department is powered by many experimental units accessible within the Department or in the Institute core facility laboratories, described in the relevant sections within this issue.
Selected publications:


Breast carcinoma HCC 1937 cells – actin filaments (green), microtubules (blue), nucleus (red)

Human osteosarcoma cells – microtubules (green), mitochondria (yellow), nucleus (red)

Human osteosarcoma cells (mitochondria)
Laboratory of Lipid Biochemistry

Head: Sławomir Pikuła
Staff: Joanna Bandorowicz-Pikuła, Anna Ćmoch (PhD student), Magdalena Domoń (PhD student), Le Duy Do (PhD student), Michalina Kosiorek (PhD student), Krzysztof J. Skowronek, Agnieszka Strzelecka-Kiliszek

Research profile:
- calcium homeostasis with special emphasis on calcium- and lipid-binding proteins, including mammalian and plant annexins
- early stages of biomineralization with a focus on biogenesis and the function of matrix vesicles
- membrane dynamics and membrane repair process
- vesicular transport with a focus on intracellular transport of cholesterol in norm and pathology
- molecular machinery involved in catecholamine secretion
- lipid metabolism in norm and pathology; calcium signal transduction; transport of ions, metabolites and xenobiotics through biological membranes
- ion channels formed by calcium- and membrane-binding proteins; nucleotides as intracellular messengers and their target proteins
- annexin-related human diseases, annexinopathies

Methods:
- cell cultures
- FACScan
- siRNA
- planar lipid bilayers
- brewster angle microscopy imaging
- immunofluorescence microscopy
- confocal microscopy
- electron microscopy
- site directed mutagenesis
- fourier transformed infrared spectroscopy
- steady-state fluorescence spectroscopy

Current research activities:
- structure-function relationship within the mammalian family of membrane- and calcium-binding proteins, annexins
- interactions of nucleotides with annexins; effects on intracellular calcium homeostasis, signal transduction and vesicular transport
- ion channel properties of annexins
- participation of annexins in transport of cholesterol and secretion of catecholamines
- factors affecting annexin and alkaline phosphatase functioning during matrix vesicles-mediated biological mineralization
Selected publications:


The effect of cytochalasin D and blebbistatin on the mineralization process in human osteosarcoma Saos-2 cells. The cells were stimulated in the presence of ascorbic acid and β-glycerophosphate and observed in the Axio Observer.Z1 light microscope. Minerals were visualized with Alizarin red-S.

Rat pheochromocytoma PC12 cells were stained with antibodies against plasma membrane Ca\(^{2+}\)-ATPase isoform PMCA4 (green), and calcineurin (red), and observed in the TCS SP5 confocal microscope. Yellow indicates merge images. From the left – control cells, cells with diminished level of PMCA2 (in the center) or PMCA3 (on the right). Scale bar – 10 μm.
Laboratory of Bioenergetics and Biomembranes

Head: Jerzy Duszyński

Staff: Małgorzata Bejtka (PhD student), Violetta Biernat, Magdalena Lebiedzińska, Dominika Malińska, Luiza Sanjuan Szklarz, Jan Suski (PhD student), Joanna Szczepanowska, Jarosław Walczak (PhD student), Mariusz Więckowski, Marta Wojewoda, Aleksandra Wojtala (PhD student), Lech Wojtczak (Professor emeritus)

Research profile:
- mitochondrial energy metabolism and energy coupling
- calcium homeostasis in normal and malignant cells
- mitochondrial stress, cytoskeleton and mitochondrial organization
- oxidative stress; p66Shc and ageing
- the role of mitochondria in apoptosis and ageing
- mitochondrial diseases

Methods:
- measurement of mitochondrial parameters
- measurement of ROS ( Reactive Oxygen Species) production
- cell subfractionation (isolation of mitochondria, ER, the plasma membrane, PAM and MAM fractions)
- Blue Native and Clear Native PAGE with the “in-gel” activity assay
- [Ca^{2+}] measurements in intracellular compartments with fluorescent and aequorin probes

Current research activities:
- regulation of calcium homeostasis in mammalian cells. The role of PAM (Plasma Membrane Associated Membranes) and MAM (Mitochondria Associated Membranes) components in calcium homeostasis
- interactions between mitochondria and the ER
- effect of mitochondrial genetic defects on cell structure, mitochondrial energy state, generation of ROS and calcium homeostasis in human cells with defined mitochondrial disorders
- the role of p66Shc protein in oxidative stress and ageing
- effect of antioxidants and inhibitors of p66Shc pathway on oxidative stress and mitochondrial energetic state in human fibroblasts harboring mitochondrial defects
- metabolic and genetic mitochondrial stress – effect of selenium
- the role of UCP (Uncoupling Protein) in energy coupling and antioxidant defense
- role of glycogen in the nervous system
Selected publications:


Research profile:
Different aspects of thymidylate biosynthesis, such as its enzymology, structure, regulation, inhibition, as well as post-translational modifications, and their influence on the enzyme properties are investigated. Problems connected with thymidylate synthase being a target in chemotherapy, including search for new inhibitors/drugs, drug resistance, specificity and mechanism of action, as well as mechanisms of enzyme inhibition and its specificity, are of particular interest. Another line of studies focuses on cell fate decision mechanisms, using two model experimental systems of senescence-like growth arrest, the nurse cell of *Trichinella spiralis* parasite and methotrexate-exposed human colon cancer cells, with bioinformatic approach applied to infer active signaling pathways. Certain molecular aspects of host immunological response to *Trichinella spiralis* infection are also studied.

Methods:
- classic enzymology, incl. kinetic studies
- genomics and genetic engineering
- purified recombinant enzyme protein production
- enzyme protein chemical modification
- molecular modeling (molecular dynamics, quantum mechanics)
- protein crystallography

Current research activities:
- developmental pattern of expression of enzymes involved in nematode thymidylate biosynthesis as potential new target for antiparasitic chemotherapy
- effects of post-translational modifications on thymidylate synthase catalytic and non-catalytic (binding repressing translation of its own mRNA) properties.
- mechanism of thymidylate synthase reaction and its inhibition, including search for new inhibitors
- mechanism of establishment of methotrexate–induced cancer cell senescence
Selected publications:


Laboratory of the Molecular Basis of Ageing

Head: Ewa Sikora
Staff: Olga Alster (PhD student), Anna Bielak-Żmijewska, Magdalena Dudkowska, Wioleta Grabowska (student), Dorota Janiszewska, Anna Karpa, Zbigniew Korwek (PhD student), Grażyna Mosieniak, Dorota Przybylska (PhD student), Halina Waś

Research profile:
The research profile of the laboratory is focused on the mechanisms of cell cycle regulation, cellular senescence and cell death of primary, immortalized and cancer cells. Particularly, we are interested in:

- the role of reactive oxygen species and DNA double strand breaks involved in the DNA damage response (DDR) leading to stress-induced premature senescence (SIPS) of normal, immortalized and cancer cells and replicative senescence of normal human cells including T cells
- the connection between DNA damage and mitotic checkpoints and its role in genomic instability and cellular senescence
- the role of apoptosis and autophagy in cellular senescence and organismal ageing
- the natural polyphenol curcumin, derived from the rhizome of Curcuma longa and its synthetic derivatives as hormetins protecting against (low concentration) and inducing (high concentration) cellular senescence - the influence on the secretome and low grade inflammation

Methods:
- flow and scanning cytometry and cell sorting
- bioimaging by using electron, confocal, fluorescent and optical microscopy
- tissue culture in vitro
- molecular biology methods such as Western blotting, RNAi technique and plasmid transfection

Current research activities:
- immunosenescence focused on searching for immunological markers (T cell phenotypes, propensity to undergo activation- and damage-induced apoptosis) possibly determining healthy ageing and longevity (in the framework of FP7 Mark-Age)
- studies on cellular senescence in vitro elucidating the mechanisms of cell cycle regulation, polyploidy formation, functional activities and the cell capacity to undergo apoptosis
- investigation of the molecular mechanisms leading to cancer senescence induced by low doses of DNA damaging agents and curcumin; cancer cell senescence as a potential anticancer strategy
Selected publications:


Human colon cancer cells undergoing senescence after doxorubicine treatment (blue)

Morphology of human colon cancer cell after treatment with doxorubicine. DNA stained with DAPI (blue) and actin stained with falloidine conjugated with rhodamine (red)
Research profile:
Intracellular ion channels regulate many key cellular functions by controlling the ion flux across different intracellular compartments. Our laboratory is particularly interested in ion channels normally found in the mitochondrial inner membrane. Recently, we have focused on intracellular ion homeostasis, pharmacology of intracellular potassium channels, pharmacology of mitochondria, interaction of potassium channel openers with mitochondria, role of mitochondria in ischemic preconditioning and cytoprotection, intracellular receptors for antidiabetic sulfonylureas and potassium channel openers, role of mitochondrial ion channels in apoptosis, regulation of chromaffin granules potassium channels by pH and nucleotides. Our overall objective is to study the role of intracellular ion translocating mechanisms in cardiovascular function during health and disease.

Methods:
- electrophysiology
- patch-clamp technique on mitoplasts
- PLM (planar lipid membrane) measurements
- oxygen consumption measurements polarographically with Clark-type electrode
- immunocytochemistry and cytometry
- primary culture of rat brain hippocampal cells
- preparation of intracellular membrane fractions

Current research activities:
The laboratory, established in June 1999, is focused on intracellular ion channels. We study the following topics:
- mechanism of cytoprotective action of potassium channel openers
- functional role of mitochondrial ATP-regulated potassium channel in hippocampus mitochondria
- mitochondrial large conductance potassium (BKCa) channel in glioma cells
- mitochondrial ion channels as early effectors of cellular apoptosis
- regulation of mitochondrial ATP-regulated potassium channels by phosphorylation
- regulation of calcium homeostasis by potassium channel openers in excitable and nonexcitable cells
Selected publications:


Electrophysiological identification of mitochondrial large conductance calcium-activated potassium channel (BKca) in the mitoplast isolated from human EA.hy 926 endothelial cells. Single channel recordings at different voltages in symmetric solution (150 mM KCl, 10 mM HEPES, pH=7.2). Recordings were low-pass filtered at 1kHz

Immunofluorescent localization of large conductance calcium-activated potassium channel (BKCa) β2 subunit in primary culture of hippocampal rat neurons. Confocal image of double immunolabeling for BKCa β2 subunit (green) and neuronal marker-MAP-2 (red).

Immunofluorescence staining of mitochondria using anti-cytochrome C oxidase antibody, in human keratinocyte cells.
Laboratory of Cellular Metabolism

Head: Krzysztof Zabłocki
Staff: Beata Drabarek (PhD student), Dorota Dymkowska, Wanda Klopotka, Elżbieta Krasowska (PhD student), Marta Onopiuk (PhD student), Marta Onopiuk (PhD student), Katarzyna Wierzbicka (PhD student), Sylwia Wojciechowska (PhD student)

Research profile:
The laboratory is focused on energy and lipid metabolism and intracellular calcium handling in relation to cellular metabolism under normal and pathological conditions. Particularly, we are interested in:

- calcium homeostasis, regulation of calcium signals and changes in energy metabolism in muscle cells derived from dystrophic mouse (mdx). In addition, potential dystrophy-related changes in calcium homeostasis in neurons are investigated
- diabetes-related alterations of energy metabolism of muscle, liver, pancreas (beta cells) and endothelium
- mitochondria as a potential pharmaceutical target in insulin resistance therapy and prevention of type 2 diabetes

Methods:
- cell culture
- spectrofluorimetry
- confocal microscopy
- selected methods of molecular biology
- polarography
- flow and laser scanning cytometry
- many standard biochemical methods are in use

Current research activities:
- investigation of dystrophy-related alterations of nucleotide receptors and store-operated calcium channels in myoblasts and neurons derived from dystrophic mdx mouse
- prevention of insulin resistance and hyperglycemia-induced pathological changes in myotubes, hepatocytes, endothelium and beta cells based on the regulation of PARP receptors activity using innovative agonists
Selected publications:


Laboratory of Cell Signaling and Metabolic Disorders

Head: Agnieszka Dobrzyń
Staff: Tomasz Bednarski (PhD student), Paweł Dobrzyń, Anna Dziewulska (PhD student), Anna Gajda, Justyna Janikiewicz, Magdalena Jazurek (PhD student), Katarzyna Kolczyńska (student), Kamil Kozinski (PhD student), Katarzyna Maleńczyk (PhD student), Małgorzata Małodobra, Katarzyna Mnich, Zofia Pilch (PhD student), Aleksandra Pyrkowska, Aleksandra Rumińska (PhD student)

Research profile:
Our research group carries out cutting edge, multidisciplinary studies on signaling and transcriptional cascades that have far-reaching implications on lipid metabolism and human metabolic diseases, i.e. diabetes and obesity-related heart dysfunctions. The long-term goal of our research is to gain in-depth understanding of the functional interaction between transcription factors and obesity related disorders. Our main priority is to understand the role of lipid metabolites in the development of lipid-induced insulin resistance and beta-cell dysfunction. The second priority is to gain insights into the functional role of stearoyl-CoA desaturase (SCD) for heart, skeletal muscle and pancreatic islet metabolism regulation because it will increase our understanding of how lipid partitioning is controlled, and may have important implications for pathogenesis of the metabolic syndrome.

Methods:
• combination of careful biochemistry, whole animal nutrition, molecular genetics and mouse genetics, putting our laboratory in the vanguard of those exploring lipid homeostasis and providing essential insights into the causes of many serious diseases that can result when metabolic homeostasis fails

Current research activities:
• identifying signaling pathways involved in the pathogenesis of insulin resistance and pancreatic beta-cell dysfunction in type 2 diabetes
• studies of transcription factors (STAT, PPAR, PGC1, SREBP) as key molecules involved in lipotoxicity
• determining the role of metabolic and genetic abnormalities in obesity-related heart dysfunction
• studies on neuronal regulation of pancreatic beta-cell function

Insulin receptor activity is significantly increased in the heart of SCD-deficient mice. Insulin receptor (IR) and IR substrate (IRS)-1 phosphorylation and association of IRS-1 with the p85 subunit of phosphatidylinositol 3-kinase (PI 3-kinase) were investigated by immunoblotting in basal condition and after insulin administration.
Selected publications:


Proposed model for the effect of SCD1 gene deletion on heart lipid metabolism and left ventricle function in leptin deficiency. Reduction in myocardial lipid accumulation and inhibition of lipid-induced apoptosis appear to be the main mechanism responsible for improved cardiac function in leptin-deficient ob/ob mice caused by lack of SCD1 function.

The effect of SCD1 deficiency on insulin signaling – proposed mechanism.
Molecular motors are systems of one or several molecules, which are capable of cyclically converting chemical energy derived from adenosine triphosphate (ATP) hydrolysis into mechanical work. The motor protein Ncd, member of kinesin-14 subfamily causes sliding and expansion of an anti-parallel microtubule array by moving one microtubule over another. By hydrolyzing one ATP molecule, Ncd generates a force of up to 7 pN and makes an 8-nm step towards the minus end of the microtubule. In the cell, Ncd plays a pivotal role in the maintenance and organization of the mitotic spindle. Our group is concerned with the force generation mechanism by this motor and particularly with the role of subunit interactions in this process. Our work is also focused on the relationship between the type of motility that Ncd exhibits and its behavior and regulation in the cell. To achieve these goals we combine protein engineering with advanced microscopic techniques and classical biochemistry.

Methods:
- protein engineering
- in vitro motility measurements of motor proteins
- total internal reflection fluorescence microscopy (TIRF)
- fluorescence resonance energy transfer (FRET)

Research activities:
- is the ability of the mitotic kinesin Ncd to recognize the relative orientation of transported microtubules associated with the subunit structure of the motor?
- reconstruction of the microtubule plus-end tracking system of Ncd by EB1. Observation of the transport in vitro using a TIRF microscope
- mapping of the interacting regions on the Ncd-EB1 complex using point mutations in the binding areas
- identification of an Ncd domain responsible for localisation of the motor in the spindle at various stages of cell division
Selected publications:


Ncd is a force generating protein that organizes microtubules into structures, such as the mitotic spindle. Cartoon showing the principle of measuring the rate of microtubule-microtubule sliding under fluorescent microscope.
Laboratory of the Molecular Basis of Cell Motility

Head: Maria Jolanta Rędowicz
Staff: Jolanta Jóźwiak, Justyna Karolczak (PhD student), Łukasz Majewski, Hanna Nieznańska, Krzysztof Nieznański, Iuliia Pavlyk (PhD student), Paweł Pomorski, Dariusz Stępkowski, Dorota Wypych, Tomasz Zajkowski (PhD student)

Research profile:
- involvement of unconventional myosins and actin-binding proteins in cell migration and intracellular trafficking
  - studies on normal and transformed mammalian cells, and amoebae
- role of myosin VI in myogenesis and skeletal muscle functioning
- plasticity of the contractile apparatus from skeletal muscles
- role of prion protein-induced oligomerization of tubulin and phosphorylation of tau protein in the pathogenesis of prion diseases
- effects of arginine deprivation on actin cytoskeleton, cell migration and invasiveness
- formation and cytoskeletal modulation of the receptor-generated calcium signal in living cells
- regulation and mechanism of capacitative calcium signal
- role of calcium signaling in the regulation of cell motility

Methods:
- protein chemistry
- biochemistry
- fluorescence spectroscopy
- molecular and cell biology (micromanipulations, measurements of intracellular ions concentration, in vivo observations of cell motility and adhesion)
- fluorescence and electron microscopy

Current research activities:
- investigation of the involvement of class VI myosin in cell locomotion and intracellular trafficking
- studies on the function of amebin, a novel actin-binding protein from Amoeba proteus
- analysis of the contractile apparatus in normal and atrophied muscles
- probing the interaction of prion protein with microtubular cytoskeleton
- fast calcium signal measurements
- imaging of receptor-induced calcium signal in primary culture neurons
- crosstalk between calcium and RhoA signaling pathways
Selected publications:


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Rat glioma C6 cells stained for Rac1 (green) and filamentous actin (red)

Mouse neuroblastoma NB2a cells stained for tubulin (green) and nuclei (blue)

Human glioma U251 cells deprived 72 hours for lysine stained for filamentous actin with Alexa546-phalloidin

U251 cells deprived for 48 hours of lysine, scanning electron microscopy
The research interests of the Department of Cell Biology encompass the fundamental issues of plasma membrane receptor activation and signal transduction under physiological and pathological conditions. Our activities are directed to study signalling cascades and the regulation of gene expression associated with (i) tumor pathology, (ii) immunoresponses, (iii) endocytosis and phagocytosis, (iv) folding of cytoskeletal proteins and cytoskeleton reorganization. Approaches range from molecular biology to electrophysiology and whole-organism physiology. The ongoing research projects in the Department are focused on:

- Molecular mechanisms regulating endocytosis and degradative pathways investigated in different cell types undergoing gene silencing (RNAi) and stimulation. Characterization of the products encoded by the genes cloned by us in a model unicellular eukaryote *Paramecium octaurelia* and indispensable for endosome/phagosome formation, sorting and membrane trafficking including Rab7 and its effectors. Studies are performed at the protein and cellular levels including proteomics, molecular biology techniques, confocal/electron microscopic immunocytochemistry and 3D imaging (Head of Laboratory – Elżbieta Wyroba)

- Identification of signalling pathways, transcriptional and epigenetic regulation of gene expression underlying brain tumour pathogenesis and neuroinflammation; development of RNAi and recombinant interfering peptide technology-based molecules to study tumour invasion and tumour-host interactions *in vitro and in vivo* (the laboratory is a member of Polish-French GDRE); development of computational methods and databases that integrate ChIP assays with DNA microarray and high-throughput sequencing technologies enabling the profiling of whole-genome histone modifications and transcription factor occupancy sites under brain inflammation (Head of Laboratory – Bożena Kamińska-Kaczmarek)

- Investigations of the function of proteins involved in folding of cytoskeletal proteins, particularly actin and tubulin, in protists and mammalian cells and its role in physiological cell responses; proteomic and functional analysis of proteins involved in ciliogenesis in protozoan cells and immortalized mammalian cell lines by genetic engineering, immunochemical, immunocytochemical and ultrastructural characteristics; the role of extracellular factors in dynamics of actin cytoskeleton in *Amoeba proteus* with the identification and determination of the function of actin binding proteins; the function of RhoA/ROCK pathway and calcium signal in the actin skeleton arrangement; the role of actin and unconventional myosins in cell migration; electrophysiological patch-clamp investigations characterizing the structure and function of mechanosensitive ion channels in *Escherichia coli* membrane (Head of Laboratory – Stanisław Fabczak)

- Studies on the mechanisms of signal generation by Fcγ and TLR4 immunoreceptors at the onset of phagocytosis and LPS recognition in macrophages and monocytes. The essential approach is to examine how activated receptors initiate a cascade of events leading to reorganisation of membrane constituents, activation of tyrosine kinases and phosphoinositide kinases. In particular, this group is focussed on: the involvement of plasma membrane rafts in receptor signalling, the role of the sphingomyelin cycle and ceramide generation in the transduction of signals by the receptors, the role of PI(4,5)P2 in modulation of submembrane cytoskeleton and cytokine generation (Head of Laboratory – Andrzej Sobota)

- Revealing the role of the Grainyhead-like (GRHL) transcription factors in signal transduction in mammalian cells. The studies are focused on understanding the regulation of gene expression by GRHL and regulation of the activity of GRHL proteins. Analysis of phenotypes of mouse strains carrying mutations in the *Grhl* genes is performed. The investigations aim at mechanisms of GRHL function in health and disease; role of the GRHL factors in neural tube closure; involvement of the planar cell polarity pathway in wound healing. (Head of Laboratory – Tomasz Wilanowski)
Selected publications:


A representative *Grhl1* null (left) and wild-type (right) littermate photographed at weaning. The hypotrichotic phenotype of *Grhl1*-deficient mice is caused by defective hair anchoring.

Activation and capping of immunoreceptor FcγIIA (red) leads to generation of ceramide in the plasma membrane (green)

Accumulation of phosphatidylinositol 4-monophosphate (green) in actin-rich filopodia (red) of spreading BHK21 fibroblasts

Overalllapping 3-D models of *Paramecium octaurelia* Rab7 isotypes
Laboratory of Cell Membrane Physiology

Head: Elżbieta Wyroba
Staff: Kamil Kobylecki (student), Karolina Miller (student), Magdalena Osińska

Research profile:
Molecular mechanisms regulating endocytosis and degradative pathways in different cell types undergoing gene silencing (RNAi) and stimulation. Evolutionary conservancy of the trafficking and sorting mechanisms are studied at the genomic, proteomic and cellular level. Components of the machinery involved in endosome/phagosome formation and membrane targeting in model unicellular eukaryote *Paramecium octaurelia*. Several genes encoding proteins indispensable in these processes were cloned in our Lab (including those first shown in unicellular eukaryotes) exhibiting a high homology to respective mammalian counterparts. Our ongoing research is focused on the functional/structural analyses of the products of these genes with special emphasis on Rab proteins and their effectors.

Methods:
- quantitative/relative real time PCR
- RT-PCR
- cloning
- 2D electrophoresis
- Southern/Northern hybridization
- mass spectroscopic analysis
- fluorometry
- Western analysis
- immunolocalization in confocal and electron microscopy
- 3D tomographic modeling

Current research activities:
- studies on evolutionary conservancy of the trafficking and sorting machinery
- revealing posttranslational modifications (PTM) as the putative mechanism of neofunctionalization of the paralogous genes
- functional analysis of Rab7 isotypes upon silencing
- identifying Rab7 effectors and cooperating proteins
- analysis of components essential in the endosomal/lysosomal pathway
- an approach with point mutagenesis and recombinant proteins to study PTM
Selected publications:


Paramecium octaurelia Rab7 proteins encoded by rab7a and rab7b paralogous genes cloned in the Lab are 62.3-63.3% identical to human counterpart and 46-47% to Trypanosoma cruzi Rab7. T.cruzi emerged earlier in the evolution and its Rab7 possesses a 20 amino acid insertion* not present in Paramecium and in the higher cells as visualized in 3-D model (PyMol) and shows different intracellular localization.

LAMP-2 homologue (one of the lysosomal membrane proteins) was localized in the vicinity of the Paramecium phagosomes during uptake of latex beads.
Research profile:
The principal focus of the laboratory is the functional analysis of key events (signalling pathways, transcriptional and epigenetic mechanisms) controlling gene expression. Of particular interest are the mechanisms that regulate and determine gene expression underlying neuroinflammation, remyelination and brain tumour pathogenesis. We study the molecular and cellular characteristics of the key transcription factors (of the STAT, NFkB, Id and Myc families), including discovery of their target genes using functional genomics, analysis of protein-DNA interactions in vitro and in vivo, combined with DNA microarray and high-throughput chIP-sequencing technologies. The high-quality transcription factor binding profile and epigenetic modification database of human, rat and mouse genomes is being developed as the Nencki Regulatory Genomics Portal. We wish to apply our findings to develop novel (RNAi or short interfering peptide-based) therapeutics applicable to human diseases.

Methods:
- cellular and animal models of inflammation and tumour-host interactions
- molecular biology and computational methods to study signalling pathways
- chromatin immunoprecipitation and reporter gene assays
- gene expression
- construction of cells expressing shRNA or recombinant proteins

Current research activities:
- deciphering mechanisms of gene expression patterns critical for the initiation of inflammation in brain injury and brain tumour pathogenesis, in particular, the contribution of “master switch” STAT, NFkB, Id and Myc transcription factors and epigenetic modifications to distinct phenotypes/functions of the innate immunity and tumour cells
- development of RNAi – and recombinant interfering peptide-based molecules to study tumour-host interactions and invasion in vitro and in vivo
Selected publications:


Laboratory of Cell Movement Physiology

**Head:** Stanisław Fabczak

**Staff:** Cezary Bregier, Hanna Fabczak, Maria Jerka-Dziadosz (Professor emeritus), Ewa Joachimiak, Piotr Koprowski, Lucja Krzemień-Ojak (PhD student), Andrzej Kubalski, Leszek Kuźnicki (Professor emeritus), Urszula Śmietanka, Ewa Waclawek (PhD student), Paulina Urbańska, Anna Wasik, Dorota Włoga

**Research profile:**
We investigate the mechanisms which affect the cell cytoskeleton assembly and its reorganization. Currently, we study the function of phosducin-like proteins (PhLPs) involved in folding of cytoskeletal proteins, particularly actin and tubulin, in protists and mammalian cells. Properly folded tubulin is essential to maintain the correct structure and function of microtubules. Cilia, the microtubules based cell extensions, are conserved organelles that play a key role in the cell motility and signal transduction. Dysfunction of cilia causes a number of human disorders known as ciliopathies. We carry out proteomic and functional analysis of the proteins involved in the ciliogenesis in protozoan cells and immortalized mammalian cell lines. Another major project concentrates on the role of extracellular factors in the dynamics of actin cytoskeleton in *Amoeba proteus* and on the identification and determination of the function of actin binding proteins. We also investigate the structure and function of mechanosensitive ion channels in *Escherichia coli*.

**Methods:**
- fluorescence resonance energy transfer (FRET) analysis
- molecular biology and genetic engineering techniques
- patch-clamp techniques
- standard biochemical and immunocytochemical methods
- ultrastructure analysis at the electron and scanning microscopy levels

**Current research activities:**
- determination of the effect of PhLPs genes konocutoff on microtubules assembly and cilia ultrastructure and function
- analysis of the PhLPs function as a modulator of chaperonin CCT during tubulin and actin folding in mammalian cell lines
- proteomic and functional analysis of proteins involved in ciliogenesis in protozoan cells and immortalized mammalian cell lines
- identification of actin binding proteins responsible for actin cytoskeleton reorganization in *Amoeba proteus*
- patch-clamp studies on mechanosensitive ion channels from the cytoplasmic membrane of *Escherichia coli* and investigation of the role of their C-termini in the channel gating
Selected publications:


Abnormally-shaped cilia in *Tetrahymena thermophila* cells with overexpression of GFP-tagged phosducin-like protein 3. Transmission Electron Microscopy

Colocalization of tubulin (blue) and chaperonin containing TCP-1 (CCT) (red) in human neuroblastoma SH-SYSY cells

Colocalization of chaperonin containing TCP-1 (CCT) (red) and phosducin-like protein 3 (PhLP3) (green) in mouse neuroblastoma NB2a cells differentiated with palmitoyl-L-carnitine (nuclei shown in blue)

Distribution of mono- (green) and polyglycylated (red) microtubules in dividing *Tetrahymena thermophila*

Patch-clamp studies on mechanosensitive channels from the cytoplasmic membrane of *Escherichia coli* including the role of large cytoplasmic chamber of MscS channel in gating
Laboratory of Plasma Membrane Receptors

Head: Andrzej Sobota
Staff: Kinga Borzęcka (PhD student), Maciej Czerkies (PhD student), Katarzyna Kwiatkowska, Anna Łukasik (PhD student), Ewelina Marszalek-Sadowska, Kazimiera Mrozińska, Agnieszka Płuciennikowska (PhD student), Agata Samonek (PhD student)

Research profile:
Our research is focused on understanding the mechanisms of signal generation by immunoreceptors of macrophages and monocytes that are involved in phagocytosis and inflammatory responses. We aim to elucidate signaling pathways behind the FcγRIIA-mediated uptake of pathogen and TLR4-dependent responses to microbial cell wall components such as LPS. The essential approach is to examine how the activated receptors initiate a cascade of events leading to reorganization of membrane constituents, activation of tyrosine kinases and phosphoinositide kinases. Specifically, we investigate the involvement of plasma membrane rafts in immunoreceptor signaling, the role of the sphingomyelin cycle and ceramide generation in the transduction of signals by the receptor, the role of PI(4,5)P2 in modulation of submembrane cytoskeleton and in internalization of membrane-associated particles.

Methods:
• cloning
• cell transfection and production of recombinant proteins
• silencing of gene expression
• confocal and immuno-electron microscopy
• surface plasmon resonance
• cell fractionation and raft isolation
• ELISA and FACS analysis

Current research activities:
• elucidating the mechanisms governing an association of activated Fcy receptor IIA and Toll-like receptors with rafts of the plasma membrane – an engagement of acid sphingomyelinase and ceramide; our approaches range from gene silencing through immunoassays to enzymatic analysis
• plasma membrane rafts as centres of PIP5-kinase activation and PIP2 turnover; expression of PIP5-kinase and its fragments is performed to reveal how the kinase is recruited to the plasma membrane
• studies on the molecular composition of detergent-resistant membrane domains (DRM) and how it affects a raft involvement in the immunoreceptors signaling
• exploration of suitability of lysenin – sphingomyelin-binding protein, as a tool for studies of sphingomyelin-cycle during Fcy receptor activation; the mechanism of interaction of lysenin with sphingomyelin in membranes is studied by variety of biophysical approaches
• ultrastructural studies on participation of plasma membrane domains (rafts) in signal generation by Fcy receptor IIA and Toll-like receptor 4
• studies of the effect of Fcy receptors and TLR4 activation on organization of cortical actin cytoskeleton during the receptor-mediated phagocytosis and inflammatory responses
Selected publications:


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Actin filaments (red) accompany TLR4 (green) at the leading lamella of LPS-stimulated cells.

TLR4 (green) and CD14 (red) colocalize at the leading edge of LPS-stimulated cell.
Laboratory of Signal Transduction

Head: Tomasz Wilanowski
Staff: Agnieszka Kikulska (PhD student), Michał Mlącki (PhD student), Magdalena Pawlak (PhD student)

Research profile:
Signal transduction in mammalian cells; signaling pathways; planar cell polarity pathway; role of the Grainyhead-like (GRHL) transcription factors in signal transduction; regulation of gene expression by the GRHL transcription factors; regulation of the activity of GRHL proteins; analysis of phenotypes of mouse strains carrying mutations in the Grhl genes; neural tube closure; wound healing; mechanisms of GRHL function in health and disease.

Methods:
- PCR
- quantitative PCR
- DNA sequencing
- histology
- immunohistochemistry
- immunofluorescence
- Western blotting
- chromatin immunoprecipitation
- electrophoretic mobility shift assays
- transfection studies
- phenotypic analyses

Current research activities:
- functions of the GRHL1 gene in human disease
- analysis of the phenotype of Grhl1 mutant mice
- mechanisms of regulation of the activity of GRHL1 protein
- regulation of gene expression by the GRHL1 transcription factor
- role of the Grainyhead-like factors in neural tube closure
- involvement of the planar cell polarity pathway in wound healing
Selected publications:


Staining for the reporter gene (β-galactosidase) activity (green) in the *Grhl1*-/- adult hair follicles: telogen (left) and anagen (right). In the adult hair follicle, the *Grhl1* gene is expressed in the inner root sheath of the hair follicle, but is absent from the dermal papilla.

*Grhl1*-null mice exhibit features of palmoplantar keratoderma. Immunofluorescence staining of the palmar surface of the forepaw of a *Grhl1*+ mouse at 7 months of age. The staining was performed with antisera against keratin 5 (green) with cell nuclei stained red.
The Department was founded in 1946 by Jerzy Konorski. Its major research is anatomical and functional connectivity of the developing and mature central nervous system in health and disease. The Department consists of eleven research groups, each focusing on a different neuroscience theme (http://www.nencki.gov.pl/en/working-groups).

**Sensory systems** (visual system of the cat and somatosensory system of the rat) are investigated by the group led by A. Wróbel and are devoted to basic functional physiology, as well as contextual mechanisms influencing perception. Additionally, the group studies the code for movement perception at the extrageniculate visual pathway.

**Regeneration and plasticity** in rats is investigated by four groups: neurodegeneration in rodent models of nerve injury potential treatments, including pharmacological, nerve grafts, locomotor training and neurotrophin signaling and cell adhesion with the use of AAV-mediated gene transfer (groups led by J. Czarkowska-Bauch and U. Sławińska); morphological changes of neural plasticity including extracellular proteolysis and glial contributions (group led by G. Wilczyński); molecular and in vivo research on the function of the basal forebrain cholinergic system and beta-amyloid-induced toxicity in Alzheimer’s disease (group led by G. Niewiadomska).

**Emotion and memory** in rats are investigated by two groups: roles of the limbic structures in emotion and social behavior, as well as the influence of psychotomimetic compounds on limbic activity (group led by S. Kasicki); learning strategies used in a variety of tests such, as defensive and alimentary conditioning, spatial tasks and recognition, and the roles of information transfer (group led by T. Werka).

**Neuropsychology** research is the conducted by two groups. Research topics include hemispheric asymmetry, cognitive functions, sex-related differences in functional brain organization, mechanisms of language, left-handedness and dyslexia. Close cooperation with colleagues at clinics and hospitals enables these groups to research cognitive deficits in stroke, epileptic and Parkinsonian patients, as well as in patients with cochlear implants and children with developmental disorders (group led by A. Grabowska and group led by E. Szeląg).

**Neuroinformatics** is researched by Daniel Wójcik and his group whose investigations are aimed at the development of tools and models, and putting them to use to understand neural processing of sensory information gathered by electrophysiological, fMRI and behavioral studies.

**Ethology** is investigated by the group directed by E. Godzińska. This group uses ants as models in comparative research devoted to ontogeny and the neurochemical basis of aggressive and social behavior.

Despite the wide scope of studies, two common topics integrate the research carried out in the Department: 1) intrinsic mechanisms of behavioral neurophysiology and 2) plasticity of the nervous system. The traditional Wednesday seminars allow for the exchange of new ideas and hot discoveries between the research groups. Seminars are also the platform for discussion of the lectures delivered by eminent scientists from all over the world, who visit the Department. Thematic seminars on ethology, behavior, neuronal systems, neuroinformatics and psychophysiology, as well as regular Journal Clubs, are designed to keep track of the modern trends in neuroscience. A two-day integration party combining scientific and social events is organized each spring for all members of the Department. On this occasion Ph.D. students report their annual achievements and awards are given for the best presentations.

Dynamic cooperation with leading international institutes facilitates implementation of new research techniques which are made available to all member of the Institute. These techniques pertain to include histology, in vitro slice electrophysiology, HPLC and modern behavioral setup equipped with digital recording, telemetry and analyzing facilities. The Department has recently established a Polish node of the international neuroinformatics network, INCF (www.neuroinf.pl).

During the last thirty years many international conferences and schools on a variety of neuroscience topics have been organized by our Departmental staff. Staff members serve frequently on committees of international brain research organizations (FENS, EBBS, INCF) and are editorial board
members of neuroscience journals (Eur. J. Neurosci., Neuroinformatics, ANE). Importantly, the Polish Neuroscience Society, founded in 1991 by former and current members of the Department, continues successfully its integrative and organizational role under the Presidency of Julita Czarkowska-Bauch (2009-2011). The recent successful organization of the first FENS Featured Regional Meeting (2009), annual Brain Awareness Weeks (www.ptbun.org.pl) and the Advanced Course in Computational Neuroscience under auspices of FENS-IBRO (www.neuroinf.pl/acrn) have been organized with substantial involvement of the Departmental staff.

Selected publications:

Secretariat:
Jagoda Michalska

Surgery Room:
Ewa Nosecka

Histology Unit:
Kępczyńska Agnieszka

Electronic Workshop:
Wojciech Borkowski
Research profile:
The research is focused on neural correlates of higher mental functions in man based on neuropsychological, neurophysiological and behavioral data. The topics involve issues ranging from basic mechanisms of attention and emotion through functional architecture of memory to self-consciousness. The main goal of studies performed on healthy human subjects, patients with brain injuries, patients with neurodegenerative (Parkinson’s and Alzheimer’s diseases) and neurodevelopmental disorders (dyslexia, ADHD) is to get a better insight into the mind-brain relationship and to provide knowledge contributing to elaboration of better tools for clinical diagnosis and remediation.

Methods:
- neuroimaging and electrophysiological methods are used enabling monitoring brain functions with high spatial and temporal resolution (functional Magnetic Resonance Imaging/Voxel Based Morphometry and Event-Related Potentials/Electromyography, respectively). These methods are coupled with studies of the effects of focal brain lesions upon cognitive and/or emotional performance
- recent studies focus more on “functional integration” (connectivity) rather than functional localization using diffusion tensor imaging (DTI) and structural equation modeling (SEM).

Current research activities:
- processing of self-related information
- neural organization of deception: an fMRI investigation in healthy subjects
- neural correlates of unconscious processing in neglect patients
- fMRI study of emotional aspect of false memory
- electrophysiological correlates of dyslexia: behavioral and ERP study of attention, magnocellular, phonological and cerebellar dysfunctions
- neuroanatomical markers of dyslexia: functional and structural magnetic resonance imaging studies
- the effect of motivation on working memory: behavioral investigation of patients with orbitofrontal damage and an fMRI study of healthy subjects
- EMG study of dynamic and static emotional expression and its relation to self – reported empathy
- neural mechanisms underlying intentional forgetting of neutral and emotional stimuli
- neural correlates of cognitive dysfunction in Parkinson’s disease

Head: Anna Grabowska
Staff: Hanna Cygan (PhD student), Marcel Falkiewicz (PhD student), Katarzyna Jednoróg, Artur Marchewka, Anna Nowicka, Krystyna Rymarczyk, Iwona Szatkowska, Paweł Tacikowski (PhD student), Aleksandra Zasada
**Selected publications:**


Head: Tomasz Werka
Staff: Janusz Błaszczyk, Ewelina Knapska, Marta Mikosz (PhD student), Aleksandra Nowak, Alicja Puścian (PhD student), Joanna Sadowska

Research profile:
Emotions shape the quality of our existence by influencing what people perceive, learn, remember and do. We conduct research on neural representations and processing of emotion using rats, mice and genetically modified animal models. In particular, we study the neural systems and cellular mechanisms underlying social communication and learning as well as the mechanisms of emotional regulation using extinction of conditioned fear. Understanding how the systems governing social communication operate could explain, e.g., why some individuals suffer from autism, in which social interaction and communication are compromised. Similarly, examining the nature and properties of fear extinction in laboratory rodents may help to optimize the treatment of human anxiety disorders such as panic disorder and post-traumatic stress disorder (PTSD).

Methods:
- state-of-the-art technical equipment for testing animal behaviour
- immunohistochemical staining
- neurotoxic brain lesions and gene delivery by intracranial infusion of viral vectors

Current research activities:
- socially transferred fear – the neural basis of empathy
- the neural mechanisms of extinction and renewal of learned fears
- designing and standardization of automated behavioral tests for mice and rats
Fear memories are long lasting and generalize broadly to many contexts. However, conditioned fear can be suppressed by repeated presentation of the CS in the absence of the US, a phenomenon called fear extinction. There is substantial evidence that extinction does not erase the original fear memory, but results in a transient inhibition of fear. For example, fear, suppressed in the extinction context (upper panel), can renew in other contexts (lower panel). Fear conditioning and extinction are widely recognized as valid models of clinical anxiety disorders and exposure therapy for anxiety disorders, respectively. The phenomenon of renewal of conditioned fear, easily observable in the laboratory, allows for studying mechanisms that restrain the effectiveness of exposure therapy.

During social interaction with a recently fear conditioned partner, observers and demonstrators exhibit social exploratory behaviors rather than aggressive behaviors: A. following anogenital area sniffing C. head area sniffing.

We study behavioral effects of socially transmitted fear. Our data suggest that a brief social interaction with a cage mate that has undergone an aversive learning experience promotes aversive learning in an otherwise naive animal.

c-Fos expression in amygdaloid nuclei of the rat subjected to a brief social interaction with a recently fear conditioned partner. Coronal sections indicating nuclei of the amygdala (Nissl stain; left) and c-Fos immunoreactivity (black dots; right) are shown; Ld – dorsal and Lv – ventral subdivisions of the lateral nucleus, BL – basal, BM – basomedial, CE- central, ME – medial and CO – cortical nuclei of the amygdala.
Laboratory of the Limbic System

Head: Stefan Kasicki
Staff: Paweł Boguszewski, Sailaja A. Goda (PhD student), Mark J. Hunt, Irena Łapińska, Karolina Nowak (PhD student), Maciej Olszewski, Joanna Piasecka, Jolanta Zagrodzka

Research profile:
Our research is focused on: (1) neurobiological correlates of emotional and social behavior in the context of temperamental traits and age (electrophysiological and immunocytochemical techniques together with advanced behavioral methods are used), and (2) neurophysiological and neurochemical mechanisms in pharmacological models of schizophrenia investigated using a variety of techniques (electrophysiology and behavior) in freely moving rats. We study the fundamental brain regions which have been implicated in these phenomena, such as the nucleus accumbens, prefrontal cortex, hippocampus and amygdala, primarily by analyzing their electrophysiological activity.

Methods:
• behavioral
• pharmacological
• electrophysiological
• immunocytochemical techniques
• typically we use several techniques simultaneously in one experiment.

Current research activities:
• behavioral and immunocytochemical studies on temperamental determinants of social behavior in psychogenetically selected RH and RL-Avoidance rats (a model of differentiated emotional reactivity and novelty seeking)
• behavioral and immunocytochemical studies on the pattern of neuronal activation in response to novel stimuli of different aversiveness levels in young and old rats
• electrophysiological, pharmacological and behavioral studies using the NMDA receptor antagonist model of schizophrenia in awake rats. Electrophysiological activity is recorded mostly from limbic structures.
Selected publications:


High frequency (~150 Hz) oscillations in an accumbal local field potential recording after systemic ketamine administration (the rodent model of schizophrenia). From the top: the filtered activities in different frequency ranges and the raw signal.
Research profile:
We work in the field of ethology, sociobiology and social neuroscience of social insects. We are particularly interested in the analysis of multidirectional information flow between various levels of organization present in ant societies and in the ontogeny and neurochemical correlates of ant aggressive and social behaviour. Our current research is focused on ethopharmacological analysis of neurochemical mechanisms underlying various forms of aggressive behaviour in formicine and myrmicine ants. We are also interested in the role of the social context in the control of expression/suppression of various elements of ant behaviour. We also try to unravel the effects of behavioural status (nurse versus forager) on behaviour and physiology of ant workers and to identify behavioural, morphological, physiological and neurochemical correlates of ant behavioural maturation and the so called behavioural reversion, i.e. the return of a forager to the behavioural status of a nurse.

Methods:
• manipulations of ant ontogeny and social context (social engineering)
• analysis of recordings of ant behaviour (“The Observer”)
• acute and chronic biogenic amine administration
• HPLC analysis of biogenic amine and amino acid contents in ant brains

Current research activities:
• context dependence of aggressive behaviour, brain neurochemistry, and effects of biogenic amine administration in ants from two subfamilies (Formicinae and Myrmicinae)
• ontogeny of ant behaviour: behavioural, anatomical and neurochemical correlates of behavioural maturation and behavioural reversion
• factors influencing brood care behaviour, exploratory behaviour and responses to potential building material in the red wood ant (Formica polyctena)
• genetic polymorphism in wood ant colonies
Selected publications:


Research profile:
Our current research focuses on understanding the dynamic operations within sensory systems of behaving animals. Using electrophysiological recording techniques and neuro-informatic methods for data analysis we try to correlate the activation of specific neuronal networks with its behavioral context. More information about the laboratory can be found on the web page (http://vslab.nencki.gov.pl).

Current research activities:
- electrophysiological correlates of visual attention in cats – temporal analysis (frequency, phase and amplitude envelope) of local field potentials recorded from different parts of cat thalamo-cortical system during behavioral task
- information processing in the rat somatosensory system – the role of primary and secondary somatosensory pathways in different behavioral situations; in vivo and in vitro electrophysiological investigations of synaptic properties and cellular connections within the cortico-thalamic loops of the somatosensory system
- the role of extrageniculate visual pathway in movement perception – electrophysiological and modeling investigations on the spatial and temporal properties of single unit receptive fields in the cat; coding of information in geniculate and extrageniculate visual pathways in the cat – electrophysiological and computational studies on temporal pattern of neuronal activity

Methods:
- in vitro intracellular recordings
- single neuron activity in the visual system
- local field recordings from behaving animals
- EEG correlates of cognitive processes in humans
- computational analysis of electrophysiological signals
Selected publications:


A, Image of a living slice of the mouse barrel cortex. Letters denote barrels. Scale bar, 500 μm. B, Firing responses to a depolarizing current pulse, characteristic for regular spiking excitatory cell (top) and an inhibitory fast spiking neuron (bottom).

Cross-trial correlation – a newly developed method for assessment of coupling between brain areas – applied to evoked potentials recorded in primary (VPM) and secondary (PoM) thalamic nuclei, and in barrel cortex of awake rats.

Activity evoked in a portion of the rat forebrain 3.5 ms after deflection of the vibrissae (current sinks red). Three coronal sections (the most anterior to the left spaced by 1 mm).

Spectral receptive field of a neuron revealing optimal response at low spatial and temporal frequencies of visual stimulation. The neuron was recorded in superficial layers of the cat superior colliculus.
Laboratory of Neuropsychology

Head: Elżbieta Szeląg
Staff: Weronika Duda (PhD student), Alicja Moczulska (PhD student), Kamila Nowak (PhD student), Anna Oroń (PhD student), Justyna Skolimowska, Aneta Szymaszek, Małgorzata Węsierska

Research profile:
We study the neurophysiology and neuropsychology of cognition in human and animal models in norm and pathology. Human studies are focused on temporal aspects of information processing, learning, language, memory and attention and are aimed at the development of innovative neurorehabilitation methods. Our research involves normal subjects (children and adults), patients suffering from various brain diseases (stroke, focal brain damage, dementia, Alzheimer’s disease), cochlear implant users, as well as children with various speech and/or language disorders, e.g. language – learning – impairment, aphasia, deafness, stuttering, infantile autism. Animal studies are focused on neural substrates of learning, memory and other cognitive processes, like cognitive coordination and flexibility. Mechanisms engaged in memory improvement induced by direct current stimulation (tDCS) of the brain are studied in the model of spatial working memory in rats.

Methods:
- temporal aspects of information processing in norm and pathology
- innovative methods of neurorehabilitation
- speech therapy in different language disorders: aphasia, stuttering, infantile autism, hearing deficits
- neuropsychology of language restoration
- cognitive deficits in infantile autism
- neuropsychology of normal chronological ageing, longevity and neurodegeneration
- neuropsychological assessment of early stages of Alzheimer’s disease
- neural basis of learning, spatial and recognition memory in rats
- comparative behavioral studies on memory in different strains of rats and other animal species
- neural basis of auditory recognition memory and auditory processing in rats
- neural substrate of cognitive processes in spatial memory model in rat
- efficacy of tDCS brain stimulation on cognitive processes in animal model

Current research activities:
- neuropsychological basis of human and animal cognition
- temporal aspects of information processing, language, hemispheric asymmetry, normal chronological aging, neurodegeneration and neurorehabilitation
- animal studies on the neural basis of memory in different strains of rats
- cognitive abilities in patients with brain damage, aphasia, hearing deficits as well as neurodevelopmental or neurodegenerative diseases
- the studies are combined with behavioral methods, electrophysiological, fMRI, molecular, pharmacological, neuroanatomical and lesion techniques
Selected publications:


Injury of the central nervous system (CNS) causes alterations in the transcriptional programs that determine neuronal fate: survival and recovery or death. One of the most powerful pro-survival/recovery programs of neuronal and glial populations in the CNS may be triggered by neurotrophins. We focus on neurotrophins, their receptors as well as on related molecules assuming that their selective upregulation may limit signaling through pro-apoptotic pathways and promote recovery processes. Several approaches to modulate an expression of these molecules after spinal cord injury have been employed: locomotor exercise, electrical stimulation of peripheral nerves and adeno-associated virus transduction mediating neurotrophins or adhesion molecules expression. These treatments cause remodeling of the spinal neuronal network and functional improvement which are evaluated with immunohistochemical, biochemical and molecular biology as well as with behavioral and electrophysiological methods.

**Methods:**
- immunocytochemical: DNA/RNA staining, cell labeling, fiber tracing
- molecular biology techniques: electrophoresis and Western blotting, RT PCR, in situ hybridization
- behavioral and electrophysiological: kinematic analysis during locomotion, EMG, H-reflex

**Current research activities:**
- modulation of the endogenous level of neurotrophic factors and their receptors in the spinal cord owing to locomotor exercise or electrical stimulation of peripheral nerves
- AAV transduction mediating neurotrophins or adhesion molecules and their effects on recovery processes following spinal cord injury
- the effect of spinal cord transection and physical exercise on the reorganization of synaptic input to motoneurons
- apoptosis and patterns of expression of transcription factors and prosurvival/proapoptotic proteins following cortical and spinal cord injuries
Selected publications:


Interinstitute Laboratory of Neuromuscular Plasticity

Head: Urszula Sławińska
Staff: Barbara Burger, Anna Cabaj*, László Gál (PhD student), Teresa Górska (Professor emeritus), Anna Leszczyńska (PhD student), Henryk Majczyński, Krzysztof Miazga (PhD student)

(Nencki Institute of Experimental Biology and *Nałęcz Institute of Biocybernetics and Biomedical Engineering)

Research profile:
We investigate the neural control of locomotor movements and the plasticity processes in the neuromuscular system in rodents. Particularly, our research involves the functional aspects of muscle recovery after central and peripheral nervous system injury in young as well as in adult rats. Moreover, the restitution of motor function related to changes in the locomotor hindlimb movements and the recovery of inter-limb and intra-limb coordination after nervous system injury are investigated. A core feature of our research is directed towards indentifying new rehabilitation methods that can stimulate the neuromuscular plasticity mechanisms responsible for restitution of motor functions after injury. Particularly the effects of the rehabilitation approaches that employ intraspinal neural transplantation, various pharmacological treatment and locomotor training are investigated.

Methods:
- behavioral and electromyographical investigation of locomotor ability of freely moving rats
- microsurgery (CNS injury, grafting, EMG electrode implantation)
- footprints or CatWalk analysis
- electrophysiological acute CNS investigations
- immunocytochemistry
- Western blotting

Current research activities:
- monoaminergic systems in control of locomotion of intact rats and on the recovery of hindlimb motor functions after partial or complete spinal cord injury
- intraspinal grafting of embryonic serotonergic cells on recovery of motor functions in adult paraplegic rats
- neuromuscular interaction on the development of muscle, motoneurone, and motor units
- different pharmacological drugs on the muscle functional recovery after PNS injury
Selected publications:


Terminals containing 5-HT (green) in coronal cross sections of spinal cord above, at the side, and below the lateral hemisection of the rat spinal cord at low thoracic (Th 9) level.

CatWalk footprints and gait diagrams of an intact rat during locomotion.

CatWalk footprints and gait diagrams of a rat 64 days after spinal cord hemisection during locomotion.

Serotonergic embryonic cells grafted into spinal cord below total transection of adult rat (green – tryptophan hydroxylase immunostaining).

EMG activity recorded from hindlimb muscles during locomotor like movement induced by tail pinching of a spinal rat on a treadmill without (top traces) and with a graft of serotonergic embryonic cells (bottom traces). Abbreviations: Sol – Soleus muscle and TA – tibialis anterior muscle; l/r – left/right hindlimb.
Head: Grzegorz Wilczyński
Staff: Małgorzata Broszkiewicz (PhD student), Joanna Dzwonek, Maciej Gawlak (PhD student), Anna Konopka, Monika Malinowska, Kamil Parobczak (PhD student), Małgorzata Siudek (student), Andrzej Szczepankiewicz, Agnieszka Walczak (PhD student), Marine Yeghiazaryan, Klaudia Ziemiańska (student)

Research profile:
Our research interest focuses on the structural and functional plasticity of the nervous system, in both health and disease. We study phenomena occurring at various levels of organization, including anatomical sub-structures of the brain, the nervous tissue with all its cellular constituents, subcellular-, and macromolecular levels. One major issue that we investigate is the role of the extracellular matrix in synaptic plasticity in the brain, and at neuromuscular junctions; this also involves studies of pathological plasticity occurring in various forms of epilepsy. Another major project focuses on the role of neuronal nuclear structure and immediate-early gene expression in learning and behaviour, and in epileptogenesis. We are also interested in advances of microscopy and tissue-visualization techniques. We cooperate extensively with several groups in the Nencki Institute and at the Medical University of Warsaw.

Methods:
- immunocytochemistry
- in situ hybridization at the level of confocal- and electron-microscopy
- high resolution in situ zymography
- neuroanatomical methods
- molecular biology techniques

Current research activities:
- investigation of the possible pathogenic role of MMP-9 in temporal lobe epilepsy
- studies on the expression and role of matrix metalloproteinases at the neuromuscular junction
- studies on the role of CD44, an adhesion and signaling receptor, in neural plasticity
- investigation of the neuronal nuclear architecture in plasticity and epileptogenesis
- studies on the neuroanatomical correlates of different forms of learning and memory in the rat
Selected publications:


MMP-9 involvement in PTZ kindling – induced epilepsy. Seizure scores of PTZ-kindled WT and MMP-9 KO mice (A) and WT and MMP – overexpressing TG rats (B) during the course of the experiment. Note that epileptogenesis is delayed in MMP-9 KO mice (repeated measures ANOVA: F(1,9) = 9.9; P < 0.05). In contrast, epileptogenesis is accelerated in MMP-9 – overexpressing TG rats (repeated measures ANOVA: F(1,13) = 4.9; P < 0.05). Note that the differences in the seizure score between WT nad TG animals do not show up upon the first few injections but progressively develop thereafter, thus indicating that a plastic progress is involved. Error bars represent SEM.

Neuromuscular junctions visualized through confocal detection of muscle acetylcholine receptors (green) and nerve fibers (red). Blue in inset – nuclei stained for DNA.
Laboratory of Neuroinformatics

Head: Daniel Wójcik
Staff: Helena Głąbska (PhD student), Jakub Kowalski (PhD student), Szymon Łęski, Piotr Majka (PhD student), Jan Potworowski (PhD student), Jacek Rogala (PhD student)

Research profile:
The main activity of the group is development of tools and models, and putting them to use to understand neural processing of sensory information. We focus on functioning of early levels of sensory systems, in particular thalamo-cortical loop, but we also study the extrageniculate pathway of the visual system and recently started to look at motor systems. While we concentrate on electrophysiology we are also interested in fMRI and behavioral data. An important part of our activity is the development of a neuroinformatics infrastructure for storage and processing of histological information and the creation of histology-based 3D brain atlases from different input sources.

More information about the laboratory on the web page: http://www.neuroinf.pl/neuroinflab

Methods:
- standard statistical frameworks
- nonlinear techniques and machine learning
- Matlab for most data analysis
- open software (Linux, Python, Neuron, VTK, Plone)

Current research activities:
- development of methods to reconstruct Current Source Density reliably in different experimental settings from local field potentials
- information processing in the cortico-thalamic part of the rat’s somatosensory system, modeling and analysis of local field potentials
- the role of extrageniculate visual pathway in movement perception, modeling and analysis of spiking activity
- development of databases to store digital representations of histology data and tools for creation of histology-based 3D brain atlases
Selected publications:

Responses of a neuron in cat superior colliculus to repetititve random stimulus. A. Position of the stimulus on the screen as a function of time. B. Raster plot of neural responses to 300 repetitions of the stimulus. C. Post-stimulus time histogram of this neuron activity (data courtesy of W. Waleszczyk, Nencki Institute)

Research profile:

Neurodegeneration is a common feature of many central nervous system diseases, such as Alzheimer’s disease, Parkinson’s disease, ALS, head trauma, epilepsy and stroke. The incidence of these devastating disorders is increasing rapidly in our ageing population and current treatments are inadequate.

Our main research interest is to understand mechanisms involved in neural ageing. Towards this end, we have tried to implement new experimental protocols and conduct longitudinal studies that can be used in Alzheimer research and other neurodegenerative disorders. The work uses rats and transgenic mice and has centred on studies of the reversal of brain dysfunction induced by aging. We attempt to link cellular and behavioral levels of the brain processes present during physiological and pathological ageing. Currently the team’s main interest is the development of novel treatments, animal models and diagnostic procedures for diseases of the central nervous system and assessment of toxicology, safety pharmacology, pharmacokinetics and complex behavioral effects of therapeutic compounds.

Methods:

• microsurgery on the brain
• histological and neuroanatomical examination
• computational image analysis
• behavioral/cognitive testing
• immunological staining: immunohistochemistry, immunocytoology, Western blotting, ELISA
• biochemical methods
• preclinical study in toxicity, CNS, cardiovascular and respiratory safety pharmacology, histopathology, and diagnostics.

Current research activities:

• cholinergic anabolism and signalling
• the retrograde transport of fluorescent NGF in basal forebrain cholinergic neurones and correlation of these changes with age-dependent structural reorganisation of the axonal cytoskeleton
• pre-synaptic TrkA receptor expression and NGF-TrkA signalling
• cytoskeletal transport and post-translational modifications of microtubule associated proteins during physiological ageing and neurodegenerative diseases in rat model systems
• profiling age-related cognitive impairments in spatial memory tasks
• development of novel treatments for neurodegenerative diseases: testing in animal models and assessment of drug safety and pharmacology
Selected publications:


Expression of tau phosphorylated at Thr231 residue in cortex of transgenic line L66 mouse (B) in comparison with wild type NMRI mouse (A) and in young (C) and aged rat (D). Staining of retrograde transport of Fluoro-Gold from cortex to NBM in young (E) and aged rat (F). Over-phosphorylation of tau protein in neurons induces changes in compartmentalisation of tau from dendrites to cell bodies and causes breakdown of cytoskeleton and malfunctioning of intraneuronal transport.
The Department of Molecular and Cellular Neurobiology is composed of eight independent laboratories headed by Anna Filipek, Leszek Kaczmarek, Małgorzata Kossut, Katarzyna Łukasiuk, Katarzyna Nałęcz, Krzysztof Pawłowski, Jolanta Skangiel-Kramska and Krzysztof Turlejski. Individual research programs in the laboratories are all complementary and interdependent within the common research area of molecular and cellular neurobiology.

The group led by Anna Filipek is focused on studying the regulation of calcium homeostasis and its impact on processes related to cell proliferation and differentiation. In particular, the group studies the role of a calcium binding protein, S100A6, and its ligands: Sgt1, CacyBP/SIP and p53 in ubiquitination, cytoskeletal organization and cellular response to stress. Another topic concerns transcriptional and epigenetic regulation of expression as well as posttranslational modifications of the above proteins in relation to their function.

Leszek Kaczmarek and his colleagues study the molecular bases of persistent neuronal responses such as: neural plasticity, including learning and memory formation, and neurodegeneration bearing features of apoptosis. Transcription factors and their target genes are the major focus of this investigation.

The group led by Katarzyna Łukasiuk works on molecular mechanisms of epileptogenesis and is interested in the role of alterations in gene expression leading to epilepsy and in designing new strategies for modifying disease development and severity.

The research of Małgorzata Kossut and her team concerns systemic and neuronal mechanisms of learning and plasticity in adult and ageing brain. The models of plasticity developed in this laboratory serve to measure the effects of genetic modifications, brain disease and trauma upon functioning of the cerebral cortex. A group within her lab investigates behavioral, cellular and molecular aspects of developmental plasticity of cat visual system.

The group led by Katarzyna Nałęcz investigates differences in function and expression of various transport systems. In particular, the expression of carnitine and amino acid transporters in highly specialized brain cells, including those making the blood-brain barrier. Other research topics cover carnitine and palmitoylcarnitine and their role in signal transduction pathways in differentiating neural cells.

The laboratory led by Krzysztof Pawłowski researches the structure and function predictions for proteins implicated in human disease, in particular uncharacterised transmembrane proteins. Another field of work is applying systems biology approaches to analysis of gene expression data and evolutionary analysis of gene expression profiles.

The group led by Jolanta Skangiel-Kramska examines cortical plasticity during postnatal development and in the adult brain. The barrel cortex of rodents is used as a model system, and plastic changes are induced by modifications in sensory input patterns. Other areas of interest are neuronal plasticity occurring after cerebral stroke in the adult brain and repopulation therapies with endo-and exogenous neural precursors. Specific research concerns the study of neurotransmitter receptors, synaptic zinc and markers of presynaptic terminals and perineuronal nets.

Krzysztof Turlejski’s group investigates development of the nervous system in the laboratory opossum (Monodelphis domestica). Another research interest of the group is the comparative investigation of neurogenesis and its regulation in adult mammals (opossum, insectivores, rodents, carnivores, bats). The third important research line is the influence of prenatal and neonatal stress on development of the nervous system, emotionality and learning abilities in mice.

The Department holds weekly seminars and journal clubs. It is also actively involved in the organization of scientific symposia, meetings, workshops and research schools, actively cooperating with the International Brain Research Organization (IBRO) and Federation of European Neuroscience Societies (FENS), European Brain and Behaviour Society and Polish Neuroscience Society.
Selected publications:


Laboratory of Calcium Binding Proteins

Head: Anna Filipek
Staff: Agnieszka Graczyk (PhD student), Ewelina Jurewicz, Ewa Kilańczyk, Jacek Kuźnicki, Wiesława Leśniak, Wiktor Prus (PhD student), Agnieszka Góral (PhD student), Agnieszka Topolska (PhD student), Urszula Wasik (PhD student)

Research profile:
The laboratory is focused on studying the regulation of calcium homeostasis and its impact on processes related to cell proliferation and differentiation. In particular, our group studies the role of the calcium binding protein, S100A6, and its ligands: Sgt1, CacyBP/SIP and p53 in cellular signaling pathways especially those involving the ERK1/2 kinases. We also investigate the involvement of complexes formed by S100A6 and its ligands in ubiquitination, cytoskeletal organization and cellular response to stress under normal and pathological conditions. In addition, we study the transcriptional and epigenetic regulation of genes encoding S100A6, Sgt1 and CacyBP/SIP as well as posttranslational modifications of these proteins in relation to their function.

Methods:
• cell culture and transfection
• plasmid construction
• immunocyto/histochemistry
• Western blot
• chemical cross-linking
• co-immunoprecipitation
• luciferase assay
• gel-shift
• chromatin immunoprecipitation (ChIP)
• bisulfite DNA modification

Current research activities:
• studies of the Sgt1 function in nucleus under stress conditions
• studies of the role of S100A6, CacyBP/SIP and ERK1/2 in cell proliferation and differentiation
• studies of the role of CacyBP/SIP in neuronal cytoskeleton dynamics through interaction with tubulin and actin
• studies of the S100A6-p53 interaction and its impact on cell physiology
• studies of the posttranslational modifications of CacyBP/SIP, Sgt1 and p53
• studies of the transcriptional and epigenetic regulation of gene expression
Selected publications:


Laboratory of Mechanisms of Transport Through Biomembranes

Head: Katarzyna Nałęcz
Staff: Magdalena Czerepys, Elżbieta Januszewicz, Karolina Jóźwiak (PhD student), Katarzyna Michalec (PhD student), Maciej J. Nałęcz, Łukasz Samluk (PhD student)

Research profile:
Transport and physiological function of carnitine and its esters in brain cells, in particular studies on carnitine and amino acid transporters (OCTN2, OCTN3, ATB8+) and their regulation at the transcriptional and post-translational level. Our research is focused on the effect of nuclear receptor activation on expression of genes coding the studied transporters as well as on the role of phosphorylation on regulation of transporters trafficking, activity and localization in organelles within the cell and membrane microdomains. Studies on targeting of carnitine transporters by interaction with other proteins are also carried out in our laboratory.

Methods:
- cell culture (primary culture of brain cells and cells transfected with vectors containing the studied genes)
- transport measurements
- immunocytochemistry
- quantitative estimation of gene expression
- proteomics of hydrophobic proteins

Current research activities:
- restructuring of plasma membrane microdomains by palmitoylcarnitine
- regulation of genes coding the high affinity carnitine transporters
- mechanisms responsible for targeting the high affinity carnitine transporters to various membranes and membrane microdomains
- involvement of protein kinase C in transporter trafficking, localization and activity
- mechanisms regulating localization of the studied transporters in detergent-resistant domains of the plasma membrane
Selected publications:


Laboratory of Neuroplasticity

Research Profile:
Cellular, molecular, and systemic mechanisms of neuroplasticity are explored using three experimental models:

• learning-induced plasticity in the somatosensory cortex in rodents. Here our major interest is regulation of inhibition and excitability. We found upregulation of inhibitory interactions, GABA-ergic markers and rapid inhibitory synaptogenesis in the cortex as a result of learning. Simultaneously, neuronal excitability was changed by regulation of potassium channels

• reorganization of cerebral cortex after stroke and during ageing. We demonstrated spontaneous remapping of the cortex after stroke. We also found that inflammatory processes impede the progress of neuroplasticity. Ageing resulted in slowing down of cortical plasticity

• developmental plasticity of cat visual system. Behavioral and anatomical investigations are conducted in parallel. Correlates of global motion impairments in pattern deprived cats at the retina level and in higher visual structures are explored

Methods:
• brain mapping with [14C]2-deoxyglucose autoradiography and fMRI
• single cell and evoked potential electrophysiology
• immunocytochemistry
• RT PCR
• in situ hybridization
• ELISA
• confocal microscopy
• photothrombotic stroke
• behavioural training
• stereotactic injections
• fMRI, MRI

Current research activities:
• brain mapping during learning
• investigations of the pattern of brain activation at various stages of learning sensory discrimination and of classical conditioning in mice, using [14C]2-deoxyglucose autoradiography and IEG immunocytochemistry
• investigation of the effects of silencing GAD67 gene upon cortical plasticity
• investigation of the role of Npas4 in cortical plasticity
• electrophysiological correlates of enriched environment in neurons of the barrel cortex – a patch clamp and evoked potentials study
• the effect of post-stroke inflammation on brain plasticity
• alterations in development and activity of visual system induced by binocular deprivation – behavioral and IEG studies
• fMRI investigations of learning-induced brain plasticity and its modulations by stress
Selected publications:


Laboratory of the Molecular Basis of Brain Plasticity

Head: Jolanta Skangiel-Kramska
Staff: Artur Czupryn, Magdalena Karetko-Sysa (PhD student), Dorota Nowicka, Grażyna Truszkowska

Research profile:
The laboratory focuses on studying neuronal plasticity during postnatal development and in the adult brain. We are especially interested in elucidating the role of the extracellular matrix (ECM) and its remodeling in plastic phenomena. Our study is concentrated on neuronal plasticity occurring after cerebral stroke in the adult brain and the potential ability of perineuronal nets – a morphologically distinguishable form of ECM – to limit plastic changes. The second avenue of investigation is deciphering factors that can modulate neuronal integration of endogenous and exogenous neuron precursors/neuroblasts/immature neurons into the mouse brain.

Methods:
- immunocytochemistry
- histochemistry
- in situ zymography
- in situ hybridization
- Western blotting
- quantitative receptor binding autoradiography
- tissue culture techniques

Current research activities:
- perineuronal nets: investigations of the involvement of extracellular matrix components in cortical plasticity especially after recovery from cortical stroke
- ECM remodeling: elucidating molecular mechanisms of ECM remodeling in the rodent brain during development and aging
- Metalloproteinases: investigations of the role of MMPs in post-ischemic phenomena
- repopulation therapies: studying integration of transplanted neurons to the postnatal brain
Selected publications:


Perineuronal net around a cortical interneuron, revealed with Wisteria floribunda lectin

Triple staining of a cortical parvalbumin neuron (green), surrounded with perineuronal net revealed with Wisteria floribunda lectin (blue) and CAT-315 antibody against aggrecan (red)

3D reconstruction of a cortical interneuron containing parvalbumin (green) surrounded with perineuronal net stained with Wisteria floribunda lectin (red)

Synaptic zinc staining in the rat spinal cord
Research profile:
The long-term goal of our work is to understand the molecular basis of persistent neuronal responses. Two sets of phenomena are under investigation: neural plasticity, including learning and memory formation, and neurodegeneration bearing features of apoptosis. Both sets of conditions share similarities in involving excitatory amino acids acting on specific receptors. Furthermore, as a result of neuronal stimulation, transduction of a signal into cell nucleus leads to activation to at least partially overlapping sets of transcription factors, and their target genes. Thus, it appears that it is not possible to understand one of these processes separately from the other.

Current research activities:
- matrix metalloproteinases (especially MMP-9) and their endogenous inhibitors (e.g., TIMP-1) in neuronal plasticity (physiological and pathological: epilepsy, addiction) and cell death
- cyclin D2 in adult brain neurogenesis; the role of adult brain neurogenesis in neuronal plasticity, learning and memory, depression and addiction
- ICER, the endogenous CREB antagonist in neuronal apoptosis and plasticity
- SRE, serum response element and its transcriptional regulators in neuronal/synaptic plasticity
- morphological changes of dendritic spines in animal models of alcohol addiction
- behavioral phenotyping of genetically modified rodents

Methods:
Biochemistry and molecular biology of macromolecular interactions in a test-tube through in vitro cell culture (stable cell lines as well as primary dissociated and organotypic animal neuronal cultures) through transgenic rodents, and behavioral analyses up to human studies (gene polymorphisms and brain imaging), cell biology techniques - fluorescent cell imaging.
Selected publications:


Hippocampal neuron in dissociated culture. GFP (green fluorescent protein) introduced by lentiviral vector (green); phalloidin staining revealing actin (red); FMRP (fragile X mental retardation protein) revealed by specific antibody staining (blue); colocalization of GFP and actin visualizing dendritic spines (yellow), harboring excitatory synapses.
Laboratory of Developmental and Evolutionary Neurobiology

Head: Krzysztof Turlejski
Staff: Agata Aniszewska (PhD student), Katarzyna Bartkowska, Natalia Chłodzińska (PhD student), Ruzanna Djavadian, Monika Gajerska-Dzieciątkowska (PhD student)

Research profile:
In our research we correlate information about development and evolution of the mammalian brain. Several lines of research are presently followed in our laboratory. First, we investigate the connections of cortical fields and thalamic nuclei in various mammalian species. Next, we investigate the rate of brain cell generation and death in various orders of mammals. This information is correlated with behavioral tests, known ecological specialization and lineage history of these species. In another line of research we investigate mechanisms of seasonal oscillations of the brain volume in Sorex shrews (the Dehnel’s effect). Another area of our research concerns the role of neurotrophins in early development of the central nervous system of the laboratory opossum Monodelphis domestica. Finally, we investigate the influence of prenatal and neonatal stress in mice on brain development as well as emotional phenotype and learning abilities in adult animals.

Methods:
- histology
- immunohistology
- Western blot
- tissue culture
- electroporation
- stereometry
- behavioral tests

Current research activities:
- the role neurotrophins and their receptors in early brain development in the opossum Monodelphis domestica
- influence of prenatal and neonatal stress on brain development in mice and related behavioral changes in adult animals
- mechanisms of spatial memory, fear and exploration in opossums, shrews and rodents
- adult neurogenesis in various species of mammals and its correlation with their ecology
- mechanisms and consequences of the evolutionary reduction of the size of body and brain
Selected publications:

Labeled dividing cells (green) and astrocytes (red) in the dentate gyrus of the gerbil

Vasculatization of the retina (lectin labeling) in the opossum
Laboratory of Epileptogenesis

Head: Katarzyna Łukasiuk
Staff: Joanna Bednarczyk (PhD student), Anna Bot (PhD student), Diana Miszczuk (PhD student), Elżbieta Wiemasz

Research profile:
Our research is concentrated on the molecular responses to brain injury and molecular events leading to the development of epilepsy. We are particularly interested in alterations in gene expression that lead to the development of spontaneous seizures in in vivo models of epileptogenesis and epilepsy. We are also interested in developing new strategies to prevent epilepsy development.

Methods:
• animal models of epileptogenesis and epilepsy
• video-EEG monitoring
• neuronal cell cultures
• gene silencing and overexpression in neurons in vitro
• in situ hybridization
• RT-PCR
• immunohistochemistry
• immunocytochemistry
• immunoblotting
• basic molecular biology methods

Current research activities:
• search for new genes involved in development of epilepsy
• the role of Ttyh1 in normal brain and in brain pathology
• investigation of compounds influencing immune system as a potential drugs for modification of epileptogenesis and epilepsy
• role of neurogenesis in epileptogenesis and epilepsy
Selected publications:


Laboratory of Bioinformatics and Systems Biology

Head: Krzysztof Pawłowski
Staff: Anna Lenart (PhD student), Teresa Szczepińska (PhD student)

Research profile:
Structure and function predictions for proteins important in human disease, in particular, the discovery and characterization of novel structural and functional domains with putative enzymatic properties. Systems biology analysis of gene expression data, in silico investigation of the relations between nuclear architecture and gene expression.

Methods:
• remote protein homology detection
• protein structure modelling
• phylogenetics
• gene expression data clustering
• gene set enrichment analysis

Current research activities:
• structure/function analysis and evolutionary history of CLCAs, a novel predicted protease family
• structure/function analysis and evolutionary history of P-DUDES, a novel predicted oxidoreductase family
• discovery and bioinformatics analysis of novel protein kinase-like families
• structure/function analysis of a novel family of putative transmembrane receptors
• searching for chromosome spatial organization rules in microarray gene expression data
Selected publications:


Model of structure of the CLCA1 protein with a hypothetical substrate peptide

Gene expression vs genomic location: overrepresentation of chromosome pairs in gene expression clusters
The Laboratory of Electron Microscopy was established in 1973 to enable new methods in electron microscopy to be introduced to the Institute and provide access/assistance to investigators from scientific institutions all over the country and their cooperating partners from abroad in the usage of the following equipment:

- High Performance Biology Transmission electron microscope JEM 1400 (JEOL Co., Japan, 2008) equipped with energy-dispersive full range X-ray microanalysis system (EDS INCA Energy TEM, Oxford Instruments, UK), tomo- graphic holder and high resolution digital camera (CCD MORADA, SiS-Olympus, Germany).

The above-mentioned equipment was installed within the project sponsored by the European Union Structural Funds: Centre of Advanced Technology BIM ‘Equipment purchase for the Laboratory of Biological and Medical Imaging’.

- JEM 1200 EX electron microscope (manufactured in 1986) with ASID scanning device linked to the X-ray microanaly- sis system AN 10000 (Link Analytical, UK).
- Scanning electron microscope JSM S1 (purchased in 1973)

Other equipment such as: Ultramicrotomes (LKB, Sweden), Critical point drying system (Polaron, UK), Vacuum evapor- ator (JEOL Co., Japan), and Cryoultramictome (Leica, Austria) are also available.

Staff provide services in the procedure of mild drying of the biological samples in liquid CO₂ (critical point), coating of dried biological samples with neutral metals and carbon evaporation of formvar-coated specimen grids for transmis- sion electron microscopy and microanalysis. Continuous maintenance of the equipment and a lot of repairs of the vacuum, electronic and mechanical systems are performed.

Public education and dissemination activities of the laboratory include:

- Modern microscopical methods series (lectures, practical training and presentations) targeting undergraduate students (including the Lab practice in scanning electron microscopy for the university students) and other guests
- Training session in application of the new instruments
- Special sessions open to public entitled “Secrets of the cells” during the twelve consecutive “Festivals of Science” (1997-2010) – presenting the details of cell ultrastructure using three different electron microscopes to more than 1400 participants – and EU event ‘Faces behind Science – Night with Researcher’ (project 044769) in 2006.

Selected publications:

The Laboratory of Confocal Microscopy was established in May 2002. This is an open laboratory available to all scientists from the Nencki Institute and other scientific institutions.

The laboratory is equipped with:

- two confocal scanning systems: Leica SP5 STED and Leica TCS SP2, both with multiphoton lasers. The appliances use HeNe 633 nm; GreNe 543 nm; Ar 458 nm, 476 nm, 488 nm, 514 nm and Mai Tai IR 710 nm-990 nm lasers as the source of light
- TCS SP5 STED covers a hi-resolution morphology system and Life Imaging techniques. STED allows spatial resolution down to 70 nm which gives possibility to explore precisely cell architecture. The resonant scanner of TCS SP5 enables to acquire high speed images at large format and to observe dynamic changes in a live cell. What is more, FRET and FRAP analyses are also available for users
- TCS SP2 system is equipped with objectives with long work distance and a heating chamber. The microscope is equipped with a unique FLIM (Fluorescence Lifetime Imaging) system used for molecules iterations
- Zeiss TIRF microscope with HeNe 633 nm; GreNe 532 nm; Ar 488 nm lasers, 405 nm diode lasers and filters: double CFC/Cy3, triple GFP/mRFP/Aleca633, GFP. Microscope allows studies of processes in plasma membrane as well as microtubules and actin filaments dynamic
- Leica Epi-Fluorescence microscope DMI6000B coupled with b/w camera, set of fluorescence filters and Differential Interference Contrast (DIC) is also available

The laboratory was enriched with a new powerful graphic station and software: Huygens Professional.

The service in the laboratory may assist users in the field of image processing and analysis as well as the advice and assistance in use of the equipment.

Selected publications:


The Laboratory of Cytometry was established in June 2010 to provide a state-of-the-art multicolor flow cytometry service. Currently, the laboratory is equipped with a BD FACSCalibur flow cytometer, BD FACS Aria cell sorter and iCys scanning cytometer, 2-laser BD FACSCalibur and 4-laser LSR Fortessa cytometer, which allows for high-quality multiparameter/multicolour analysis. The Laboratory of Cytometry also provides cell culture unit and all necessary laboratory facilities.

- Cytometer BD FACSCalibur – equipped in the 488 nm laser and red diode 635 nm
- Cell sorter BD FACS Aria – equipped in the 488 nm, 635 nm lasers and UV lamp
- Cytometer BD FACSCalibur – equipped in the 488 and 635 nm lasers
- BD LSR Fortessa Analyser – equipped in the 355 nm, 405 nm, 488 nm and 635 nm lasers

**Activities:**

- the laboratory provides the core-facility service for investigators from the Nencki Institute and other scientific and R&D institutions
- expertise and technical assistance is offered in flow cytometry, cell sorting as well as laser scanning cytometry. Expert consultation for experiment design, fluorochrome selection and data analysis is also provided
- the laboratory is involved in basic research and innovative projects, based on the high-tech flow cytometry applications. Lab members perform their own research projects and collaborative projects with other scientific groups
- education – we organise lectures, training courses and hands-on workshops for beginners and advanced researchers

**Methods:**

- immunophenotyping
- analysis of apoptosis and viability
- analysis of proliferation, cell cycle and mitosis
- analysis of DNA damage/breaks
- analysis of calcium flux, free radicals production and mitochondrial membrane potential
- immunofluorescence of surface and intracellular markers expression
- cytokine production
- cell sorting
- multiparameter flow cytometry
- others, designed individually, dependently on needs

**Selected publications:**


The Laboratory of Cell Engineering was established at the Nencki Institute of Experimental Biology in March 2011. The facility is a fully equipped professional laboratory specialized in the production of genetically modified animals as well as viral vectors. The Laboratory provides the core facility service for investigators from the Nencki Institute and other scientific and R&D institutions.

Genetically modified animals (mice and rats) are produced by use of classical and lentiviral transgenesis methods. We possess high expertise in producing transgenic rats, which compared to mice, represent far more useful in vivo models to study mechanisms of human diseases. We are also introducing the “knock-out” technology into our Laboratory.

We have substantial experience in obtaining lentiviral vectors with tissue-specific (mainly neurospecific) expression pattern as well as the shRNA expressing vectors. Lentiviruses are currently extensively used in scientific and medical approach, as they constitute the most efficient tool able to incorporate transgene of interest into genome of non-dividing as well as dividing cells.

Genetically Modified Animal Models:
- preparing of constructs (choosing the promoter, cloning, confirming the expression by in vitro assays)
- microinjection of zygotes
  - traditional method (injecting of DNA solution into one of the pronuclei of fertilized embryo)
  - using the lentiviral vectors (incorporating of viruses under the zona pellucida)
- oviduct transfer of the injected zygotes into pregnant/pseudopregnant females
- vasectomy in males
- tail or ear tissue biopsy, DNA isolation
- genotyping

Viral vectors technology:
- expertise and technical assistance in selecting tissue specific promoters, projecting and producing vectors carrying silencing sequences
- cloning, preparing the plasmids for production of viruses
- production of the viral vectors (lenti, adenoviral)
- titer analysis (Real-Time PCR)
- further experiments with created viral vectors (e.g. developing of stable cell lines by use of lentiviral vectors)

Selected publications:
The Animal House is divided into separate areas for breeding and experimental purposes.

The breeding house has been in operation since 2000 – an independent building technically prepared for maintaining animals (air conditioning system, double-door autoclave, automatic washing machines for bottles, barrier system for personnel entrance). Breeding of experimental rats (outbred stock Long Evans Rat SimTac:LE), mice (outbred stock Crl:NMRI, inbred strains C57Bl6/J and C57Bl10/J), the Gray Short-Tailed Opossums (Monodelphis domestica) and cats is also performed in the Animal House. The majority of our breeding colony is from several different transgenic strains. The breeding pairs were obtained from internationally renowned breeding centres: Harlan Netherlands B.V.; Harlan UK C; Southwest Foundation for Biomedical Research, Department of Genetics, San Antonio The Jackson Laboratory and Taconic USA.

Our animals periodically undergo pathological, parasitological, bacteriological and virusological control. Bacteriological and viral controls are done in cooperation with the Institute of Oncology, the Department of Veterinary Medicine of the Agriculture Academy in Warsaw, IDEXX Laboratories and QM Diagnostics in the Netherlands.

The Animal House provides animals for experiments (selected according to age, sex, weight, and phase of the cycle) at the laboratories of the Nencki Institute. The team provide comprehensive animal care following neurosurgical treatment. Rearing of cats used in experiments on plasticity of the nervous system is also done by our experienced staff.

The approval of the First Ethical Commission in Warsaw that supervises animal experiments at our Institute is required for all planned experiments.

Head: Anna Passini
Staff: Katarzyna Błaszczak, Małgorzata Cira, Wioletta Góral, Teresa Just, Małgorzata Kielak, Marta Nowak, Hanna Śliwa, Wojciech Wiśniewski, Tomasz Włodarczyk
Information Technology Unit

Main Activities:
Planning, deploying and supporting the Institute’s networking infrastructure.

The Nencki Institute local area network (LAN) is based on the Cisco Nexus 7000 Series Switch, which constitutes the network core. Cisco Catalyst 2960 devices are used for access switching. They are interconnected with 2*1 Gb/s fibre optics (Gigabit Ethernet). Connection to wide-area Internet (100 Mb/s) is secured by a firewall.

Managing the data center infrastructure.
The infrastructure is based on the Cisco Unified Computing System (UCS), VMware vSphere software and NetApp storage systems. The Cisco UCS architecture includes a 10 Gigabit Ethernet network, x86 blade servers and a management system. The network is based on the Cisco Unified Fabric concept, in which 10 Gigabit Ethernet is used for all types of transmissions (Ethernet and Fibre Channel, using the Fiber Channel over Ethernet standard). During the deployment 40 virtual servers were implemented on seven physical servers.
Deploying, supporting and administering the Digital Library Repository of Scientific Institutes (rcin.org.pl).
The repository stores digitalized research papers, archive materials, research documentation and written cultural heritage, selected from collections of 16 Polish research institutes libraries.

Deploying, supporting and administering the Institute servers, which includes:
• WWW servers (www.nencki.gov.pl, intra.nencki.gov.pl, bioimagine.nencki.gov.pl)
• mail and DNS server
• web mail server (poczta.nencki.gov.pl)
• internet calendar server (kalendarz.nencki.gov.pl)
• remote access server, terminal services servers
• Accounting Department servers
• internal file server
• NAS and SAN storage systems
• proxy, DHCP, time and local upgrade servers
• print servers
Providing front line IT support to staff of the Institute in all aspects of computer operations (Helpdesk system).

Additional Activities:
• providing digital imaging and printing facilities
• developing and coding content for WWW servers
• supervising implementation of databases application software in the Institute’s Accounting Department
• predicting and planning for the Institute’s future hardware and software needs.

Head: Mirosław Sikora
Staff: Agnieszka Kowaluk, Arkadiusz Kuczewski, Maciej Maszewski, Anna Mirgos, Justyna Osmulska, Piotr Redel
The Library was founded together with the Institute in 1918 and was originally located at 8 Śniadeckich Street, Warsaw. The main collection contains books and journals of the Libraries of the Hydrobiological Station in Wigry, of the Sea Station in Hel, of the Biometrical Department in Warsaw and the library of Biological Station in Pińsk. In September 1939, the main collection was destroyed by German authorities. When the World War II ended, both the Institute and the library were rebuilt in Łódź, and remained there until 1954, when they relocated to the current address in Warsaw.

Nowadays, the library gathers books, periodicals, CD-s, microfilms and old prints. The methods of acquisition are purchase, subscription, exchange, gifts and others. The collection amounting to 25,130 volumes of books also includes 441 doctoral and postdoctoral theses. It currently receives 126 periodicals, including 61 as a foreign subscription. At present, there are 1,484 titles and 48,817 volumes of journals. The library exchanges periodicals published by the Nencki Institute with several contractors in Poland and abroad. The profile of the collection is connected with the following scientific fields: cell biology, molecular biology, biochemistry, ethology, neurobiology and psychophysiology.

In the library there are traditional alphabetical catalogues of books and periodicals, the subject catalogue of books and the on-line catalogues of books and periodicals dating back to the year 1975.

The library automation:
- library software – the “Horizon” system
- the number of on-line connections – 9 seats
- cooperation with other libraries: the Polish and foreign libraries of the same scientific profile as well as the group of Warsaw libraries cooperating within the integrated computer system “Horizon” (since 1997 the library has been a member of the Consortium of Scientific Libraries in Warsaw)
- access to many databases: Science Citation Index Expanded, Pub-Med, ISI Journal Citation Reports, Ebscohost, CogNet
- on-line access to periodicals: SpringerLink, ScienceDirect, Wiley-Blackwell, Ebscohost and journals subscribed to by the library

Since 2011 Nencki Institute Library participates in creation of Digital Repository of Scientific Institutes. The Project: Digital Repository of Scientific Institutes: POIG.02.03.02-00-043/10 is being implemented owing to funds from European Regional Development Fund, The Innovative Economy Operational Programme, Objective 2. The aim of the Project is to create a worldwide available, multidisciplinary, full-text searchable repository of digitalized resources of scientific publications, archival materials and research documentation, as well as digital publications collected from 16 Polish research institutes associated with in the RCIN Consortium. (http://rcin.org.pl/dlibra)

The librarians prepare the annual “List of the Institute employees’ publications”.

For further information e-mail: bibli@nencki.gov.pl

More information at http://biblioteka.nencki.gov.pl/
The Nencki Institute and Polish Neuroscience Society jointly publish the quarterly journal Acta Neurobiologiae Experimentalis.

Acta Neurobiologiae Experimentalis (ANE) is a continuation of Acta Biologiae Experimentalis, a quarterly founded in 1928 as the main Polish journal publishing original articles in the broad area of experimental biology. In 1970, the name was changed ANE and the scope was redirected towards behavior, neuroanatomy, neurophysiology and neuropsychology. The first Editor after the change of title was Professor Jerzy Konorski. ANE has always been edited in the Nencki Institute and has an international Board of Editors. PWN (state-owned Polish Scientific Publishers) acted as the journal publisher till 1989. In 1990, the Nencki Institute became its independent publisher, and the Polish Neuroscience Society became its co-publisher in 2002.

Today, ANE is a fully peer-reviewed quarterly with an international Board of Editors and an Impact Factor of 1.322 (in 2010). Its scope covers broad aspects of neurobiology and neuropathology, including genetics, biochemistry, molecular and cellular neurobiology of the nervous system, electrophysiology and fMRI, functional and comparative neuroanatomy, development and evolution of the nervous system, behavior, brain modeling and also its aging and pathology. ANE publishes original research reports, theoretical papers, reviews, short communications, descriptions of new methods, book reviews and letters to the editor.

Chronicle of the Polish Neuroscience Society is printed on separate pages in the issues of ANE. The average time from receiving a manuscript to print is 6 months. Dates of submission and acceptance are specified at the end of each manuscript. Last issue of each year contains the list of contents of the volume, index of authors and the list of reviewers.

ANE is indexed by Current Contents/Life Sciences, Index Medicus, Biological Abstracts, Science Citation Index, EMBASE/Excerpta Medica, Cambridge Scientific Abstracts USA, Medline and Polska Bibliografia Lekarska GBL. Circulation of ANE varies from 300 (standard issues) to 950 (conference issues). Libraries and individual subjects from over 20 countries subscribe to ANE. Electronic submission and processing of manuscripts is possible from the page of ANE. An electronic version of the journal has recently become available free of charge on-line in PDF format at http://www.ane.pl and http://www.icm.edu.pl. ANE is consecutively placing PDFs of earlier issues on its page. They are linked to specific titles in Medline, to be downloaded for free. At present, articles published from mid 1970’s and onward are available.
The Office of International Relations and Project Management (OIRPM) plays an important role in the Institute’s operations and scientific development. Among its many functions:

- OIRPM facilitates all formal and organizational aspects of international relations, including organization of international conferences and workshops, supporting scientific exchange programmes, managing organizational, legal, and financial aspects of hosting foreign visitors at the Institute as well as aiding Institute employees in their missions abroad.
- OIRPM assists Institute scientists in development and preparation of proposals for external funding from national and international sources, monitors the financial and administrative aspects of submitted proposals and all on-going projects. It also informs the scientists about the existing funding opportunities within the EU Framework Programmes (FP) and other international initiatives as well as European Funds at the national and regional level.
- OIRPM employees act in the capacity of project managers for large and complex projects financed from the European Funds and the Framework Programmes, such as the multi-partner consortia in Innovative Economy Operational Programme (2007-2013) or FP7. The office acts as a liaison with the European Commission (Marta Rucińska is the designated LEAR for FP7) and with the coordinators and funding agencies for large scale investment and R&D projects.

Since 2009 OIRPM has been responsible for stimulating innovation and overseeing technology transfer at the Institute. OIRPM developed and launched the Nencki Institute Innovation Platform (NIIP) that supports intellectual property (IP) protection and management. OIRPM supports and oversees preparation and submission of invention disclosures and the patenting process as well as initiates the technology transfer process. OIRPM employees act as first contact points for the Institute scientists and their industry partners. OIRPM activities stimulating innovation and technology transfer are realised in close collaboration with BTM Mazowsze Ltd, a bio-tech-med cluster management company providing professional support for scientific entities in the transfer of technologies from science to industry and commercialisation of research results.

OIRPM specialists contribute to the promotion of the Institute and dissemination of knowledge by publishing and editing the contents of the Nencki Institute Web Site, the bi-annual NenckiNewsletter and by facilitating media relations. OIRPM staff also actively participate in recruitment, counselling and career advancement of international students, post doctoral fellows and international scientists.

OIRPM prepares annual reports for the Ministry of Science and Higher Education and a report on the Institute’s international cooperation for the Polish Academy of Sciences. The office Head reports to the Deputy Director for Scientific Research and/or directly to the Institute Director.

Head: Marcin Szumowski
Staff: Joanna Kalka-Krakowska, Joanna Kołodziejczyk, Paweł Nowicki, Marta Rucińska, Anna Sadlik-Paskalec
Although the Nencki Institute has a long history of training and awarding PhD degrees, its PhD programme was not formally established until the spring semester of 2001. The main subject areas of the curriculum are Neurobiology, Biochemistry and Molecular and Cell Biology. Currently, 130 enrolled PhD students are advised by working group leaders from among 150 full–time staff participating in the programme. English proficiency is a pre-requisite for enrollment in the programme, and additional language training is available to all doctoral students. Master’s degree in Biology, Biotechnology, Psychology, Chemistry, Physics, Engineer or Medical decoy or equivalent is a formal requirement to enroll in the 4-year programme, during which each student is required to work on research in a field directly related to his/her PhD thesis. All students must attend a series of mandatory lectures as well as participate in the Institute Seminar Series (both give and attend other presentations). All students participate in international workshops and conferences, and report periodically to their supervisors on the progress of their research. Although all students have full access rights to the created knowledge and always receive credit for its generation (co-authorship of papers and conference presentations), the research results remain the property of the Institute.

International PhD Studies in Neurobiology ‘NeuroPhD’

International PhD Studies in Neurobiology ‘NeuroPhD’ programme is designed to addresses the fundamental mechanisms of neuronal function in health and disease that may eventually lead to improved therapeutic strategies. The programme consists of seventeen 4-year brain research projects whose common goal is to understand basic brain mechanisms from health to disease. The project is funded by the Foundation for Polish Science (http://www.fnp.org.pl) within the Innovative Economy Operational Programme (project period: October 2009 – September 2014).

The NeuroPhD programme is designed in cooperation between the Nencki Institute, a Consortium coordinator, and following 17 international research Partner Institutions:

- Katholieke Universiteit, Leuven, Belgium
- Institute of Medical Sciences, University of Aberdeen, Scotland, U.K.
- Vanderbilt University Center for Structural Biology, Nashville, USA
- Department of Experimental and Diagnostic Medicine, University of Ferrara, Italy
- Department of Biomedicine, University of Bergen, Norway
- Université Lyon 1, UFR Chimie-Biochimie, Villeurbanne Cedex, France
- University of Artois, Faculty of Science – Jan Perrin, LENS Cedex, France
- Linköping University, Linköping, Sweden
- Indian Institute of Chemical Technology (IICT), Hyderabad, India
- Institute of Cell Biology, National Academy of Sciences of Ukraine, Lviv, Ukraine
- Max Delbrueck Center for Molecular Medicin (MDC) Berlin, Germany
- K.U. Experimental Genetics Group (LEGTEGG) Leuven, Belgium
- University of Nice-Sophia Antipolis, France
- Virtanene Institute, University of Kuopio, Kuopio, Finland
- Department of Ophthalmology, University of Szeged, Hungary
- School of Pharmacy and Biomedical Sciences, University of Portsmouth, U.K.
- Bonn University, School of Medicine, Bonn, Germany
Administration Units

Administration
Head: Anna Jachner-Miśkiewicz

Finance and Account
Head: Hanna Michalska
Staff: Małgorzata Chmiel, Dorota Chylińska-Krzemińska, Dorota Krakowska, Iwona Marchewka, Krystyna Piechowska, Anna Rasztęborska, Teresa Skórzyńska, Sylwia Szulc, Renata Szymańczak, Justyna Tutaj-Śledziewska
Human Resources and Recruitment Office
Head: Urszula Dziewulska

Staff: Ewa Leśniczuk, Agata Siudek, Ewa Zadykowicz, Katarzyna Żak

Administrative Support:

Secretary to the Director of the Institute
Beata Kuźniarska

Secretary to the Administrative Director
Elżbieta Stefaniuk

Secretary to the Scientific Council
Agata Siudek
For many years the Nencki Institute of Experimental Biology has been involved in various public events aimed at the popularization of science, such as the Warsaw Science Festival (http://www.festiwalnauki.edu.pl) and The Science Picnic of the Polish Radio and the Copernicus Science Centre (http://www.pikniknaukowy.pl). Both of these events have greatly contributed to the general public’s appreciation of science and scientists.

The staff of the Nencki Institute has been involved in the organization of workshops for teachers under the Centre for Innovative Bioscience Education (http://www.biocen.edu.pl) and seminars for the Polish Children’s Fund recipients (http://www.fundusz.org). Meetings with smaller groups of students have been arranged for those interested in research activity of individual scientific teams.

Coordinator: Anna Wasik
Science Picnic
Science Festival
Science Festival
Science Picnic
Workshops under the Centre for Innovative Bioscience Education
Science Picnic
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<td>217, 218</td>
<td>36</td>
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<td>374, 474</td>
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<td>137, 134</td>
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<td>494, 295</td>
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<td>322, 628</td>
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<td>374, 474</td>
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<td>629, 526</td>
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The Neurobiology Centre at the Nencki Institute has been established as part of a strategic project entitled the Centre for Preclinical Research and Technology (CePT).

Within the Innovative Economy Operational Programme (2007-2013) several strategic investments in research infrastructure have been funded from the European Regional Development Fund (ERDF). CePT is the one of the leading projects on that list and the first approved by the European Commission. The Neurobiology Centre investment is executed by the Nencki Institute under a bilateral agreement with the CePT project coordinator, the Medical University of Warsaw (MUW). The value of the Neurobiology Centre (CN) investment is 52 million PLN, which constitutes over 15% of the total value of the CePT project (359 million PLN). About 30 million PLN will be used to purchase research equipment; 15 million PLN will be spent on construction work to extend both wings of the Institute building, while the remaining funds will be allocated to other project-related activities (project management and promotion, personnel costs, training, audit and indirect costs).

After two years of intense preparatory work, and following the settlement of a public tender for architectural design, construction began in May of 2010 and will be completed by the first quarter of 2012. The CN investment is supervised by a team overseeing implementation of the CePT project at the Nencki Institute. The team, working under the supervision of the Nencki Institute’s Director, Adam Szewczyk, consist of Marcin Szymowski (WUM Cooperation coordinator), Anna Jachner (construction coordinator), Hanna Michalska (financial coordinator) and Jerzy Duszyński (scientific coordinator). During the preparatory phase the following people have also been actively involved: Leszek Kaczmarek (scientific coordinator for the CePT research programme representing all seven institutes of the Polish Academy of Sciences) and Urszula Sławińska (coordinating the analysis of functional requirements of the CN investment).

A number of core facilities will be established at the Institute after the CN investment is completed in 2012. These laboratories will be furnished with state-of-the-art research equipment and will provide services not only to researchers working at the Nencki Institute and partners of the CePT consortium, but also to scientists from other research centres in Poland and abroad. Execution of the CN investment will enable the Institute to become a leader in pan-European initiatives, such as the Euro-BioImaging project (www.eurobioimaging.eu) listed on the roadmap of the European Strategy Forum for Research Infrastructures (ESFRI).

The cluster of core facilities within the Neurobiology Centre shall, among others, create a favourable environment enhancing professional development of the most talented researchers in the fields of neurobiology, biochemistry and molecular biology. We hope that the CN investment, strengthened by an inflow of human capital and execution of ambitious, international research projects shall, within the next ten years, place the Nencki Institute among the best research institutions in the field of biology in Poland as well as among the leading European research centres.
NEuro-BioImaging Poland (NEBI)

The main objective of NEuro-BioImaging Poland (NEBI) is to provide open access to imaging technologies across biological and medical applications, with an emphasis on neuroimaging. NEBI will bring together technologies from basic biological imaging with Advanced Light Microscopy (ALM) through in vivo molecular imaging of single cells to animal models through human brain imaging. Its core facilities (reference centres) will be established in Warsaw and Cracow to provide main access points for the Polish research community. These will be partly based on completed or ongoing investments financed from the European Regional Development Fund (ERDF) and partly on newly constructed facilities to devote a significant part of the infrastructure capacity to external users. NEBI operations will be coherent with the goals and objectives as well as the organisational and management approach of Euro-BioImaging (NEBI) pan-European research infrastructure (RI).

Consistently with the NEBI structure, NEBI will operate as a distributed infrastructure with three main research nodes (Neurobiology Centre, Brain Imaging Centre, and Neuroeconomics Centre) and a broader network of associated centres (11 legal entities). NEBI will be coordinated by the Nencki Institute of Experimental Biology. Each open access laboratory within each of the NEBI nodes will follow the access policy developed by NEBI partners together with the EBI consortium. Two levels of participation in NEBI are foreseen: i) Partner (legal entities involved in management, maintenance and technical support for access to the RI) and ii) Associated Partner (having access to the RI, executing joint research projects training and technical workshops with the use of the RI, etc). NEBI will develop management structures, access policies and sustainability strategy that will allow the network to operate successfully as an effective arm of EBI for at least 20 years.

**Timeline:**
Preparatory phase: 2010–2012;
Construction phase: 2011–2013;

**Estimated costs:**
Preparatory phase: 6M EURO (of which 4,6M EURO has been secured)
Construction phase: 41M EURO (of which 28M EURO has been secured)
Annual operations: 3,6M EURO
Decommission cost: N/A
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2. **Nencki Institute of Experimental Biology, Polish Academy of Sciences**
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4. Institute of Biochemistry and Biophysics, Polish Academy of Sciences
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