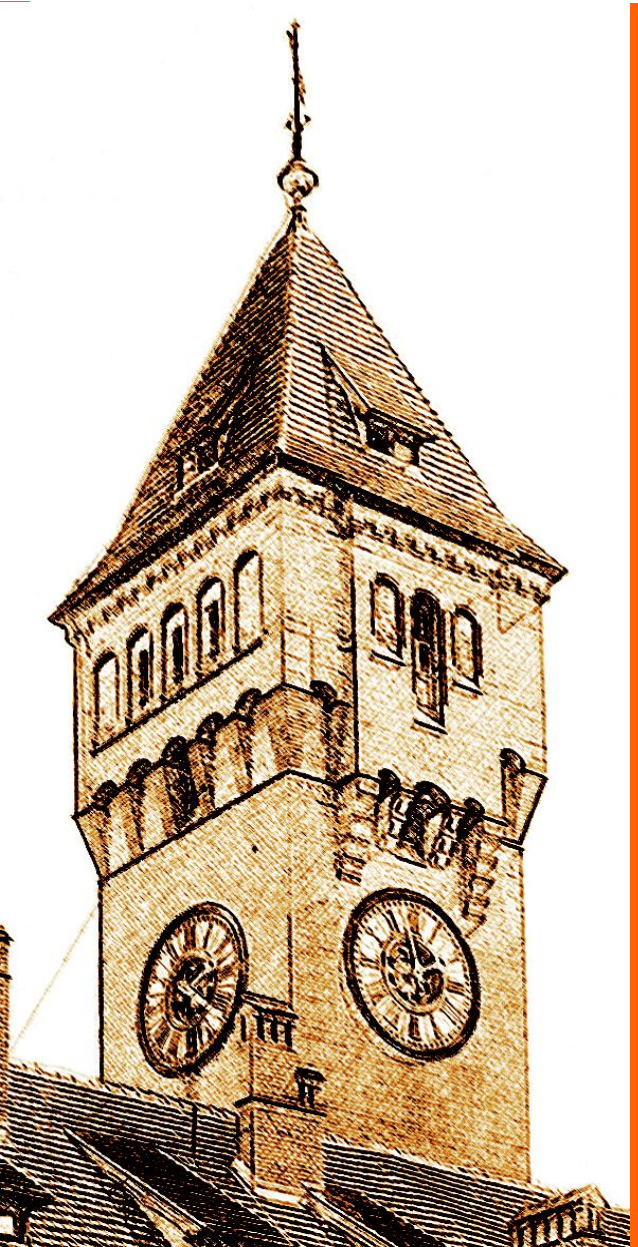
INNOWACYJNA GOSPODARKA
NARODOWA STRATEGIA SPÓJNOŚCI

Wrocławskie Centrum Badań EIT+

UNIA EUROPEJSKA
EUROPEJSKI FUNDUSZ ROZWOJU REGIONALNEGO



Focus on Biomedical Applications

Jacek Otlewski
(Scientific coordinator of the BioMed project)

Wrocławskie Centrum Badań EIT+ Sp. z o.o.

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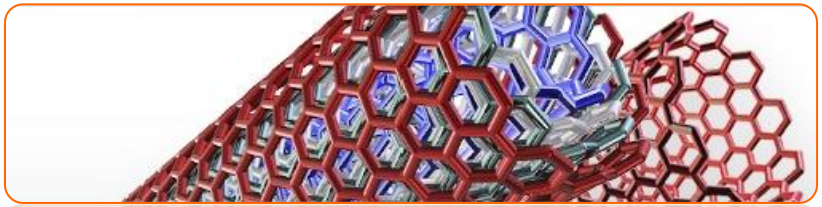
European Research Infrastructures for Innovation and Development,
Wroclaw, June 16-17, 2010

Wroclaw Research Centre EIT+

Two major EU-sponsored projects

Biotechnology and medical technologies
BioMed (27,6 mln Euro)



Nanotechnology and nanomaterials
NanoMat (31 mln Euro)

plus

146 mln Euro – for infrastructure
(labs and instrumentation at Pracze Campus)

BioMed Project: Cooperation with scientists and research institutions

Project contractors – selected in tenders:
Universities and research organizations from Lower Silesia and Poland, including:

- University of Wroclaw
- Wroclaw Medical University
- Wroclaw University of Environmental and Life Sciences
- Wroclaw University of Technology
- Institute of Immunology and Experimental Therapy, Polish Academy of Sciences
- Opole University

Laboratory base:

- existing labs of the contractors (years 2009-2012)
- new laboratory centre at Campus Pracze (years 2013-2014)

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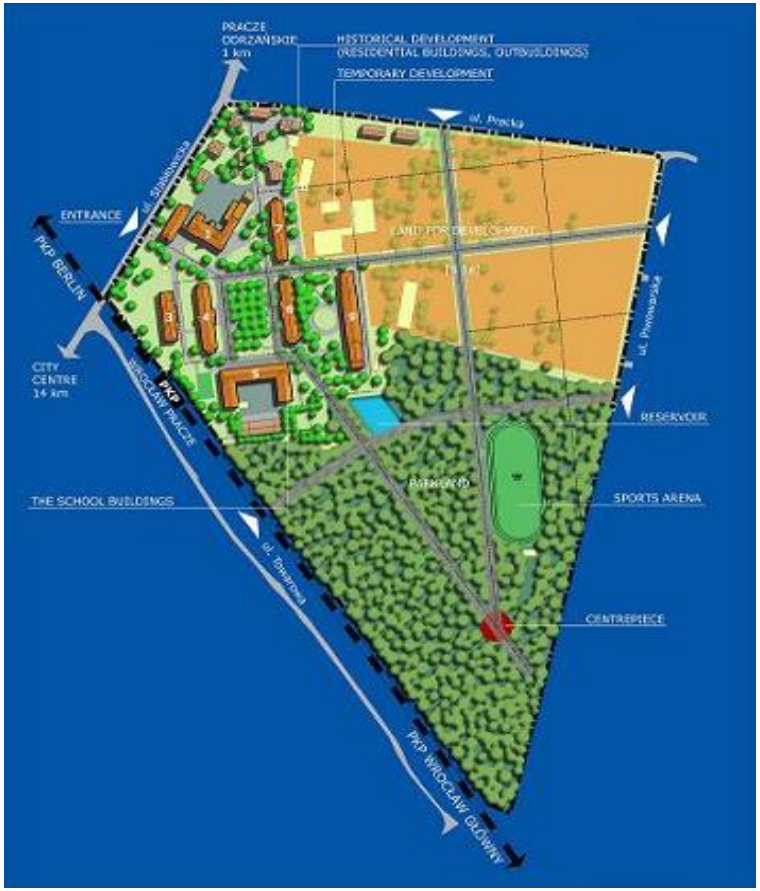
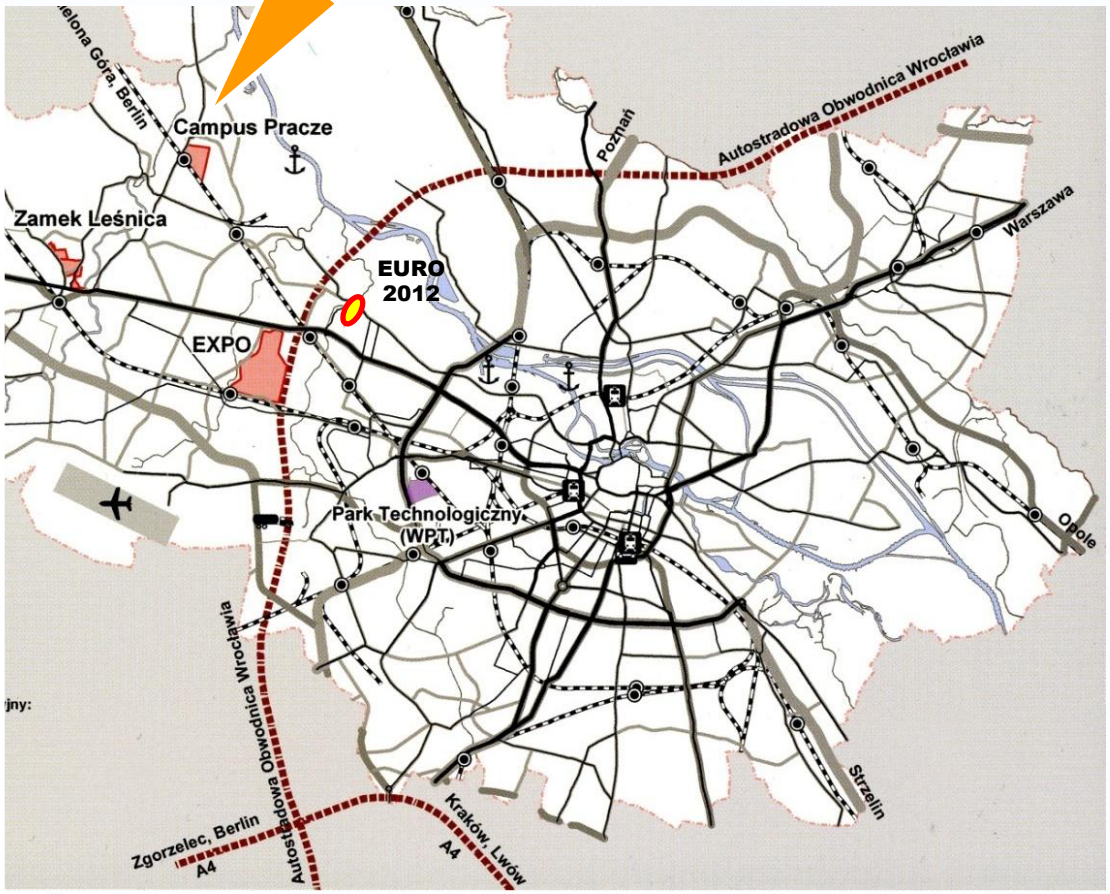
Location





BIOMED Project

General goal of BioMed project:

- development of novel drugs, drug delivery systems, and biomaterials for disease treatment, diagnostics, and prevention,
- in summary, 15 individual tasks, 14 of them have been initiated in December, 2009.

Selected tasks objectives:

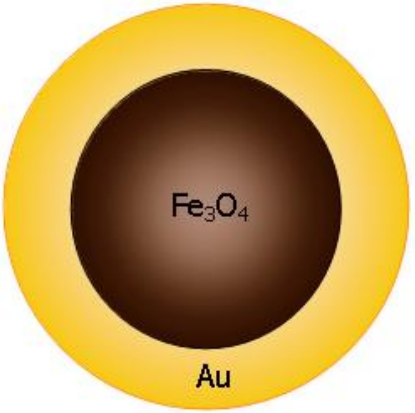
- construction of multifunctional bionanoparticles applicable in directed drug delivery, imaging and diagnostics,
- generation of new forms of pharmaceuticals for more effective treatment of cancer diseases and bacterious infections,
- development of a standard method for the detection of hallucinogenic substances in biologic materials, including blood and urine,
- mechanisms and regulation of iron/heme uptake in *Porphyromonas gingivalis*: application in diagnostics and treatment of periodontitis,
- design of novel compounds effective in anti-leukemic therapies.

Synthesis and applications of bionanomaterials for specific medical applications

Leader: Professor Jacek Otlewski

Main biotechnological objectives:

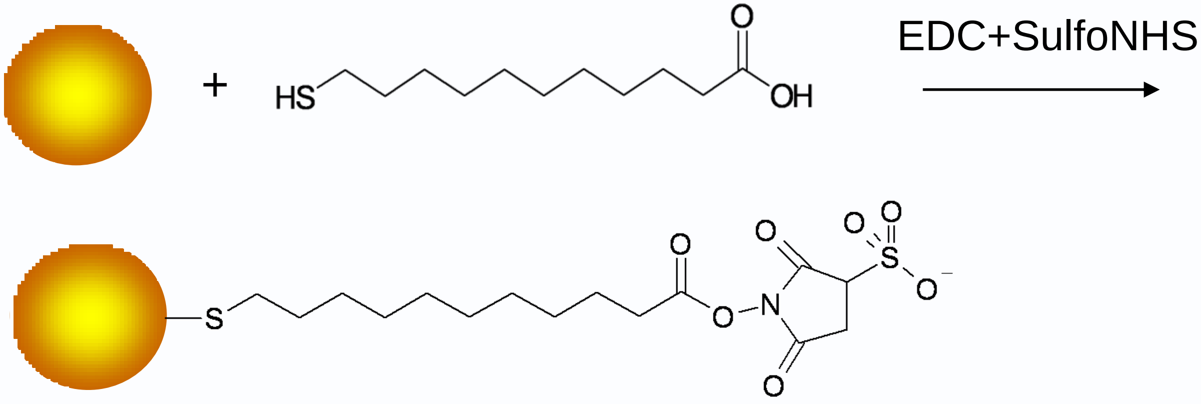
- development of magnetic bionanoparticles as tumor destroying agents via hyperthermic effect
- synthesis of nanoparticles based on superparamagnetic metal oxides coated with gold
- development of novel methods of nanoparticle coating with protein-based drug
- development of phage-display selected non-IgG proteins for specific recognition of breast and prostate cancer markers
- construction of temperature-inducible drug release linkers

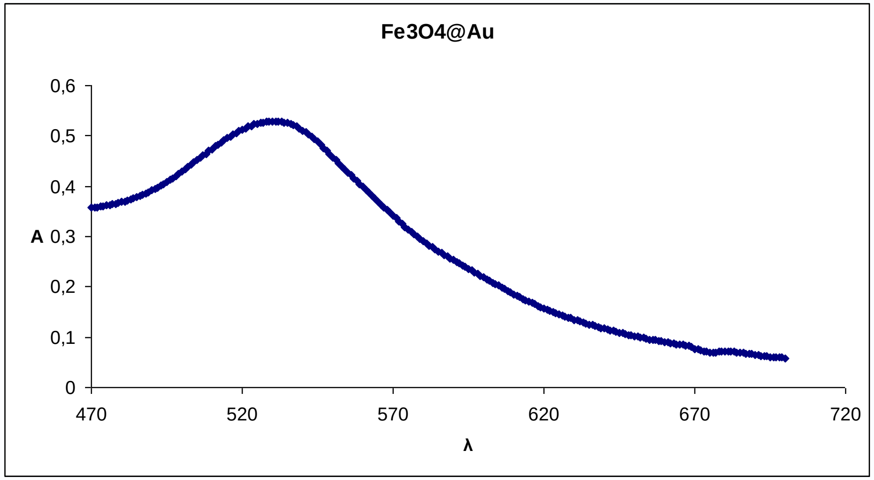


Schematic structure of gold coated ferrite nanoparticle (Fe_3O_4@Au)

Synthesis and applications of bionanomaterials for specific medical applications

Modification of nanoparticles with 11-mercaptoundecanoic acid, activation of carboxylic groups



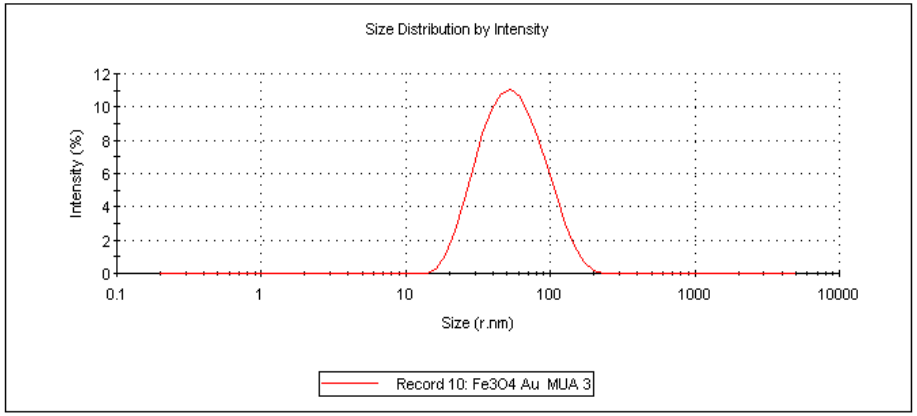


Absorption spectra of Fe_3O_4@Au

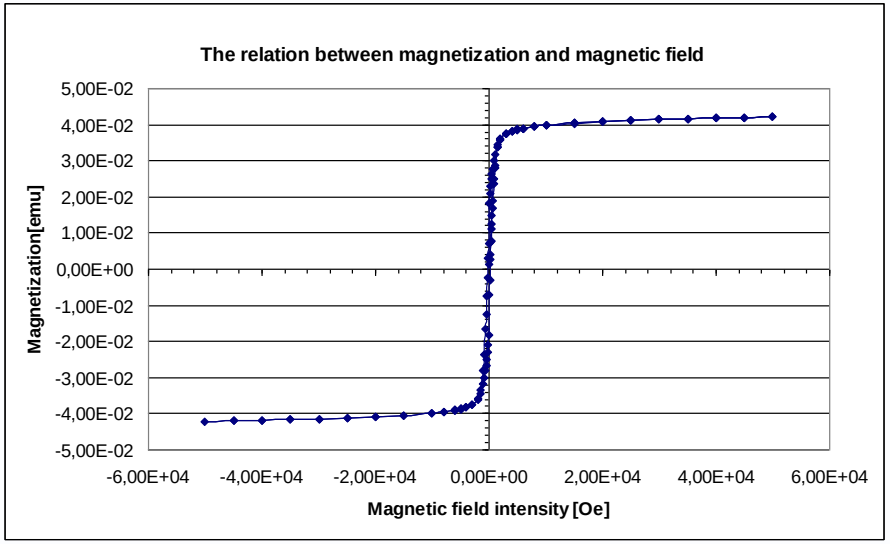
Synthesis and applications of bionanomaterials for specific medical applications

DLS and SQUID analysis of nanoparticles

		Diam. (nm)	% Intensity	Width (nm)
Z-Average (r.nm): 45,28	Peak 1:	60,32	100,0	30,46
PdI: 0,255	Peak 2:	0,000	0,0	0,000
Intercept: 0,927	Peak 3:	0,000	0,0	0,000
Result quality : Good				



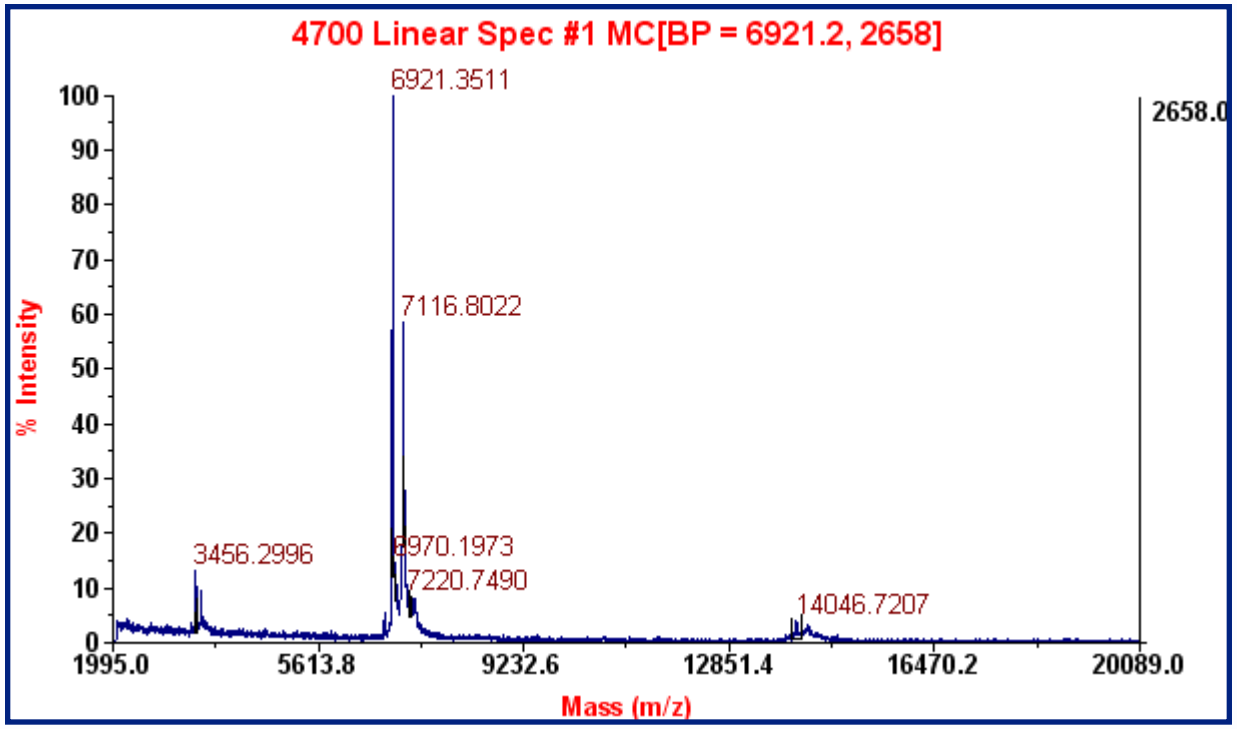
DLS analysis of Fe_3O_4@Au nanoparticles coated with 11-mercaptoundecanoid acid



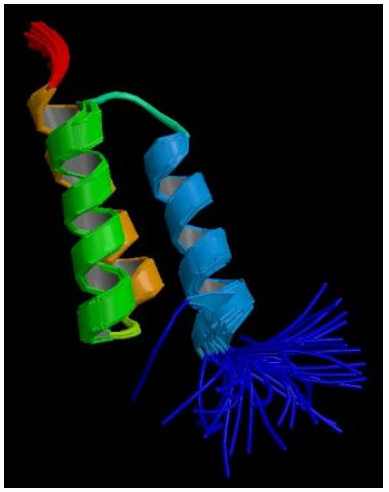
The relation between magnetization and magnetic field intensity at constant temperature (2K). The maximum value of magnetization is 9,76 emu/g.

Synthesis and applications of bionanomaterials for specific medical applications

MS-spectrum of MUA-linked affibody anti-Her2 after reduction with 2-mercaptoethanol



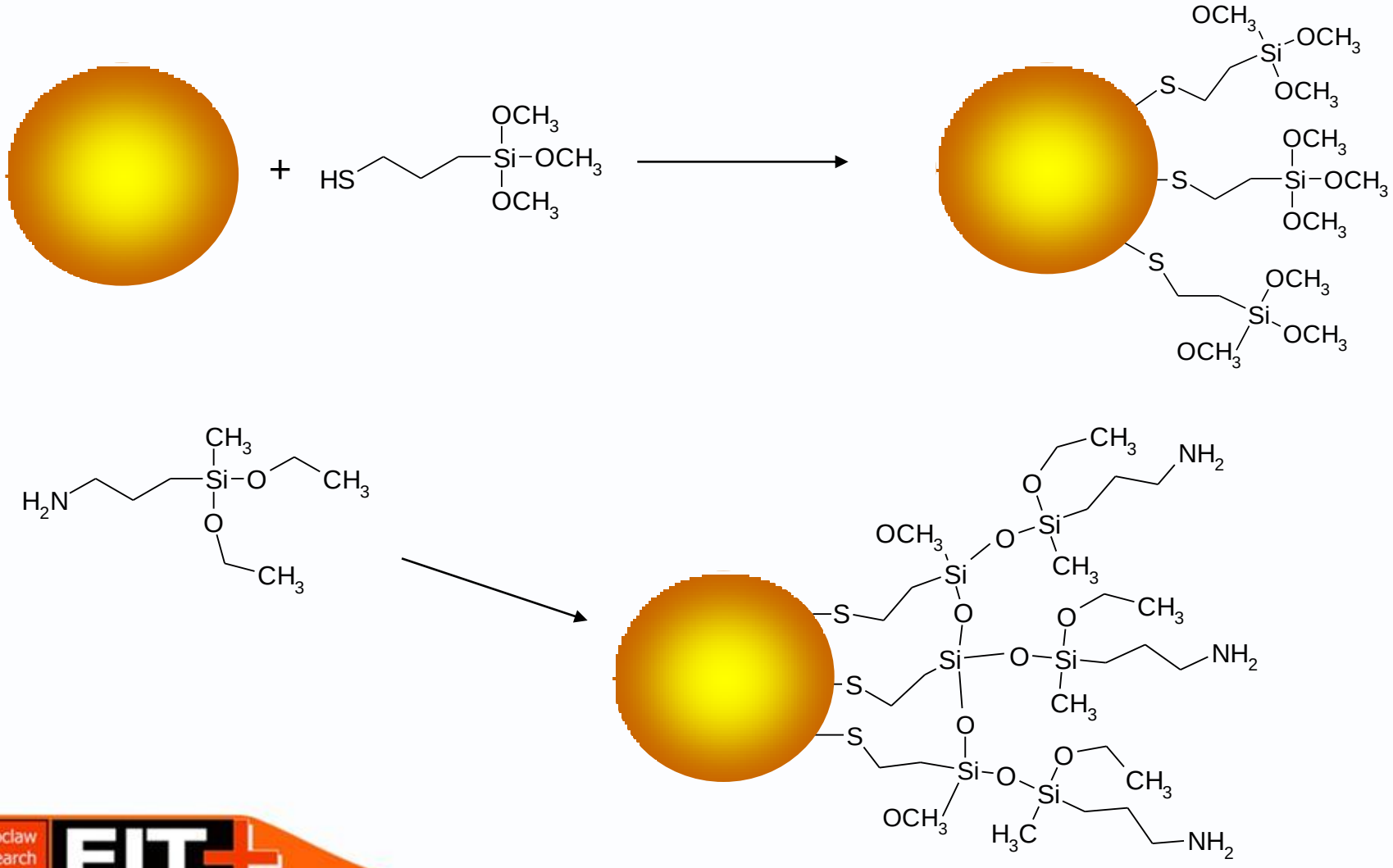
Affibody



PDB: **2B88**

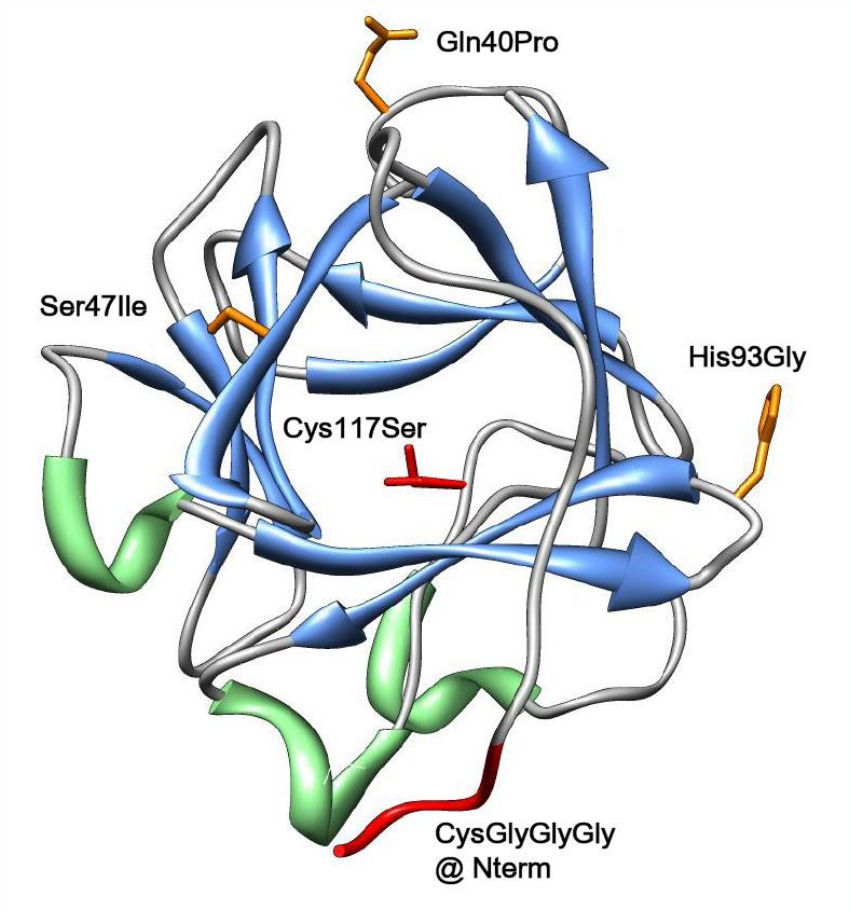
Synthesis and applications of bionanomaterials for specific medical applications

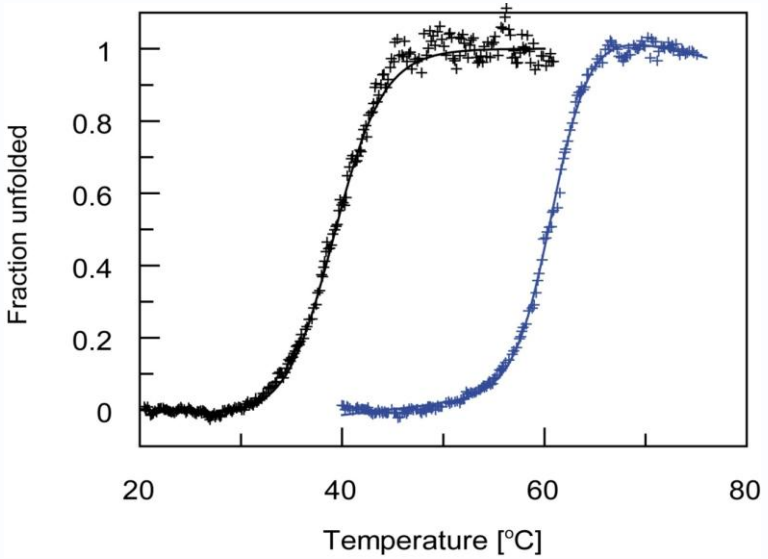
Presentation of amine groups on the surface of nanoparticles by modification with silanes



Synthesis and applications of bionanomaterials for specific medical applications

FGF1 variant designed for conjugation



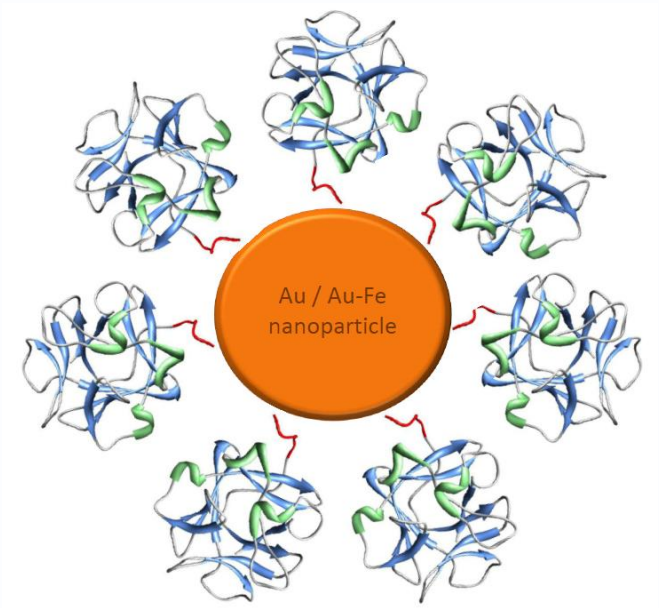


— FGF1 WT

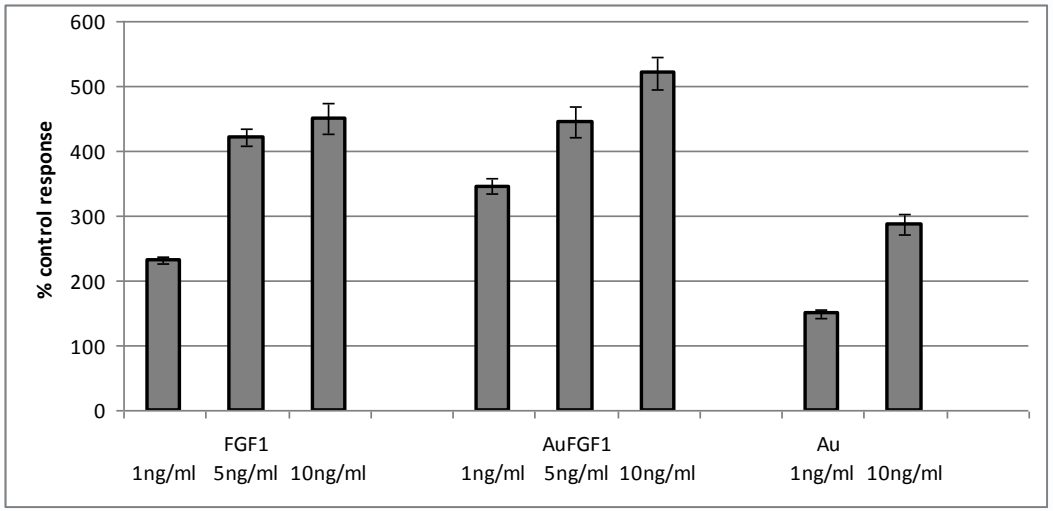
— FGF1 mut

Synthesis and applications of bionanomaterials for specific medical applications

FGF1 mutant conjugated to gold nanoparticles



NIH 3T3 response (proliferation assay)

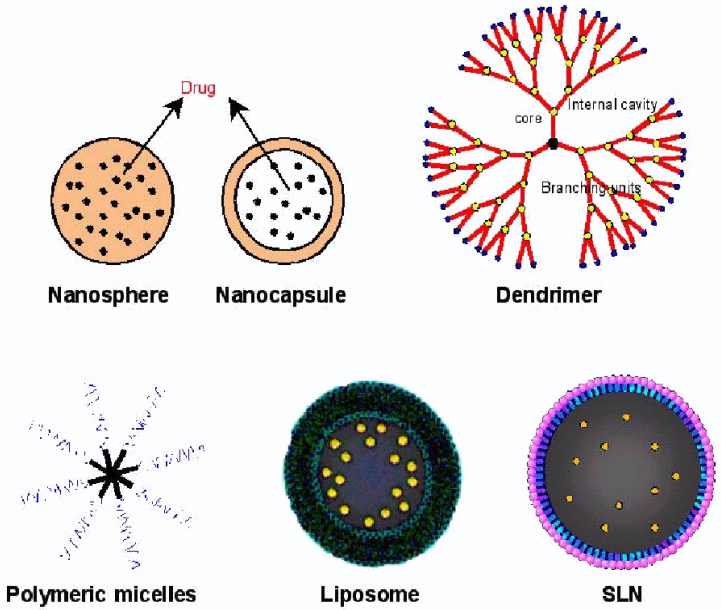


Supramolecular forms of bioactive substances - from projects to products

Leader: Professor Aleksander Sikorski

Main biotechnological objective:

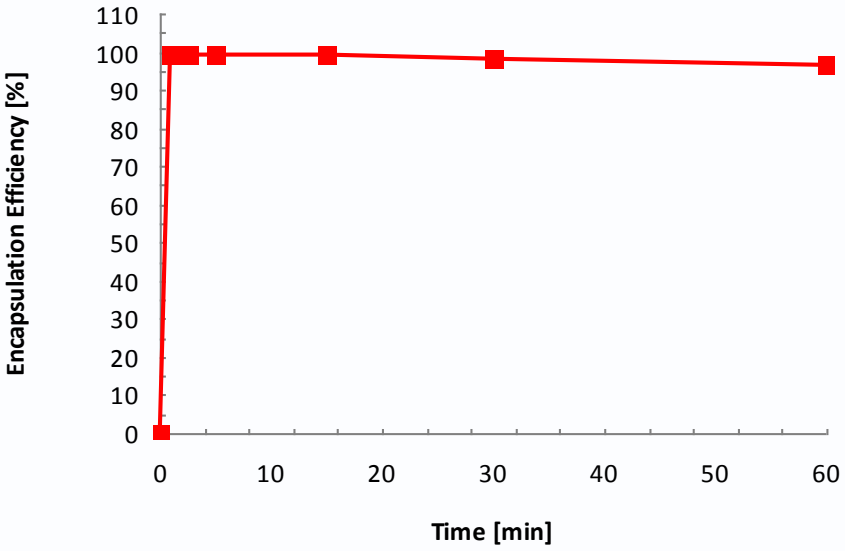
- development of novel liposomal compositions
- characterization nanoencapsulated bioactive substances:
  - low molecular weight anticancer drugs,
  - anti-inflammatory drugs,
  - antibacterial substances,
  - siRNA



Different forms of supramolecular drugs

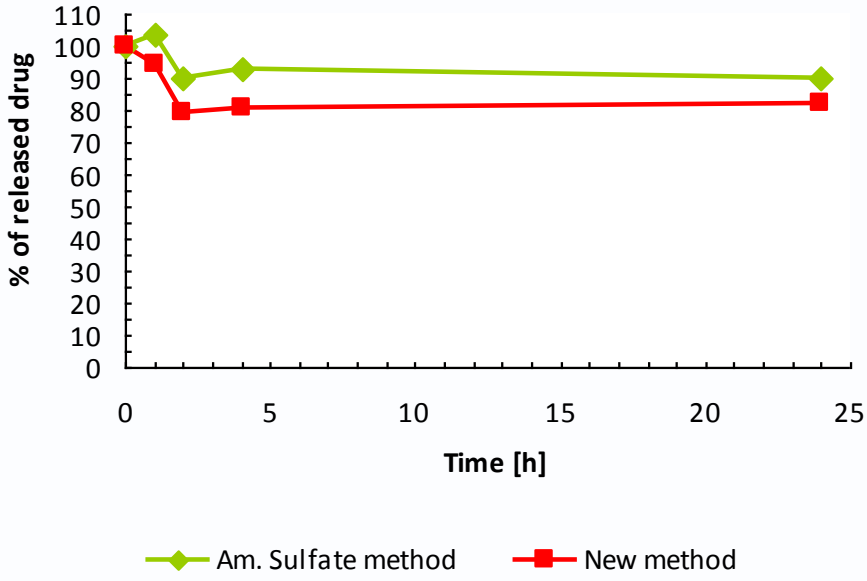
Supramolecular forms of bioactive substances - from projects to products

Encapsulation of the doxorubicin within liposomes using a new active loading method



Loading kinetics of the doxorubicin into the HSPC/Chol/DSPE-PEG 2000 (mol/mol 5.5:4:0.5) liposomes using the new ion gradient method. The process was performed at 60ºC at the drug to lipid 1:5 molar ratio.

Plasma stability of the doxorubicin-loaded liposomes



Stability of the doxorubicin containing HSPC/Chol/DSPE-PEG 2000 (mol/mol 5.5:4:0.5) liposomes in the 50% human plasma at 37ºC. The drug was encapsulated using ammonium sulfate method and the new method at the 1:5 molar ratio.

Identification of hallucinogenic substances

Leader: Professor Paweł Kafarski

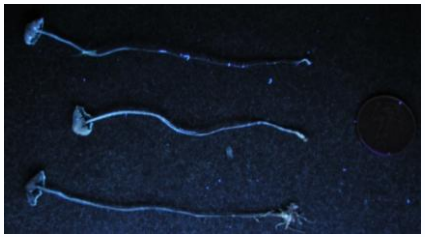
Main technological objective:

- identification of hallucinogenic mushrooms and edition of their photographic register (for the police use)
- isolation and purification of hallucinogenic compounds
- determination of the structures of major hallucinogens
- elaboration of suitable techniques for quantification of these substances in mushroom tissues and body fluids

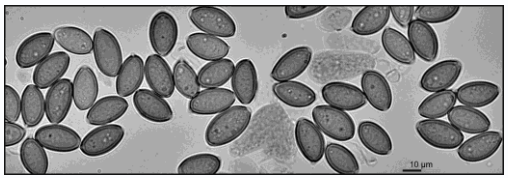
Psilocybe semilanceata

Naturally occurring fungi

Dried fungi



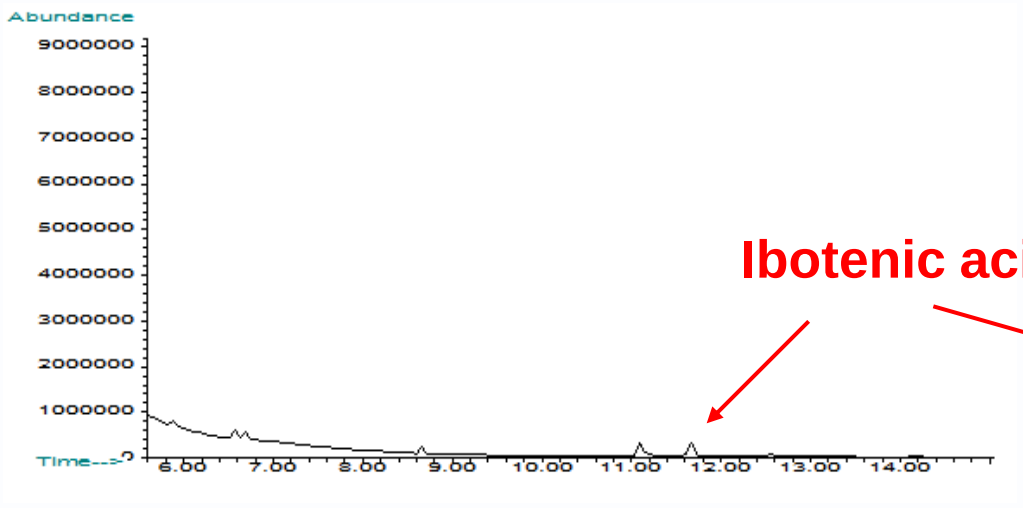
Dried fungi in UV light



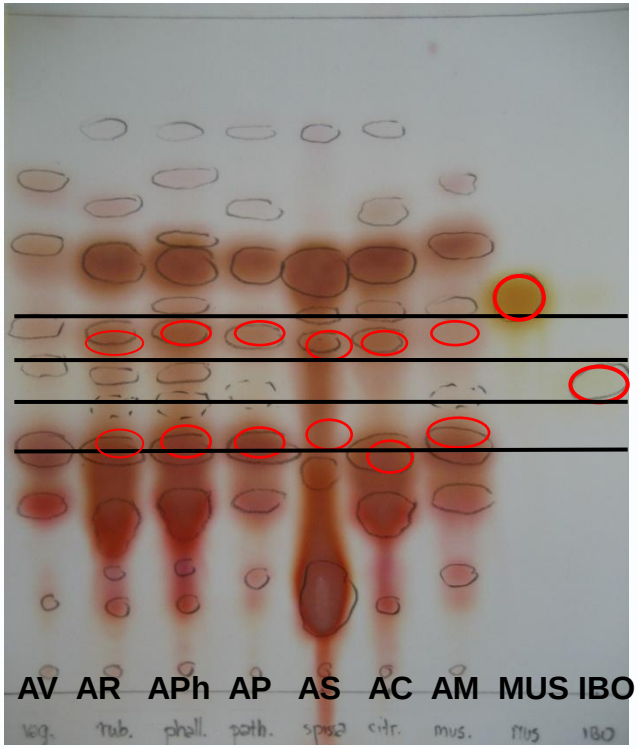
Spores

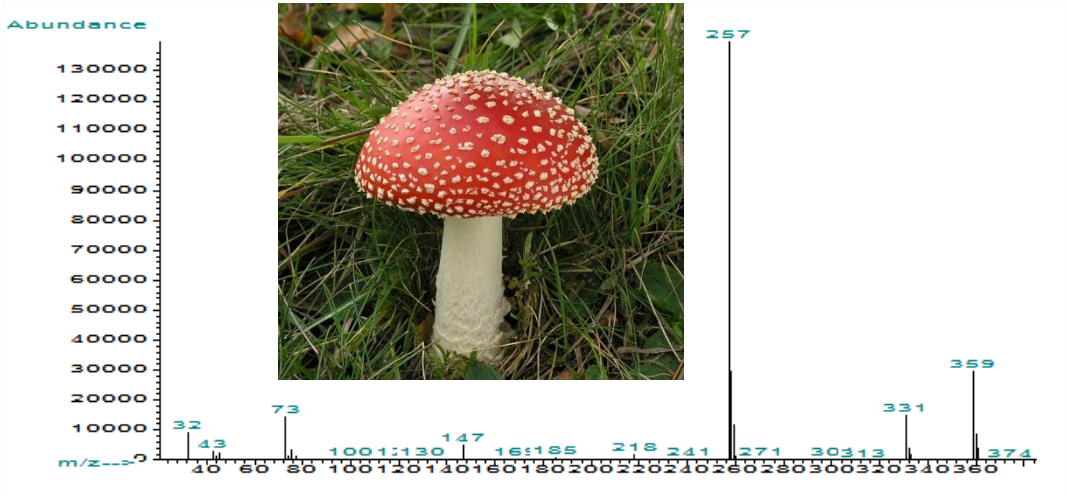
Identification of hallucinogenic substances

Detection, identification and quantification of hallucinogenic substances



Ibotenic acid



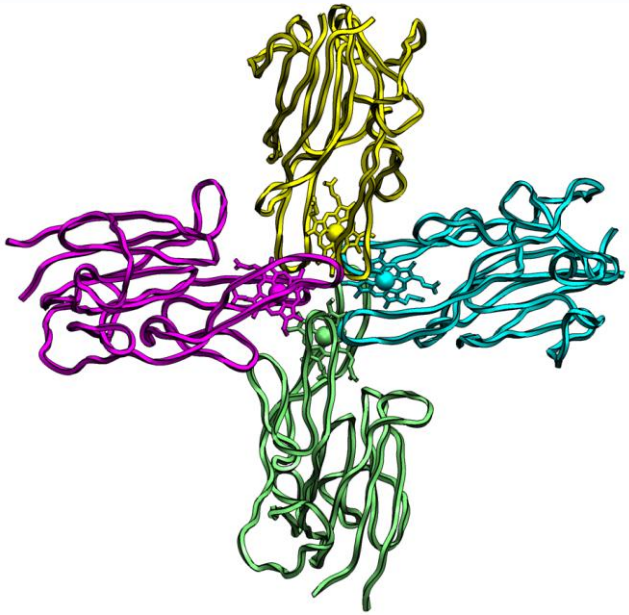


Mechanisms and regulation of iron and heme uptake in *Porphyromonas gingivalis* and their practical use in periodontitis treatment

Leader: Professor Teresa Olczak

Main biotechnological objectives:

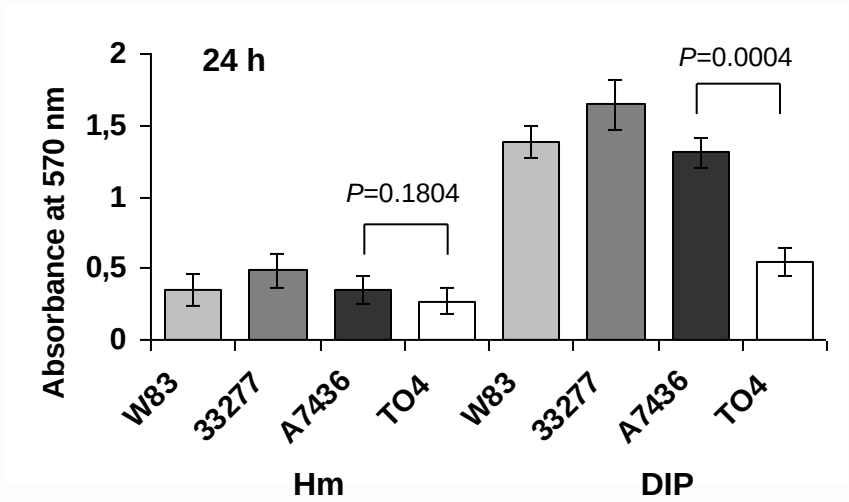
- analysis of the heme-binding outer membrane receptors and lipoproteins, regulatory Fur protein and other ferric uptake modulators
- research of host-pathogen interactions based on lipoprotein recognition through Toll-like receptors
- design of therapeutic agents blocking the heme uptake and host-pathogen interactions

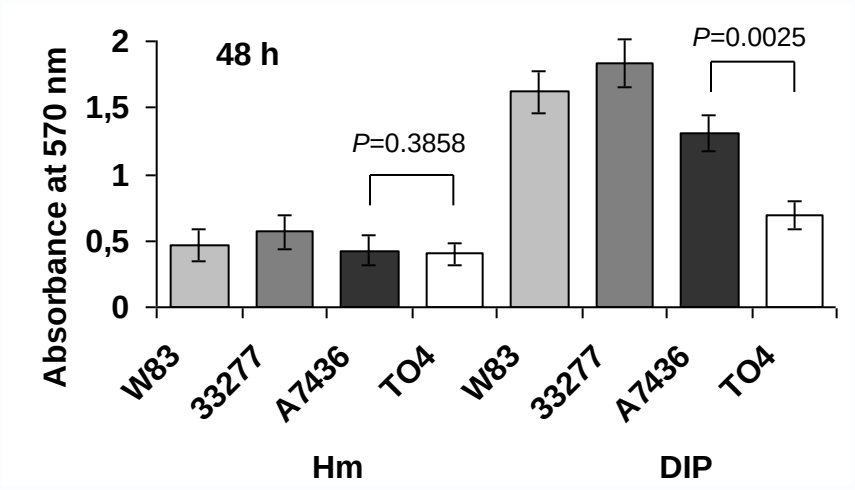


HmuY, protein involved in heme uptake in *P. gingivalis*

Mechanisms and regulation of iron and heme uptake in *Porphyromonas gingivalis* and their practical use in periodontitis treatment

HmuY is involved in biofilm formation by *P. gingivalis*





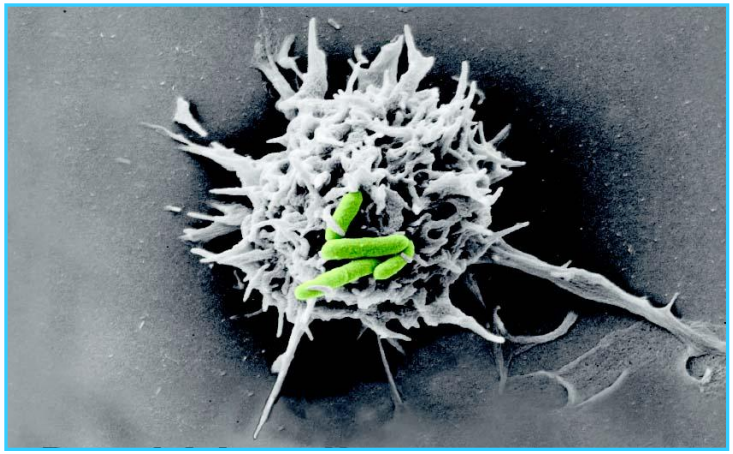
Hm - high iron/heme conditions;
DIP - low iron/heme conditions.

Molecular markers of diseases related to nuclear receptor dysfunctions – targets for diagnostics and therapy

Leader: Professor Ewa Marcinkowska

Main biotechnological objectives:

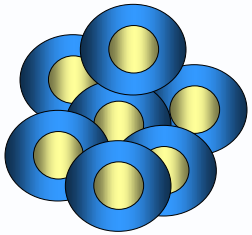
- introduce new therapeutic strategies using vitamin D analogs (VDAs) which induce differentiation of acute myleoid leukemias (AMLs) cells
- identify molecular markers that differentiate leukemias which are susceptible to treatment with VDAs
- design of diagnostic tests that allow to select patients for therapy using VDAs
- identification of cell surface markers specific for AML cells



Molecular markers of diseases related to nuclear receptor dysfunctions – targets for diagnostics and therapy

Methods

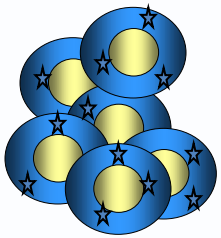
Isolate AML cells from patients



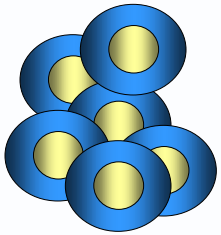
Study *in vitro* cell differentiation in response to VDAs

Define subpopulations of:

VDA-susceptible cells

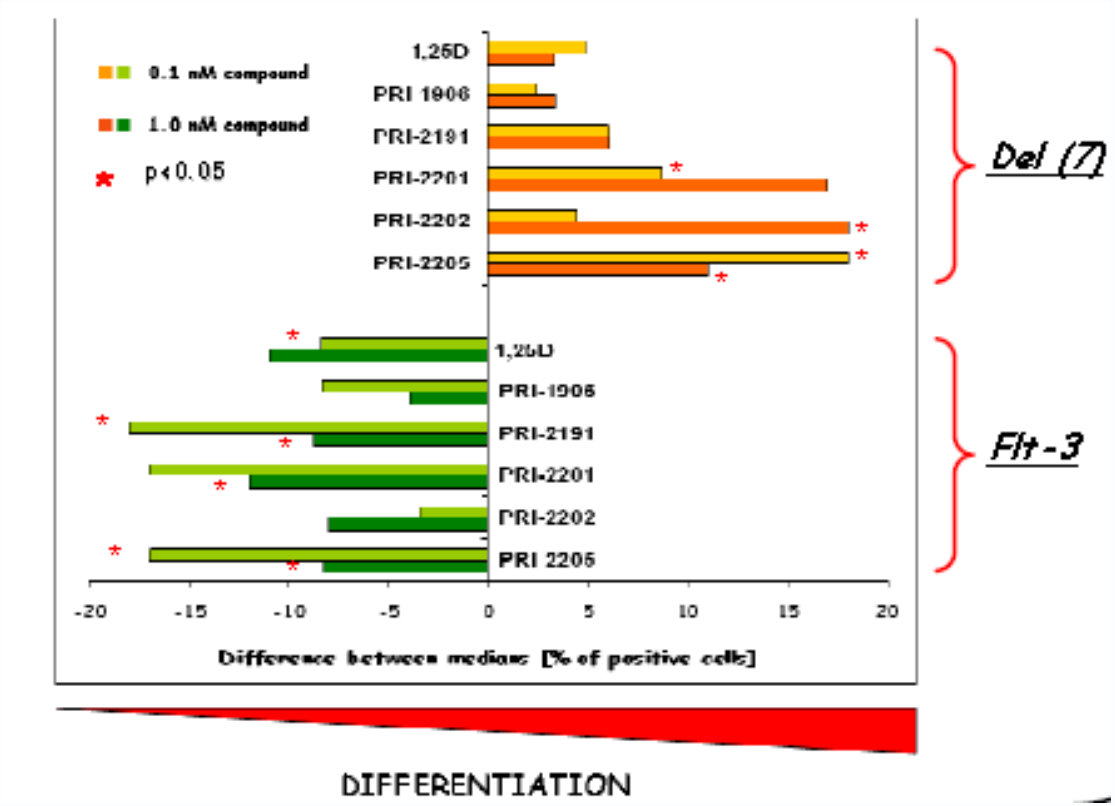


VDA-resistant cells



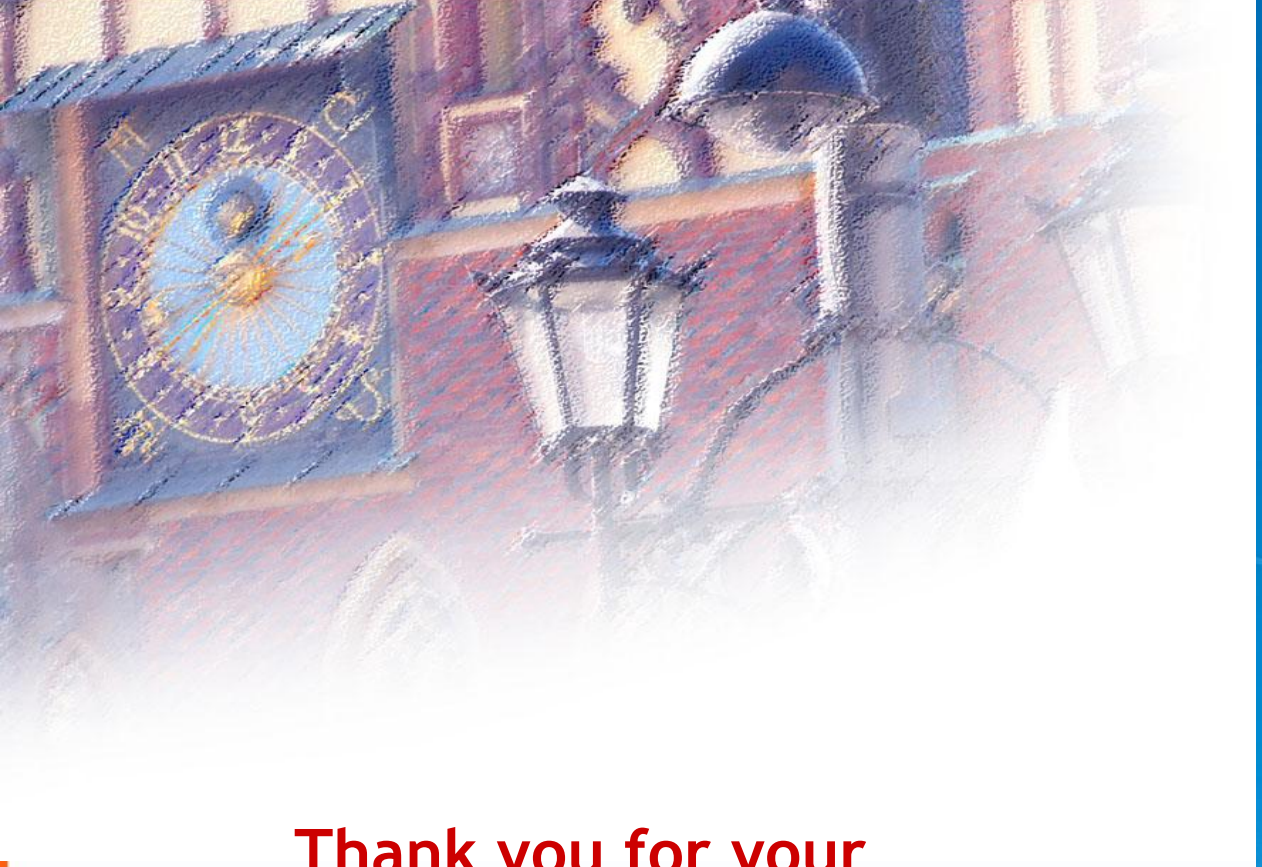
Molecular markers of diseases related to nuclear receptor dysfunctions – targets for diagnostics and therapy

Effect of chromosome 7 deletion and Flt-3 receptor mutations



Cells carrying deletion of chromosome 7 (or its fragment) are **sensitive** to VDAs-induced differentiation, while the cells with Flt-3 tyrosine kinase receptor mutations are **resistant** to the treatment.

Campus Pracze



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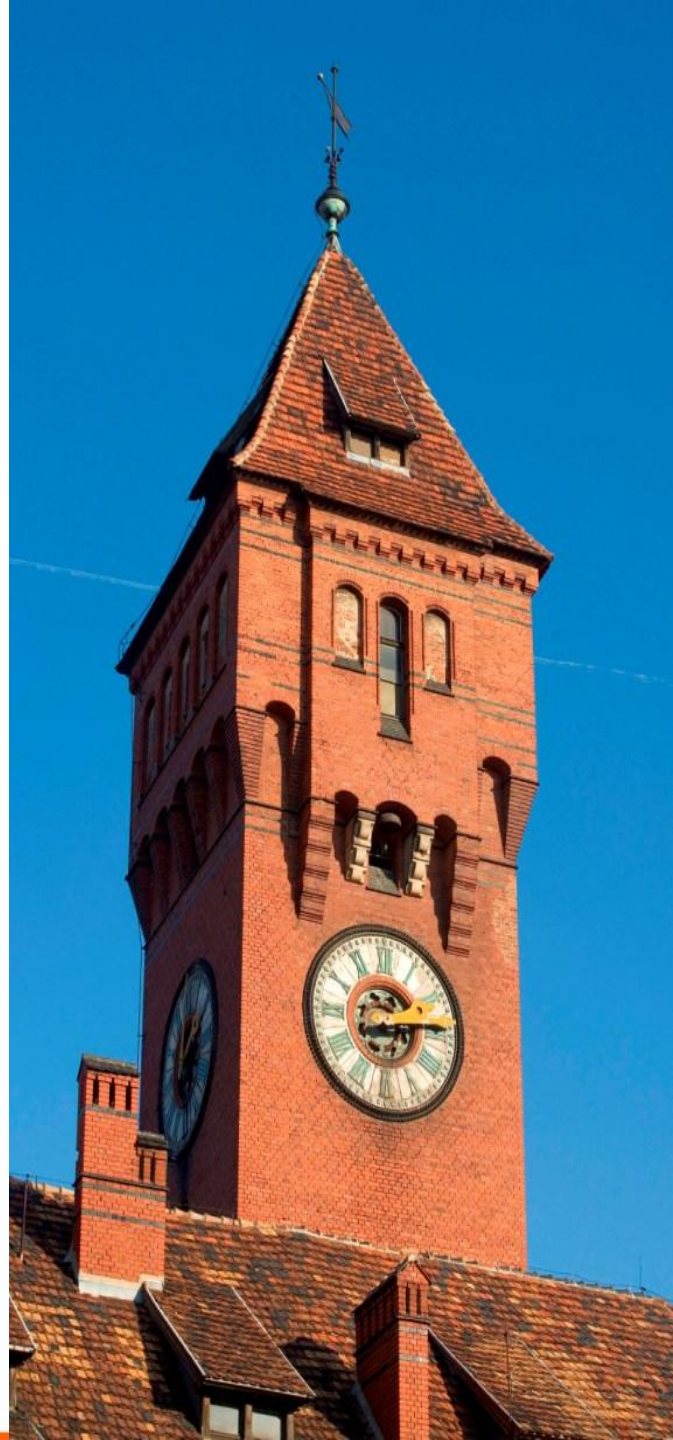

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