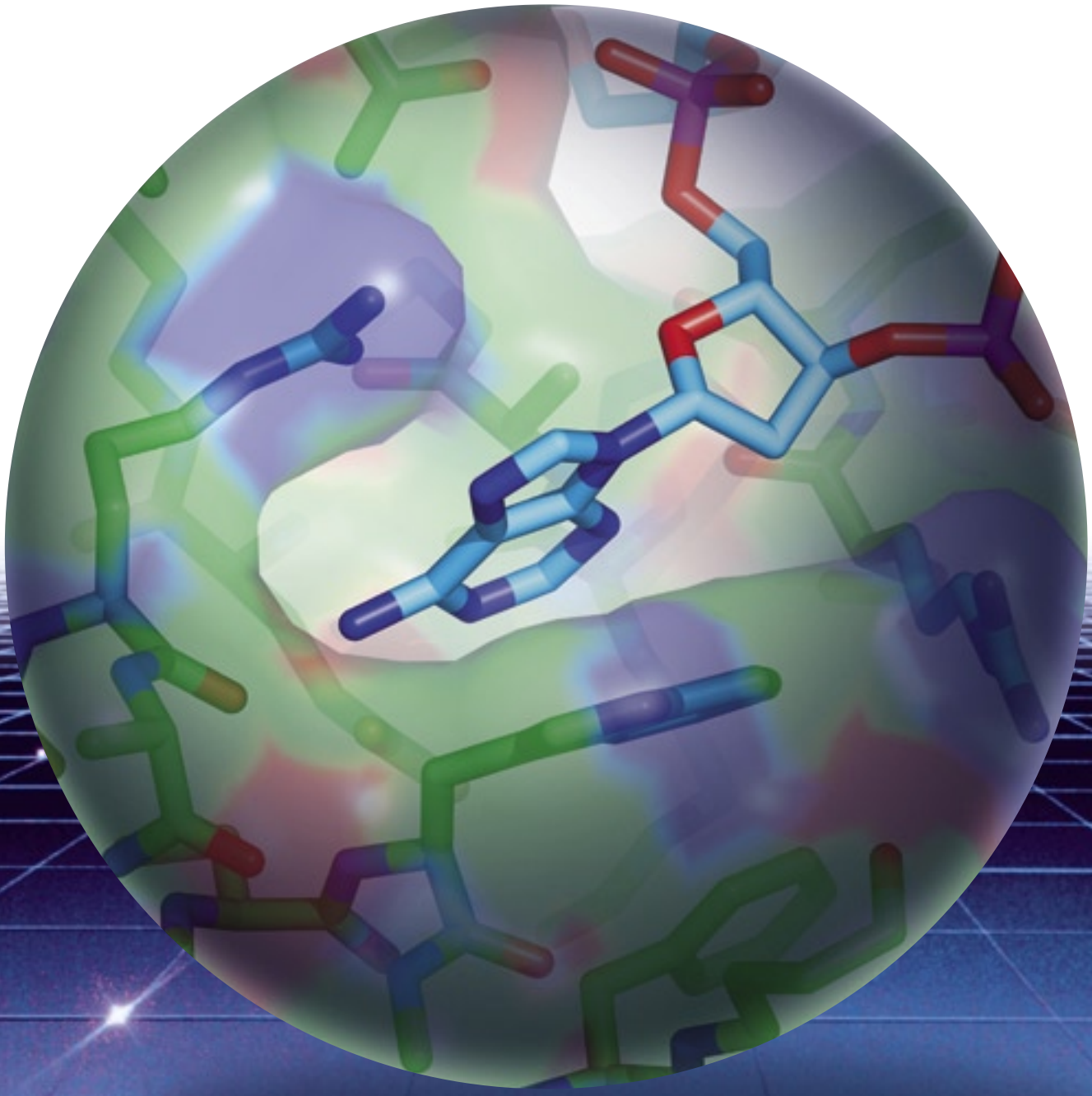

Annual Report **2005**

INTERNATIONAL INSTITUTE OF MOLECULAR AND CELL BIOLOGY IN WARSAW

Director

Jacek Kuznicki

Deputy Director for scientific matters

Michal Witt

Deputy Director for administrative matters

Maria Kleska

Financial Manager

Hanna Iwaniukowicz

Chairman of the International Advisory Board

Angelo Azzi

Deputy Chairman of the International Advisory Board

Leszek Kaczmarek

International Institute of Molecular and Cell Biology in Warsaw

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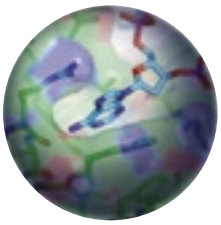
Cover illustration:

Nucleotide flips explain the specificity of restriction endonuclease Ecl18kI. The extruded bases are accommodated in pockets of the enzyme (Bochtler et. al, EMBO J., in press, 2006).

Contents



Map of the Ochota Campus

1 **International Institute of Molecular and Cell Biology in Warsaw**

Polish Academy of Sciences

2 Nencki Institute of Experimental Biology
3 Medical Research Center
4 Institute of Biochemistry and Biophysics
5 Institute of Biocybernetics and Biomedical Engineering

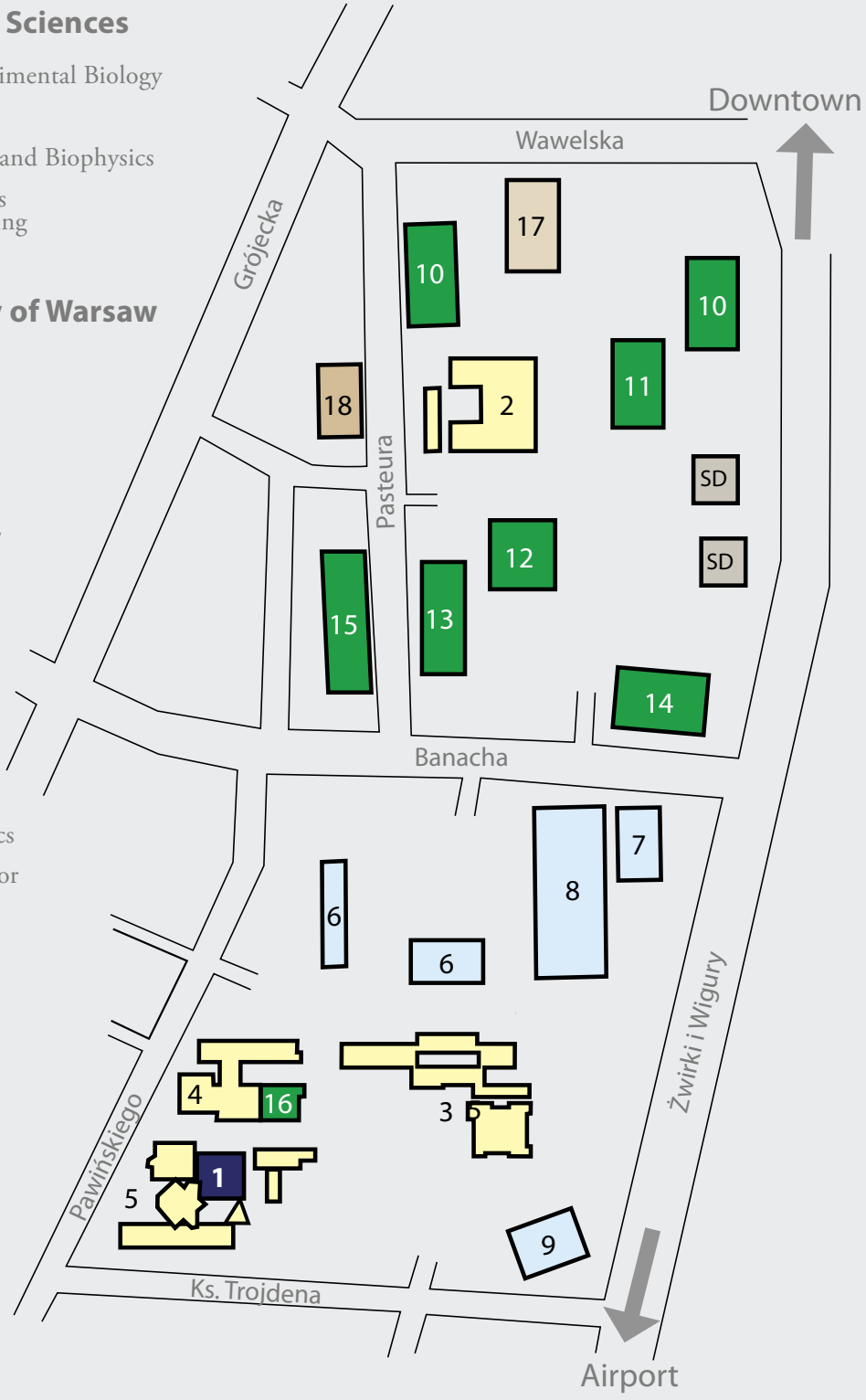
Medical University of Warsaw

7 Faculty of Pharmacy
8 Hospital
9 Rector's office

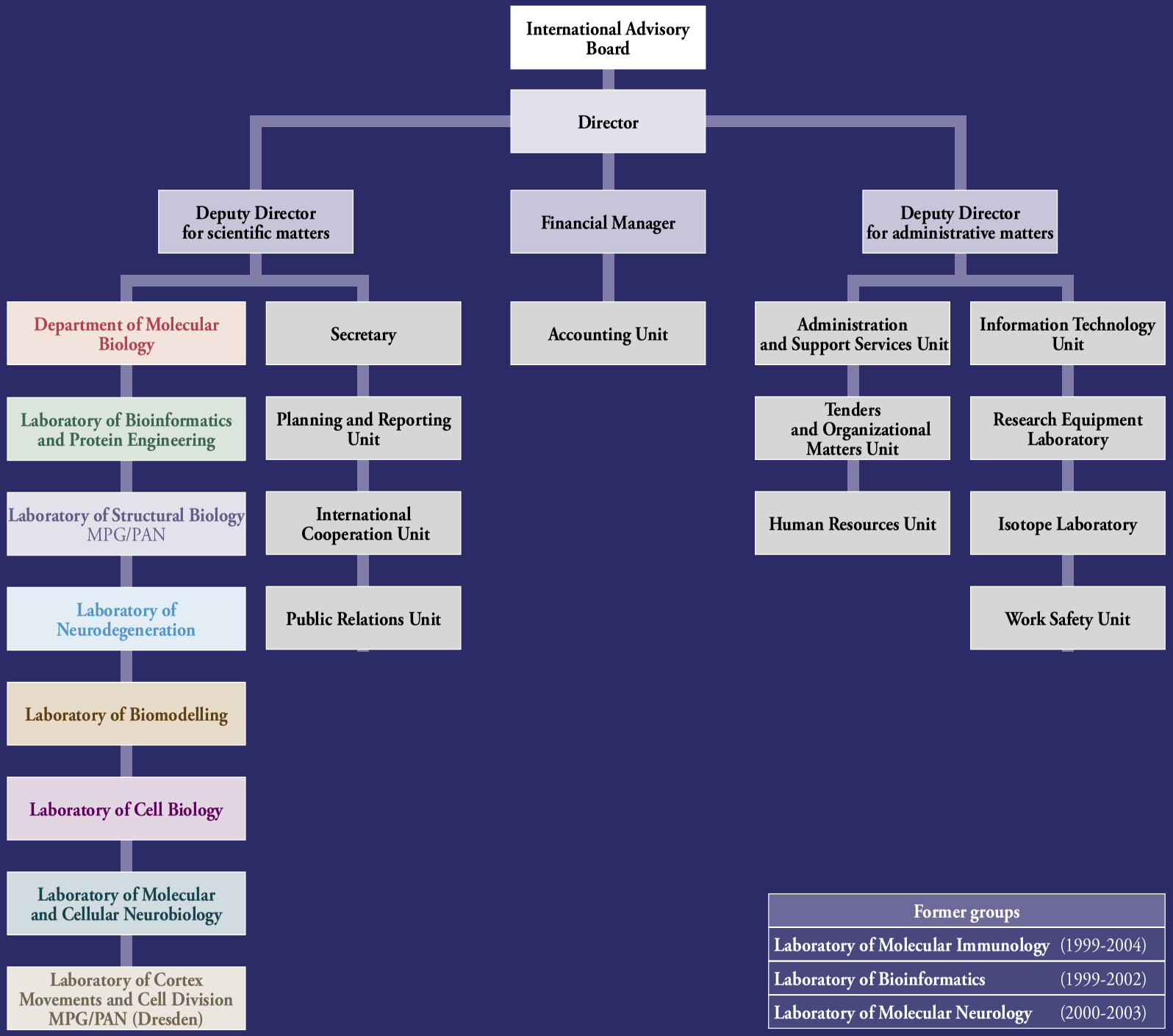
Warsaw University

10 Faculty of Chemistry
11 Faculty of Biology
12 Heavy Ion Laboratory - cyclotron
13 Faculty of Geophysics
14 Faculty of Geology
15 Faculty of Matematics, Informatics and Mechanics
16 Interdisciplinary Centre for Mathematical and Computational Modeling

17 Oncology Hospital
18 Pulmonology Hospital
SD Student Dormitories



Structure of the International Institute of Molecular and Cell Biology in Warsaw



Former groups	
Laboratory of Molecular Immunology	(1999-2004)
Laboratory of Bioinformatics	(1999-2002)
Laboratory of Molecular Neurology	(2000-2003)

Directors and Administration

Jacek Kuznicki
Director

Beata Tkacz
Director's Assistant

Urszula Bialek-Wyrzykowska
International Cooperation Manager

Krystyna Domanska
Human Resources Specialist

Michal Witt
Deputy Director for scientific matters

Agnieszka Ziemka
Planning and Reporting Manager

Dorota Libiszowska
Foreign Grants Specialist

Ewa Blazewicz
Secretarial Assistant

Maria Kleska
Deputy Director for administrative matters

Agnieszka Karbowska
Tenders Specialist

Magdalena Glogowska
PR Specialist

Rober Banasiak
Maintenance Specialist

Hanna Iwaniukowicz
Financial Manager

Sylwia Adamiec
Accounting Specialist

Monika Nowicka
Payroll Specialist

Rafal Flis
IT Specialist

Przemyslaw Slusarczyk
IT Specialist

International Advisory Board of the International Institute of Molecular and Cell Biology in Warsaw

2002-2006 term

Chairman:
Angelo Azzi

Deputy Chairman:
Leszek Kaczmarek

Members:

Ken-ichi Arai

Director, Institute of Medical Science, University of Tokyo 4-6-1, Shiroganedai, Minato-ku, Tokyo 108, Japan

Angelo Azzi

Director, Institute of Biochemistry and Molecular Biology, University of Berne, Buhlstrasse 28, CH-3012 Berne, Switzerland

Alexey A. Bogdanov

Head, Department of Chemistry and Biochemistry of Nucleoproteins, Chemistry Department, Moscow State University, 119899 Moscow, Russia

Robert P. Erickson

Department of Pediatrics, Section of Medical and Molecular Genetics, The University of Arizona Health Sciences Center, 1501 N Campbell Ave, PO Box 245073, Tucson, AZ 85724-5073, USA

Frank Gannon

Executive Director, European Molecular Biology Organisation, Postfach 10.2209, D-69012 Heidelberg, Germany

Willem H. Gispen

Rector Magnificus Utrecht University, Universiteitsweg 100, 3584 CG Utrecht, PO BOX 80125, 3508-TC, The Netherlands

Robert Huber

Head, Department of Structure Research, Max Planck Institute of Biochemistry, Am Klopferspitz 18a, D-82152 Martinsried, Germany

Wieland Huttner

Scientific Member and Director, Max Planck Institute of Molecular Cell Biology and Genetics, Pfotenhauerstrasse 108, D-01307 Dresden, Germany

Leszek Kaczmarek

Chairman, Division II Biological Sciences, Polish Academy of Sciences; Nencki Institute of Experimental Biology, Polish Academy of Sciences, 3 Pasteur St, 02-093 Warsaw, Poland

Oleg A. Krishtal

Deputy Director, The Bogomoletz Institute of Physiology, Head of the Department of Cellular Membranology, Bogomoletz Institute of Physiology, Kiev, Ukraine

Andrzej B. Legocki

President, Polish Academy of Sciences, PKiN, Pl. Defilad 1, 00-901 Warsaw, Poland

Slawomir Majewski

Vice-Chairman, Division VI Medical Sciences, Polish Academy of Sciences; Head, Department of Sexually Transmitted Diseases, Institute of Venorology, Warsaw School of Medicine, 82a Koszykowa St, 02-008 Warsaw, Poland

Jacques Mallet

Laboratoire de Genetique Moleculaire de la Neurotransmission et des Processus Neurodegeneratifs, CNRS UMR 9923, Hopital de la Pitie-Salpetriere, Batiment CERVI, 83 Boulevard de l'Hopital, Paris, France

Maciej J. Nalecz

Director, Division of Basic and Engineering Sciences, UNESCO, 1, rue Miollins, 75732 Paris Cedex 15, France

Ryszard Przewlocki

Head, Department of Molecular Neuropharmacology; Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna St, 31-343 Cracow, Poland

Mariusz Z. Ratajczak

Director, Stem Cell Biology Program, 418 James Graham Brown Cancer Center, University of Louisville, 529 South Jackson St, Louisville, KY, 40202, USA

Wojciech Stec

Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, 112 Sienkiewicza St, 90-363 Lodz, Poland

J. Gregor Sutcliffe

Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

Participants of the meeting of the International Advisory Board, June, 2005

From left (first row): J. Kuznicki, U. Bialek-Wyrzykowska, J. G. Sutcliffe, A. Azzi, (second row) W. Stec, J. Mallet, M. J. Nalecz, L. Kaczmarek, A. A. Bogdanov, (third row) W. Huttner, R. Przewlocki, R. P. Ericsson, M. Witt, J. Duszynski, M. Zylicz.

Important Dates in the Institute's History

Sept. 1991	The proposal to create the Institute was published in the UNESCO Bulletin of MCBN
June 1994	State Committee for Scientific Research (KBN) accepts the activities aimed at establishing the Institute
Oct. 1994	Presidium of Polish Academy of Sciences (PAN) votes to support the Institute
May 1995	An agreement between Poland and UNESCO to establish the Institute
June 1996	The Molecular and Cell Biology Department is created by PAN
June 1997	Polish Parliament passes a bill to found the Institute
May 1998	Prof. A. Azzi is nominated as the Director of IIMCB
Jan. 1999	The Institute commences its independent activities; Prof. J. Kuznicki appointed as Acting Director
July 1999	Dr. J. Dastych is appointed as Leader of the Laboratory of Molecular Immunology
Oct. 1999	Prof. M. Zylicz is appointed as Chair of the Department of Molecular Biology
April 2000	An agreement between the Max Planck Society (MPG) and the Polish Academy of Sciences (PAN) to launch a Joint MPG-PAN Junior Research Group
Nov. 2000	Dr. M. Bochtler is appointed as Leader of the Laboratory of Structural Biology (Joint MPG-PAN Junior Research Group), and Dr. M. Hetman as Leader of the Laboratory of Molecular Neurology
Dec. 2000	Dr. J. Rychlewski is appointed as Leader of the Laboratory of Bioinformatics
Jan. 2001	The MPG-PAN Junior Research Group commences its activities
June 2001	Prof. J. Kuznicki is elected by the International Advisory Board as Director of the Institute, begins to complete the Laboratory of Neurodegeneration. After consultation with UNESCO, the official nomination was signed by the President of PAN on February 1, 2002
Mar. 2002	Dr. J.M. Bujnicki is nominated as Acting Leader of the Laboratory of Bioinformatics and in June being appointed as Leader of the Laboratory of Bioinformatics
June 2002	Dr. S. Filipek is appointed as Leader of the Laboratory of Biomodelling
Nov. 2002	New members of the International Advisory Board nominated for 2002-2006 term
Jan. 2003	Status of the Centre of Excellence in Molecular Bio-Medicine is granted by the European Commission within 5th Framework Programme
June 2003	Evaluation of first two research groups
June 2005	Professor J. Kuznicki re-elected as Director of the Institute (term 2006-2010). Dr. J. Jaworski accepted as a new lab leader.

Directors' note

As time passes, the Institute grows, and more and more people are involved in research activities. In 1999, with the support of PAN, UNESCO, and a few politicians we started with a beautiful new, but empty building, with no people, no funds for research, and rather dim perspectives for the future, but with a lot of enthusiasm instead. The enthusiasm and eagerness are still here, but focused on making progress in science rather than on the organization of the Institute. We have already filled a major part of the building – levels 3 to 5 are full, with some space left on the 1st, 2nd and 6th floors. Three new labs appeared during last 12 months: the Laboratory of Cell Biology headed by Marta Miaczynska, the Laboratory of Molecular and Cellular Neurobiology – by Jacek Jaworski, and the Laboratory of Cortex Movements and Cell Division MPG/PAN – by Ewa Paluch. The latter laboratory is located at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, and is an organizational equivalent of the Structure Biology MPG-PAN lab at our Institute. Within the next few years we expect to hire new young and talented lab leaders, who will fill out the remaining lab space. We will select them through an open international competition based on their professional achievements and scientific plans, which should complement existing research groups and bridge their interest and activities. New leaders will be provided with a supportive and professional administration, good infrastructure and modern equipment, and we will share a friendly climate and dedication to good science with them. The other indicator of growth is a number of foreign grants: we tripled the number of 6th FP grants compared to 2004 and received substantial new ones from the Howard Hughes Medical Institute, Wellcome Trust and Max Planck Gesselschaft with old ones from EMBO and NIH still being continued. Finally, we can proudly announce that among more than 200 papers published since the start of the Institute's activities the number of publications in the best journals has significantly increased. This has allowed us to climb to the top shelf of Polish institutes, with which we share the optimism that reorganization of the funding system of research in Poland will help good institutes to become even better.

Description of the Institute's Activities

The Organization of Research at IIMCB

IIMCB's structure consists of eight research groups: Department of Molecular Biology (Zylicz), Laboratory of Bioinformatics and Protein Engineering (Bujnicki), Laboratory of Structural Biology MPG/PAN (Bochtler), Laboratory of Neurodegeneration (Kuznicki), Laboratory of Biomodelling (Filipek), Laboratory of Cell Biology (Miaczynska), Laboratory of Molecular and Cellular Neurobiology (Jaworski), Laboratory of Cortex Movements and Cell Division MPG/PAN in Dresden (Paluch).

The scope of research carried out at IIMCB is mainly focused on fundamental biomedical problems. Among the major research topics are:

1. The role of molecular chaperones in cell transformation - analysis of interactions between human p53, stress kinases and molecular chaperones, the characterisation of novel human testes specific protein kinase and regulation of its activity, factors of adverse prognosis in non-small lung cancer (Zylicz's group)
2. Theoretical and experimental studies of enzymes acting on nucleic acids (restriction nucleases, methyltransferases, RNA-modification enzymes, DNA repair systems) and proteins from human pathogens (bacteria, viruses, protozoa): protein structure prediction, evolutionary analyses, mutagenesis, protein engineering (Bujnicki's group)
3. The crystallographic structure determination of proteins.
4. The search for a functional bio-marker of familial Alzheimer disease (FAD); the analysis of calmyrin and its interaction with presenilins; the molecular characterisation of Polish patients with FAD, sporadic Alzheimer disease (SAD) and frontotemporal-dementia (FTD); studies of environmental and genetic aspects of longevity - Polish Centenarians Program (Kuznicki's group)
5. The structural modelling of membrane proteins and their complexes involving rhodopsin and other G-protein coupled receptors – structures and processes; the molecular role of mutations of presenilins in neurodegenerative diseases (Filipek's group)
6. Interdependence between intracellular endocytic transport and nuclear signal transduction (Miaczynska's group)
7. Molecular processes underlying neuronal development, plasticity, and "physiological" programmed cell death, including gene transcription, kinase-dependent cell signaling and intracellular trafficking (Jaworski's group)
8. Movements of the actomyosin cortex; mechanism of triggering of cortical flows and of their contribution to the establishment of the mitotic division ring (Paluch's group).

Awards, Honors and Titles

- Habilitation degree to Dr. Janusz M. Bujnicki
- Habilitation degree to Dr. Matthias Bochtler
- Ministry of Health Group Award to DSc.Habil Janusz M. Bujnicki for publications on the role of protein K in cell signaling with particular focus on RNA binding mechanisms
- Foundation for Polish Science Scholarships to Renata Filipek, PhD; Monika Klejman, PhD; Marcin Klejman, PhD; Dawid Walerych, MSc

Education

IIMCB continues its doctoral program in partnership with other research and educational institutes of the Ochota Campus (20 students). International PhD program run in collaboration with Utrecht University have entered the second phase: currently four students are enrolled in this program. Additionally, the doctoral program of the Postgraduate School of Molecular Medicine (three students) and of the Foundation for Polish Science (six students) continue; (see section „Educational Activities" p. 59).

Media Visibility and Popularization of Science

In 2005, IIMCB faculty and staff members were very active in the popularization of science. They presented results of their research on the Academic Internet Television Network and other TV channels and gave numerous press interviews. The articles about IIMCB and research conducted here were published by leading Polish newspapers and journals: Wprost, Polityka, Rzeczpospolita, Gazeta Wyborcza, Przekroj, Swiat Nauki, Przeglad Techniczny, Sprawy Nauki. A comprehensive description of IIMCB history and research activity was published in a leading Polish biochemical review journal, Postepy Biochemii. IIMCB researchers were present in various radio broadcasts and Internet portals (www.onet.pl, www.esculap.pl, www.naukawpolsce.pl). IIMCB, together with the Polish Children`s Fund, organised a special event for talented high school students: Prof. Maciej Zylicz lectured on the biology of molecular chaperones and afterwards students visited IIMCB labs. Furthermore, IIMCB scientists presented several topics during the Warsaw Science Festival, the most popular and successful event bringing science to society in Poland. Popularization activities for teachers and pupils at IIMCB have been performed mostly through the Science Festival School (SFN). SFN together with Institute of Biochemistry and Biophysics PAN and Nencki Institute of Experimental Biology PAN runs two open laboratories: at IIMCB and Warsaw Agricultural University. A total number of 1000 young participants visited laboratory workshops in 2005; 115 biology teachers and about 600 students of various levels attended lectures organized by SFN.

A former Minister of Finance, currently the President of the Polish National Bank, Prof. Leszek Balcerowicz visited research institutes of Ochota Campus; meetings with researchers were concluded during the „Can we achieve economic growth without supporting research?" discussion. The visit was covered by local media.

Publishing NEWSKO

Since 2000 e-bulletin NEWSKO provides the Ochota Campus community with current information on seminars, symposia, conferences, job opportunities and other essential events.

NEWSKO, which has been published at the Institute every Thursday for the last six years, integrates scientists, students and medical doctors at the Ochota Campus and plays a role as the communication platform for all Centres of Excellence at Ochota Campus.

Computer Network

The IIMCB computer network, managed by Rafal Flis, is implemented over a structured network of copper fifth category cable. Active elements of the network are: four optic fiber transceivers, seven 3Com/HP 24-port Ethernet 10/100 Mb/s switches and two HP 8-port Ethernet, 10/100/1000 Mb/s switches. We are connected directly to several different Research Institutes in Ochota Campus through fiber optics. There are more than 100 workstations, notebooks, tablets and pads in the network protected by a local firewall operating under Windows NT/W2K/XP/CE, Linux, BSD, Solaris and Mac OS. We have twelve Institute servers (Intel-based) used for e-mail, Intranet, Internet, DNS, DHCP, applications files, remote access, proxy, firewall, terminal services, multimedia and video streaming. These servers operate under Windows NT/W2K/2003, BSD and Linux. Users can remotely access the local network through VPN from home or elsewhere. We have a connection to the Ochota Campus through the Gigabit Ethernet. Next year, we are planning to develop the connection to upgrade the local network to the Gigabit Ethernet bone. A plan for future purchases includes mass storage and multimedia for common usage of the Institute labs.

It has already become IIMCB tradition to organize together with Polish Children`s Fund yearly special lectures for talented high school pupils. This year, a group of brilliant youngsters listened to Prof. Maciej Zylicz lecture on molecular chaperones.

Activities of the Centre of Excellence in Molecular Bio-Medicine

Activities of the Centre of Excellence in Molecular Bio-Medicine focus on (i) improvement of research quality in biomedical sciences, (ii) extension of the range and scope of education and training in the field, (iii) promotion and popularisation of molecular medicine and human genetics as innovative and modern branches of basic and applicable research, and (iv) strengthening the international position of IIMCB as a centre, where basic and applied research, as well as education and training, are carried out at the highest level. These objectives were taken into consideration while implementing the Centre's activities depicted in the workplan throughout all work packages.

Workpackage 1

The third International Annual Symposium took place in the 30th month of the project. It consisted of an open research symposium and a closed meeting of International Advisory Board of IIMCB. Research symposium included lectures given by candidates for the new lab leader position at IIMCB: **Dr. Pawel Bieganowski**, IIMCB, **Dr. Jacek Jaworski**, USA; **Dr. Agnieszka Kobielak**, USA and **Dr. Krzysztof Kobielak**, USA.

Workpackage 2

This work package is devoted to twinning activities with: **Max Planck Institutes in Germany; the Utrecht University in The Netherlands**; and **the Italian National Research Centre on Ageing in Ancona, Italy**. As a part of co-operation with Max Planck Institutes **Prof. Maciej Zylicz** took part in the symposium "The Science & Art in Europe" organized by the Max Planck Society in Berlin and **Anna Zarembska, Marta Brewinska and Dr. Marta Miaczynska** visited the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden. As a part of co-operation with the Utrecht University **Prof. Maciej Zylicz** and **Marta Bucko-Justyna** visited the Department of Physiological Chemistry and Centre for Biomedical Genetics at the University Medical Centre in Utrecht.

Workpackage 3

Within this work package fourteen scientists from various European laboratories visited the Centre: **Prof. Guido Tarone** (Italy), **Dr. Mara Brancaccio** (Italy), **Dr. Kathryn Ball** (United Kingdom), **Dr. Maura Wallace** (United Kingdom), **Dr. Henri Grosjean** (France), **Dr. Bruno Lapeyre** (France), **Dr. Ewa Paluch** (France), **Dr. Berta Alsina** (Spain), **Dr. Jordi Villa-Freixa** (Spain), **Dr. David T. F Dryden** (United Kingdom), **Prof. Pierre Formstecher** (France), **Prof. Renata Polakowska** (France), **Dr. Iwona Pilecka** (Switzerland), and **Prof. Eric Westhof** (France). The visitors presented seminars for scientists from the Centre and the Ochota Campus and led extensive scientific discussions with the researchers at the Centre. A number of scientific co-operations were initiated that are expected to result in common research projects and publications. These visits were particularly important for young scientists at the Centre who gained an opportunity to discuss their projects with experts in the field and to develop new research ideas. Three IIMCB fellows visited their European collaborators: **Dr. Janusz Bujnicki** went to: (i) CEA-VALRHO, DSV-DIEP-SBTN, Service de Biochimie post-genomique & Toxicologie Nucleaire in Bagnols-sur-Ceze, France, (ii) Enzymology and Structural Biochemistry Laboratory, CNRS in Gif-sur-Yvette, France and (iii) Laboratoire de Microbiologie, Université Libre de Bruxelles, Belgium; **Jan Kosinski** went to Laboratoire d'Enzymologie et Biochimie Structurales, CNRS in Gif-sur-Yvette, France; and **Dr. Slawomir Filipek** to the Center of Biotechnology, University of Technology in Dresden, Germany.

Workpackage 4

In the third year of the project exchange of students and postdocs between the Centre and established European laboratories was intensified. Three foreign guests worked at the Centre, **Aneta Kaczmarczyk** (Sweden), **Ewa Chovancova** (Czech Republic), and **Luis Giron** (Germany). Nine Polish researchers from the Centre worked in various European laboratories:

- **Dominika Trzaska** in the Clinical Immunology and Allergy Unit, Department of Medicine, Karolinska Institutet, Karolinska University Hospital Solna in Stockholm, Sweden
- **Maciej Olszewski** at the Department of Dermatology and Allergology, University Medical Center in Utrecht, The Netherlands

- **Magdalena Kaus** at the Institute for Medical Microbiology and Hygiene in Regensburg, Germany
- **Malgorzata Gutkowska** at the Institute of Biochemistry, Faculty of Sciences, Università Politecnica delle Marche in Ancona, Italy
- **Bartosz Wawrzynow** in the CRUK Interferon and Cell Signaling Group, Cell Signaling Unit Cancer Research Centre and the University of Edinburgh, United Kingdom
- **Maciej Geremek** in the Complex Genetics Group, Department of Medical Genetics, Utrecht Medical Center in Utrecht, The Netherlands
- **Izabela Sabala** at the Department of Rheumatology and Inflammation Research, University of Gothenburg, Sweden
- **Iwona Cymerman** at the Institute of Biochemistry, Justus-Liebig-Universität in Giessen, Germany
- **Katarzyna Modrzynska** at the Center of Research in Macromolecular Biochemistry in Montpelier, France

Workpackage 5

The conference **„Molecular Mechanisms of Neurodegeneration and Neuroprotection"**, a joint event organized by Prof. Jacek Kuznicki from the Centre and Prof. Bozena Kaminska from the Nencki Institute of Experimental Biology, took place in 2003 and was described in the First Annual Periodic Report.

Workpackage 6

EMBO-FEBS Workshop on Biology of Molecular Chaperones: Heat Shock Proteins in Molecular Medicine, Misfolding Diseases and Cancer took place in 29th /30th month of the project in Zakopane, Poland. The event was sponsored by European Molecular Biology Organisation (EMBO), The Federation of European Biochemical Societies (FEBS) and **the Centre of Excellence in Molecular Bio-Medicine of the International Institute of Molecular and Cell Biology in Warsaw.** The workshop was organized and chaired by **Prof. Maciej Zylicz** from IIMCB, Poland and **Prof. Ulrich Hartl** from MPG, Germany. Over 130 researchers from 25 countries around the globe came to hear, present and discuss various aspects of research on molecular chaperons. Several invited speakers took part in the session sponsored by the Centre: **Prof. Ari Helenius** (Switzerland), **Prof. Peter Csermely** (Hungary), **Prof. Simon Pacey** (United Kingdom), **Prof. Borek Vojtesek** (Czech Republic), **Prof. Marija Jäättelä** (Denmark), **Prof. Wiesława Widlak** (Poland), **Prof. Carmen Garrido** (France), **Dr. Andrea Zgaga-Griesz** (Germany), **Dr. Theo Rein** (Germany), **Prof. Ulrich Hartl** (Germany), **Prof. Didier Picard** (Switzerland), **Rolf Issels** (Germany), **Prof. Gabriele Multhoff** (Germany), **Prof. Giorgio Parmiani** (Italy), **Prof. Lorenzo Pilla** (Italy), **Prof. Ted Hupp** (United Kingdom), and **Prof. Harm H. Kampinga** (The Netherlands).

Molecular Medicine Lecture Series: „Pneumology, Haematology and Psychiatry" included lecture by **Dr. Heymut Omran** from the Universitäts-Kinderklinik in Freiburg, Germany.

Workpackage 7

The third of the Integrated Courses of the Postgraduate School of Molecular Medicine (SMM) planned within this work package: **„Advances in molecular medicine: focus on molecular endocrinology"** was held in 30th month of the project and consisted of a conference ***„Molecular endocrinology – from gene to disease"*** and a practical course ***„Molecular endocrinology in clinical practice"***. The Integrated Course took place at the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology in Gliwice, Poland. This event included lectures of invited guests: **Prof. Tomasz Bednarczuk** (Poland), **Prof. Catharina Larsson** (Sweden), **Prof. Gerry Thomas** (United Kingdom), **Prof. Ilpo Huhtaniemi** (United Kingdom), **Prof. Klaus Badenhoop** (Germany), **Prof. Patrick Gaudray** (France), **Prof. Katarzyna Lacka** (Poland), and **Prof. Liliana Konarska** (Poland). The course included lectures, laboratory workshops, and clinical presentations.

Workpackage 8

One of the main objectives of the Centre of Excellence project is a promotion of the International Institute of Molecular and Cell Biology as a leading research centre in molecular biomedicine, both domestically and internationally, and popularization of science in the society. To meet those objectives two IIMCB fellows **Magdalena Glogowska** and **Agnieszka Ziemka** have taken postgraduate training in Public Relations. The Centre is very active in bringing science to society: it organized seven different events within 9th Warsaw Science Festival and supported numerous activities of the Science Festival School. Other promotional activities included **Prof. Jacek Kuznicki's** lecture on achievements of 18 CoEs at the Centres of Excellence Workshop organized by the Nencki Institute of Experimental Biology and IIMCB, 9-10 November 2005. Also, **Prof Michal Witt** has presented the Institute and its achievements at the VII World Congress of the International Council for Central and East European Studies in Berlin 28-29 July 2005.

Scientific Meetings and Lectures

- 4th International Conference *„Inhibitors of Protein Kinases"*, 25-29.06.2005, Warsaw, Poland, organizer: Interdisciplinary Center for Mathematical and Computational Modeling; coorganizers: Institute of Biochemistry and Biophysics PAN, Institute of Biocybernetics and Biomedical Engineering, Division of Biophysics – Institute of Experimental Physics, University of Warsaw and IIMCB
- EMBO Workshop *„Frontiers of Molecular Biology"*, 14-18.10.2005, Jachranka, Poland, organized by EMBO and IIMCB
- SMM 5th Integrated Course – *„Advances in molecular medicine: focus on molecular endocrinology"* consisted of a conference *„Molecular endocrinology – from gene to disease"* and a practical course *„Molecular endocrinology in clinical practice"*, 26.06-1.07.2005, Gliwice, coorganized by IIMCB within the „Centre of Excellence in Molecular Bio-Medicine" project
- SMM Lecture Course on Human Genetics, 1-2.06.2005, Warsaw, organized by SMM and IIMCB
- International Annual Symposium, 10-11.06.2005, Warsaw, Poland, IIMCB within the „Centre of Excellence in Molecular Bio-Medicine" project
- IIMCB Annual Report Session, 6.05.2005, Mierki, Poland
- 28.05-2.06.2005 EMBO-FEBS Workshop on Biology of Molecular Chaperones: *Heat Shock Proteins in Molecular Medicine, Misfolding Diseases and Cancer,* Zakopane, Poland; sponsored by European Molecular Biology Organisation (EMBO), The Federation of European Biochemical Societies (FEBS) and the Centre of Excellence in Molecular Bio-Medicine of the International Institute of Molecular and Cell Biology in Warsaw; organized and chaired by Professor Maciej Zylicz from IIMCB and Prof. Ulrich Hartl from MPG, Germany
- SMM Annual Scientific Report Session, 10-11.10.2005, Warsaw, organized by SMM, Medical University of Warsaw and IIMCB.

Lectures within Centre of Excellence in Molecular Bio-Medicine project

Guido Tarone (Department of Genetics, Biology and Biochemistry, University of Torino) *Integrin signaling and mechanotransduction in the heart.* 14.02.2005

Kathryn Ball (CRUK Interferon and Cell Signalling Group, Cancer Research Centre, University of Edinburgh) *Defining steps on the pathway leading to activation of the IRF-1tumour suppressor.* 9.03.2005

Heymut Omran (Universitaets-Kinderklinik, Freiburg) *DNAH5 and DNAI1 mutations cause mis-localization of the outer dynein arm heavy chains DNAH5 and DNAH9.* 17.03.2005

Henri Grosjean (Director of Research CNRS, Laboratory of Structural Enzymology and Biochemistry (LEBS) Gif-sur-Yvette) *Comparative analysis of tRNA sequences in genomes of the 3 biological domains.* 26.04.2005

Bruno Lapeyre (Centre de Recherche de Biochimie, Macromoleculaire du CNRS, Montpellier) *RNA MTases in yeast: bending the rules.* 3.06.2005

Pawel Bieganowski (IIMCB) *Hints from the histidine triad family.* 10.06.2005

Jacek Jaworski (Howard Hughes Medical Institute & Picower Center for Learning and Memory, Massachusetts Institute of Technology, Cambridge, MA) *Regulation of dendritic arbor development by the PI3K- Akt-mTOR signaling pathway.* 10.06.2005

Agnieszka Kobielak (Laboratory of Mammalian Cell Biology and Development, The Rockefeller University, New York, NY) *Alpha-catenin: at the junction of intercellular adhesion and actin dynamics.* 10.06.2005

Krzysztof Kobielak (Laboratory of Mammalian Cell Biology and Development, The Rockefeller University, New York, NY) *Regulation of hair follicle morphogenesis by BMP signaling.* 10.06.2005

Ewa Paluch (UMR168 Physico-Chimie Curie, Institut Curie/ CNRS, Paris) *How actomyosin contractility and cortical flows govern cell shape dynamics.* 27.06.2005 (lecture given at the Nencki Institute of Experimental Biology PAN, Warsaw)

Berta Alsina (Development Biology Group, Department of Health and Experimental Sciences, Universitat Pompeu Fabra) *Neurogenesis and compartment formation in the inner ear development.* 11.07.2005

Villa-Freixa Jordi (Computational Biochemistry and Biophisics, Universitat Pompeu Fabra) *From micro – to macroscopic approaches to the dynamics of biochemical processes.* 11.07.2005

David T. F. Dryden (University of Edinburgh) *Making and breaking a biomolecular machine.* 30.08.2005

Pierre Formstecher (Inserm U459, Université Lille 2, Faculté de Medecine Henri Warembourg) *From stem cell to cell death. A new concept in epithelial cell biology and cancer.* 26.09.2005

Iwona Pilecka (Serono Pharmaceutical Research Institute, Geneva) *Downregulation of receptor tyrosine kinases by Cbl and CIN85.* 13.10.2005

Eric Westhof (Université Louis Pasteur, Strasbourg) *RNA self-assembly motifs.* 3.11.2005

IIMCB researchers seminars

Marcin Klejman (Department of Molecular Biology) *Transcription by eukaryotic RNA polymerase II: regulation of the TATA-binding protein function.* 6.01.2005

Monika Mysiak (Laboratory of Neurodegeneration) *From pre-initiation complex formation to initiation of adenovirus DNA replication.* 20.01.2005

Anna Modzelewska (Laboratory of Biomodelling) *Chemistry of wine.* 27.01.2005

Renata Filipek (Laboratory of Structural Biology Max Planck/PAN) *Crystallographic studies of staphopain inhibition.* 3.02.2005

Marta Wisniewska (Laboratory of Neurodegeneration) *Specificity of transcription factor(s) AP-1 - comparative studies on some promoters.* 10.02.2005

Marta Bucko-Justyna (Department of Molecular Biology) *From gene to protein properties and its interactions: TSSK3 example.* 17.02.2005

Honorata Czapinska (Laboratory of Structural Biology Max Planck/PAN) *Crystallographic analysis of BPTI mutants and their complexes with bovine chymotrypsin.* 24.02.2005

Malgorzata Marcyjaniak (Laboratory of Structural Biology Max Planck/PAN) *TRIM5α-selective weapon against retroviruses.* 3.03.2005

Joanna Sasin (Laboratory of Bioinformatics and Protein Engineering) *Known unknowns' and 'unknown unknowns'- 'top 10' lists of highly attractive targets for experimental study.* 10.03.2005

Agnieszka Chmiel, (Laboratory of Bioinformatics and Protein Engineering)

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Circular permutatioN. 31.03.2005

Michal J. Pietal (Laboratory of Bioinformatics and Protein Engineering) *Support Vector Machines - an example of mathematical method in protein classification.* 14.04.2005

Pawel Bieganowski (Department of Molecular Biology) *Histidine Triad Protein Family.* 21.04.2005

Marta Miaczynska (Laboratory of Cell Biology) *Studies of proteins regulating endocytic transport - part I.* 12.05.2005

Mathias Bochtler (Laboratory of Structural Biology Max Planck/PAN) *Asymmetric protein, symmetric crystal?* 16.05.2005

Marta Miaczynska (Laboratory of Cell Biology) *Studies of proteins regulating endocytic transport - part II.* 19.05.2005

Beata Bielinska (Department of Molecular Biology) *Analysis of deletions of the ovo promoter region in Drosophila melanogaster germline.* 02.06.2005

Michał Boniecki (Laboratory of Bioinformatics and Protein Engineering) *Continous, intermediate resolution protein model - Refiner. Construction and example results of protein structure modeling.* 9.06.2005

Magdalena Lipka (Laboratory of Structural Biology MPG/PAN) *If only we can keep youth forever.* 30.06.2005

Marta Miaczynska (Laboratory of Cell Biology) *Endosomes in signal transduction: not just a sink.* 20.10.2005

Matthias Bochtler (Laboratory of Structural Biology MPG/PAN) *X-ray sources for protein crystallography.* 27.10.2005

Krzysztof Skowronek (Laboratory of Bioinformatics and Protein Engineering) *Chaos Engineering. Strategies of protein randomization.* 10.11.2005

Janusz M. Bujnicki (Laboratory of Bioinformatics and Protein Engineering) *Jedi vs Sith: physics and evolution in protein structure prediction.* 24.11.2005

Maciej Zylicz (Department of Molecular Biology, IIMCB) *HSPs vaccines.* 15.12.2005.

Grants

International

6th Framework Programme

- "Tracking the endocytic routes of polypeptide growth factor receptor complexes and their modulatory role on signalling" (019050 LSH 2006); 428,400 EUR; 2006-2010; M. Miaczynska
- "A multidisciplinary approach to the study of DNA enzymes down to the single molecule level" (MRTN-CT-2005-019566); 254,452 EUR, matching funds 606,181 PLN; 2005-2009; J.M. Bujnicki
- "From cell-cell recognition to memory formation. New strategies for the treatment of dysfunctional plasticity, learning and memory" (LSHM-CT-2005-512012); 478,000 EUR, matching funds 1,203,600 PLN; 2005-2009; J. Kuznicki
- "Co-ordinated internet-linked networks for promoting innovation, exchanging knowledge and encouraging good practice to enhance bioscience education in European schools" (Sub-contract No1 to EC Contract 511180; SAS6); 38,534 EUR, matching funds 77,520 PLN; 2005-2008; J. Lilpop (SFN)
- "Genetic Testing in Europe - Network for test development harmonization, validation and standardization of services" (LSHB-CT-2004-512148); 30,000 EUR, matching funds 70,591 PLN; 2005-2009; M. Witt
- "Abnormal proteins in the pathogenesis of neurodegenerative disorders" (LSHM-CT-2003-503330); 161,200 EUR, matching funds 457,000 PLN; 2004-2006; J. Kuznicki
- "Mechanisms of transgene integration and expression in crop plant plastids: underpinning a technology for improving human health" (LSHG-CT-2003-503238); 164,160 EUR, matching funds 477,000 PLN; 2004-2007; J.M. Bujnicki

5th Framework Programme

- "Centre of Excellence in Molecular Bio-Medicine" (QLK6-CT-2002-90363); 350,000 EUR and supplementary grant from KBN 996,000 PLN, matching funds 30 000 PLN 2003-2006; J. Kuznicki
- "Novel non-antibiotic treatment of staphylococcal diseases" (QLK2-CT-2002- 01250); 238,382 EUR, matching funds 776,000 PLN; 2002-2006; M. Bochtler

Other International Funds

- International Research Scholars: "Signaling from endosomes to the nucleus: The role of APPL proteins and their interacting partners"; Howard Hughes Medical Institute; 500,000 USD; 2006-2010; M. Miaczynska
- The MPI-CBG/IIMCB Partner Group at the IIMCB: "Biochemical and microscopical characterization of APPL-positive endosomes"; 60,000 Euro; 2006-2008; M. Miaczynska
- "Communication between intracellular organelles in trafficking and signalling: The role of APPL proteins", International Senior Research Fellowship of the Wellcome Trust (UK); 4,315,706 PLN; 2006-2010; M. Miaczynska
- Grant NIH "Kinetoplastid SL RNA biogenesis"; 100,000 USD; 2004-2009; J.M. Bujnicki
- Grant NIH "Discovering new human DNA repair genes by bioinformatics"; 89,401 USD; 2003-2005; J.M. Bujnicki
- Utrecht University fellowships for five PhD students (M. Witt's lab, IIMCB and Institute of Human Genetics PAN, Poznan; M. Zylicz's lab, IIMCB; A. Lipkowski's lab, Center for Experimental and Clinical Medicine, PAN, Warsaw; L. Kaczmarek's lab, Nencki Institute PAN, Warsaw; R. Przewlocki's lab, Institute of Pharmacology PAN, Cracow); 10,000 EUR annually from 2004 to 2007
- EMBO & HHMI Young Investigator Programme Award (Project No. 741) 26,000 USD and 50,000 PLN annually from 2002 to 2005; J.M. Bujnicki
- EMBO & HHMI Young Investigator Programme Award; 26,000 USD and 50,000 PLN annually from 2004 to 2006; M. Bochtler
- Polish National Commission for UNESCO program "Science of modern biology – exploratory resources for biology teachers and students"; 20,000 USD; 2004-2005; J. Lilpop

- The Max Planck Society (MPG) – the Polish Academy of Sciences (PAN) MPI-CBG Junior Research Group Program -Laboratory of Structural Biology MPG/PAN; 1,500,000 EUR, 2001-2006; M. Bochtler

Polish

Research Grants from the Ministry of Education and Science

- The Max Planck Society (MPG) – the Polish Academy of Sciences (PAN) MPI-CBG Junior Research Program - Laboratory of Cortex Movement and Cell Division MGP/PAN; 3,024,200 PLN; 2006-2008; E. Paluch
- „Role of mTOR-regulated proteins in development of dendritic tree of hippocampal and cortical neurons" (0966/P01/2006/30); 220,800 PLN; J. Jaworski
- "Biochemical and microscopical characterization of APPL-positive endosomes" (0394/P04/2005/28); 390,040 PLN; 2005-2008; M. Miaczynska
- "Identification of natural substrates for enzymes from the HINT family of phosphoroamidases and identification of enzymes that synthesize these substrates" (0453/P04/2005/29); 352,000 PLN; 2005-2008; P. Bieganowski
- "Investigation of structure of presenilin protein and significance of its mutations in Alzheimer's disease development" (0695/P05/2005/29); 220,000 PLN; 2005-2007; K. Jozwiak
- "STRUF- the novel software for classification and prediction of proteins functions " (1581/T11/2005/29); 105,000 PLN; 2005-2007; J. Sasin
- "Differences in action of stress-induced and constitutively synthesized Hsp70" (KBN-0408/P04/2004/27); 550,200 PLN; 2004-2007; M. Zylicz
- "Combating bacterial resistance against MLSb antibiotics by design of a novel type of inhibitors against Erm methyltransferases" (KBN-0611/P05/2004/27); 93,000 PLN; 2004-2006; M. Feder
- KBN-Polonium "Etude comparitive d'ARN-methyltransferases de differents organismes: un modele pour l'evolution des systemes enzimatiques de modification des acides nucleiques"; 2004-2005; J.M. Bujnicki
- Polish-German project (KBN-DAAD) "Protein-nucleic acid and protein-protein interactions in biomedically important enzymes involved in nucleic acid metabolism (DNA repair and degradation)"; 2004-2005; J.M. Bujnicki
- Polish-Czech project "Protein engineering of dehalogenating biocatalysts"; 2004-2005; J.M. Bujnicki
- "Modelling of G Protein-Coupled Receptor and their interactions with drugs in case of opioid receptors" (KBN-0624/P05/2003/25); 120,000 PLN; 2003-2006; S. Filipek
- "Identification of specificity determinants of restriction endonucleases by bioinformatics and mutagenesis" (KBN-0344/P04/2003/24); 300,000 PLN; 2003-2006; J.M. Bujnicki
- "Hsp90 in Cancerogenesis" (KBN-0203/P04/2002/22); 462,000 PLN; 2002-2005; A. Wawrzynow

Doctoral grant

- "Investigation of the structure of arrestin-rhodopsin complex by theoretical methods" (0121/P01/2006/30); 33,000 PLN; 2006-2007; S. Filipek

Ordered Grants from the Ministry of Education and Science

- "New bioinformatic tools for proteomics and structural genomics" (KBN-K089/P04/2004); 1,800,000 PLN; 2004-2007; 5 groups in Poland, including 2 in IIMCB (Bujnicki and Bochtler); Director: J.M. Bujnicki
- "Advanced molecular methods in haematology. Development and implementation of standardized research procedures for minimal residual disease, posttransplantation chimerism and marker translocations" (K126/P05/2005); 3,027,500 PLN; 2005-2007; Director: M. Witt; 13 groups in Poland
- "Search for diagnostic methods of Alzheimer's disease and identification of pathogenic mechanisms as potential targets of therapies based on proteomic research in human lymphocytes"(K129/P05/2005/UMED6); 400,000 PLN; 2005-2008; U. Wojda (within ordered grant directed by Medical University of Lodz)
- Bilateral Polish-German Ordered Research Grant (KBN-K064/P05/2003) "The transduction of neuronal Ca^{2+}-signals via EF-hand calcium-binding proteins caldendrin and calmyrin in Alzheimer's disease and psychotic disorders"; 955,400 PLN; 2003-2006; Director: U. Wojda with cooperation with Dr. M.R. Kreutz, Department of Neurochemistry, Molecular Biology, Leibniz Institute for Neurobiology, Magdeburg
- "Genetic and environmental longevity factors in a group of Polish centenarians" (KBN-022/ P05/1999); 1,500,000 PLN; 2001-2005; Director: J. Kuznicki; 22 groups in Poland
- "Addiction: neurobiological basis, mechanisms, methods of prophylaxis and treatment" (KBN-033/P05/2000); 3,400,000 PLN; 2001-2005; Director: R. Przewlocki

Other Research Grants

- Professorial Grant from Foundation for Polish Science (SP 10/04) „Beta-catenin metabolism in health and disease"; 240,000 PLN; 2004-2006; J. Kuznicki

International Cooperation

With the Max Planck Society

The success of Dr. Matthias Bochtler's joint Junior Research Group operating at IIMCB since 2001 under the agreement between the Max Planck Society (MPG) and the Polish Academy of Sciences (PAN) resulted in the organisation of a second edition of an international competition for setting up a mirror joint Group at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden (MPI-CBG), financed by the Polish Ministry of Education and Science. The new Laboratory of Cortex Movements and Cell Division started its activities on the 1st of February 2006 and is headed by Dr. Ewa Paluch. The equipment and running costs for the lab, including personnel, are provided by the Polish site. MPI-CBG covers local operational costs, maintenance and provides administrative support. Dr. Ewa Paluch's group focuses on biochemical and physical mechanisms of cell shape and deformations. The research is concentrated on movements of the actomyosin cortex, a thin gel of actin that underlies the cell membrane. The group is now working on the involvement of spontaneous cortical ruptures and flows in cell division.

The project-oriented cooperation between IIMCB and MPI-CBG has been further intensified by the establishment of the Partner Group of the MPI of Molecular Cell Biology and Genetics called the MPI-CBG/IIMCB Partner Group at the International Institute of Molecular and Cell Biology. Dr. Marta Miaczynska, head of the Laboratory of Cell Biology is the leader of the Partner Group and Prof. Marino Zerial is the cooperation partner and a scientific mentor at MPI-CBG. The Partner Group, set up for 3 years with the possibility of a 2-year extension, commenced its work on the 1st of January 2006. The project entitled "Biochemical and microscopical characterization of APPL-positive endosomes" aims at the further molecular characterisation of a novel signal transduction pathway, essential for cell proliferation and operating between the plasma membrane and the cell nucleus.

With Utrecht University

A research collaboration program with Utrecht University was initiated by Prof. Willem Gispen, Rector of Utrecht University. The main goal of this program was to foster Polish – Dutch exchange of scientific information and to strengthen the research cooperation through bilateral visits of staff members and their students. Furthermore, eight Polish doctoral students received four-year fellowships to work in Poland on their doctoral thesis. In the spring of 2005 Marta Bucko and Katarzyna Starowicz defended their thesis in Utrecht.

With the Italian National Research Centre on Ageing (INRCA), Ancona

After a few years of successful cooperation, existing collaborations of scientists between the Italian National Research Centre on Ageing in Ancona and IIMCB were formalized. Prof. Claudio Franceschi representing INRCA and Prof. Jacek Kuznicki representing IIMCB have signed an agreement on the creation of an exchange program in the area of biomedical sciences.

With the Palladin Institute of Biochemistry of NAS of Ukraine

In September 2005, IIMCB represented by Director J. Kuznicki and the Palladin Institute of Biochemistry of NAS of Ukraine represented by Director S. V. Komissarenko have signed an official agreement on scientific cooperation. As a result, the Laboratory of Neurodegeneration of IIMCB hosted Dr. Tatiana Borisova, Senior Scientist from the Department of Neurochemistry from NAS Institute of Ukraine in November 2005. Dr. Borisova met with IIMCB's researchers and gave a seminar "Artificial gravity loading of animals as a tool to investigate the presynaptic processes in brain".

Foreign Visits to IIMCB:

1. 23.03.2005: Prof. Alexander S. Spirin, Professor of Biochemistry and Molecular Biology, Member of the Russian Academy of Sciences, Institute of Protein Research and Dept. of Molecular Biology Moscow State University, Russia
2. 29.03.2005: visit of delegation from Deutsche Forschungsgemeinschaft: Prof. Ernst-Ludwig Winnacker, President

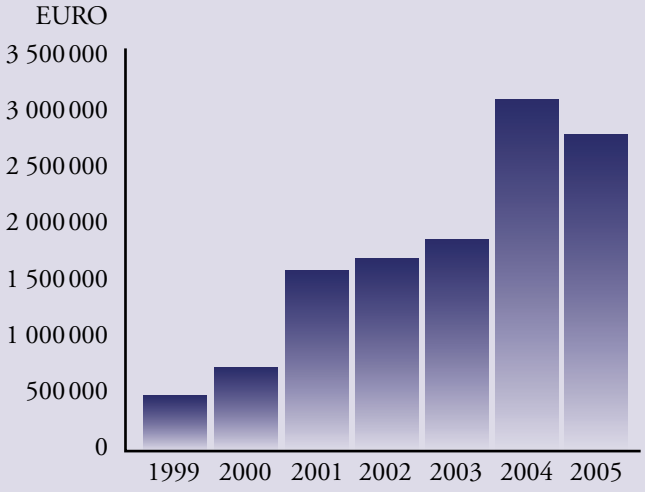
of the DFG; Dr. Beate Konze-Thomas, Director General Programmes and Research Infrastructure; Dr. Alice Rajewsky, Programme Director, International Cooperation with Central and Eastern Europe; Dr. Torsten Fischer, Programme Officer for European Research Cooperation

3. 29.06.2005: Prof. Vaclav Paces, President of the Academy of Sciences of the Czech Republic
4. 6.07.2005: Prof. Konstantin Skryabin, Director of Center „Bioengineering", Russian Academy of Science and Prof. Marc Van Montagu, Director of the Laboratory of Genetics at the Faculty of Sciences, Ghent University, Belgium
5. 19.07.2005: Prof. Reza Davari Ardakani President of Academy of Sciences of Islamic Republic of Iran (ASI), Prof. Mohammad Reza Shams Aredkani, Vice President of ASI
6. 10.08.2005: Dr. Kieran Rooney, Business Development Director, Pharmaceutical Profiles; Brendan Vickers, Network Manager of International Technology Promoter (ITP); Philip Oliver, Life Science – Europe, ITP; Izabela Van den Bossche, Director of Science and Innovation Section, Embassy of Great Britain
7. 30.08.2005: Dr. Kathie Olsen, Associate Director with the Office of Science and Technology Policy in the Executive Office of the President USA
8. 16.11.2005: Prof. Baatar Chadraa, President of Mongolian Academy of Sciences; Prof. Dugeriin Regdel, Secretary General of Mongolian Academy of Sciences
9. 9.12.2005: Dr. Jean-Claude Beloeil, Director of Research CNRS, Centre de Biophysique Moleculaire CNRS, Orlean, France
10. 14.12.2005: Dr. Mark A. Suskin, Head of Europe Office, National Science Foundation, France

Seminars of invited speakers

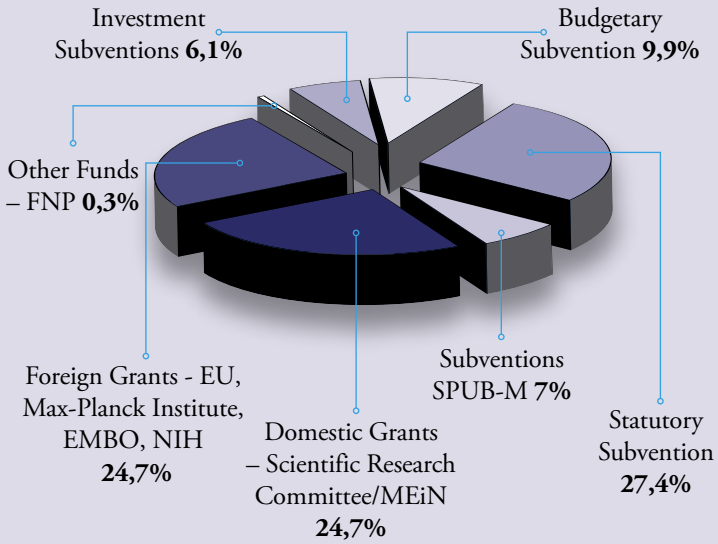
1. Daniel Krowarsch (Institute of Biochemistry and Molecular Biology University of Wroclaw) *Circular dichroism as a tool for protein structure analysis.* 4.01.2005
2. Marek Cieplak (Institute of Physics PAN, Warsaw) *Mechanical stretching of proteins: calmodulin and titin.* 13.01.2005
3. Jan A. Miernik (Plant Genetics Research Unit USDA and University of Missouri) *Multiplicity of the Arabidopsis thaliana J-domain proteins: redundancy or specialization?* 1.02.2005
4. Grzegorz Grynkiewicz (Pharmaceutical Research Institute, Warsaw) and Wieslaw Szeja (Silesian University of Technology, Gliwice) *Synthetic approaches to modulation of small ligand interactions with biological targets.* 24.03.2005
5. Dorota Religa (Karolinska Institute, Stockholm and Medical Research Center, Warszawa) *Role of amyloid ß-peptide in the pathogenesis of Alzheimer's disease and other neurological and psychiatric disorders.* 29.03.2005
6. Veli-Pekka Jaakola (Macromolecular Structures Group, University of Helsinki, Finland) *Expression and purification of G protein-coupled receptors for structure determination.* 15.04.2005
7. Jan Loewe (MRC, Cambridge) *Rotary mechanism of DNA translocation.* 17.10.2005
8. Peggy Stolt (Max Planck Institute for Biophysics, Frankfurt) *Structure and function of the PTB domain of the lipoprotein receptor adaptor protein disabled-1.* 19.10.2005
9. Tatiana Borisova (Palladin Institute of Biochemistry NAS of Ukraine, Kiev) *Artificial gravity loading of animals as a tool to investigate the presynaptic processes in brain.* 17.11.2005
10. Przemyslaw Bozko (University of Illinois, Chicago) *Reactivation of p53 – strategy for anticancer therapy.* 18.11.2005
11. Sajid Rashid (Institute of Human Genetic, George-August University, Goettingen) *Exploring the role of dynein light chain.* 6.12.2005
12. Alina Oknianska (Lund University, Lund) *Regulation and functions of phosphodiesterase 3B (PDE3B) in adipocytes.* 8.12.2005

Diversity of Funding IIMCB `2005



Sources	amounts in PLN	amounts in EURO*
Budgetary Subventions	1 080 000	279 807
Statutory Subvention	2 996 000	776 206
Subventions SPUB-M	765 000	198 197
Domestic Grants Scientific Research Committee	2 700 865	699 742
Foreign Grants – EU, Max-Planck Institute, EMBO, NIH	2 701 416	699 885
Other Funds – FNP	28 400	7 358
Investments Subventions	664 143	172 067
Total	**10 935 824**	**2 833 262**

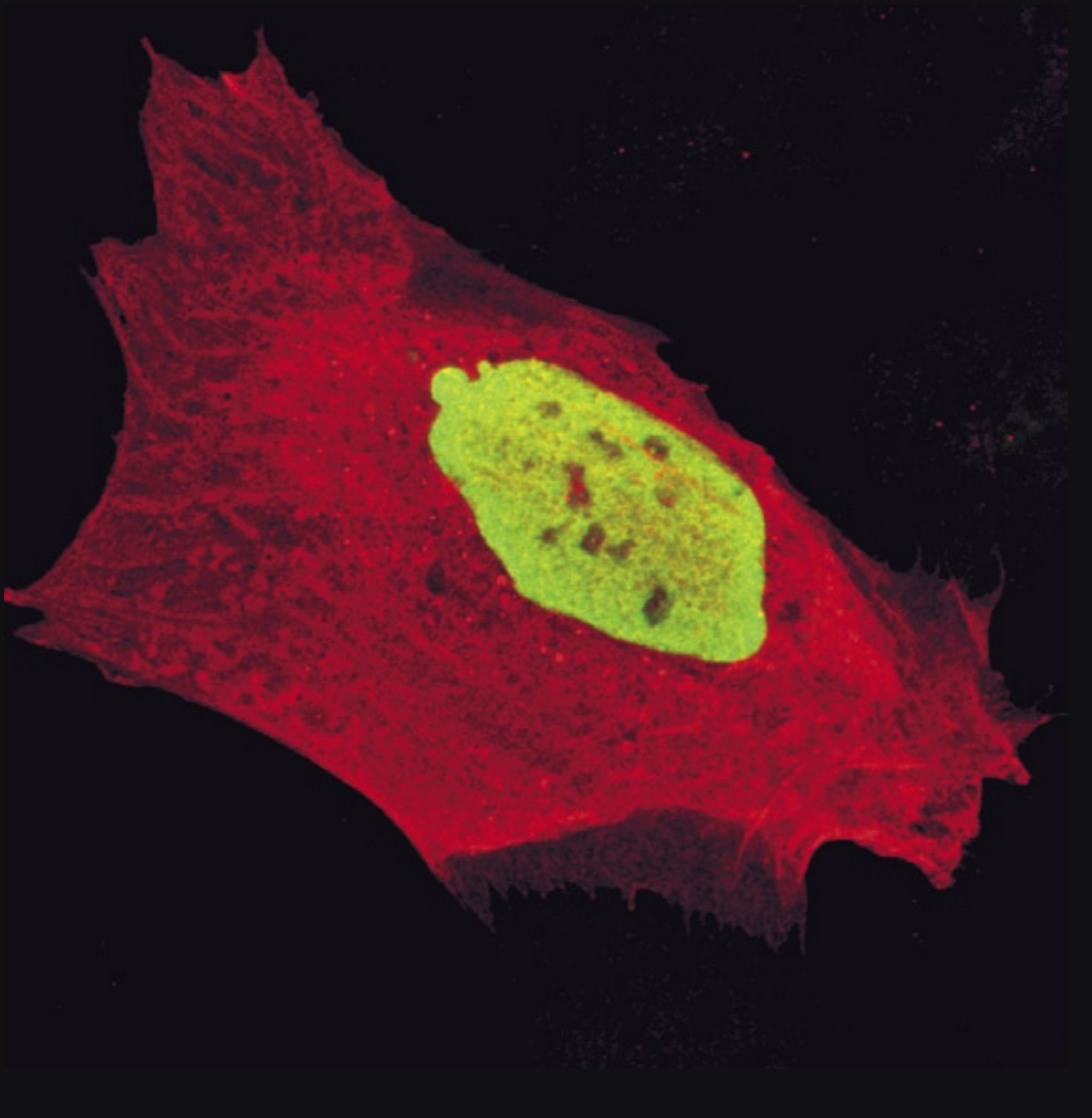
**1 EURO = 3,8598 PLN @31st Dec `2005*



Expenses of IIMCB

PROFIT & LOSS STATEMENT	amounts in PLN
NET REVENUE ON SALES AND EQUIVALENTS:	9 380 290
Net revenue on sales of products	8 854 698
Change of work in progress (increase /+/, decrease /-/)	525 592
OPERATIONAL ACTIVITY COSTS	10 362 636
Depreciation	1 100 857
Materials and energy	2 663 500
Services	945 595
Fees and taxes	422 696
Salaries and wages	2 990 770
Social and health insurance	675 613
Other operational expenses	1 563 604
PROFIT / LOSS ON SALES	-982 346
OTHER OPERATIONAL INCOME	784 701
Subventions	782 250
Other operational income	2 451
OTHER OPERATIONAL EXPENSES	7 990
PROFIT / LOSS ON OPERATIONAL ACTIVITY	-205 635
FINANCIAL INCOME	61 252
Interests	49 079
Others	12 173
FINANCIAL EXPENSES	35 201
Interests	140
Others	35 061
PROFIT / LOSS ON BUSINESS ACTIVITY	-179 584
EXTRAORDINARY ITEMS	0
GROSS PROFIT / LOSS	-179 584
INCOME TAX	0
NET PROFIT / LOSS	-179 584

Department of Molecular Biology



Lab Leader

Maciej Zylicz, PhD, Professor

Vice Head: :
Alicja Zylicz, PhD, Professor

Research Associate:
Pawel Bieganowski, PhD
Marcin Klejman, PhD

Research Assistant:
Maciej Olszewski, MSc (since January 2006)

Graduated PhD students:
Marta Bucko-Justyna (until April 2005),
Grzegorz Kudla, PhD (until April 2005)

PhD students:
Joanna Boros (until May 2005), MSc;
Malgorzata Gutkowska, MSc; Aleksandra Helwak, MSc (until October 2005); Leszek Lipinski, MSc; Dawid Walerych, MSc, Bartosz Wawrzynow, MSc, Jakub Urbanski, MSc

Secretary:
Grazyna Orleanska, MSc

Technician:
Wanda Gocal

Maciej Zylicz, PhD

Degrees

Professor, 1992

DSc.Habil. in molecular biology, Institute of Biochemistry and Biophysics PAN, Warsaw, Poland 1986

PhD in biochemistry, Medical University of Gdansk, Poland 1979

MSc in physics and biology, University of Gdansk, 1977

Post-doctoral Training

1993-1994 Visiting Professor, University of Utah, Medical Center, Institute of Oncology, Salt Lake City, UT, USA

1982-1984 University of Utah, Department of Cellular, Viral and Molecular Biology, Salt Lake City, UT, USA

1979-1981 University of Gdansk, Department of Biochemistry, Gdansk

Professional Employment

since September 1st 2005 President, Executive Director of the Foundation For Polish Science, FNP

since 1999 Head of Department of Molecular Biology, IIMCB

1994-1999 Head of Department of Molecular and Cellular Biology, Faculty of Biotechnology, University of Gdansk

1991-1994 Head of Department of Molecular Biology, University of Gdansk

1990-1993 Vice President, University of Gdansk

1988-1991 Associate Professor, Department of Molecular Biology, University of Gdansk

1981-1988 Assistant Professor, Department of Biochemistry, University of Gdansk

Other Professional Activities

2000-2004 Chair of Biology, Earth Sciences and Environmental Protection Commission of State Committee for Scientific Research

Membership in Scientific Societies, Organizations and Panels

- Member of EMBO
- Member of EMBO Council
- Member of Advisory Editorial Board of EMBO Journal and EMBO Reports and IUBM Life
- Polish delegate to EMBC (2001-2004)
- Polish delegate to Life Science Committee of ESF
- Member of the Selection Committee for EMBO YIP (2001-2003)
- Member of the Selection Committee for the special DFG programs
- Member of Polish Academy of Sciences
- Member of American Society of Biochemistry and Molecular Biology
- Member of Academia Europaea
- Member of the State Committee for Scientific Research (1997-2004)
- Member of Polish Academy of Arts and Sciences

Honors, Prizes, Awards

1. Prime Minister Award for Scientific Achievements, 2002
2. "L. Marchlewski" Award of Biochemistry and Biophysics Committee PAN, 2001
3. Award of Foundation for Polish Science (FNP), 1999
4. Award of the Polish Biochemical Society for the best biochemistry work performed in Polish laboratories, 1996
5. Award of Ministry of Education, 1994
6. "Heweliusz" Prize for the Scientific Achievements, awarded by the President of Gdansk, 1993
7. Award of Polish Academy of Sciences, 1990
8. Individual Award of Polish Academy of Sciences for Scientific Achievements, 1986

Doctorates

K. Liberek, D. Skowyra, J. Osipiuk, B.Banecki, D.Wojtkowiak, J. Jakobkiewicz, J. Puzewicz, P. Barski, F. King, M. Bucko-Justyna, G. Kudla

DSc Habil. Performed in Department

Liberek K., Werel W., Marszalek J., Konieczny I., Wawrzynow A., Banecki B.

Professor Titles Received:

Liberek K., Marszalek J., Konieczny I., Wawrzynow A.

Publications

80 publications in primary scientific journals including: two papers published in Cell, six in EMBO J., six in PNAS and 25 in J. Biol. Chem. These papers were cited more then 4,500 times with an average citation per paper of 60.

Selected publications since 2001

- *Galazka G, Stasiolek M, Walczak A, Jurewicz A, Zylicz A, Brosnan CF, Raine CS, Selmaj K Brain-Derived Heat Shock Protein 70-Peptide Complexes Induce NK Cell-Dependent Tolerance to Experimental Autoimmune Encephalomyelitis. J Immunol, 2006; 176:1588-99
- Ilyushik E, Pryce DW, Walerych D, Riddell T, Wakeman JA, McInerny CJ, McFarlane RJ Psc3 cohesin of Schizosaccharomyces pombe: cell cycle analysis and identification of three distinct isoforms. Biol Chem, 2005; 386:613-21
- Klejman MP, Zhao X, van Schaik FMA, Herr W, Timmers HTM Mutational analysis of BTAF1-TBP interaction: BTAF1 rescues DNA-binding defective TBP mutants. Nucl Acids Res, 2005; 33:5426-36
- *Bucko-Justyna M, Lipinski L, Boudewijn M, Burgering T, Trzeciak L Characterization of Testis Specific Serine-threonine Kinase 3 and its activation by Phosphoinositide-Dependent Kinase-1-dependent signaling. FEBS J, 2005; 272:6310-23
- *Mycko PM, Cwiklinska H, Szymanski B, Kudla G, Kilianek L, Odyniec A, Brosnan CF, Selmaj KW Inducible heat shock protein 70 promotes myelin autoantigen presentation by HLA Class II. J Immunol, 2004; 172: 202-213
- *Kudla G, Helwak A, Lipinski L Gene conversion and GC-content evolution in mammalian Hsp70. Mol Biol Evol, 2004; 21:1438-44

- *Jassem J, Jassem E, Jakobkiewicz-Banecka J, Rzyman W, Badzio A, Dziadziuszko R, Kobierska-Gulinda G, Szymanowska A, Skrzypski M, Zylicz M P53 and K-ras mutations are frequent events in microscopically negative surgical margins from patients with non-small cell lung carcinoma. Cancer, 2004; 100: 1951-60
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- *Kaczanowski R, Trzeciak L, Kucharczyk K Multitemperature single-stranded conformation polymorphism. Electrophoresis, 2001; 22:3539-45

*Papers marked with an asterisk have the IIMCB affiliation of the authors

Description of Current Research

The scientific objective of the Department is focused mainly on human molecular chaperones and their role in cell transformation.

The p53 tumour suppressor gene encodes a sequence specific transcription factor, which is mutated in the vast majority of human cancer. One of the foremost characterized target genes of p53 is the *mdm2* gene. MDM2 protein possesses E3 ubiquitin ligase activity towards p53. Through its ability to ubiquitinate p53 and target it for proteasomal degradation, MDM2 plays key role in retaining p53 at very low levels in non stress conditions. In such circumstances MDM2 and p53 form a negative feedback loop in which p53 induces *mdm2* transcription and MDM2 targets p53 for degradation. In stress situation MDM2–dependent degradation of p53 is inhibited what results in an increase of a steady-state level of p53 transcription factor and consequential flux in the expression of more than a hundred genes including those involved in apoptosis and cell arrest. Fine balance between the level of p53 and MDM2 is required for normal cell growth. MDM2 oncoprotein also possesses numerous p53-independent activities, which contribute to the development of tumours where mdm2 is overexpressed, mostly by gene amplification. However, the biochemical mechanism of these activities remains elusive. Indeed, despite the fact that MDM2 interacts with proteins fulfilling a variety of cellular functions (p300, pRb, Numb, MTBP, ARF, E2F1, TBP, TAFII250, Sp1, ribosomal L5, TSG 101), the biological significance of these multiple interactions remains to be elucidated. It should be stressed that not all MDM2 client proteins are targeted by it for proteasome degradation, hence not all involvements of MDM2 can be explained by its E3 ligase activity. Several findings, namely: binding to nascent p53 polypeptide chain, activation of transcription factors, protection and activation of DNA polymerases, involvement in ribosome assembly suggest that MDM2 possesses similar activities of that described for molecular chaperones. Recently we have shown that Hsp90, in an ATP-dependent reaction, retains wt p53 in the conformation which allows binding to the specific promoter sequence (Walerych et al., 2004). Hsp90 binds also to the mutant p53, but this interaction is indirect. With the use of highly purified proteins, we identified intermediate reactions that lead to the assembly of the multichaperone complex (mutp53-Hsp40-Hsc70-Hop-Hsp90) (King et al., 2001)

In this year's report, we demonstrate that:

A. MDM2 is a novel molecular chaperone.

B. silent site GC content correlates with gene expression efficiency in mammalian cells (effects of GC content on the expression of Hsp70, GFP and IL2 genes).

MDM2 is a novel molecular chaperone

We purified human recombinant MDM2 protein to high homogeneity and showed that it is active as an E3 ligase in reconstituted *in vitro* p53 polyubiquitination reaction. We assayed MDM2 molecular chaperone activity by means of: suppression of aggregation of citrate synthase and refolding of heat inactivated luciferase. In both cases we showed that MDM2 possesses much more potent molecular chaperone activity than Hsp90. Moreover, MDM2 could also substitute Hsp90 and CHIP in polyubiquitination reaction of luciferase. To our surprise, MDM2 protein can also substitute for Hsp90 molecular chaperone in the reaction of p53 binding to the *p21* promoter derived sequence at 37°C. MDM2-dependent binding of p53 to *p21* promoter sequence is ATP dependent. In control experiments we showed that the MDM2 K454A mutant which is unable to bind ATP, can act as an E3 ligase in view of p53 polyubiquitination, however it lacks MDM2 molecular chaperone activity required for p53 binding to the *p21* promoter sequence at 37°C. The results show that, apart from E3 ligase, MDM2 protein also possesses molecular chaperone activity required for folding of wt p53 to the transcriptionally active conformation. Moreover, molecular chaperone activity of MDM2 could also explain the molecular mechanism of MDM2 action in p53-independent reaction involved in tumorigenesis or as a facilitator of translation.

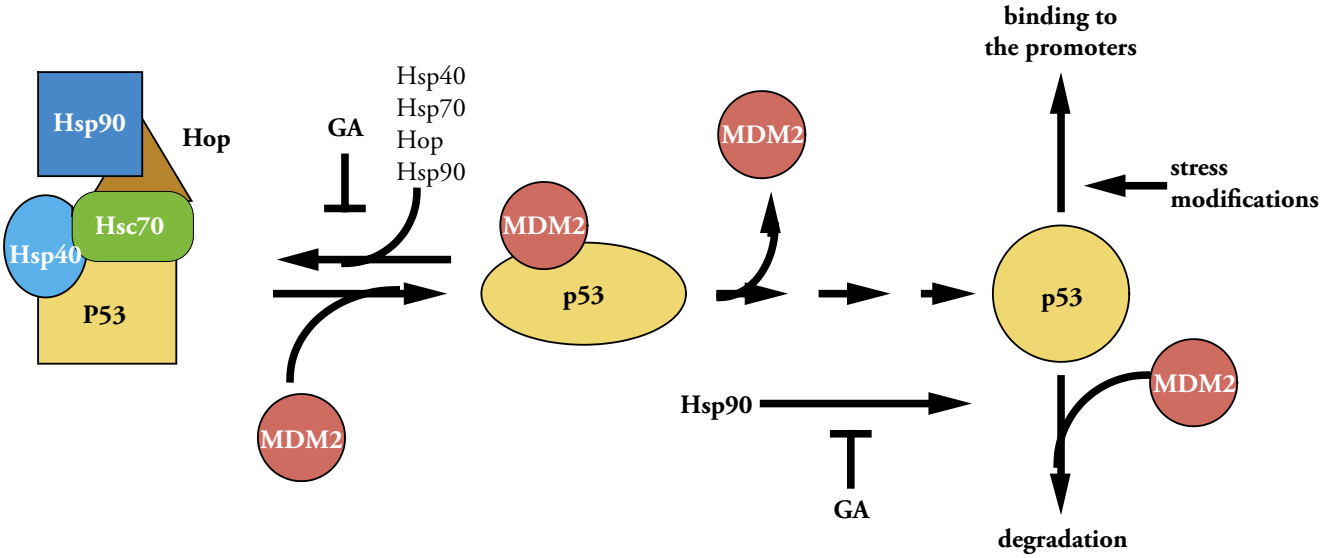

Figure 1. Proposed model for MDM2 activity as a molecular chaperone.

Molecular chaperone activity of MDM2 is required for partial unfolding of p53. After dissociation of MDM2, p53 could spontaneously fold to the active conformation which, in the presence of posttranslational modification induced by stress conditions, could work as a transcription factor. In the absence of stress, MDM2 E3-ligase activity is required for polyubiquitination of p53 and in the consequence degradation of p53. Hsp90 molecular chaperone could work sinergistically with MDM2. In stress situation the conformational equilibrium of p53 is shifted towards mutant-like conformation which could be stabilized by multichaperone complex, where Hsp90, indirectly via Hop protein, interacts with Hsc70/Hsp40 chaperone machine. The presence of geldanamycin (GA), a specific inhibitor of Hsp90, not only inhibits Hsp90 chaperone activity involved in folding of p53 but also inhibits formation of multichaperone complex.

Silent site GC content correlates with gene expression efficiency in mammalian cells

Mammalian genes are highly heterogeneous with respect to their nucleotide composition, but the functional consequences of this heterogeneity are not clear. In the previous studies, weak positive or negative correlations have been found between the silent site GC content and expression of mammalian genes. However, previous studies disregarded differences in the genomic context of genes, which could potentially obscure any correlation between GC content and expression. In the present work, we directly compared the expression of GC-rich and GC-poor genes, placed in the context of identical promoters and UTR sequences. In the first set of experiments, we compared the expression of genes from the mammalian Hsp70 family. We have recently shown

that despite the very high similarity of their encoded proteins, mammalian Hsp70-family genes display large differences in their nucleotide usage (Kudla et al., 2004). We performed transient and stable transfections of mammalian cells with GC-rich and GC-poor versions of *Hsp70, GFP* and *IL2* genes. The GC-rich genes were expressed several-fold to over a hundred-fold more efficiently than their GC-poor counterparts. This effect was not due to different translation rates of GC-rich and GC-poor mRNA. On the contrary, an efficient expression of GC-rich genes resulted from their increased steady-state mRNA levels. mRNA degradation rates were not correlated with GC content, suggesting that efficient mRNA transcription or processing is responsible for the high expression of GC-rich genes. We conclude that silent site GC content correlates with gene expression efficiency in mammalian cells.

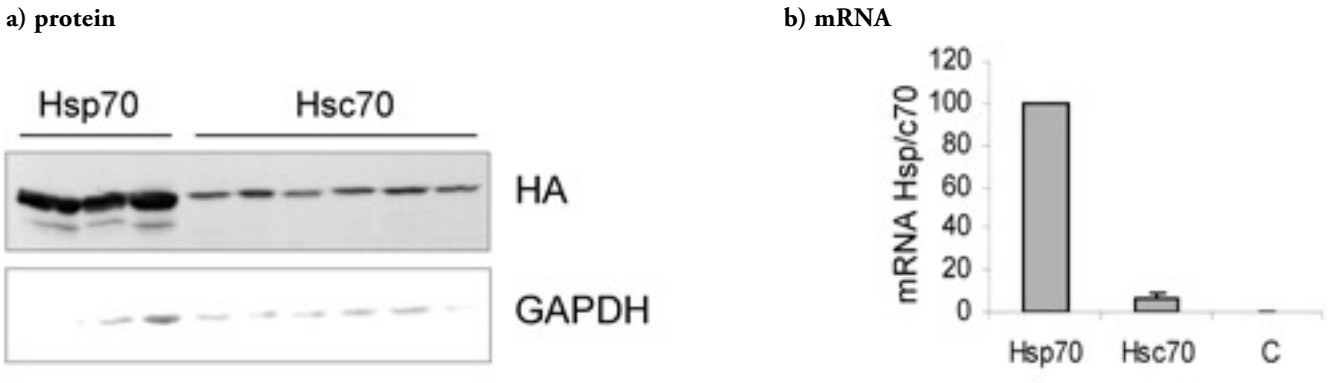

Figure 2. Expression of Hsp70 (GC3=92%) and Hsc70 (GC3=46%). (a) Both genes were cloned under the same promoter. Three independent clones of pcDNA3-Hsp70-HA (GC3=92%) and six clones of pcDNA3-Hsc70-HA (GC3=46%) were used to transfect HeLa cells. Twenty-four hours following transfection the cells were harvested and the Hsc70-HA or Hsp70-HA protein levels were analyzed by western-blotting using an anti-HA antibody. An anti-GAPDH antibody was used as loading control.(b) HeLa cells were transfected with equal amounts of pcDNA3-Hsp70-HA or pcDNA3-Hsc70-HA plasmids. After 24 hours, total cellular RNA was isolated and analyzed by qRT-PCR. The graphs represent Hsp/c70 mRNA amounts. Hsp70, cells transfected with pcDNA3-Hsp70-HA; Hsc70, cells transfected with pcDNA3-Hsc70-HA; C, untransfected cells. The error bars represent standard deviations from 3 to 4 independent transfections.

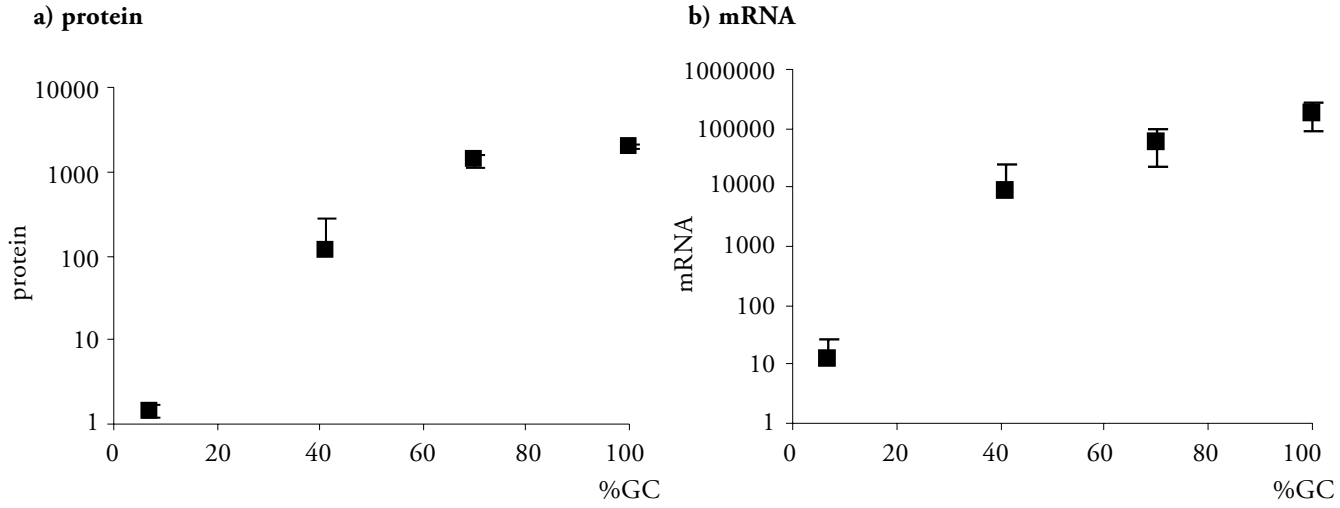

Figure 3. Correlation between silent-site GC content and expression of IL2 variants in stably transfected MCF-7 cells.
MCF-7 cells were stably transfected with expression plasmids containing wIL2 (GC3=7%), IL2 (GC3=41%), IL2-eIL2 (GC3=70%), eIL2 (GC3=100%). Protein and mRNA was quantified in 3 to 5 individual clones for each transgene. (a), ELISA measurements of the IL2 protein levels. (b), real-time RT-PCR measurements of IL2 mRNA levels. IL2 mRNA levels were normalized to GAPDH mRNA. The vertical axis in each graph represents arbitrary units. The error bars represent standard deviations from 3 to 4 independent clones.

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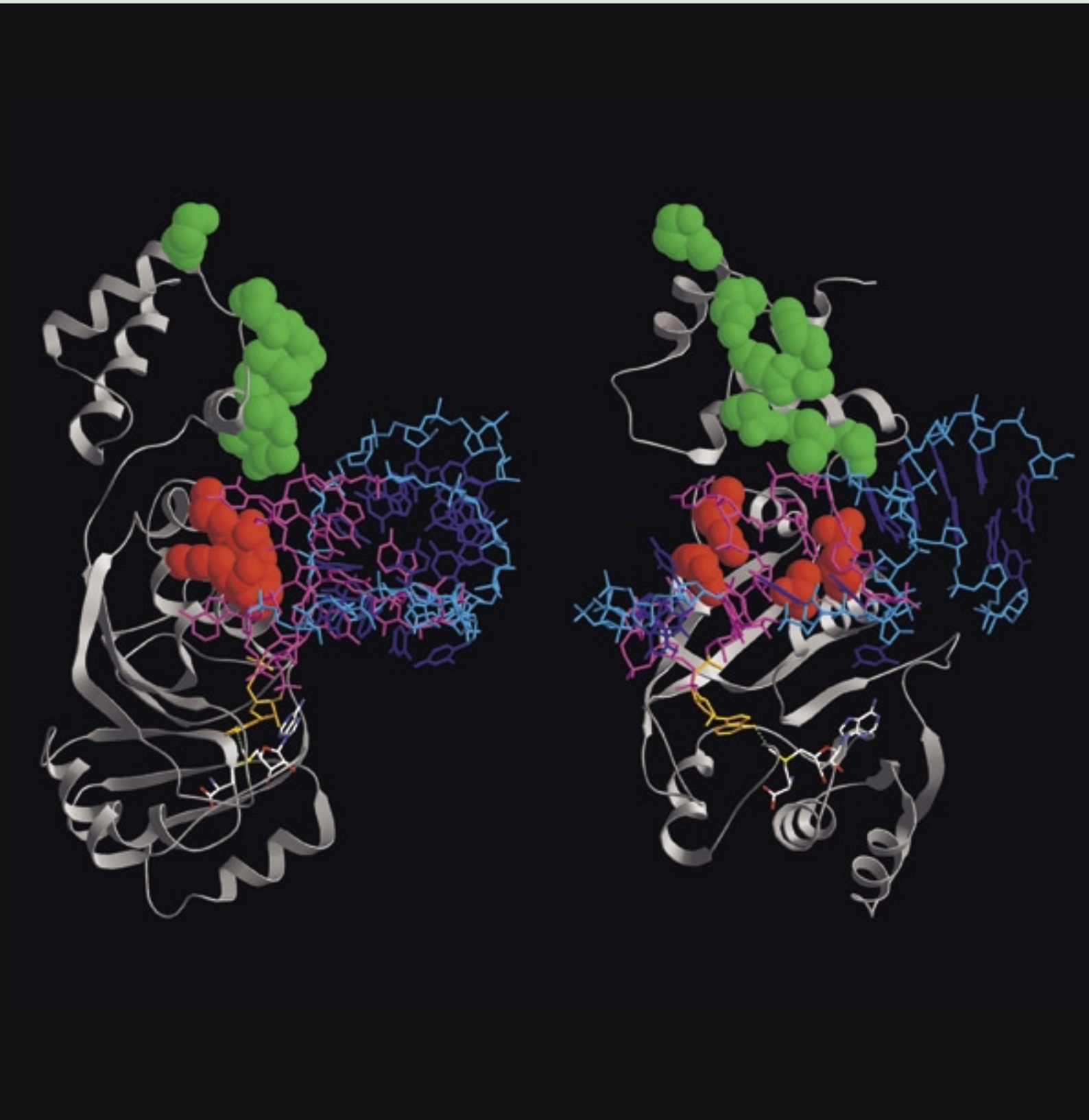

Lab Leader

Janusz M. Bujnicki, PhD, DSc.Habil.

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Krzysztof Skowronek, PhD

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Undergraduate students:
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Katarzyna Filip, Agnieszka Obarska, BSc

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Michal Wrzesinski, MSc

Computer administrator:
Jan Kogut

Janusz Bujnicki, PhD

Degrees

2005 DSc.Habil, Institute of Biochemistry and Biophysics, PAN, Warsaw

2001 PhD in bioinformatics; University of Warsaw, Faculty of Biology

1998 MSc in microbiology; University of Warsaw, Faculty of Biology

Professional Experience

since 2002 Head of the Laboratory of Bioinformatics and Protein Engineering IIMCB

2001-2002 Group Leader, Molecular Evolution Research Group, Laboratory of Bioinformatics, IIMCB

2001 Visiting Scientist, Computational Biology Branch, National Center for Biotechnology Information, NLM, NIH, Bethesda, MD, USA (with Dr. E.V. Koonin)

1999-2000 Research Scientist, Bioinformatics Laboratory, IIMCB (with Dr. L. Rychlewski)

1998-2000 Senior Research Assistant, Molecular Biology Research Program, Henry Ford Health System, Detroit, MI, USA (with Dr. L.C. Lutter)

Awards

2005 Group prize of the Ministry of Health for co-authorship of series of publications regarding the biological function of protein K (head of the team: Prof. J. Ostrowski)

2002 EMBO/Howard Hughes Medical Institute Young Investigator Program award 2003, Fellowship for Young Scientists of the Foundation for Polish Science

2002 Award of the Polish Society of Genetics (the best Polish genetics-related publication in the year 2001: Trends Biochem Sci. 2001 Jan; 26(1): 9-11)

2001 Award of the Polish Biochemical Society (the best Polish publication on nucleic acid biochemistry in the year 2000: FASEB J. 2000 Nov; 14(14): 2365-2368)

Papers published by the Bujnicki group in 2005

- Armalyte E, Bujnicki JM, Giedriene J, Gasiunas G, Kosinski J, Lubys A. Mva1269I: a monomeric type IIS restriction endonuclease from *Micrococcus varians* with two EcoRI- and FokI-like catalytic domains. J Biol Chem, 2005; 280:41584-94
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- Kosinski J, Feder M, Bujnicki JM. The PD-(D/E)XK superfamily revisited: identification of new members among proteins involved in DNA metabolism and functional predictions for domains of (hitherto) unknown function. BMC Bioinformatics, 2005; 6:172
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- Kosinski J, Steindorf I, Bujnicki JM, Giron-Monzon L, Friedhoff P. Analysis of the quaternary structure of the MutL C-terminal domain. J Mol Biol, 2005; 351:895-909
- Radlinska M, Piekarowicz A, Galimand M, Bujnicki JM. Cloning and preliminary characterization of a GATC-specific beta2-class DNA:m6A methyltransferase encoded by a transposon Tn1549 from *Enterococcus spp.* Pol J Microbiol, 2005; 54:249-252
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- Kolinski A, Bujnicki JM. Generalized protein structure prediction based on combination of fold-recognition with de novo folding and evaluation of models. Proteins, 2005 CASP6 special issue; 61 Suppl 7:84-90
- Pingoud V, Geyer H, Geyer R, Kubareva E, Bujnicki JM, Pingoud AM. Identification of base-specific contacts in protein-DNA complexes by photocrosslinking and mass spectrometry: a case study using the restriction endonuclease SsoII. Mol BioSyst, 2005 1(2):135-141. DOI: 10.1039/b503091a
- Purushothaman SK, Grosjean H, Bujnicki JM, Lapeyre B. Trm11p and Trm112p are both required for the formation of 2-methylguanosine at position 10 in yeast tRNA. Mol Cell Biol, 2005; 25:4359-70
- Chmiel AA, Radlinska M, Pawlak SD, Krowarsch D, Bujnicki JM, Skowronek KJ. A theoretical model of restriction endonuclease NlaIV in complex with DNA, predicted by fold-recognition and validated by site-directed mutagenesis and circular dichroism spectroscopy Protein Engineering, 2005; 18:181-9
- Pawlak SD, Radlinska M, Chmiel AA, Bujnicki JM, Skowronek KJ. Inference of relationships in the "twilight zone" of homology using a combination of bioinformatics and site-directed mutagenesis: a case study of restriction endonucleases Bsp6I and PvuII. Nucleic Acids Res, 2005; 33:661-71
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- Chmiel AA, Bujnicki JM, Skowronek KJ. A homology model of restriction endonuclease SfiI in complex with DNA. BMC Struct Biol, 2005; 5:2
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- Pingoud V, Sudina A, Geyer H, Bujnicki JM, Lurz R, Luder G, Morgan R, Kubareva E, Pingoud A. Specificity changes in the evolution of type II restriction endonucleases: a biochemical and bioinformatic analysis of restriction enzymes that recognize unrelated sequences. J Biol Chem, 2005; 280:4289-98
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Current Research

The research in the Laboratory of Bioinformatics and Protein Engineering is focused on bioinformatics, biochemistry, and evolution of protein-nucleic acid interactions. In particular we are involved in the development and applications of software tools for the analysis of data concerning protein sequence-structure-function relationships and in experimental analyzes of enzymes that catalyze covalent modifications or cleavage of nucleic acids, such as methyltransferases, nucleases and proteins involved in DNA repair. We integrate theoretical and experimental analyzes to study the rules that govern the sequence-structure-function relationships in proteins. The knowledge of these rules can be used to facilitate the discovery of new proteins with interesting functions or to alter the function of already known proteins and to engineer new enzymes.

From the theoretical end, our current focus is on the development of tools and protocols for purely theoretical prediction of protein structures (see for instance our protein structure prediction "meta server" at (http://genesilico.pl/meta/) as well as for determination of protein structures based on heterogeneous, low-resolution, noisy and ambivalent experimental data. We are also involved in genome-scale phylogenetic analyses, with the focus on identification of genes/proteins, which belong to particular families. Structural and evolutionary predictions obtained from bioinformatics analyses are then combined to infer the protein function. From the experimental end, the goal is to characterize the function of new genes/proteins identified by bioinformatics and to use the theoretical prediction to guide protein engineering, using rational and random approaches, as well as the combination of both. The ultimate goal is to design proteins with new properties, in particular enzymes with new desired functions, which have not been observed in nature.

Projects

The development of new software tools for structural genomics and proteomics – in collaboration with Prof. Andrzej Kolinski (University of Warsaw) and Dr. Matthias Botchler (IIMCB); funded by KBN, also in collaboration with Prof. David Baker (University of Washington, Seattle, WA, USA, funded by NIH).

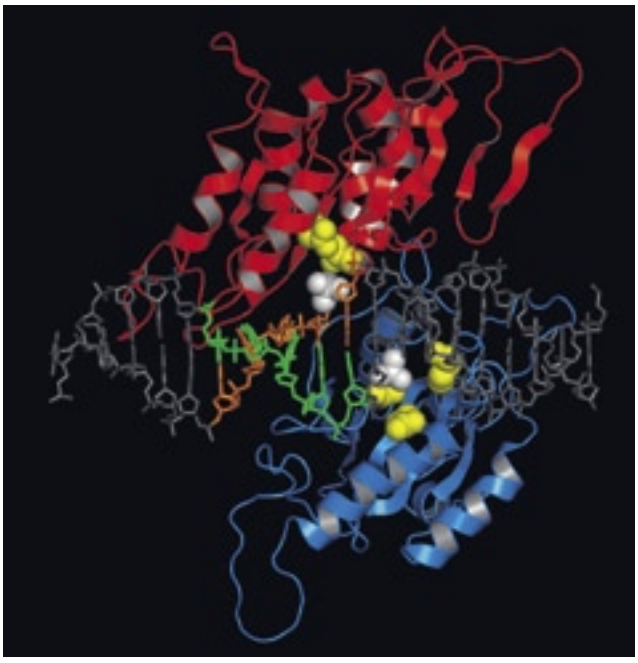
Theoretical and experimental characterization of protein-DNA recognition in various enzymes – as a part of a Marie Curie Research and Training Network 'DNA enzymes (see the website at https://genesilico.pl/DNAenzymes/), funded by the 6th Framework Programme of the EU.

The analysis of the plant and plastid genomes to characterize the mechanisms of plastid transformation and foreign gene expression in tobacco, tomato and potato – as a part of a consortium funded by the 6th Framework Programme of the EU (see the website https://genesilico.pl/Plastomics/).

The evolution of structure-function relationships in RNA MTases. Key collaborators: Dr. Bruno Lapeyre (CNRS, Montpellier, France), Dr. Henri Grosjean (CNRS, Gif-sur-Yvette, France), Dr. Louis Droogmans (University of Bruxelles, Belgium).

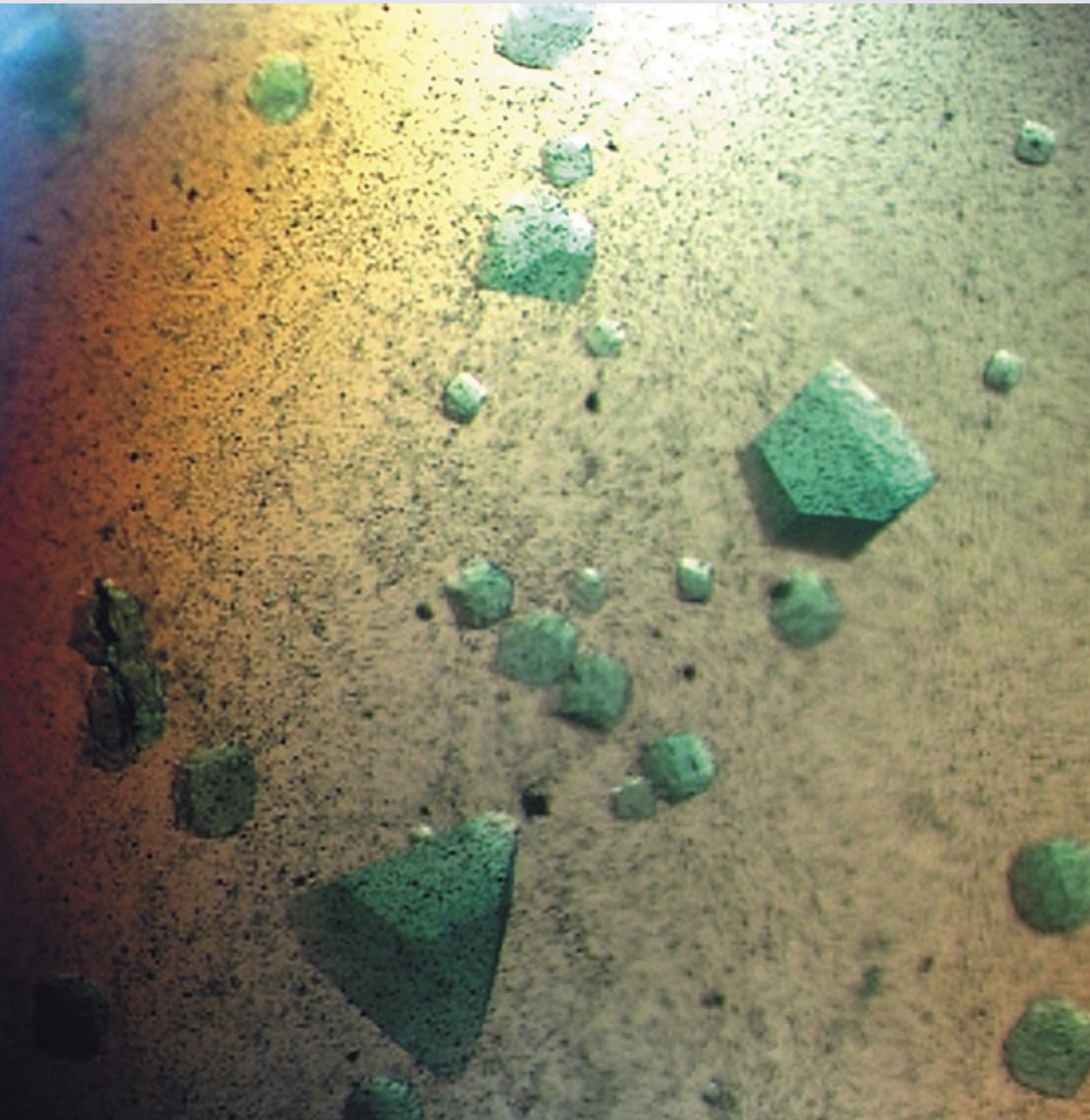
The bioinformatics-guided engineering of DNA methyltransferases with new properties – in collaboration with Dr. Monika Radlinska (Warsaw University); funded by KBN.

Theoretical model of an unusual restriction enzyme Mva1269I comprising two different nuclease domains (shown in red and blue) in a single polypeptide. Two strands of the target sequence in the DNA are indicated in orange and green. For more information see Armalyte et al, J Biol Chem 2005; 280:41584-94.



Theoretical model of an unusual restriction enzyme Mva1269I comprising two different nuclease domains (shown in red and blue) in a single polypeptide. Two strands of the target sequence in the DNA are indicated in orange and green. For more information see Armalyte et al., J Biol Chem 2005 Dec 16;280(50):41584-94.

Laboratory of Structural Biology MPG/PAN



Lab Leader

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Honorata Czapinska, PhD
Renata Filipek, PhD
Aneta Kaczmarczyk, Ph D

PhD students:
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MAX-PLANCK-GESELLSCHAFT

INTERNATIONAL INSTITUTE OF MOLECULAR AND CELL BIOLOGY

The equipment and running costs for the lab, including personnel, are provided by the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden (MPI-CBG).

Matthias Bochtler, PhD, DSc.Habil.

Degrees

DSc. Habil, Institute of Bioorganic Chemistry PAN, Poznan, Poland, 2006

PhD in biochemistry, Technische Universitaet München, Germany, 1999

MSc in experimental physics, Ludwig Maximilians-Universitaet München, Germany, 1995

Research Training

1999-2000 the Max Planck Institut für Biochemie, Martinsried, Germany

1996-1999 Research Assistant, MPI für Biochemie, Martinsried, Germany

1995-1996 internship, the Department of Medical Microbiology, University of Regensburg, Germany

1992-1993 guest student, Cambridge University, United Kingdom

1990-1992 studies in physics, Munich University, Germany

Honors, Prizes, Awards

Pienkowski award, 2005

EMBO/HHMI Young Investigator award, 2004

Crystal award, Germany, 2000

Crystal award, Germany, 1998

Scholarship from Deutsche Studienstiftung and the Bavarian State, 1990-1992

Papers published by the group in 2005/2006

- Bochtler M, Szczepanowski RH, Tamulaitis G, Grazulis S, Czapinska H, Manakova E, Siksnys V, Nucleotide flips determine the specificity of the Ecl18kI restriction endonuclease. EMBO J 2006, in press
- Azim MK, Goehring W, Song HK, Ramachandran R, Bochtler M, Goettig P, Characterization of the HslU chaperone affinity for HslV protease. Protein Sci, 2005; 14:1357-62
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- Firczuk M, Mucha A, Bochtler M, Crystal structures of active LytM. J Mol Biol, 2005; 354:578-90
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- Korza HJ, Bochtler M, Pseudomonas aeruginosa LD-carboxypeptidase, a serine peptidase with a Ser-His-Glu triad and a nucleophilic elbow. J Biol Chem, 2005; 280:40802-12

Description of Current Research

We use protein crystallography to study peptidases, proteases and enzymes that are involved in protein degradation. In 2004 and 2005, we have also spent some time on crystallographic method development.

Structures of peptidases and their inhibitors

We have focused on bacterial peptidases of unknown structure and discovered several new folds, prompting others to define several new peptidase clans (see http://www.merops.ac.uk).

The definition of the first clan (now clan MO) was the result of our structural analysis of LytM, which was studied as a model protein for the pharmacologically interesting peptidase lysostaphin. The fold of this protein turned out to be unprecedented in peptidases and proteases, but there were local similarities between the active sites of LytM and previously characterized peptidases, namely D-Ala-D-Ala-peptidases and the N-domain of sonic hedgehog. Using consensus motifs from the structural work, we predicted that MepA-like enzymes, would also have similar active sites. Taken together, our work defines a group of metallopeptidases with currently over 300 member sequences in the database, and it provides an example for the successful exploitation of structural information for biological predictions.

Another clan (now clan MQ) emerged, when we solved the structure of AmpS, a peptidase that had been picked in a genomic screen for its importance for Staphylococcus aureus cell growth in vitro. The first crystal structure confirmed the expectation that there would be novel active site, but was of unclear relevance, because the enzyme had been crystallized in an inactive conformation. This has now been remedied with the successful determination of the crystal structure of a homologue, which traps several molecules of the enzyme, in active and inactive states, and firmly establishes the new clan.

A novel serine peptidase clan (now clan SS) emerged from our study of a LD-carboxypeptidases, for which neither the fold nor the catalytic type were known prior to our work. Our crystal structure, at high resolution, showed a novel fold, and more importantly, a very unusual active site. Instead of the usual Ser-His-Asp triad, LD-carboxypeptidase has a highly unusual Ser-His-Glu triad. The active site serine residue has a strained, almost "forbidden" conformation. Interestingly, the arrangement is reminiscent of the "nucleophilic elbow" in αβ-hydrolases. Therefore, the LD-carboxypeptidase structure provides an excellent example for the reinvention of mechanistic strategies in new contexts.

The laboratory has also been involved in the search for new mechanisms of protease inhibition. In collaboration with Professors Dubin and Potempa of the Jagiellonian University in Krakow, we could show that staphostatins, the highly specific inhibitors of the major secreted proteases of Staphylococcus aureus, (i) have lipocalin-like folds (11), (ii) act as competitive, active site directed inhibitors that span the active site clefts of their target proteases in the same orientation as substrates. We have now reported the structure of staphostatin B in complex with wild-type staphopain B and found an intriguing similarity to the "ion-molecule" binding modes which has been proposed by Peter Kollman and coworkers for the Michaelis complex of papain-type enzymes and their substrates. Our findings prompted a detailed comparison between staphostatins and standard-mechanism serine protease inhibitors and may have general implications on the question how exactly peptidases cleave amide bonds.

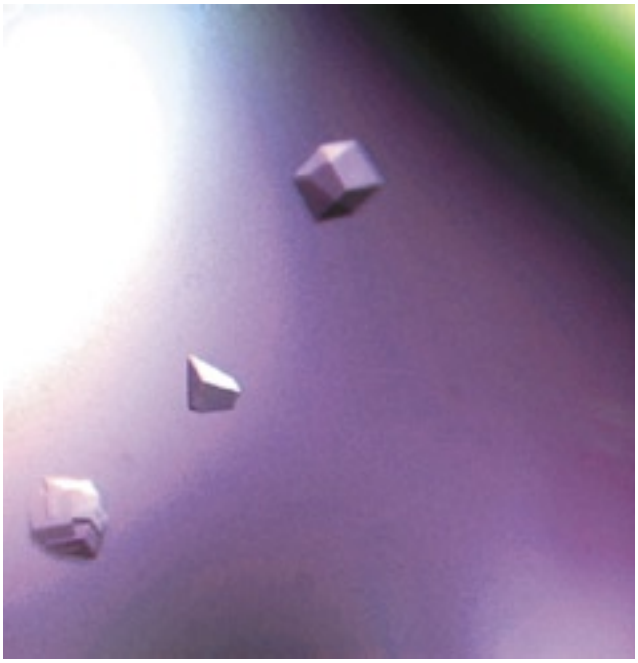
Structures of enzymes of the ubiquitin-proteasome pathway

Protein degradation by the ubiquitin-proteasome pathway requires the sequential action of a ubiquitin-activating enzyme (E1), a ubiquitin-conjugating enzyme (E2), and a ubiquitin-ligase (E3). The ubiquitin-transfer machinery is hierarchically organized: for every ubiquitin-activating enzyme, there are several ubiquitin-conjugating enzymes, and most ubiquitin-conjugating enzymes can in turn interact with multiple ubiquitin-ligases. Despite the central role of ubiquitin-activating enzyme in this cascade, a crystal structure of this protein is not available. The enzyme is thought to consist of an adenylation domain, a catalytic cysteine domain, a four-helix bundle, and, possibly, a ubiquitin-like domain. The ubiquitin adenylation domain can be modeled based on its homology to the adenylation domains of the NEDD8- and SUMO-activating enzymes, but low sequence similarity and vastly different domain lengths make this difficult for the catalytic cysteine domain that results from the juxtaposition of two catalytic cysteine half-domains. We expressed and purified several fragments of ubiquitin-activating enzyme, and now solved the structure of the second catalytic cysteine half-domain (SCCH) of mouse ubiquitin-activating enzyme. We show that the domain is organized around a conserved folding motif that is also present in the NEDD8- and SUMO-activating enzymes, and we propose a tentative model for full-length ubiquitin-activating enzyme. Work on the first cysteine catalytic half-domain (FCCH) is a collaboration with I. Zhukov and A. Ejchart.

Structures of restriction endonucleases

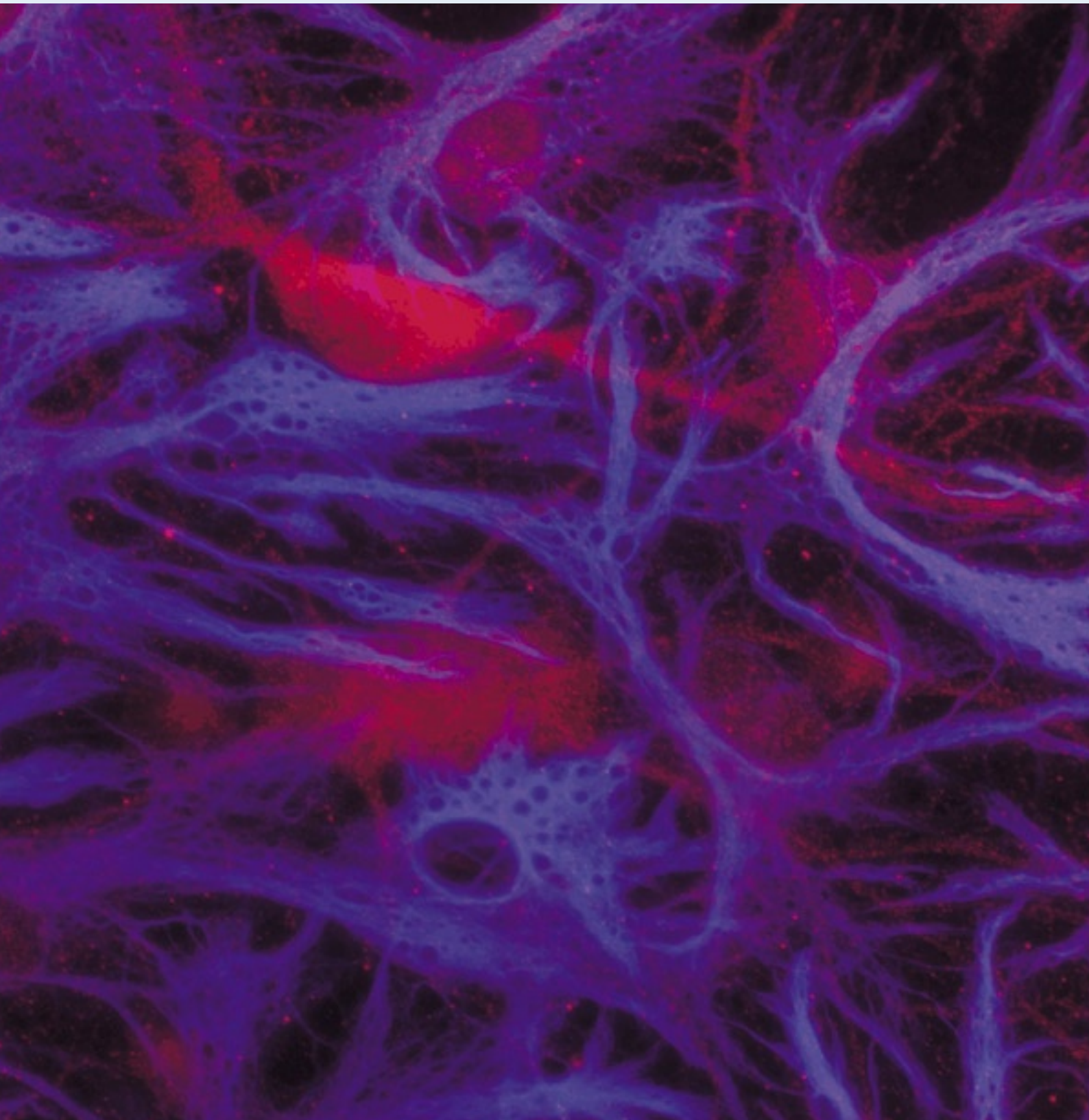
Type II restriction endonucleases are very diverse in sequence, yet nearly all of them share the fold and the metal-dependent catalytic mechanism. Most are active as dimers that match the two-fold symmetry of their recognition sequences. Although thousands of restrictases have been described, fewer than 20 crystal structures are available. To date, mostly "palindrome-cutters" that recognize true palindromes and generate overhangs with an even number of bases have been studied in detail. Based on these data, a few general rules have been deduced: (a) "phenotype" predicts "genotype", (b) changes in the recognition sequence, which do not affect the cleavage pattern, require mutations, but no alterations in quaternary structure, (c) changes in the cleavage pattern require radically different dimerization modes. Interestingly, recent data indicate that "pseudopalindrome-cutters" that recognize pseudopalindromic sequences and generate overhangs with an odd number of bases violate these rules, at least in some cases.

Pseudopalindrome cutters are similar to palindrome cutters, especially in their dimerization modes, yet generate different cleavage patterns. We have selected the pseudopalindrome cutter Ecl18kI (/CCNGG) and the related palindrome cutter NgoMIV (G/CCGGC) for a detailed comparison. A high resolution structure of NgoMIV with DNA has been reported previously. We have now crystallized Ecl18kI with DNA and solved the structure at high resolution. The comparison of the cocrystal structures shows that Ecl18kI and NgoMIV use a conserved "recognition module" to interact with their target sequences as predicted. To accommodate the extra nucleotides (N) at the center, Ecl18KI flips them out from the DNA duplex. This flip and the accompanying DNA kink cause a register shift by 1 bp making the distances between scissile phosphates in the NgoMIV and Ecl18kI cocrystal structures nearly identical. Ecl18kI is the first example of a restriction endonuclease that flips nucleotides to achieve specificity for its recognition site.



Crystals of a ubiquitin-activating enzyme fragment (second catalytic cysteine half domain) in the H3 crystal form

Laboratory of Neurodegeneration



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Associate Professors:
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Cezary Zekanowski, PhD, DSc.Habil.

Post-doctoral fellows:
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Monika Mysiak, PhD
Marta Wisniewska, PhD

PhD students:
Magdalena Blazejczyk, MSc; Lukasz Bojarski, Wojciech Michowski, MSc; Adam Sobczak, MSc; Aleksandra Szybinska, MSc

Centenarian Program:
Malgorzata Mossakowska, PhD (co-ordinator)

Collaborations:
Dr. Anna Filipek, Nencki Institute of Experimental Biology
Prof. Maria Barcikowska, MD, Institute of Experimental Medicine
Dr. Slawek Filipek and Krzysztof Jozwiak, Laboratory of Biomodelling, IIMCB
Dr. Malgorzata Mossakowska (IIMCB) and Dr. Katarzyna Broczek MD, Department of Clinical Geriatrics, Medical University of Warsaw
Dr. Jakub Golab, Medical University of Warsaw
Dr. Michael Kreutz, Department of Neurochemistry/Molecular Biology, Leibniz Institute for Neurobiology, Magdeburg, Germany
Dr. Guido Tarone, Department of Biology, University of Turin

Jacek Kuznicki, PhD

Degrees

Professor, 1993

DSc.Habil., Nencki Institute of Experimental Biology PAN, Warsaw, Poland, 1987

PhD in biochemistry, Nencki Institute of Experimental Biology PAN, Warsaw, 1980

MSc in biochemistry, Warsaw University, 1976

Post-doctoral Training

1981-1984 Visiting Fellow, Laboratory of Cell Biology headed by E.D. Korn, National Institutes of Health, Bethesda, MD, USA

Professional Employment

since 2002 Director of Institute and Head of the Laboratory of Neurodegeneration, IIMCB

2000-2001 Director, Centre of Excellence for Studies on Mechanisms of Neurodegeneration Phare Sci-Tech II located at the Nencki Institute of Experimental Biology PAN, Warsaw

1999-2001 Acting Director, IIMCB; Organizer and Director of Centenarian Program

1996-2002 Head of Laboratory of Calcium Binding Proteins, the Nencki Institute of Experimental Biology PAN, Warsaw

1992-1995 Visiting Professor at the National Institute of Mental Health, Laboratory of Clinical Science, Bethesda, MD, USA

1991-1992 Deputy Director (Scientific Director), Nencki Institute of Experimental Biology PAN, Warsaw

1986-1992 Associate Professor and Head of Laboratory of Calcium Binding Proteins, Nencki Institute of Experimental Biology PAN, Warsaw

1984-1985 Research Associate, Nencki Institute of Experimental Biology PAN, Warsaw

1981-1984 Visiting Fellow, NIH, Laboratory of Cell Biology, Bethesda, MD, USA

1980-1981 Post-doctoral Fellow, Nencki Institute of Experimental Biology PAN, Warsaw

1976-1980 PhD Student, Nencki Institute of Experimental Biology PAN, Warsaw

Membership in Scientific Societies, Organizations and Panels

- Member of the Polish Academy of Science - since December 2004
- Member of American Society for Biochemistry and Molecular Biology, since 2003
- Head of Advisory Board of the Science School Festival, since 2002
- Member of the Biochemical Society (England), since 1995
- Member of the Polish Neuroscience Society, since 1991
- Member of the Polish Society for the Advancement of Science and Arts, since 1991
- Vice-president of the Polish Biotechnology Committee, 1996-1999 and 2000-2002
- Member of the Polish Biotechnology Committee, 1990-2002
- Co-Editor of Advances in Biochemistry (published in Polish), 1989-1992
- Member of the Polish Biochemical Society, since 1977
- General Secretary of the Polish Biochemical Society, 1989-1991

Honors, Prizes, Awards

- Professorship Award of Foundation for Polish Research (FNP), 2004-2006
- Prime Minister Award for the scientific achievements, 2003
- Award from Division of Biological Sciences PAN for the work on calcium binding proteins, 2001
- Polish Anatomical Society Award for the article on calcium binding proteins published in "Advances in Cell Biology", 1987
- Skarzynski Award of Polish Biochemical Society for the best review article in Advances in Biochemistry, 1986
- Parnas Award of Polish Biochemical Society for the publishing of the best paper in biochemical research, 1977
- Mozolowski Award, Polish Biochemical Society for outstanding Polish young biochemists, 1977
- Magna cum laude, University of Warsaw, 1976

Publications in 2005

- *Zekanowski C, Golan MP, Krzysko KA, Lipczynska-Lojkowska W, Filipek S, Kowalska A, Rossa G, Peplonska B, Styczynska M, Maruszak A, Religa D, Wender M, Kulczycki J, Barcikowska M, Kuznicki J Two novel presenilin 1 gene mutations connected with frontotemporal dementia-like clinical phenotype: genetic and bioinformatic assessment. Exper Neurol, 2006 in press
- *Spiechowicz M, Bernstein H-G, Dobrowolny H, Leśniak W, Mawrin C, Bogerts B, Kuznicki J, Filipek A Density of Sgt1-immunopositive neurons is decreased in the cerebral cortex of Alzheimer's disease brain. Neurochem Inter., 2006 in press
- *Lesniak W, Kuznicki J Binding and functional characteristics of two E-box motifs within the S100A6 (calcyclin) gene promoter. J Cell Bioch, 2006; 97:1017-24
- *Blazejczyk M, Wojda U, Sobczak A, Spilker C, Bernstein H-G, Gundelfinger ED, Kreutz MR, Kuznicki J Ca^{2+}-independent binding and cellular expression profiles question a significant role of calmyrin in transduction of Ca^{2+}-signals to Alzheimer's disease-related presenilin 2 in forebrain. Biochim Biophys Acta - Molecular Basis of Disease, 2005; 1762:66-72
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- *Broczek K.M, Pawlinska-Chmara R, Kupisz-Urbanska M, Mossakowska M Antropometric chest structure of Polish centenarians. J Physiol Pharmacol, 2005; 56, Supp 4:9-13
- *Lesniak W, Szczepanska A, Kuznicki J Calcyclin (S100A6) expression is stimulated by agents evoking oxidative stress via the antioxidant response element. Biochim Biophys Acta, 2005; 1744:29-37

- Lewandowicz A, Ringia EA, Ting LM, Kim K, Tyler PC, Evans GB, Zubkova OV, Mee S, Painter GF, Lenz DH, Furneaux RH, Schramm VL Energetic mapping of transition state analogue interactions with human and Plasmodium falciparum purine nucleoside phosphorylases. J Biol Chem, 2005; 280:30320-30328
- *Palczewska M, Batta G, Groves P, Linse S and Kuznicki J Characterization of calretinin I-II as an EF-hand, Ca^{2+}, H^{+} - sensing domain. Protein Sci, 2005; 14:1879-87
- *Puzianowska-Kuznicka M, Kuznicki J Genetic alterations in accelerated ageing syndromes. Do they play a role in natural ageing? Int J Biochem Cell Biol, 2005; 37:947-60
- *Sobczak A, Blazejczyk M, Piszczek G, Zhao G, Kuznicki J, Wojda U Calcium-binding calmyrin forms stable covalent dimers in vitro, but in vivo is found in monomeric form. Acta Biochim Pol, 2005; 52:469-76
- Ameyar-Zazoua M, Wisniewska MB, Bakiri L, Wagner EF, Yaniv M, Weitzman JB AP-1 dimers regulate transcription of the p14/p19ARF tumor suppressor gene. Oncogene, 2005; 24:2298-306
- *Zekanowski C, Religa D, Safranow K, Maruszak A, Dziedziejko V, Styczynska M, Gacia M, Golan M, Peplonska B, Chlubek D, Kuznicki J, Barcikowska M The -22c/t polymorphism in presenilin 1 gene is not connected with late-onset and early-onset familial Alzheimer's disease in Poland. J Neural Transm, 2005; 112:839-45

*Papers marked with an asterisk have the IIMCB affiliation of the authors

Current Projects

We are interested in molecular mechanisms involved in learning and memory, as well as in neurodegeneration, and we study these processes at the genomic, protein, cellular level, and by bioinformatics methods. Our five major projects are:

1. Mutations in presenilins, amyloid precursor protein and few other proteins in a group of Polish patients with early onset of dementia or mild cognitive impairment
2. Structure and function relationship of human components of γ-secretase complex with special emphasis on Aph-1 and presenilins
3. Ca^{2+}-signals that might contribute to the pathological processes in brains of Alzheimer's disease (AD) patients.
4. β- and δ-catenins in signaling pathways connected with neuronal cell adhesion molecules
5. Characterization of biological function of CHORD (Cys and His Rich Domain) containing proteins in the nervous system

1. Identification of mutations in presenilins, amyloid precursor protein and few other proteins in a group of Polish patients with early onset of dementia or mild cognitive impairment (Cezary Zekanowski in collaboration with Maria Barcikowska and her group at the Medical Research Center, Polish Academy of Sciences)

The γ-secretase enzyme is an intramembrane-cleaving aspartyl protease complex consisting of four proteins: presenilin, nicastrin, Aph-1 and Pen-1. Presenilin is believed to be the catalytic component of the complex. More than 100 mutations have been identified in this protein, which are linked to early-onset Alzheimer's disease. Most of these mutations are located in the transmembrane domains, indicating that the intramembrane interactions play a crucial role in the stabilization and correct functioning of the enzyme. Presenilins interact with β-catenin and several other proteins. Despite of the extensive efforts presenilin structure and mechanism of its activity remain unknown. Even presenilin topology is a matter of controversy: few models are under consideration.

To determine the spectrum of mutations in a group of Polish patients with clinically diagnosed early-onset Alzheimer's disease, frontotemporal dementia and related dementias we performed a screening for mutations in presenilin 1 (PSEN1), presenilin 2 (PSEN2), amyloid precursor protein (APP), tau protein (MAPT), and prion protein (PRNP) genes. Previously recognized pathogenic mutation in PSEN1 gene (L153V) was identified. The total frequency of mutations in a group of familial AD patients was 21%. A mutation P102 in PRNP gene was identified in a patient with atypical Gerstmann-Sträussler-Scheinker syndrome.

Prion protein gene polymorphism M129V represents a known risk factor for Creutzfeldt-Jacob disease. Recently, the meta-analysis revealed that homozygosity at codon 129 is connected with increased risk of Alzheimer's disease. We decided to determine whether M129V polymorphism is a risk factor for late-onset Alzheimer's disease in Polish patients. We analyzed a group of 53 early-onset, and 113 late-onset patients, and observed that in late-onset patients there is a statistically significant increase of MM and decrease of MV genotype frequency, as compared to controls. Stratification of the group according to APOE4 status revealed significant association only in the subgroup with no APOE4, however no interaction was found between APOE4 status and M129V polymorphism. We concluded that MM genotype increases late-onset Alzheimer's disease risk in Polish population independently from the APOE4 status.

An association was reported recently for a Russian population between a promoter polymorphism in the PSEN2 gene in late-onset Alzheimer's disease, patients lacking APOE4 allele.

However a study from Italian population reported conflicted results. The deletion has a putative functional role, increasing PSEN2 expression. We started to examine the impact of the polymorphism in a group of 200 Polish late-onset patients. Preliminary results confirm association between the polymorphism and late-onset Alzheimer's disease.

2. Studies of structure and function relationship of human components of γ-secretase complex with special emphasis on presenilins (wild type and with familial Alzheimer's disease mutations) and Aph-1 (Lukasz Bojarski, Andrzej Lewandowicz, Urszula Wojda, Aleksandra Szybinska in collaboration with Krzysztof Jozwiak and Slawek Filipek from Laboratory of Biomodelling at IIMCB)

Lymphocytes of patients with identified mutations have been immortalized and collected in the cell bank consisting of about 200 lymphoblasts lines including those obtained during Polish Centenarian Project. Stable clones of HEK293 cells overexpressing wild-type presenilin 1 and mutated variants carrying a novel familial Alzheimer's disease mutation (F226L) connected with clinically diagnosed frontotemporal dementia, and *post mortem* diagnosis of Alzheimer's disease were prepared. Human embryonic kidney Flp-In-239 cells stably expressing APP mutation KM670/671NL (obtained from Dr. Jessie Theuns, University of Antwerp) were stably transfected with the constructs. We also examined novel, identified by us, presenilin 1 (I213F, P117R) and presenilin 2 (Q228L) mutations on β-amyloid production. Stable clones of HEK 293 cells overexpressing APP, with so called Swedish mutation, were stably transfected with constructs bearing the above-mentioned mutations or empty vector. β-amyloid 1-40 and 1-42 levels in serum-free culture media were estimated by ELISA. Cells with mutated presenilins produced much more β-amyloid than control cells and β-amyloid 42 / β-amyloid 40 ratio was significantly increased comparing to controls.

We analyse topology of endogenous presenilin 1 in plasma membrane of human lymphoblasts using limited tryptic digestion of live cells, fluorescence microscopy, flow cytometry, and biotynylation of membrane proteins *in vivo*. Preliminary data indicate that N-terminal end is extracellular, supporting Devi's et al. model of 7^{TM} domains. This is not a widely accepted presenilin topology. Bioinformatics model of PS1 and APH-1 complex allowed us to establish a possible interface between these two proteins and to explain effects of several FAD mutations. We developed procedure to separate from native sources PS1 and PS2 complexes to establish their composition and understand difference in their activities. This project will be completed in collaboration with participants of APOPIS consortium.

We look for a source of presenilin 1 for structural studies in lipid bilayer/detergent systems with plans of collaboration with NMR/X-ray structural laboratories in case protein purification is successful. Bacterial plasmids used such as one encoding a fused presenilin 1 with mistic protein tag and use of C43 E. coli to facilitate membrane protein expression gave insufficient yields. Thus, further screening for appropriate expression method has been extended to Baculovirus /*Spodoptera frugiperda* system. The procedures of transfection, virus amplification, protein overexpression and purification are now being optimized. However, the bacterial system has been used for overexpression and purification of milligram amounts of His-tagged N-terminal end (72 amino acids tail) of presenilin 1. This fragment was successfully used to saturate anti PS1 antibodies in flow cytometry and fluorescence microscopy assays. The Aph-1 expressing vectors have been successfully transfected in eukaryotic cells and expression has been proved by western blotting and fluorescence microscopy techniques. We now apply 2D SDS-PAGE and mass spectroscopy to search for posttranslational modification(s) supposed to affect γ-secretase assembly and activity.

3. Analysis of transduction of Ca^{2+}-signals that might contribute to the pathological processes in brains of Alzheimer's disease patients (Magdalena Blazejczyk and Adam Sobczak under supervision by Urszula Wojda)

We investigated how the transduction of Ca^{2+}-signals might contribute to the pathological processes in brains of Alzheimer's disease patients. Specifically, we analyzed structural and biochemical features, expression, signal transduction and possible pathophysiological role of calcium-binding protein calmyrin1 (CaMy1), implicated in these disease. Our immunocytochemical studies, employing obtained by us antibodies against CaMy1, provided first evidence for a neuronal localization of CaMy1 in normal human brain and showed its altered distribution in AD patients, suggesting CaMy1 involvement in the Alzheimer's disease pathogenesis (Bernstein et al, Neuropathol Appl Neurobiol. 2005, 31(3):314-24). We found also that CaMy1 interacted specifically with Alzheimer's disease associated presenilin 2 *in vitro* and *in vivo*, as assayed by affinity chromatography, pull-down, and immunoprecipitation (Blazejczyk et al, Biochim Biophys Acta. 2005;1762(1):66-72). However, CaMy1/PS2 binding proved Ca-independent and we demonstrated limited colocalization of CaMy1 with PS2 at the cellular level in human and rat forebrain (major area affected by Alzheimer's disease). Accordingly, subfractionation of rat brain forebrain yielded only a limited overlap of both proteins. In summary, our studies indicated CaMy/PS2 interaction could not represent a major link between deregulation of Ca-homeostasis and PS2 in Alzheimer's disease brain (Blazejczyk et al,

Biochim Biophys Acta. 2005;1762(1):66-72). We also demonstrated that CaMy1 is monomeric *in vivo* (Sobczak et al, Acta Biochim Pol. 2005; 52(2):469-76). Additionally, based on search in genomic databases we realized that CaMy1 is a member of a protein family. We have cloned another member of this family and called it CaMy2. We now compare the neuronal localization, structure, Ca^{2+}-binding, myristoylation and target interactions of CaMy2 and its homolog CaMy1. We expect that this work will provide an insight into structure-function relationship of a new CaMy family among Ca^{2+}-binding proteins, sharing some structural similarities with Neuronal Calcium Sensors and calcineurin.

4. Analysis of β- and δ-catenins' role in signaling pathways connected with neuronal cell adhesion molecules (Monika Klejman, Marta Wisniewska, and Aleksandra Szybinska)

β-catenin plays a crucial role in cell proliferation and development, and is a component of the adherens junctions. In addition to the membrane-localized protein there is also a cytosolic pool of β-catenin, which is controlled by phosphorylation and subsequent ubiquitination and degradation. After wnt signaling activation, β-catenin phosphorylation is inhibited, the protein translocates to the nucleus and activates gene transcription as a cofactor of Lef1/Tcf4 transcription factor.

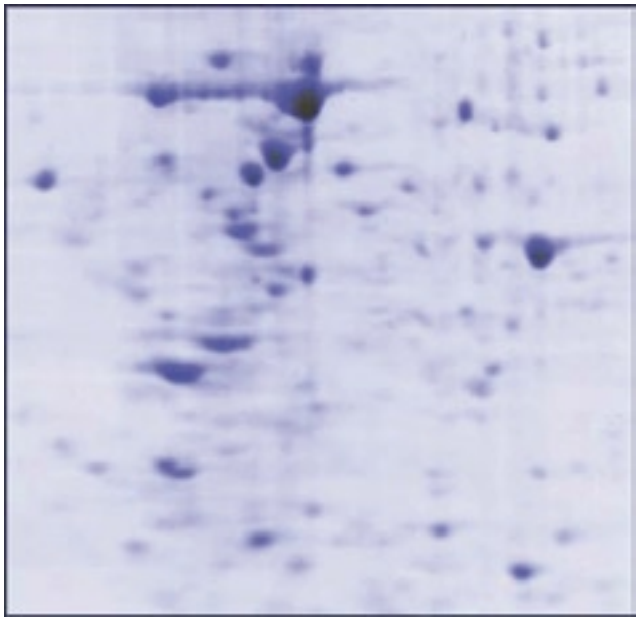
We are interested in the function of β-catenin in the adult brain. New data suggests that β-catenin might be also involved in a process of learning and memory formation. We analyze β-catenin expression in the forebrain of adult mice and rats using immunocytochemistry and immunofluorescent methods, as well as biochemical analysis of the brain protein extracts. We also analyze the level and distribution of proteins potentially involved in β-catenin degradation in the brain, namely Siah 1, Sgt1 and presenilin 1. The influence of Ca^{2+}-signaling on β-catenin ubiquitination has been studied in mouse embryonic fibroblasts and HEK293 cell lines. Immunoprecipitates by anti β-catenin antibody were analyzed by western blots to identify either unmodified, or phosphorylated and ubiquitinated protein.

δ-catenins is a component of cell adhesion complex and is exclusively expressed in the nervous system. It was shown to be important for the processes of learning and memory. However, the mechanism of δ-catenins activity is not fully understood. The aim is to identify all interacting partners for δ-catenins in the brain using affinity chromatography with recombinant δ-catenin expressed in baculovirus system. The baculoviruses carrying δ-catenin gene were constructed and protein expression achieved. Proteomic analyses of brain samples obtained from partners participating in PROMEMORIA project using 2D-PAGE and western blotting have been initiated.

5. Studies aiming at characterization of biological function of CHORD (Cys and His Rich Domain) containing proteins in nervous system (Wojciech Michowski)

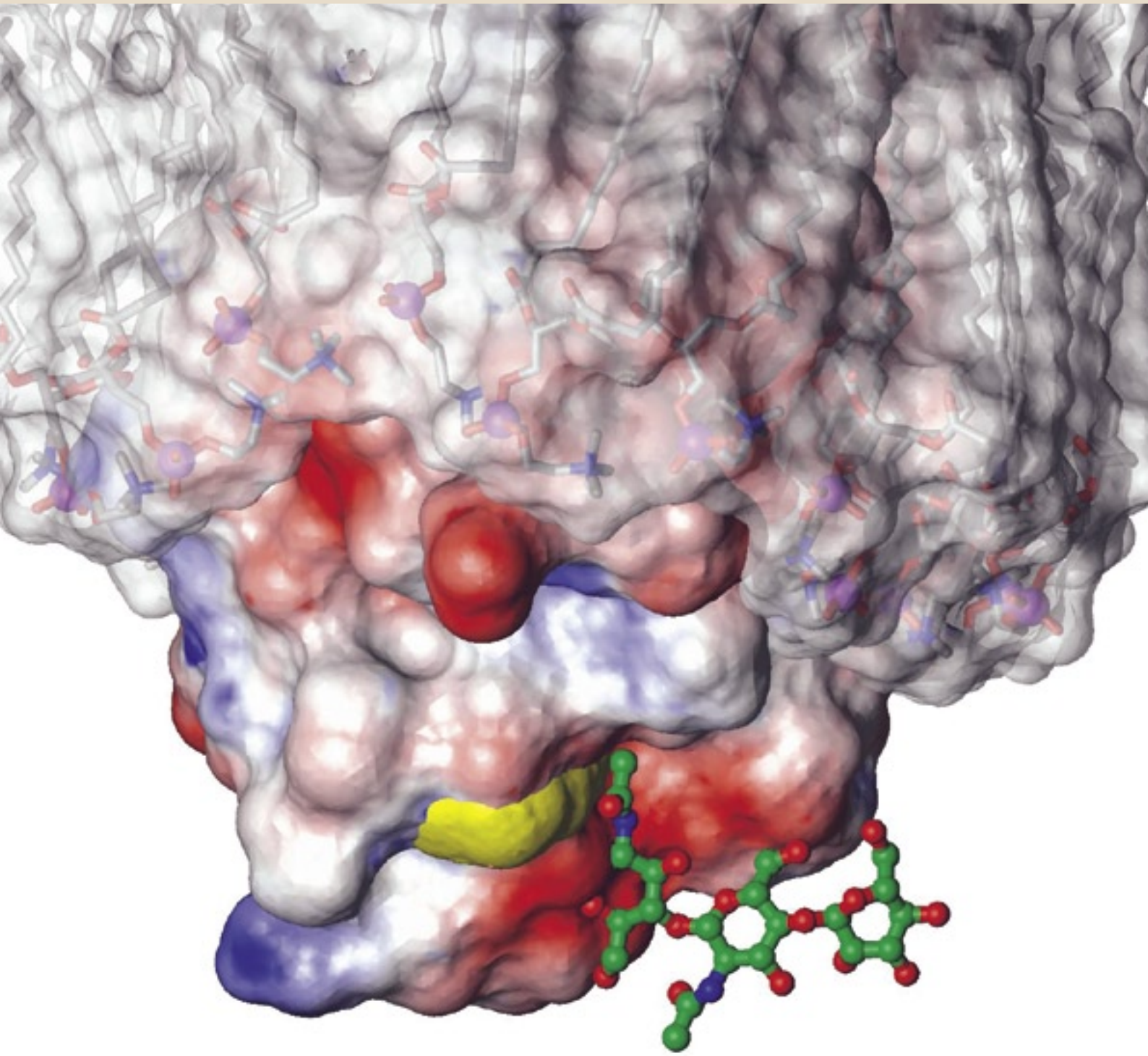
Two genes for CHORD containing proteins are present in mammalian genome, melusin and chp-1. Melusin is a protein expressed in heart and skeletal muscles. It specifically senses mechanical stress induced by chronic aortic hypertension, mediates development of adaptive cardiac hypertrophy and protects cardiac muscle from consequences of pressure overload. We identified melusin as a novel protein target of the S100 Ca^{2+}-signal sensing proteins.

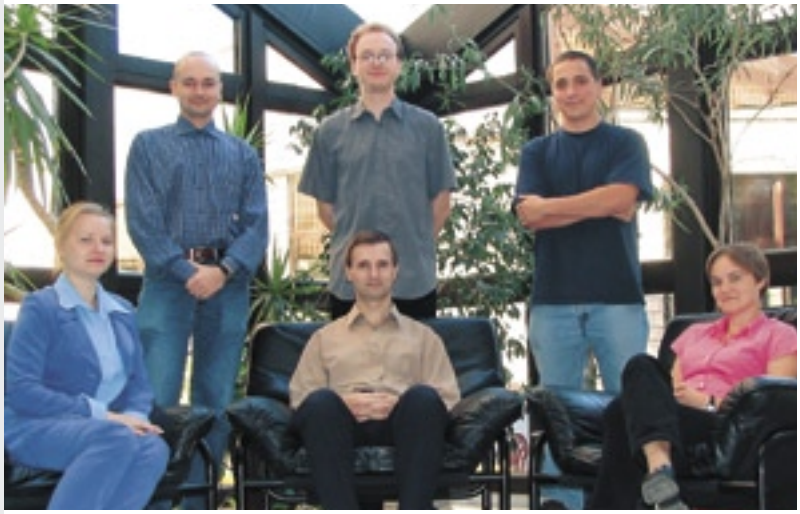
Chp-1 is ubiquitously expressed protein with suggested function under stress conditions. It exhibits chaperoning activity and its mutants show mitotic aberrations. Since high level of chp-1 is observed in neuronal tissue we decided to explore the function of chp-1 in primary rat hippocampal neurons. Using imunofluorescence technique we monitor the level and changes in the distribution of chp-1 in neurons upon different stimulations. We study the effect of chp-1 on neuronal apoptosis by evaluating the response to apoptotic stimuli of cortical neurons that overexpress chp-1. In parallel, we look at molecular pathways, in which chp-1 takes part by searching for its new protein targets. These experiments are conducted by means of affinity chromatography, immunoprecipitation, 2D-PAGE and mass spectrometry.



2D Gel Electrophoresis of HEK-293 cells extract stained with Coomassie blue.

Laboratory of Biomodelling





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Krzysztof Jozwiak, PhD

PhD students:
Anna Modzelewska, MSc;
Krystiana Krzysko, MSc;
Michał Kolinski, MSc

Undergraduate students:
Aleksander Debinski

Slawomir Filipek, PhD, DSc.Habil.

Degrees

DSc.Habil. in medicinal chemistry, Warsaw University, Faculty of Chemistry, 2004

PhD in theoretical chemistry, Warsaw University, Faculty of Chemistry, 1993

MSc in quantum chemistry, Warsaw University, Faculty of Chemistry, 1985

Post-doctoral Training

2001, 2002 Visiting scientist, Department of Ophthalmology, University of Washington, Seattle, WA, USA

Professional Employment

since 2002 Head of the Laboratory of Biomodelling, IIMCB

1993-2002 Post-doctoral fellow, Warsaw University, Faculty of Chemistry

1985-1993 Assistant, Warsaw University, Faculty of Chemistry

Honors, Prizes, Awards

2000-2002 Scientific awards-stipends of Rector of Warsaw University

Professional Memberships

Molecular Graphics and Modelling Society
Biophysical Society

Publications

34 publications since 2001 in primary scientific journals

Selected publications

- *Sapra KT, Park PS-H, Filipek S, Engel A, Muller DJ, Palczewski K. Detecting molecular interactions that stabilize native bovine rhodopsin. J Mol Biol, 2006; in press
- *Zekanowski C, Golan MP, Krzysko KA, Religa D, Lipczynska-Lojkowska W, Filipek S, Kowalska A, Rossa G, Peplonska B, Styczynska M, Maruszak A, Wender M, Kulczycki J, Barcikowska M, Kuznicki J. Two novel presenilin-1 gene mutations connected with frontotemporal dementia-like phenotype: genetic and bioinformatic assessment. Exp Neurol, 2006; in press
- *Modzelewska A, Filipek S, Palczewski K, Park PS-H. Arrestin interaction with rhodopsin: conceptual models. Cell Biochem Biophys, 2006; in press
- *Filipek S, Modzelewska A, chapter. "Molecular Modelling of Membrane Proteins" in "Structural Genomics on Membrane Proteins", K. Lundstrom ed., Marcel Dekker, New York, 2006; pp. 331-347
- *Filipek S Organization of rhodopsin molecules in native membranes of rod cells - old theoretical model compared to new experimental data. J Mol Model, 2005; 11:385-391
- *Park PS-H, Filipek S, Wells JW, Palczewski K. Oligomerization of G protein-coupled receptors: past, present, and future. Biochemistry, 2004; 43:15643-15656
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*Papers marked with an asterisk have the IIMCB affiliation of the authors

Current major research projects

1. Oligomerization of G Protein Coupled Receptors based on the rhodopsin case

G-protein-coupled receptors (GPCRs) constitute a large superfamily of receptor proteins responsible for signal transduction. These receptors mediate recognition of environmental stimuli like light, odor, and taste, but also involve responses to peptides, hormones, proteases, chemokines and other ligands across plasma membranes. They are also important targets for pharmacological intervention via activating or blocking their action. The current state of research is that GPCRs exist and act as dimers. However, a couple of years ago the monomeric state of GPCR was commonly accepted and a few cases of dimerization (like $GABA_B$ receptors) were treated as an exception. Gradually, due to growing evidence of experimental data the hypothesis of dimerization became a dominant one.

Based on distances between rhodopsin (Rh) monomers, measured by Atomic Force Microscopy (AFM), we built a model of rhodopsin oligomer. The model was subsequently enhanced by simulation in membranes specific to native rod outer segment (ROS) discs. Such membranes contain unsaturated lipids (docosahexaenoyl chains) in high concentrations.

Recently, our model of rhodopsin oligomer was experimentally confirmed by Guo *et al. PNAS* 2005 (Fig. 1). They used cysteine mutants of amino acids from the putative interface between two GPCR molecules and found that only amino acid residues from TM-4 and TM-5 were able to crosslink. Additionally, they discovered that after binding of an agonist to the receptor (they used D_2 dopamine receptor) the interface is changing and involves another face of TM-4. This unexpected problem makes oligomerization research still advantageous and we will try to reveal how the change of interface is possible in the oligomeric structure (rotation of TM-4, mutual movement of the adjacent receptor molecules etc.) and also how it affects activation and inactivation processes GPCRs are involved in.

2. Transduction of the signal from GPCR to G protein

The existence of oligomeric assemblies of GPCRs has been confirmed by biochemical and biophysical studies including direct AFM imaging of rhodopsin in native membranes. The present question is how they work together to transduce the signal into the cell and, further on, how the oligomeric state influences all aspects of their biological function. Crystallographic structure of rhodopsin revealed that its cytoplasmic surface is too small to bind the whole trimeric G protein and accommodate all interactions predicted from crosslinking data.

According to our modelling, transducin (Gt) binds to rhodopsin tetramer. After dissociation of the $Gt_{\beta\gamma}$ subunit, the remaining alpha subunit can bind to a second molecule of transducin and facilitate docking to the adjacent rhodopsin tetramer, providing positive cooperativity for binding of another trimer $Gt_{\alpha\beta\gamma}$. Currently, we continue to elucidate the model and the role of post-translational modifications on binding of Gt to rhodopsin.

3. Quenching of GPCRs - phosphorylation and binding to arrestin

Deactivation of GPCRs is associated with binding of arrestin. But before this process can start it is necessary that receptor become phosphorylated. We built a model of a complex of rhodopsin dimer and then, subsequently, tetramer with rhodopsin kinase. The kinase domain of RK binds and phosphorylates the C-terminus of activated rhodopsin while the second domain of RK (RGS homology domain) is in contact with another, inactive rhodopsin molecule.

During a formation of the arrestin - rhodopsin dimer complex the long range electrostatic forces pull the two interacting parts together since there is a strict complementarity of the electrostatic potentials between binding surfaces of both arrestin and the rhodopsin dimer (Fig. 2). Our modelling revealed that arrestin, composed of two stiff lobes, can undergo a 40° rotation which is a maximal value because the hinge region of arrestin is maximally stretched in this conformation (Fig. 3). In the rotated conformation arrestin can bind the rhodopsin dimer very firmly and, what was also found by the modelling, recognizes the active state of rhodopsin. The activated rhodopsin structure is characterized by displaced transmembrane helix VI. Arrestin can recognize the new position of this helix and binds only when rhodopsin is activated (Fig. 4).

4. The structure of the γ-secretase complex and explaining the role of Alzheimer's disease mutations

Familial form of Alzheimer's disease (FAD) is associated with mutations in several genes. Most of them were found in presenilin-1 (PS-1), a protein involved in formation of γ-secretase. This membrane-embedded complex is a key player in AD development generating toxic β-amyloid peptide. The core of this complex consists of four membrane proteins: PS-1, APH-1, PEN-2 and NCT. To explain why some mutations of PS-1 are harmful and some neutral, and to predict which amino acid mutations may be potentially dangerous, we created a molecular model of PS-1. It was known that mutations are forming linear patterns on the putative transmembrane helices of PS-1. We confirmed this idea based on much bigger database of AD mutations and extended these patterns to areas spanning even to three faces of hydrophobic regions (HRs) of PS-1. The complementary areas of residues free of AD mutations were identified based on location of silent polymorphism and PS-1 vs. PS-2 amino acid discordances. The created model of PS-1, although preliminary, properly classifies different faces of HRs based on the contact to adjacent HRs of PS-1 or to putative locations of other membrane proteins from γ-secretase complex.

5. Investigation of molecular interactions that stabilize membrane proteins

Using Atomic Force Microscopy cantilever in single-molecule force spectroscopy (SMFS) method (Fig. 5), it was possible to probe molecular interactions within native bovine rhodopsin and discover structural segments of well-defined mechanical stability. Such structural segments stabilize secondary structure elements of the native protein. They also position and hold the highly conserved residues at functionally important environments. The changes in unfolding pattern may underlie dysfunctions associated with particular mutations. Theoretical investigations that we started recently in our lab focus on the pulling of individual helices of these proteins out of the membrane and observing the changes that occur during this process. This also involves investigations of the membrane-protein interface.

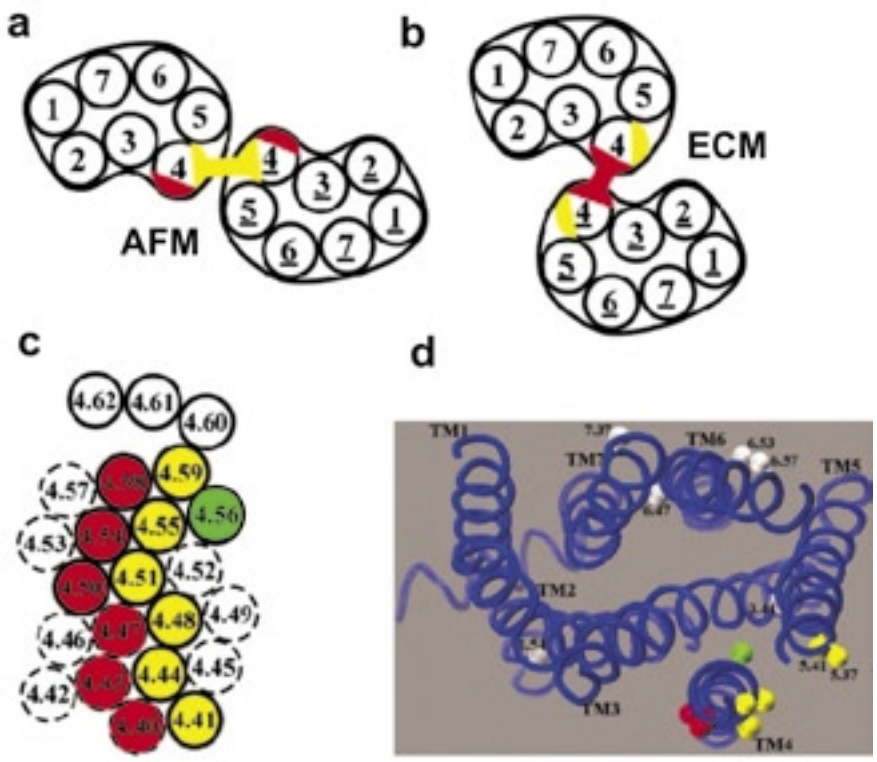

Figure 1. Models of the rhodopsin dimer interface. **a.** The interface involving TM-4 and TM-5 found by us based on AFM measurements for bovine Rh. **b.** The interface involving TM-4 deduced by Guo et al. from ECM (electron cryomicroscopy) of squid Rh. **c.** TM-4 of Rh. Solid circles denote positions of amino acids for which the corresponding cysteine mutants were crosslinked. Colors mark particular interfaces. **d.** Homology model of D_2R. Residues belonging to AFM predicted interface are shown in yellow, belonging to ECM one are shown in red. Residue 4.56 not belonging to any of these interfaces is shown in green.

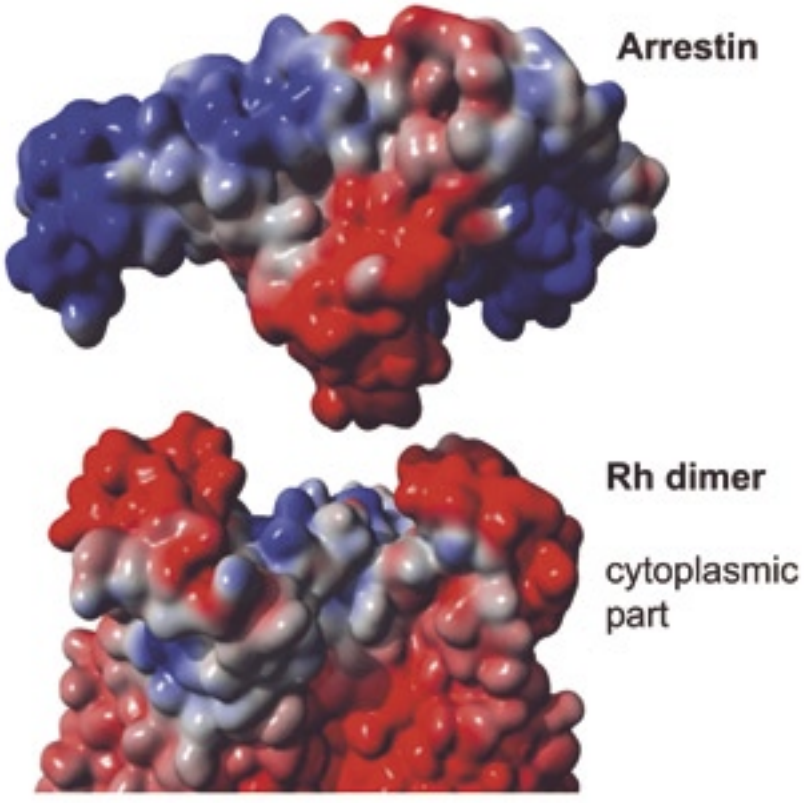

Figure 2. The complementarity of electrostatic potentials of arrestin and cytoplasmic part of rhodopsin dimer. Colour red denotes negative potential, blue – positive.

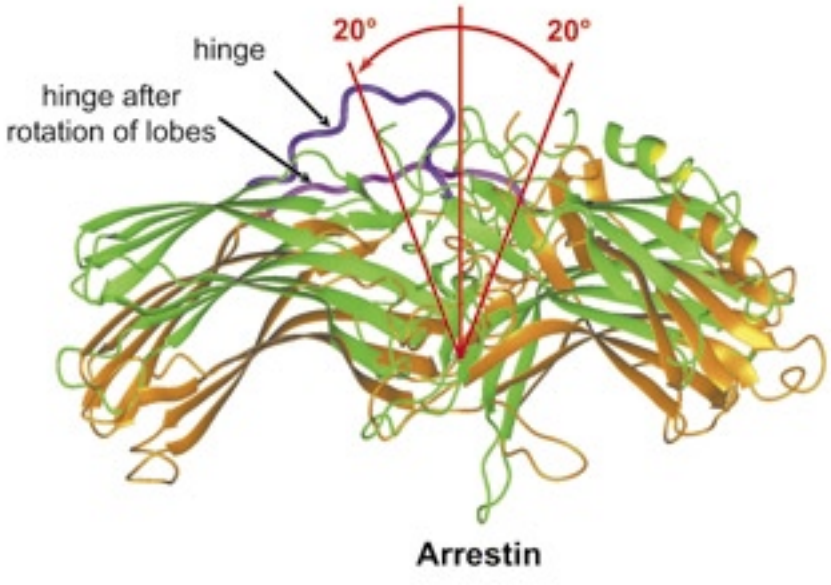

Figure 3. Superimposition of arrestin in basal (green) and with lobes 40° rotated (orange) conformations. Hinge region before (purple) and after (magenta) rotation.

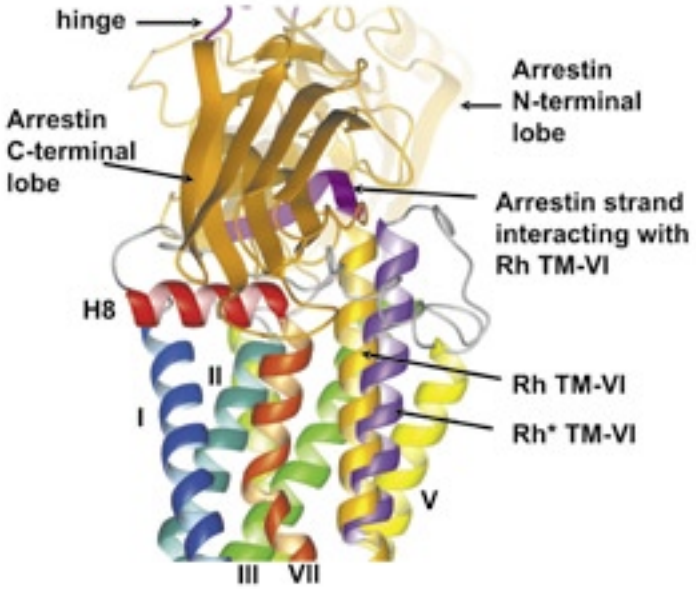

Figure 4. Arrestin recognizes active rhodopsin. View rotated 180°. Arrestin's strand from C-terminal lobe (magenta) interacts with rhodopsin TM-VI and goes down more only if this helix is moved away in activated rhodopsin (Rh*).

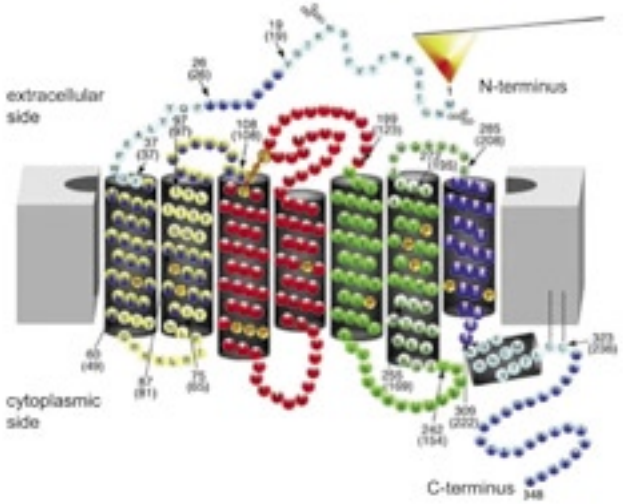

Figure 5. Secondary structure of Rh mapped with structurally stable segments observed by SMFS. Different colours mark each structural segment of Rh.

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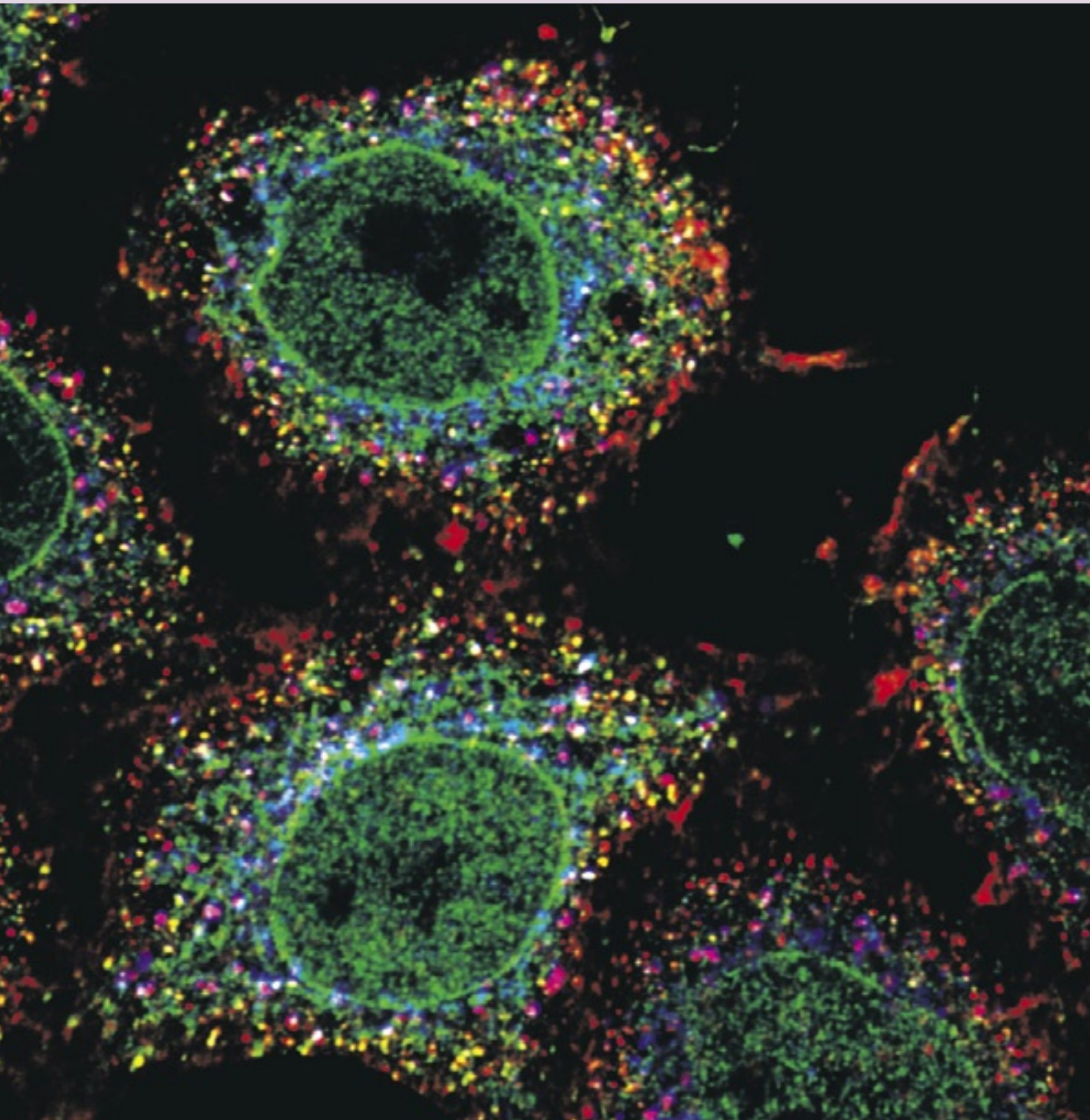

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Lukasz Sadowski, MSc (since 2006)

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Vanessa Formas, MA (since 2006)

Marta Miaczynska, PhD

Degrees

1997 PhD in genetics, University of Vienna, Austria

1993 MSc in molecular biology, Jagiellonian University, Cracow, Poland

1991 BSc in biological sciences, University of Wolverhampton, UK

Research Training

2001-2005 senior postdoctoral fellow in the Max Planck Institute for Molecular Cell Biology and Genetics (MPI-CBG) in Dresden, Germany

1997-2000 postdoctoral training at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany

1993-1996 PhD studies in the Institute of Microbiology and Genetics, University of Vienna, Austria

1990-1991 exchange student at the University of Wolverhampton, Wolverhampton, UK

Fellowships and awards

2005 International Research Scholar of Howard Hughes Medical Institute, USA, (2006-2010)

2005 International Senior Research Fellowship of the Wellcome Trust, (UK), (2006-2011)

2005 Partner Group grant from the German Max Planck Society, (2006-2008)

2001-2004 Postdoctoral Fellowship of the Max Planck Society, Germany

1999-2000 Long Term Postdoctoral Fellowship of the Human Frontier Science Program Organization (HFSPO)

1998-1999 Erwin Schrödinger Postdoctoral Fellowship from the Austrian Science Fund (FWF)

1993-1996 Bertha von Suttner PhD Scholarship from the Austrian Ministry of Science

1990-1991 Studentship of the European Community Tempus Scheme

Selected publications:

- Mace G, Miaczynska M, Zerial M, Nebreda AR Phosphorylation of EEA1 by p38 MAP kinase regulates μ opioid receptor endocytosis, EMBO J, 2005; 24:3235-46
- Miaczynska M, Pelkmans L, Zerial M Not just a sink: endosomes in control of signal transduction. (Review) Curr Opin Cell Biol, 2004; 16:400-406
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Research

The relationship between the processes of intracellular membrane transport and signal transduction is the major interest of our laboratory. Although studied individually for several years, these processes appear to be tightly linked and mutually interdependent on each other.

Signal transduction in response to growth factors is initiated at the plasma membrane by binding to specific receptors which upon activation initiate a series of protein-protein interactions and stimulate kinase cascades, thus transmitting signals through the cytoplasm to the nucleus, where gene expression is modulated. Activated receptor-ligand complexes are eventually cleared up from the cell surface by endocytosis and targeted for degradation in lysosomes, thus terminating the signalling. In the traditional view, no intracellular organelles were considered required for signal propagation from the plasma membrane to the nucleus which should occur exclusively through cytoplasmic mediators. In this model, endocytosis was regarded merely as a mechanism for switching off the signalling. More recent studies reveal, however, that transduction of signals initiated on the cell surface can continue within the endocytic pathway, in part via endosome-specific signalling complexes, different from those assembled on the plasma membrane. Therefore, endosomes can be considered as intracellular platforms for active signal propagation, enabling a precise spatial and temporal control of cellular responses. Accumulating evidence indicates that endocytosis plays an active role in modulating signal transduction but also vice versa, signal transduction cascades may regulate endocytic trafficking.

Our laboratory focuses on the role played by the endosomal compartments and endocytic transport in modulating intracellular signal transduction. Recent studies characterising endosomal APPL proteins as signal transducers provided a striking example of the involvement of endosomes in signalling (Miaczynska et al., 2004). Two homologous proteins APPL1 and APPL2 are effectors of the small GTPase Rab5, a key regulator of early steps of endocytosis. They are localized to a subpopulation of Rab5-positive endosomes that appear segregated from the well-characterized canonical early endosomes marked by another Rab5 effector EEA1. APPL-harbouring endosomes are accessible to certain endocytic cargo such as epidermal growth factor (EGF), thus raising a possibility that they may represent a specialized endosomal compartment devoted to signalling.

Further analysis of APPL1 demonstrated that its intracellular distribution is dynamic and changes in response to extracellular stimuli such as EGF or oxidative stress (Fig. 1). In our current model, EGF is internalized into APPL- and EEA1-positive endosomes and upon EGF endocytosis, GTP hydrolysis on Rab5 releases APPL1 from the membrane. Cytosolic APPL1 translocates into the nucleus where it interacts with the histone deacetylase and chromatin remodelling complex NuRD/MeCP1. The nuclear accumulation of APPL1 subsides within 30 mins after EGF addition, with APPL1 re-localising to the endosomes. Knockdown of APPL proteins by RNAi demonstrated that each of them is required for efficient cell proliferation. By identifying an endocytosis regulator Rab5 and a nuclear chromatin remodelling complex NuRD/MeCP1 as interacting partners of both APPL proteins, these data pointed for the first time to a direct molecular link between the processes of endocytosis and chromatin remodelling. As histone deacetylase activities are essential for cell cycle progression, APPL binding to NuRD/MeCP1 may serve the purpose of subjecting this function to regulation by extracellular signalling.

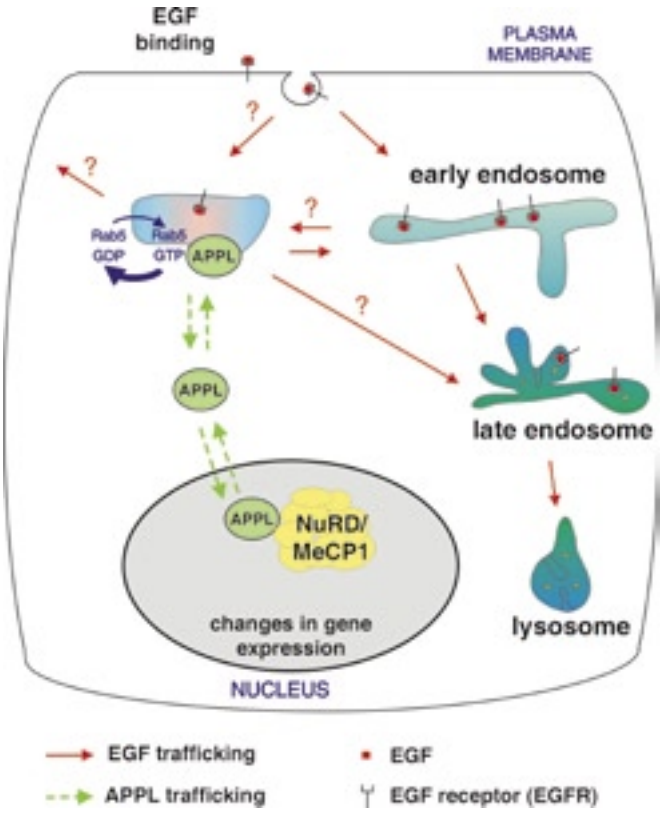

Figure 1. Functional cycle of APPL1 re-localization after EGF administration. See text for description. Possible trafficking pathways into and out of APPL-positive endosomes are labelled with the question marks.

Cumulatively, these data identified a novel signalling pathway that is essential for cell proliferation and involves an endosomal compartment as an intermediate in signalling between the plasma membrane and the nucleus. They posed several new and fascinating questions, some of them we attempt to address at present. We would like to understand the mechanisms responsible for APPL1 shuttling in the cell, its importance for cell proliferation and the exact roles played by various intracellular pools of APPL1 (endosomal, cytoplasmic and nuclear). Furthermore, we will attempt to determine the molecular identity of the endosomal compartment occupied by APPL proteins, both in terms of its biochemical composition and cargo trafficking routes connecting these structures to other endosomal compartments. Finally, we would like to extend our studies to determine the significance of the APPL pathway in signalling downstream of other growth factors besides EGF. The latter task will be undertaken in collaboration with other laboratories participating in a European Union Integrated Project entitled: Tracking the Endocytic Routes of Polypeptide Growth Factor Receptor Complexes and their Modulatory Role on Signalling (acronym EndoTrack).

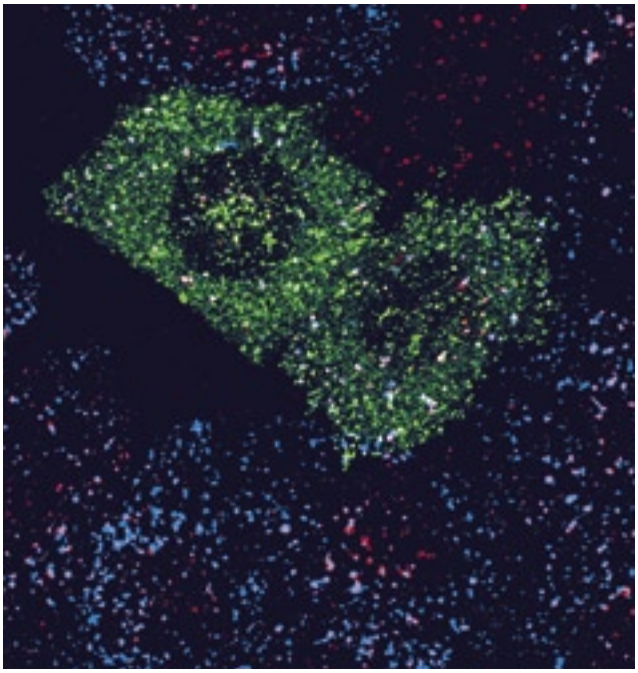

Figure 2. Confocal image of HeLa cells, which were transfected with GFP-APPL1 (green), and then allowed to internalize Transferrin-Alexa 647 (blue) for 30 seconds and left for 3 minutes in medium without Transferrin till fixation. EEA1, the marker of early endosomes was labelled with Alexa 555 (red).

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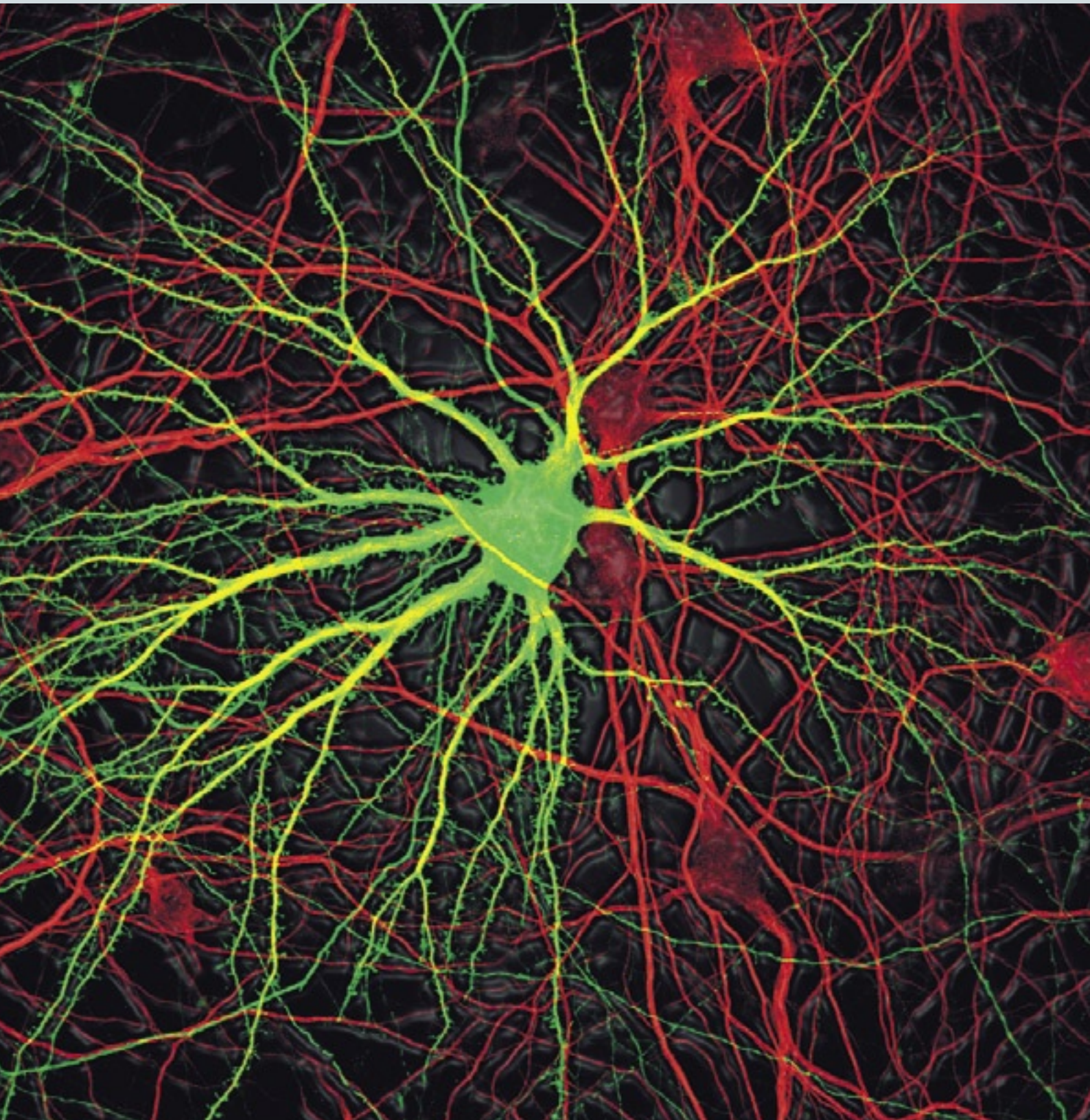

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Degrees

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1996 MSc in Biology, Department of Genetics, Warsaw University, Poland

Research Training

2002-2005 Picower Center for Learning and Memory, Massachusetts Institute of Technology and Howard Hughes Medical Institute, Prof. Morgan Sheng, Cambridge, MA, USA; postdoctoral associate

2000 ARL Division of Neural Systems, Memory and Aging, University of Arizona, Dr. J. Guzowski, Tucson, USA (1 month), research training

1997-2001 Laboratoire de Genetique Moleculaire de la Neurotransmission et des Processus Neurodegeneratifs (L.G.N.), Prof. J. Mallet, UMR 9923 C.N.R.S., Paris, France (seven months in total), research training

1996-2002 Laboratory of Molecular Neurobiology, Nencki Institute of Experimental Biology, Prof. Leszek Kaczmarek Warsaw, Poland; PhD student until 2001; postdoctoral associate until May 2002

1995-1996 Department of Genetics, Prof. P. Weglenski, Warsaw University, Poland, master degree

Fellowships and awards

2005 Konorski Award of Polish Neuroscience Society and Polish Academy of Science for the best publication of year 2004 in the field of Neuroscience (for publication by Kowalczyk et al, 2004 JCB, 167:209-213)

2002 Polish Prime Minister Award for the PhD thesis

2001 Foundation for Polish Science National Scholarship for Young Investigators, 1 year scholarship.

2000 EMBO Short Term Fellowship 2000

1999 Polish Network for Cell and Molecular Biology UNESCO/PAN Scholarship

1997 Bourse de stage du Gouvernement Francaise (French Government Scholarship)

Selected publications:

- Szymczak S, Kalita K, Jaworski J, Mioduszewska B, Savonenko A, Markowska A, Merchenthaler I, Kaczmarek L Estrogen Receptor beta regulates synaptic plasticity in the rat hippocampus. Hippocampus, 2006; in press
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Research

The research of the Laboratory of Molecular and Cellular Neurobiology focuses mostly on the link between protein kinase mTOR, phenomenon of local protein synthesis and development of dendritic arbors in the mammalian brain.

Dendrites are the main site of information input onto neurons, and different neurons have distinctive and characteristic dendrite branching patterns. Advances in electrophysiology and

computational modeling have clearly shown that dendritic arbor shape is one of the crucial factors determining how signals coming from individual synapses are integrated. In fact several neuropathologic conditions are characterized by abnormalities in dendritic tree structure including a number of mental retardation (MR) syndromes (such as Down's, Rett's as well as Fragile X syndrome), schizophrenia and Alzheimer disease. In addition even mild but prolonged stress to the animals can induce shrinkage of dendritic fields in hippocampus.

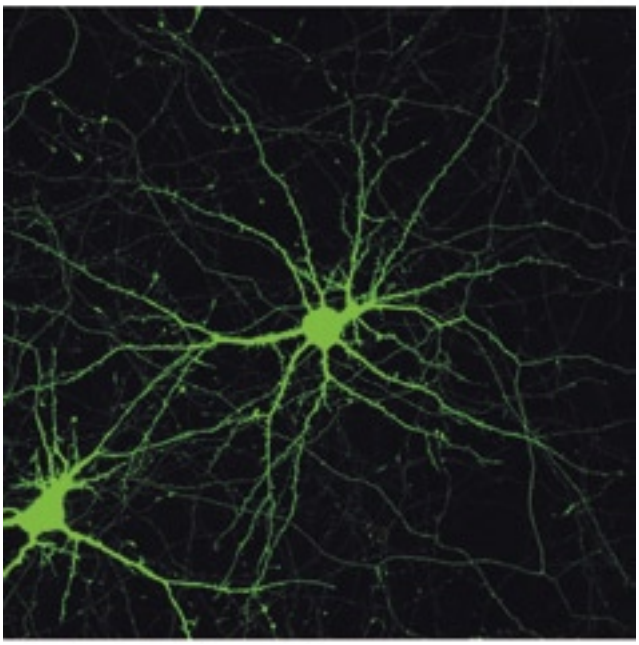
Dendritic arbor development is a multi-step process that is controlled by both external signals and intrinsic genetic programs. Only in recent years have molecular mechanisms been elucidated for dendritic arbor development. Among the proteins that transduce extracellular or cell surface signals into changes in dendritic shape are several protein kinases. Our recent work demonstrated for the first time that PI3K and its downstream kinase Akt regulate the complexity of dendritic branching in neurons by protein kinase mTOR (mammalian target of rapamycin).

mTOR is a serine/threonine protein kinase that controls cell size in both non-neuronal and neuronal. In addition, mTOR activity has been implicated in long-term synaptic plasticity. mTOR is thought to act primarily by phosphorylating eIF-4E binding protein (4E-BP) and p70 ribosomal S6 protein kinase (p70S6K), which are important regulators of protein translation. Moreover, recent findings have shown mTOR involvement to be important for local protein synthesis in neuronal dendrites. In the context of these findings our recent data describing mTOR-4EB-P1 and p70S6 kinase involvement in dendritic branching raises the interesting question whether local or general mTOR signaling is required for dendrite morphogenesis. It serves as a starting point for studying the more general question of the potential role of local protein synthesis in dendritic tree development. However, "chemical genomics" performed on yeast identified 400 rapamycin-dependent mutants, the analysis of which suggested that mTOR might be involved in cellular functions other than translation such as transcription, ubiquitin-dependent proteolysis and microtubule stability. That raises general question that should be answered first - what are mTOR dependent proteins and cellular processes involved in dendritogenesis process?

To answer these questions we want to:

1) Identify mTOR-regulated proteins in neurons by a proteomic approach.
2) Design siRNA library against mTOR-regulated proteins expressed in neurons and perform systematical screen for these mTOR-dependent proteins that are involved in process of dendritic branching.
3) Establish a link between local protein translation and physiological dendritic arbor development. This task requires first establishing strategy for specific inhibition of local protein synthesis. This unique technology will help us to check how local protein production in dendrites contributes to their development.
4) Characterize both, mTOR-regulated cellular processes and local protein synthesis in dendritic arbor pathologies observed in MR, stress and schizophrenia.

control vector



4E-BP1-AA

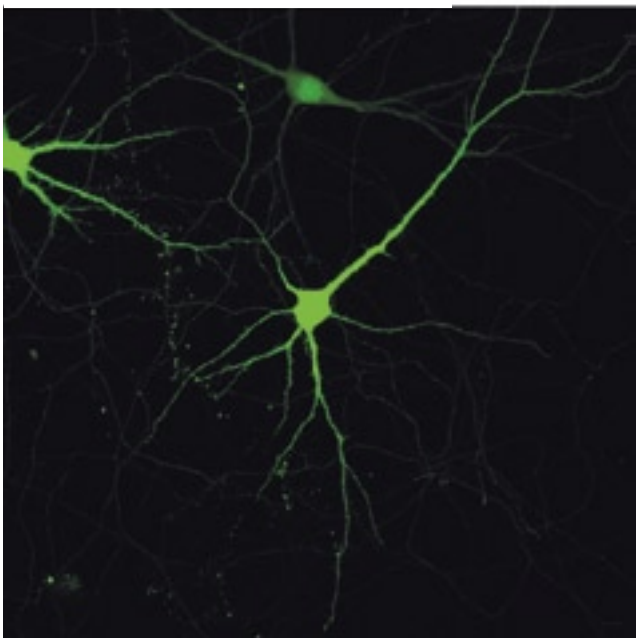
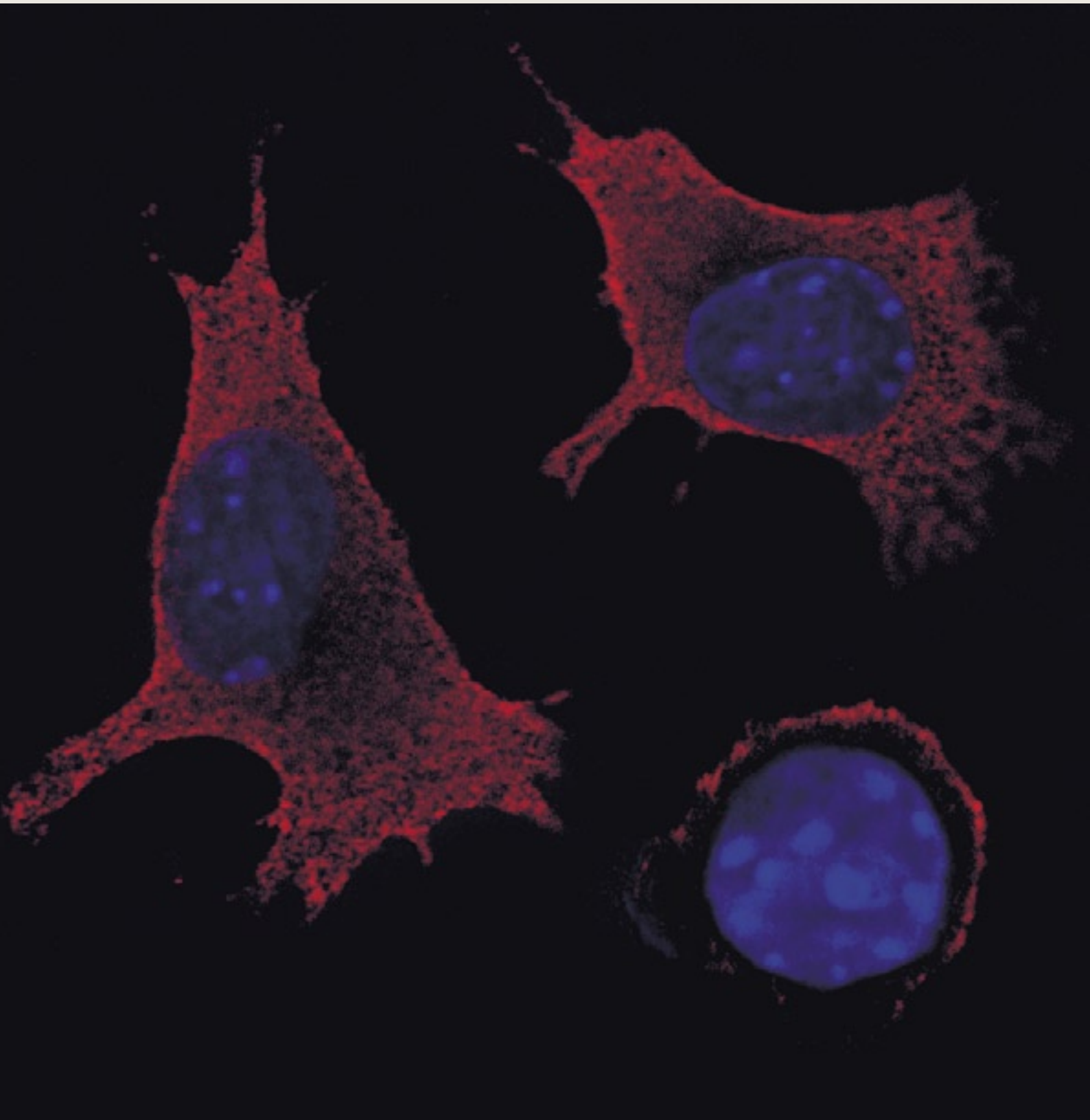


Figure. Overexpression of 4E-BP1, mTOR-regulated protein, involved in translation control inhibits dendritic branching of hippocampal neurons cultured in vitro. Representative micrographs of hippocampal neurons transfected at DIV7 for one week with control vector or 4E-BP1-AA mutant (permanently active mutant of 4E-BP1). Neuron morphology was visualized by cotransfected GFP.

Laboratory of Cortex Movements and Cell Division MPG/PAN

(located at the Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, started its activity on the 1st of February 2006)



Lab Leader

Ewa Paluch, PhD

MAX-PLANCK-GESELLSCHAFT

INTERNATIONAL INSTITUTE OF MOLECULAR AND CELL BIOLOGY

The equipment and running costs for the lab, including personnel, are provided by IIMCB (MEiN special research project).

Ewa Paluch, PhD

Degrees

2005 PhD in Biophysics, University Paris 7, Paris, France.

2001 DEA (Masters degree) "Interfaces Physique-Biologie", University Paris 7 (rank: 1st)

2000 Agrégation of Physics

1999 Maîtrise (equivalent BSc) in Physics at Ecole Normale Supérieure de Lyon, France

1998 Licence in Physics at Ecole Normale Supérieure de Lyon

Research Training

2001-2005 PhD studies at the Institut Curie, Paris, France

2000-2001 DEA (equivalent Masters) research project in Biophysics, Institut Curie, Paris, France

1999 Maîtrise (BSc) research project in particle Physics, CERN, Geneva, Switzerland

1998 Licence (part of BSc) research project in relativistic Astrophysics, Paris-Meudon Observatory, France

Professional Employment

since 2006 Joint MPI-CBG/PAN group leader at the Max Planck Institute of Molecular Cell Biology and Genetics, Dresden

Oct.-Dec. 2005 Scientist position at the Max Planck Institute of Molecular Cell Biology and Genetics, Dresden

Honors and Fellowships

2005 Joint MPI-CBG/PAN group leader at the Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany

2004-2005 PhD scholarship from the Ligue Nationale contre le Cancer, France

2001-2004 PhD scholarship from CNRS, France

2000 Agrégation in Physics (French national competition, rank: 6th)

1998-2001 full salary from the Ecole Normale Supérieure de Lyon, France (recruitment by national competition)

1995 Prize of Scientific and Technical Vocation of girls, awarded by the Regional Delegation for Women Rights, region of Paris, France

Research

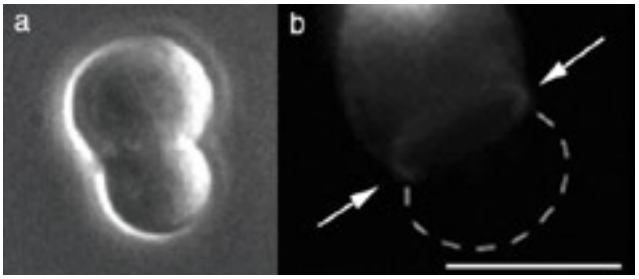
The laboratory focuses on biochemical and physical mechanisms of cell shape and deformations. Cell shape changes, e.g. during migration or division, are driven by remodeling of the cytoskeleton, and primarily of cellular actin networks. The research focuses on movements of the actomyosin cortex, a thin gel of actin that underlies the cell membrane. Due to the presence of myosin motors, the cortex can undergo contractions that lead to concerted flows of actin, myosin, associated proteins and cortical organelles. Such flows have been observed in various modes of cell locomotion as well as at the onset of cytokinesis, and are thought to result from gradients of tension that pull cortical components from regions of relaxation to regions of high tension.

Our group members have previously studied the behavior of cells, in which cortical contractility was increased by disassembly of the microtubules. Under these conditions and in the absence of substrate adhesions, the cell cortex spontaneously ruptures and a bulge of bare membrane is expelled through the hole. Cortex flows triggered by the rupture then lead to the oscillation of a constriction ring across the cell. Based on these experiments, we proposed that bleb formation and cortical flows reveal an intrinsic behavior of the actomyosin cortex and that they are direct consequences of cortical contractility. By controlling cortex contractions, the cell could use these spontaneous behaviors for locomotion and shape changes.

Our research now focuses on the involvement of these spontaneous cortical ruptures and flows in cell division. At the onset of anaphase, cortical flows from the poles towards the equatorial region have been observed. They seem to directly lead to the formation of the cleavage furrow, although how this happens is not well understood. We study the mechanism by which these cortical flows are triggered and how they contribute to the establishment of the mitotic division ring.

To address these questions, we combine biophysical and biochemical approaches. Our research projects include:

- charaterization of the flows and identification of the molecular players involved
- study of the physics of cortical flows and furrow formation from the experimental side (local perturbations of the cell cortex) and from the theoretical side (collaboration with the groups of Karsten Kruse and Frank Jülicher, Max Planck Institute of the Physics of Complex System, Dresden)
- study of the cortex contribution to accurate mitotic spindle positioning



Oscillating rings in cell fragments.

a. A bulge of membrane is expelled after rupture of the cortex. The bulge is limited by a constriction ring.

b. Actin-GFP reveals that the expelled bulge has no actin cortex (the dashed line underlines the bulge contour). The arrows point out the accumulation of actin at the constriction ring. Bar: 5µm.

Selected publications:

E. Paluch, M. Piel, J. Prost, M. Bornens, C. Sykes Cortical actomyosin breakage triggers shape oscillation in cells and cell fragments, Biophys J, 2005; 89:724-33

J. van der Gucht, E. Paluch, J. Plastino, C. Sykes Stress release drives symmetry breaking for actin-based movement, Proc Natl Acad Sci USA, 2005; 102:7847-52

E. Paluch, C. Sykes, J. Prost, M. Bornens Dynamic modes of the cortical actomyosin gel during cell locomotion and division. Trends Cell Biol, 2006; 16:5-10.

Educational Activities

Utrecht University Doctoral Program

The Utrecht University international doctoral program is based on an agreement between the Polish Network for Cell and Molecular Biology UNESCO/PAN and the Utrecht University (The Netherlands). This is a part of the research collaboration program initiated by Prof. Willem Gispen to facilitate the exchange of scientific information and ideas among Polish and Dutch scientists and graduate students and to allow for short-term research visits of the staff members and their students from Poland to Utrecht and vice versa. The first turn of the doctoral program offered three four-year doctoral positions. The doctoral thesis were to be defended in front of the dissertation committee of the Medical Faculty of Utrecht University. As a result till now two students M. Bucko-Justyna (M. Zylicz's lab, IIMCB) and K. Starowicz (R. Przewlocki's lab, Institute of Pharmacology PAN, Cracow) defended their theses in due course. Because of the success of this part of the program, the next recruitment has been announced in 2003. Currently three students are enrolled in the program: M. Geremek (M. Witt's lab, IIMCB and Institute of Human Genetics PAN, Poznan: Genetic analysis of primary ciliary dyskinesia/Kartagener Syndrome [PCD/KS]), M. Lukowiak (A. Lipkowski's lab, Center for Experimental and Clinical Medicine PAN, Warsaw: Pharmacology of opioid peptides. The application of polymers as carriers of the opioid peptides), P. Michaluk (L. Kaczmarek's lab, Nencki Institute PAN, Warsaw: Role of MMP-9 in neuronal plasticity). The fourth student is supposed to join the program under the supervision of M. Zylicz. IIMCB coordinates the entire program on the Polish site.

After a defence of the doctoral thesis of Katarzyna Starowicz, Utrecht. From left: B. Przewlocka, K. Starowicz, W. Gispen, R. Przewlocki.

Postgraduate School of Molecular Medicine (SMM) (www.iimcb.gov.pl/smm/index.html)

Medical Universities in Warsaw, Poznan, Szczecin, Gdansk, Wroclaw, Lodz, as well as the International Institute of Molecular and Cell Biology, the Nencki Institute and the Foundation for Experimental and Clinical Oncology have jointly founded the Postgraduate School of Molecular Medicine. The main goal of the School is to offer a new post-graduate PhD program in the field of molecular medicine, which is addressed to medical, biology and pharmacy postgraduate students in Poland. Since the year 2002, SMM has been opened to foreign students. SMM is formally affiliated with the Medical University of Warsaw, which is responsible for the administration of the school. According to its by-laws, the School is managed by the Director and the Scientific Council elected by the founding institutions. At present the Director's position is held by Prof. L. Konarska from the Faculty of Pharmacy Department of Biochemistry and Clinical Chemistry, Medical University of Warsaw. SMM admits students (up to ten per year) for the four-year doctoral program. The candidates are requested to present a scientific program of their doctoral research, the scientific merit of which is carefully evaluated by the Recruitment Committee of SMM as well as independent reviewers in Poland and from abroad. Eight groups of students were accepted during the period of 1998-2005, including six foreign individuals. Successful candidates accomplish their scientific program, under supervision of their tutors, in home laboratories throughout Poland. The members of SMM Scientific Council evaluate stu-

dent progress annually. The tutorial program offered to the students includes theoretical (lectures, seminars) and practical courses (laboratory sessions) on selected topics of modern molecular biology and medicine. Each SMM student is awarded a stipend (full or supplemental). Furthermore, SMM helps students to participate in short-term scientific training in leading Polish and foreign laboratories. In parallel to funds generated by founding institutions, SMM activities are supported by subsidies from the Polish Ministry of Health, Ministry of Education and Science, the Kronenberg Foundation, UNESCO-ROSTE, the European Commission within the 5th Framework Programme (Centre of Excellence in Molecular Bio-Medicine of IIMCB), CNRS (France). Additional financial support comes from the French government supporting the costs of participation of outstanding French scientists in tutorial and organizational activities of SMM as well as short-term scholarships for the training of SMM students in laboratories in France.

In 2005 the following courses were organized:

- SMM Lecture Course on Human Genetics, 1-2.06.2005, Warsaw, organized by SMM and IIMCB. This annual obligatory course for all first-year students was organized by Prof. Michal Witt. The lectures were given by eleven eminent Polish scientists from major clinical and research institutions in Poland. The course was open for the public.
- Practical course "Molecular methods applied in medicine", 20-24.06.2005, Poznan, within the Summer School „Progress in Molecular Biology".
- 5th Integrated Course - "Advances in molecular medicine: focus on molecular endocrinology" consisted of a conference "Molecular endocrinology – from gene to disease" and a practical course "Molecular endocrinology in clinical practice", 26.06-1.07.2005, Gliwice. The Integrated Course took place at the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology in Gliwice, and included laboratory workshops, clinical presentations and lectures by invited guests from abroad: Catharina Larsson (Sweden), Gerry Thomas (United Kingdom), Ilpo Huhtaniemi (United Kingdom), Klaus Badenhoop (Germany), Patrick Gaudray (France), Josef Kohrle (Germany), Maria Luisa Brandi (Italy), Ralf Pasche (Germany) and twenty two speakers from Poland, including Barbara Jarząb, Liliana Konarska and Elżbieta Gubała (organizers).
- 7th Annual Inaugural and Research Report SMM Session, 10-11.10.2005, Warsaw, organized by SMM, Medical University of Warsaw and IIMCB. Invited lecture "Gene deregulation in melanoma leading to immunosuppression" Prof. Catherine Alcaide-Loridan, Institut Jacques Monod, UMR 7592, CNRS, Universite Paris VI & Paris VII, France. During the session 27 SMM students presented their research results obtained during the academic year 2004/2005.

5th Integrated Course of SMM (Gliwice 2005) – international conference and workshop „Molecular endocrinology in clinical practice: from gene to disease". From left: Prof. Liliana Konarska (director of SMM), SMM students during lecture and workshop.

Popularization of Science

Activities within Science Festival School

The aim of the School of Science Festival is to reduce the gap between science and society in Poland by conducting educational activities popularising biology - open lectures, workshops for students and all interested participants, courses for biology teachers. All activities are focused on improving biology education and awareness of biology in society. The co-founders of the Science Festival School are four biological institutes: International Institute of Molecular and Cell Biology (IIMCB), Nencki Institute of Experimental Biology PAN (IBD), Institute of Biochemistry and Biophysics PAN (IBB), Warsaw Agricultural University (WAU) and Warsaw Festival of Science. IIMCB hosts SFN' laboratory, office and administration. Science Festival School leads another laboratory at Warsaw Agricultural University. Total number of 1000 young participants visited laboratory workshops in 2005, 115 biology teachers and about 600 listeners of lectures.

IX Warsaw Science Festival (16-25 September 2005)

- Do we still evolve? Open lecture – **A. Lorenc**
- Laboratory workshops: How to wring jellyfish out from bacteria? – the miracles of biotechnology – **S. Pawlak**
- Laboratory workshops: Explore your own DNA – **J. Lilpop**
- Computer workshops Bioinformatical investigation – the history of the protein – **G. Papaj**
- Laboratory in the kitchen – IX Science Festival in Jabłonna Palace – **K. Brewczynski**
- Physics in service for biology – IX Science Festival in Jabłonna Palace – **K. Brewczynski**
- The incredible enzymes – science show – **A. Lorenc**

IX Science Picnic (4 June 2005)

BioEducation Foundation, Science Festival School and molecular biology student's association organized exhibition and science shows:

- Physics in service for biology
- How was DNA discovered?
- Beyond the reaches of the microscope - showing proteins and other molecules.
- Translation – let's build a protein!

Laboratory workshops

The public-oriented laboratory workshops cover various topics of modern biology such as DNA research, proteomics or biotechnology. Participants take part in real–life experiments like DNA examining and analysis, protein isolation and purification, bacterial transformation, etc.

Courses for biology teachers

A programme aim at training biology teachers has been continued this year. The goal of the two-day laboratory workshops is to present the most recent achievements and laboratory techniques in biological sciences. The participants of such courses not only have a chance to learn how to use modern laboratory equipment, but also how to make some

easy and cheap biology experiments in the classroom. With the support of most popular daily newspaper Gazeta Wyborcza and Board of Directors of Mazovian Voievodship, SFN organized 7 weekend meetings at Teachers Excellence Centres throughout the country.

Open lectures

SFN presents theoretical issues of modern biology by organizing open lectures given by top Polish scientists. In 2005, every two weeks lectures on genomics, evolution, Nobel Prizes, biotechnology and proteomics were carried out.

The 4th Mini Symposium for biology teachers was organized on the 3rd December 2005 together with Centre of Excellence BRAINS at The Nencki Institute of Experimental Biology. 60 teachers took part in 6 lectures given by scientists from The Institute and Warsaw University.

Educational projects:

- **"VOLVOX" project under FP6**

  School of Science Festival has started the implementation of the Volvox Specific Support Action project funded by the European Commission within FP6 and officially entitled: 'Co-ordinated Internet-linked networks for promoting innovation, exchanging knowledge and encouraging good practice to enhance bioscience education in European schools.' Volvox consists of 9 partners from Denmark, Estonia, Germany, Italy, Luxembourg, Poland, Portugal, Sweden and UK. Volvox network will provide teachers with authoritative briefings, proven laboratory protocols, classroom activities addressing the social impact of bioscience, accounts of the careers of young scientists and numerous other educational resources to help motivate them and their students. Furthermore, Volvox will provide a dynamic forum for the exchange of creative ideas and good educational practices across the European Union. Available to read, this amount of resources should encourage more young people to develop positive attitudes towards studying science and to consider a scientific career.

- **"Science of Modern Biology – Exploratory Resources for Biology Teachers and Students"**

  Project was financed from UNESCO and International Institute of Molecular and Cell Biology in Warsaw funds. The main goal of the project was to develop various resources to supplement existing biology curricula and help teachers engage young people in current issues of modern biology. A set of standards for the modern and innovative exploratory resources in biological education was established, including experimental kits to be used in classrooms, lesson scripts, and educational games. Three practical kits

  for schools were developed: "Explore DNA", "Secrets of photosynthesis" and "Enzymes around us" supplemented by various theoretical materials. Practical workshops for 40 biology teachers from all over the country were organized to evaluate those resources.

- **"Biology of 21st century – innovative lesson screenplays"**

  This project was founded by Polish Insurance Company (PZU) Foundation and implemented in cooperation with BioEducation Foundation, Polish Biology Olympiad, "Akcja z klasą" and "Biologia w szkole" periodic. Two innovative scenaries were developed together with biology teachers form small Polish towns:

  – bioethical problems with molecular diagnostics

  – science experiment methodology

  The scenarios and all materials were tested during 12 lessons in high-schools and were very positively evaluated by students and teachers.

Laboratory training for talented secondary school pupils

Laboratory training for four gifted secondary school pupils was organized during summer holidays. One of laureates of Polish Biology Olympiad joined for a week the research group at Laboratory of Neurodegeneration, IIMCB. SFN organized initial training in laboratory practice and covered costs of travelling and accommodation in Warsaw for young researchers.

Staff at IIMCB

(as of April 2006)

Name		Funding
Jacek Kuznicki	Director	IIMCB
Michal Witt	Deputy Director for sicientific matters	IIMCB(1/2)
Maria Kleska	Deputy Director For administrative matters	IIMCB
Hanna Iwaniukowicz	Financial Manager	IIMCB
Sylwia Adamiec	Accounting Specialist	IIMCB
Monika Nowicka	Payroll Specialist	IIMCB
Beata Tkacz	Directors' Assistant	IIMCB
Agnieszka Karbowska	Tender Specialist	IIMCB
Urszula Bialek-Wyrzykowska	International Cooperation Manager	IIMCB/CoE(1/2)
Dorota Libiszowska	Foreign Grants Manager	IIMCB/CoE
Magdalena Glogowska	PR Specialist	IIMCB/CoE
Agnieszka Ziemka	Planning and Reporting Manager	IIMCB
Krystyna Domanska	Human Resources Specialist	IIMCB
Ewa Blazewicz	Secretarial Assistant	IIMCB
Rafal Flis	IT Manager	IIMCB
Przemyslaw Slusarczyk	IT Specjalist	IIMCB
Robert Banasiak	Maintenance Specialist	IIMCB

Department of Molecular Biology

Name		Funding
Maciej Zylicz	Lab Leader	IIMCB
Alicja Zylicz	Vice Head	IIMCB
Marcin Klejman	Research Associate	IIMCB
Pawel Bieganowski	Research Associate	IIMCB/MEiN grant
Maciej Olszewski	Research Assistant	MEiN grant
Leszek Lipinski	PhD Student	IBB
Magdalena Gutkowska	PhD Student	Nencki Fellowship
Dawid Walerych	PhD Student	SMM
Bartosz Wawrzynow	PhD Student	Nencki
Jakub Urbanski	PhD Student	SMM
Grazyna Orleanska	Secretary	IIMCB

Laboratory of Bioinformatics and Protein Engineering

Name		Funding
Janusz M. Bujnicki	Lab Leader	IIMCB
Krzysztof Skowronek	Research Coordinator	EU
Michal Boniecki	PhD Student	MEiN program
Agnieszka Chmiel	PhD Student	MEiN program
Iwona Cymerman	PhD Student	SMM/MEiN grant
Malgorzata Durawa	PhD Student	MEiN program(1/2)
Marcin Feder	PhD Student	SMM/NIH
Michal Gajda	PhD Student	EU
Andrzej Kaminski	PhD Student	IIMCB
Jan Kosinski	PhD Student	SMM/MEiN grant
Michal Kurowski	PhD Student	IIMCB
Grzegorz Papaj	PhD Student	MEiN program
Sebastian Pawlak	PhD Student	MEiN program
Marcin Pawlowski	PhD Student	IIMCB
Michal Pietal	PhD Student	MEiN grant
Elżbieta Purta	PhD Student	MEiN program
Karolina Tkaczuk	PhD Student	MEiN grant
Irina Truszynska	PhD Student	NIH
Joanna Sasin	PhD Student	IIMCB/Nencki Fellowship
Katarzyna Filip	Msc Student	Volunteer
Stanisław Dunin-Horkawicz	Msc Student	Volunteer
Agnieszka Obarska	Msc Student	Volunteer
Michal Wrzesinski	Office Manager	MEiN grant
Jan Kogut	Computer Administrator	EU
Maciej Fijalkowski	Computer Administrator	NIH
Ryszard Matlak	Research Assistant	Volunteer

Laboratory of Structural Biology MPG/PAN

Name		Funding
Matthias Bochtler	Lab Leader	Max Planck
Izabela Sabala	Post doctoral Fellow	EU/Max Planck
Honorata Czapinska	Post doctoral Fellow	MEiN program
Renata Filipek	Post doctoral Fellow	Max Planck
Aneta Kaczmarczyk	Post doctoral Fellow	CoE/Young Inv. Program
Grzegorz Chojnowski	PhD Student	MEiN grant
Henryk Korza	PhD Student	Max Planck/MEiN program
Magdalena Lipka	PhD Student	Max Planck
Malgorzata Firczuk	PhD Student	EU/Max Planck
Monika Sokolowska	PhD Student	Max Planck
Roman Szczepanowski	PhD Student	EU/Max Planck
Magdalena Kaus	PhD Student	Max Planck/Nencki Fellowship

Laboratory of Biomodelling

Name		Funding
Sławomir Filipek	Lab Leader	IIMCB
Krzysztof Jozwiak	Post doctoral Fellow	MEiN grant
Anna Modzelewska	PhD Student	IIMCB/UW
Krystiana Krzysko	PhD Student	IIMCB
Michal Kolinski	PhD Student	SMM
Aleksander Debinski	MSc Student	Volunteer

Laboratory of Neurodegeneration

Name		Funding
Jacek Kuznicki	Lab Leader	IIMCB
Urszula Wojda	Associate Professor	IIMCB
Monika Klejman	Post-doctoral Fellow	MEiN program
Andrzej Lewandowicz	Post-doctoral Fellow	EU
Marta Wisniewska	Post-doctoral Fellow	EU
Magdalena Blazejczyk	PhD Student	MEiN grant/Nencki Fellowship
Lukasz Bojarski	PhD Student	IIMCB/Nencki Fellow
Wojciech Michowski	PhD Student	Nencki Fellowship
Adam Sobczak	PhD Student	MEiN grant/Nencki Fellowship
Aleksandra Szybinska	PhD Student	IIMCB
Malgorzata Mossakowska	Project - coordinator	IIMCB

Laboratory of Cell Biology

Name		Funding
Marta Miaczynska	Lab Leader	IIMCB
Beata Bielinska	Research Assistant	HHMI(1/2)
Marta Brewinska	PhD Student	IIMCB/Nencki Fellowship
Anna Zarebska	PhD Student	IIMCB/Nencki Fellowship
Anna Hupalowska	PhD Student	EU
Lukasz Sadowski	PhD Student	EU
Vanessa Formas	Grant Administrator	HHMI

Laboratory of Molecular and Cell Neurobiology

Name		Funding
Jacek Jaworski	Lab Leader	IIMCB
Malgorzata Perycz	PhD Student	IIMCB/Nencki Fellowship
Lukasz Swiech	PhD Student	IIMCB/Nencki Fellowship
Malgorzata Urbanska	PhD Student	Volunteer
Izabela Szamreta	Technician	IIMCB

Laboratory of Cortex Movements and Cell Division MPG/ PAN in Dresden

Name		Funding
Ewa Paluch	Lab Leader	IIMCB*

*MEiN program (special research project)

Research Equipment Laboratory

Name		Funding
Pawel Bieganowski	Fellow	IIMCB(1/2)
Beata Bielinska	Fellow	IIMCB(1/2)
Malgorzata Durawa	Fellow	IIMCB (1/2)
Wanda Gocal	Technician	IIMCB
Izabela Szamreta	Technician	IIMCB(1/2)

School of the Science Festival

Name		Funding
Joanna Lilpop	Head	IIMCB
Marta Badurek	Organizer	Volunteer
Agnieszka Chołuj	organizer	Volunteer
Anna Lorenc	consultant	Volunteer
Takao Ishikawa	Teacher, consultant	Volunteer
Aleksandra Kwiatkowska	Teacher	Volunteer
Berenika Pokorska	Teacher	Volunteer
Agata Rogowska	Teacher	Volunteer
Anna Zarebska	Teacher	IIMCB
Maciej Kotlinski	Teacher	Volunteer
Sebastian Pawlak	Teacher, consultant	IIMCB
Wojciech Grajkowski	Teacher	Volunteer
Grzegorz Papaj	Teacher	Volunteer
Krzysztof Brewczynski	Teacher, organizer	Volunteer
Anna Karnkowska	Teacher	Volunteer
Michał Mlacki	Teacher, technician	Volunteer
Jakub Urbanski	UNESCO grant coordinator	IIMCB/UNESCO grant
Eliza Glodkowska	Teacher	Volunteer
Piort Mrowka	Teacher	Volunteer
Katarzyna Gieczewska	Teacher	Volunteer
Roman Szczesny	Teacher	Volunteer
Monika Hejnowicz	Teacher	Volunteer
Justyna Rudzka	Teacher	Volunteer
Bartosz Tarkowski	Teacher	Volunteer
Weronika Wronowska	Teacher	Volunteer

Infrastructure and Working Environment

The building of the Institute offers 16820 m^3 of cubic space, with 4032 m^2 of internal surface. It is divided into seven floors and a basement. The administrative sector is located on the ground floor (Directors' offices, the lecture hall for 60 people, Institute's library/meeting room, other offices and social rooms). Five floors, from the 1st till the 5th, are arranged as a typical laboratory space, a "Faraday - cage" lab for sensitive electronic measurements (e.g. electrophysiology), a cold-room, a dark room, several offices, social rooms and common space for heavy laboratory equipment (see: http://www.iimcb.gov.pl/equipment.php). On the 4th floor there is a computer facility of the Institute (including servers) and on the 5th floor a part of the laboratory space is prepared to accommodate a cell and molecular biology school (training laboratory for 18 students).

The infrastructure of the Institute is fully adapted to the safety and biosafety regulations for chemistry and molecular biology laboratories. All laboratories have been equipped with modern apparatus in accordance with the highest international standards. In addition to the regular equipment in each wet laboratory, there are pieces of apparatus shared by all researchers. There are centrifuges and ultracentrifuges, sets of FPLC and HPLC systems, chromatography system ACTA, a real-time thermocycler, fluorescence microscopes, phosphoimagers, incubators and shakers for bacterial cultures, electroporators for transfections and transformations, freezers (-70°C). There are also seven cell culture labs fully equipped with incubators, laminar-flow hoods, and microscopes, three cold-rooms, and two sets of water deionizing units. The isotope laboratory has been recently equipped (including a new scintillation counter) compliant with the Polish and EU law regulations. The Laboratory of Structural Biology, fully financed by the Max Planck Society, Max Planck Institute of Molecular Cell Biology and Genetics in Dresden, is furnished with the most modern research equipment including a high brilliance rotating anode generator (RU-H3RHB from MSC), Max-Flux confocal optical mirrors, a MAR345 low noise X-ray detector and a cryosystem.

Due to its uniqueness, this equipment serves members of the entire scientific community interested in protein crystallography analysis. Among new pieces of equipment recently acquired at IIMCB are: surface plasmon resonance measuring system Biacore 3000, confocal microscope, flow cytometer, CD spectropolarimeter, microplate reader.

The building is equipped with ventilation, air conditioning, smoke alarms and fire escapes according to current regulations. Offices and lecture halls are separated from the laboratory space. Three lecture halls allow for intensive seminar programs, without any restrictions concerning time schedules. The practical courses are organized in a separate laboratory that is an important element for comfort and work safety. Being part of a large building complex, IIMCB has access to the following: six lecture halls (from 20 to 300 people), an exhibition hall, a hotel, a cafeteria, as well as other facilities belonging to the neighboring research institutes of the Ochota Campus.

The IIMCB facilities, as well as the whole campus complex, are fully accessible for the disabled. Medical, social and legal services are accessible to the entire staff on-site. A security guard system operates on the entire campus around the clock.