



Introduction to BIOMEDREG Project as a Research Platform for Molecular and Translational Medicine: from Discovery to Clinical Trials and Use



Marian Hajduch, MD, PhD

Laboratory of Experimental Medicine,
Institute of Molecular and Translational Medicine,
Faculty of Medicine and Dentistry,
Palacky University in Olomouc
Czech Republic



EUROPEAN UNION
EUROPEAN REGIONAL DEVELOPMENT FUND
INVESTING IN YOUR FUTURE



OP Research and
Development for Innovation



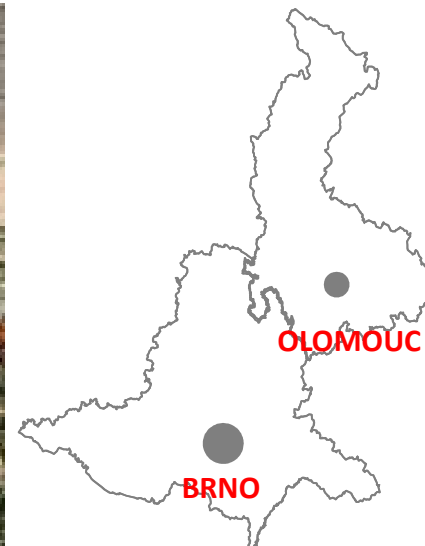
Content

1. Historical and regional consequences
2. Project BIOMEDREG
3. Cluster MedChemBio
4. EATRIS-CZ
5. Conclusions – Collaborative Opportunities



Palacký University in Olomouc

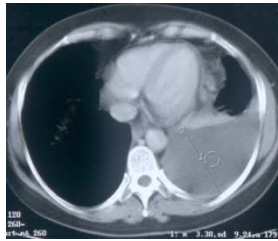
- Established in 1573
- The second oldest university after the Charles University in Prague
- Olomouc Archbishop – center of Moravian religion and education – alumni or region associated scientists: John Amos Comenius, Vincenz Priessnitz, **Johann Gregor Mendel**, Sigmund Freud, Konrad Zirm, Otto Wichterle, Frantisek Santavy, Jiri Bartek
- Currently 25.000 students, approx. 10% of Czech university students and 2.800 employees



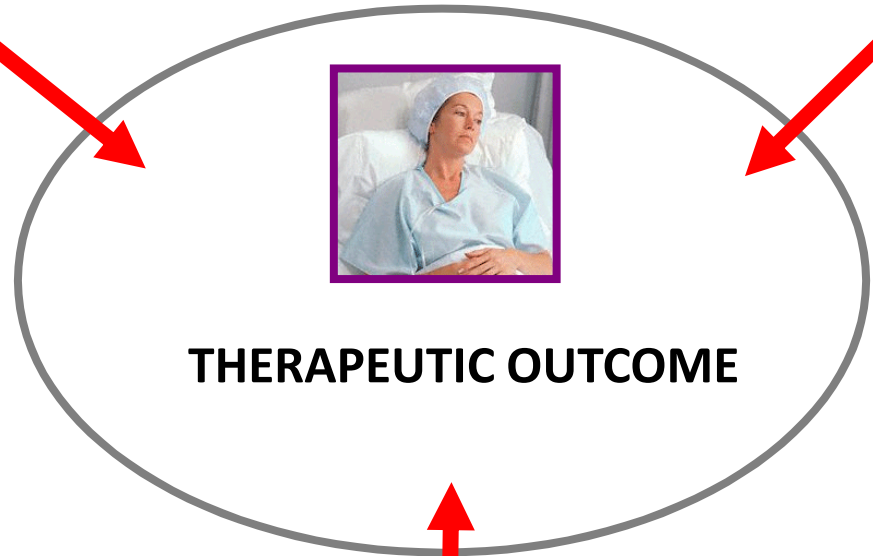
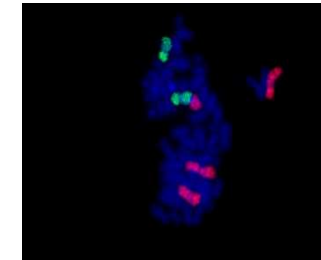


Major Determinants of Therapeutic Outcome

ANATOMIC STAGE
OF DISEASE
(DIAGNOSTICS)



TUMOR BIOLOGY
(BIOMARKERS & MOLECULAR
TARGETS)



THERAPEUTIC OUTCOME

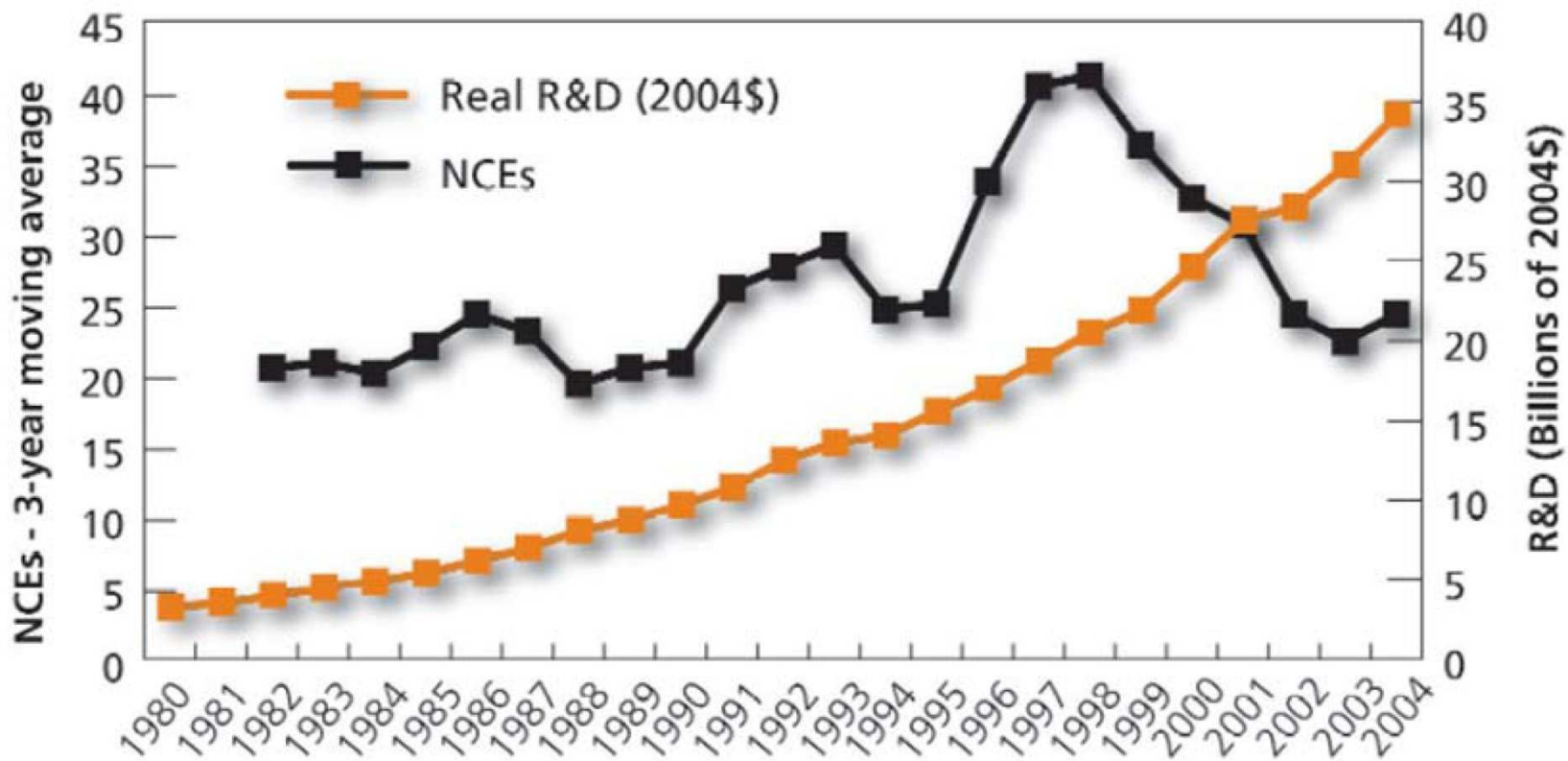
THERAPIES

(SMALL MOLECULES, BIOLOGICS, ATMPs)





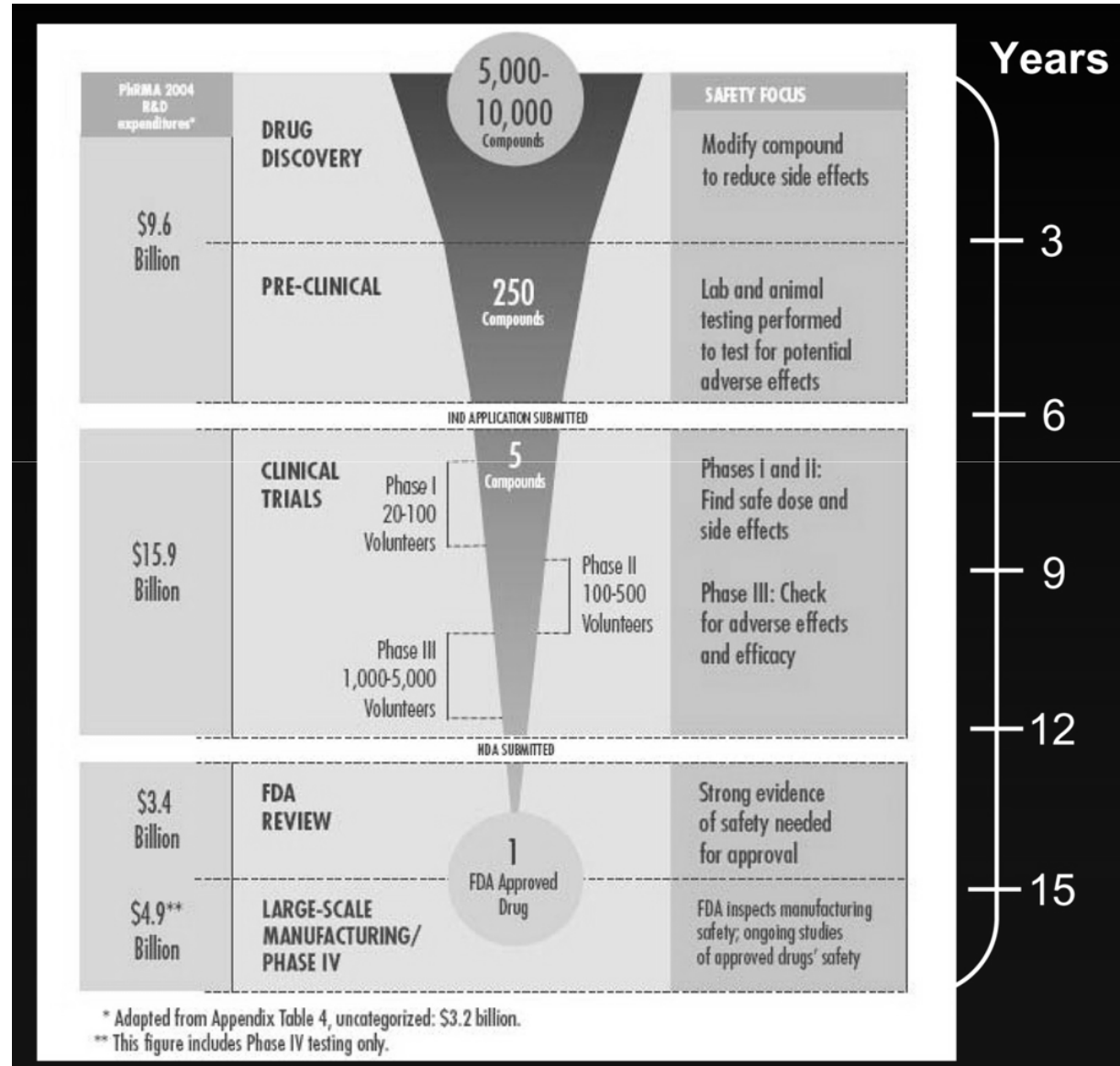
U.S. Pharmaceutical Industry Inflation-Adjusted R&D Expenditures and NCE Approvals, 1963-2004



Source: Tufts CSDD Approved NCE Database; PhRMA



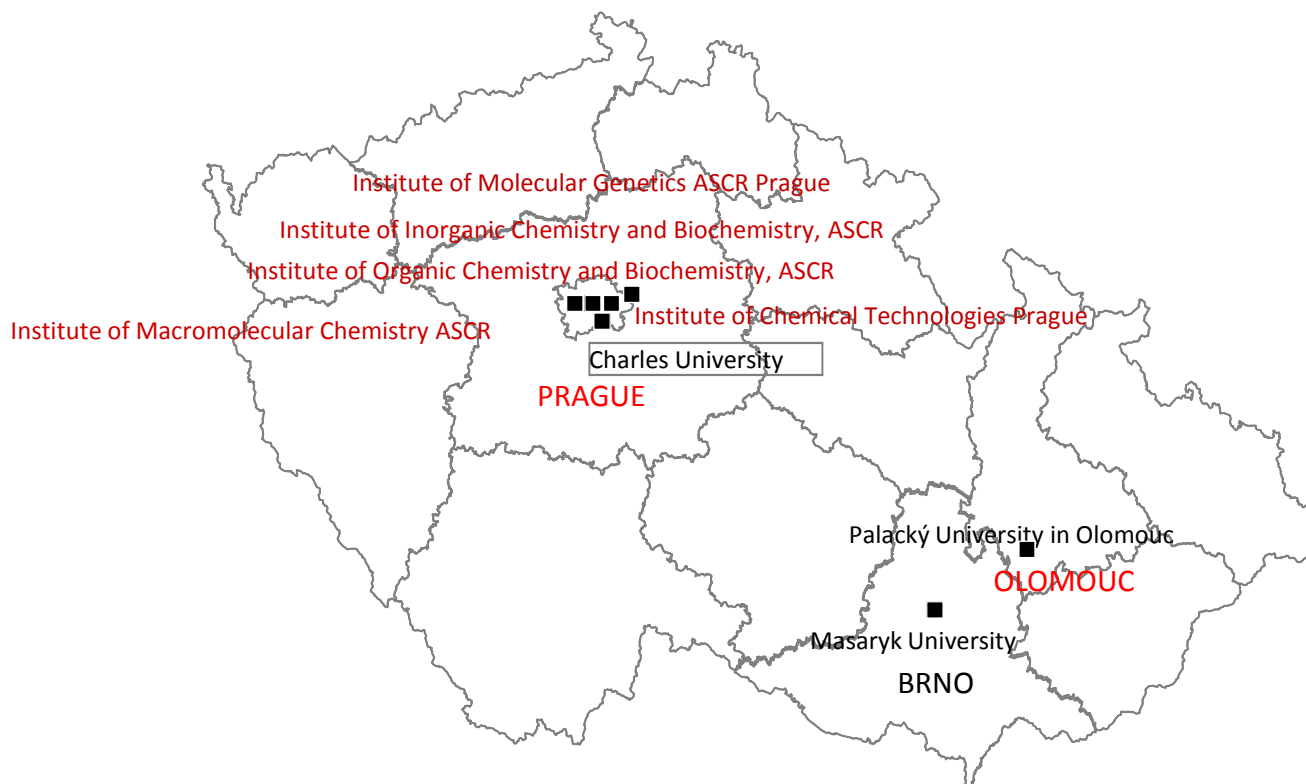
Compound Success Rates





Long-lasting tradition of chemistry in the country

Main medicinal chemistry, drug development and chemical biology centers
in the Czech Republic



BIOMEDREG



INSTITUTE OF MOLECULAR AND
TRANSLATIONAL MEDICINE

Biomedicine for regional development and human resources

BIOMEDREG

2nd Priority Axis OP VaVpl

Project Leader:

Palacký Universty in Olomouci

Partners:

University Hospital in Olomouc

Institute of Organic Chemistry and Biochemistry AS CR

Institute of Chemical Technologies in Prague

Allocation:

Approx. 40 M €

Phase of the Project:

Realization phase started on April 1, 2010

Information:

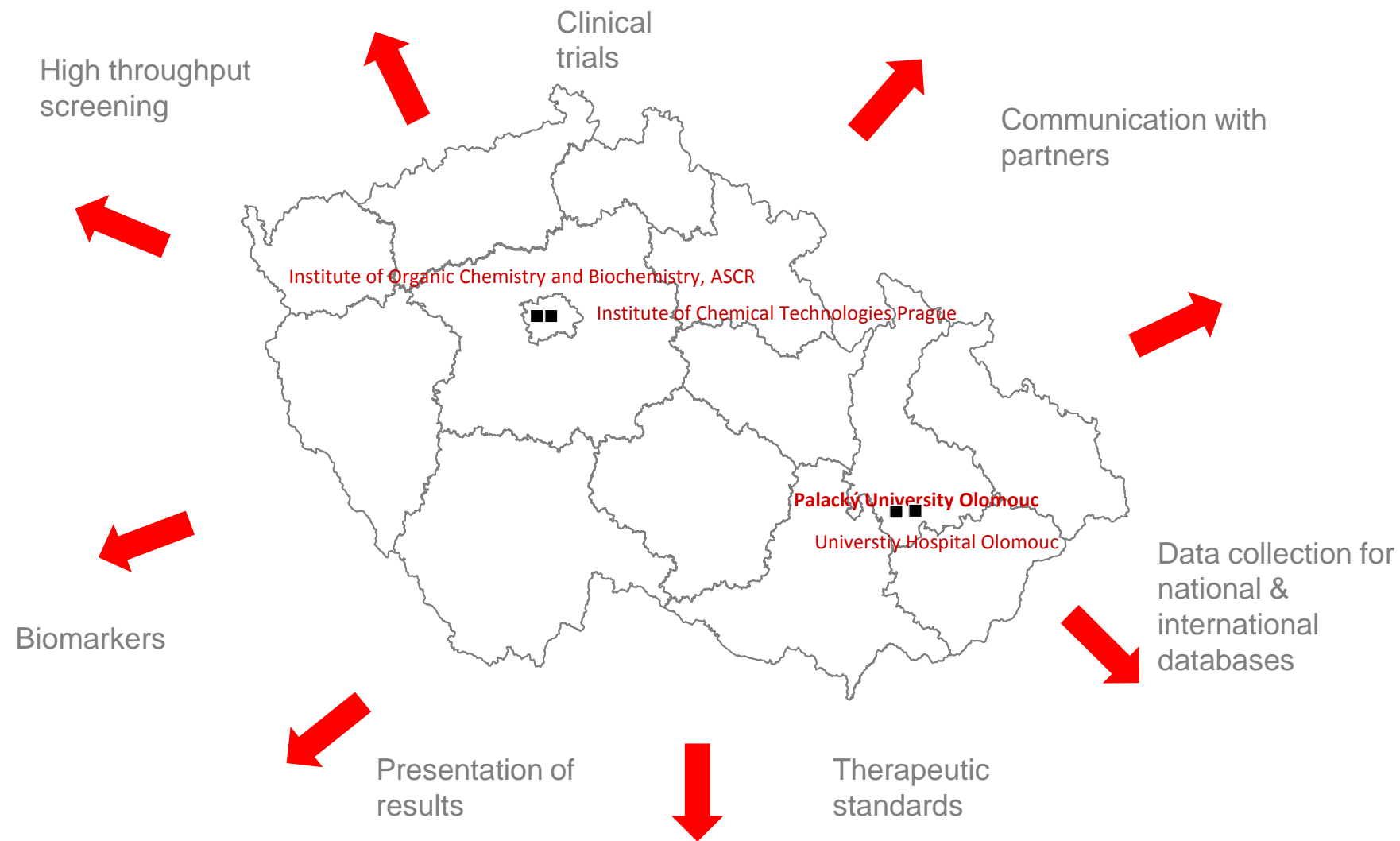
www.biomedreg.eu

BIOMEDREG



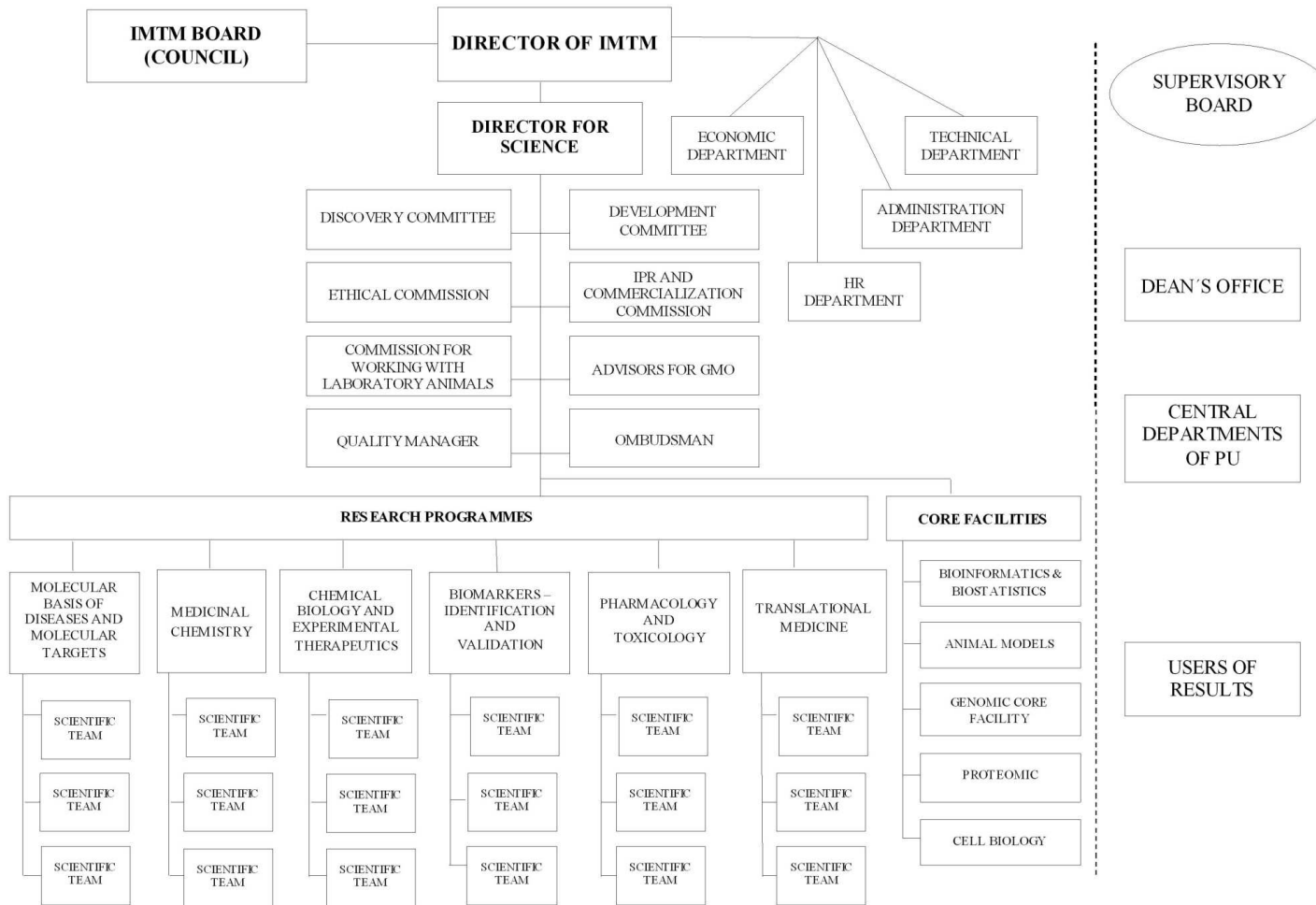
INSTITUTE OF MOLECULAR AND
TRANSLATIONAL MEDICINE

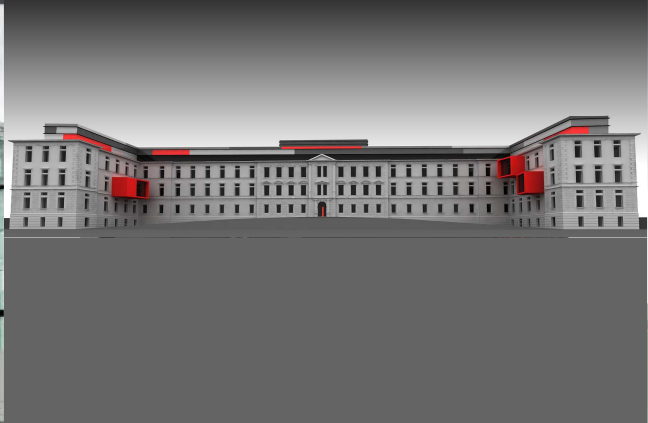
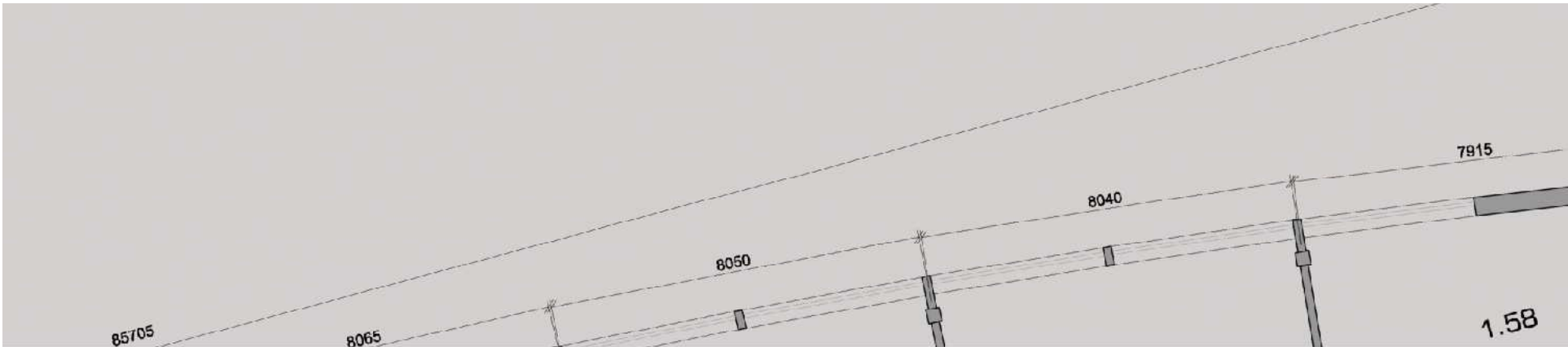
Infrastructural project for chemical biology and translational medicine (BIOMEDREG) – concentrating, evaluating and developing the national chemical knowledge





Institute of Molecular and Translational Medicine Management







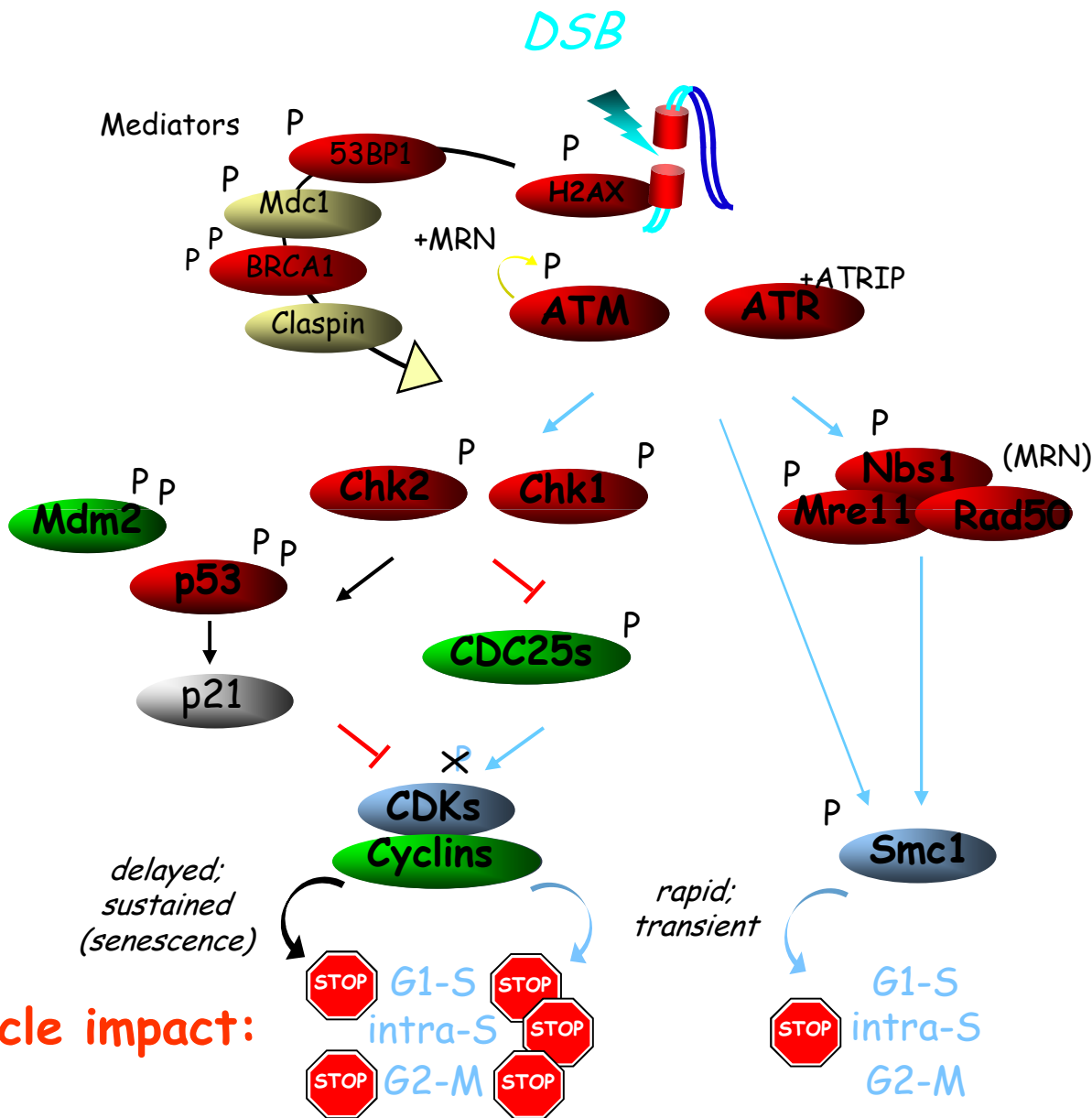
Research Program #1- Molecular Mechanisms of Diseases and Molecular Targets

(Jiri Bartek & Martin Petrek)

- Mechanistic understanding of pathways activated in response to DNA damage
- Specific features of cancer stem cells (CSC) biology and DDR
- Identification of potential targets for cancer treatment, including CSCs
- Polymorphisms of inflammatory genes
- New molecular targets in microbes
- High-throughput siRNA and drug/siRNA screens and target validation

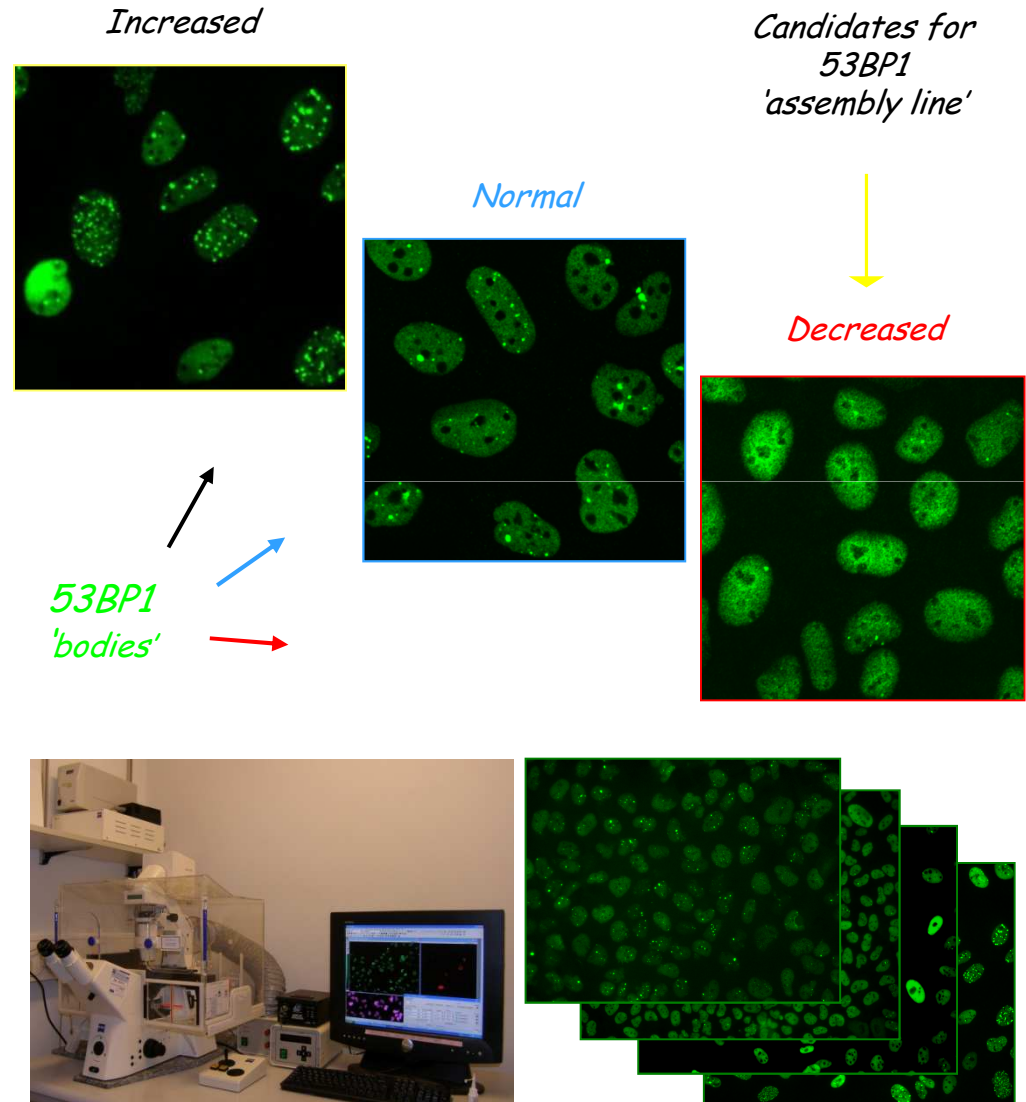
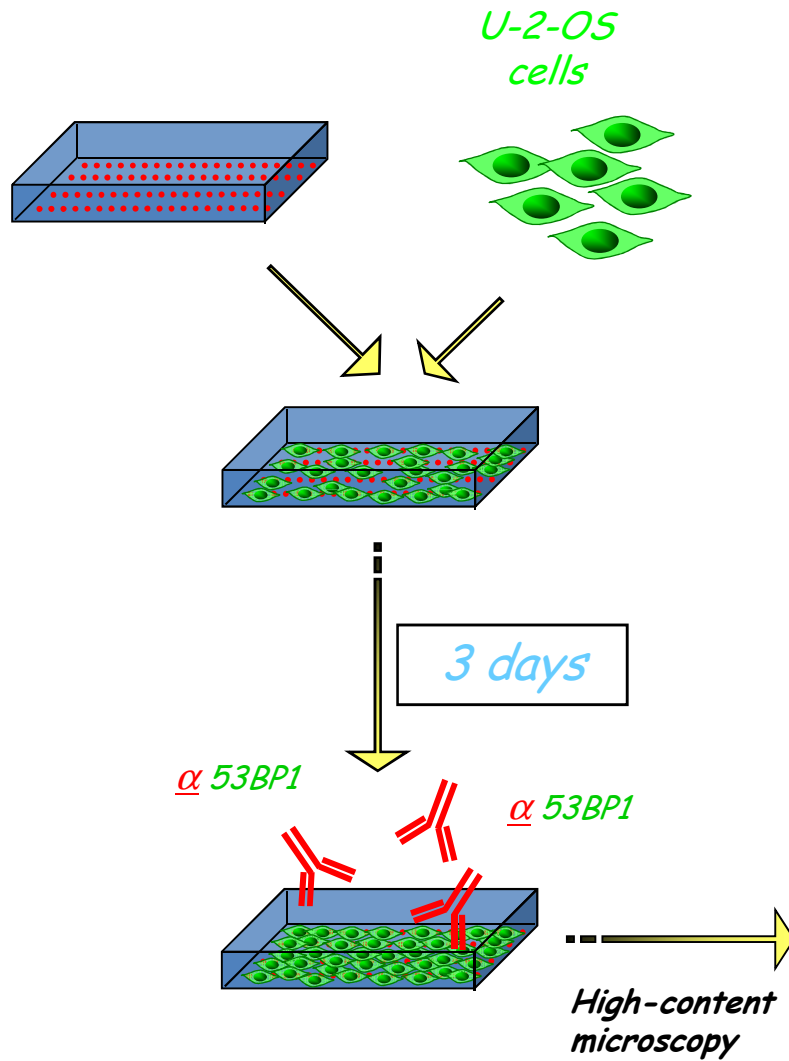


Tumour suppressors in DNA damage checkpoint signalling



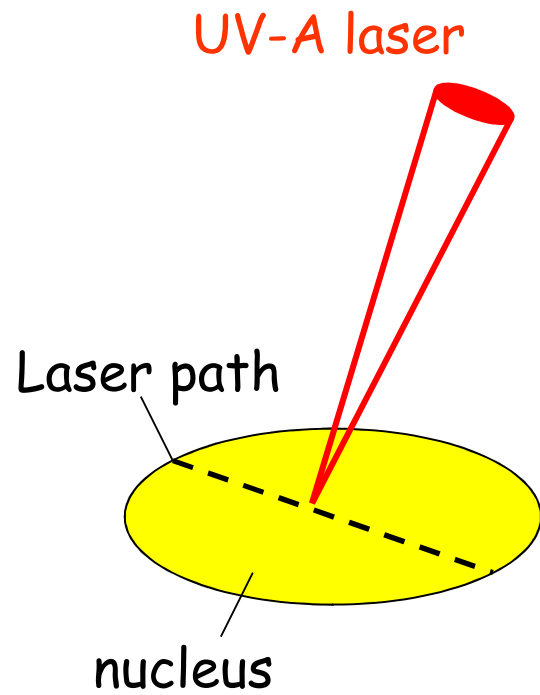


Readout & workflow of the siRNA screen

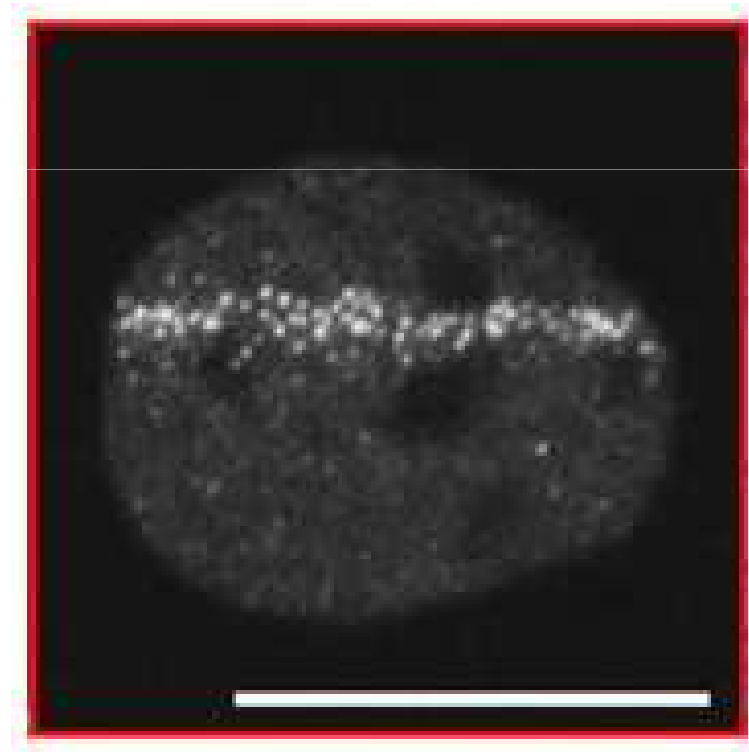




Laser micro-irradiation screening

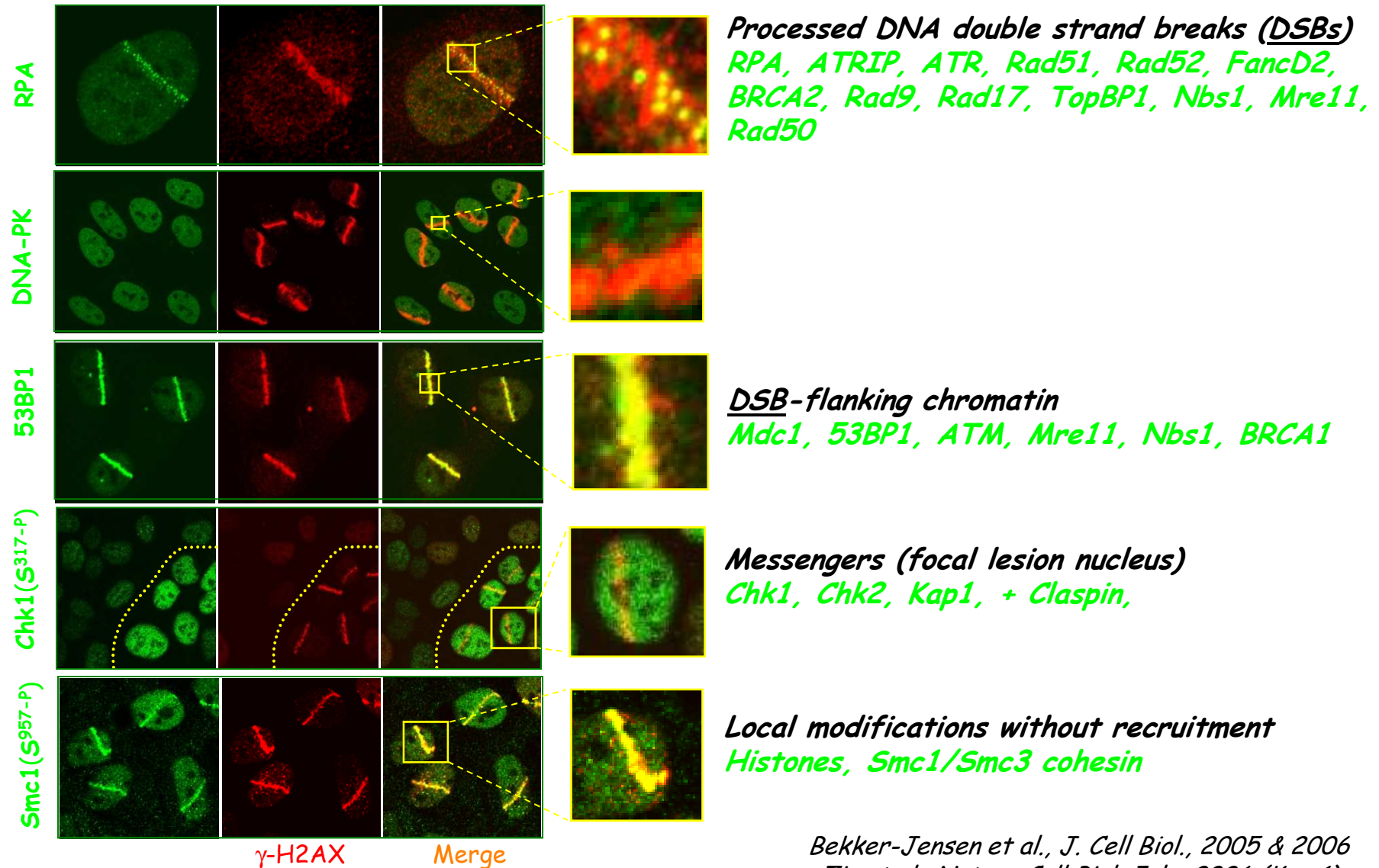


GFP-tagged protein



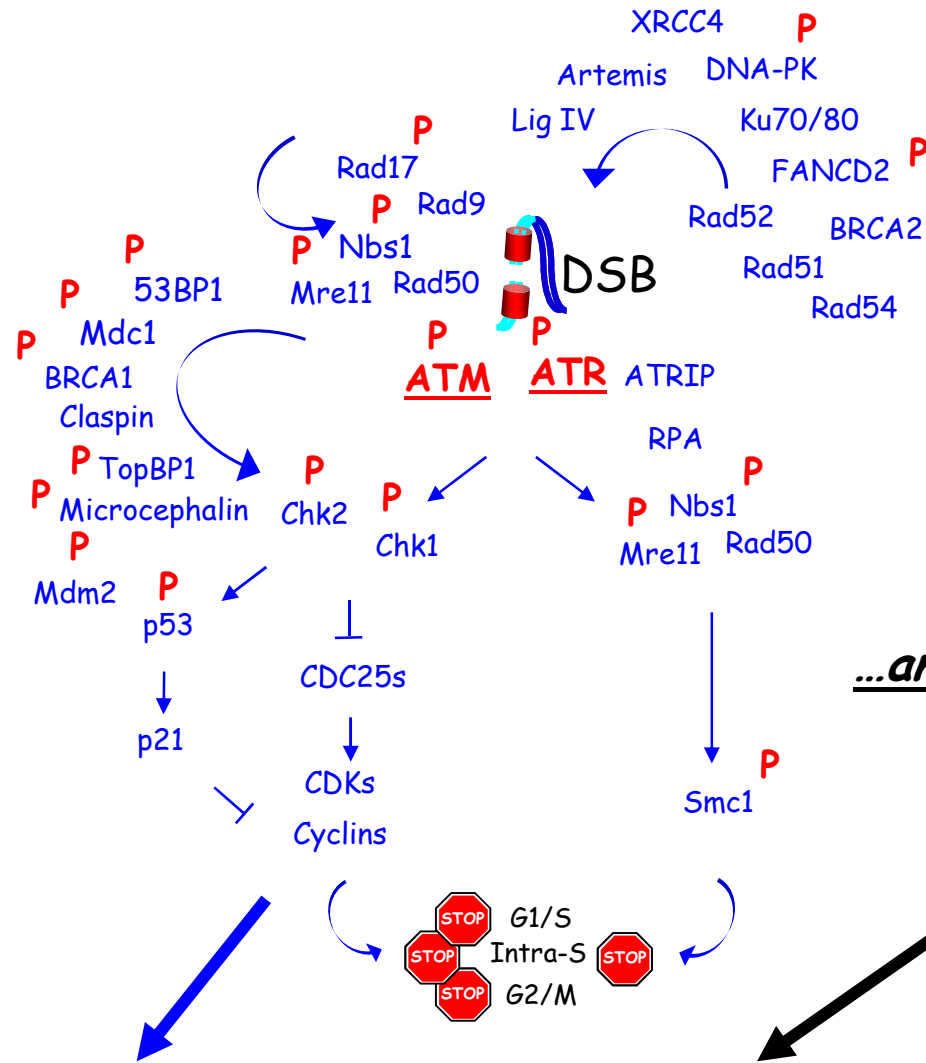


Laser micro-irradiation used for basic characterization of proteins (spatial 'map' of nuclear sub-compartments)





DNA damage response is propelled by *protein phosphorylations...*



...and other modifications

- Ubiquitylation
- Sumoylation
- Acetylation
- Methylation
- Parylation (olaparib)

Complex genomics, proteomics and metabolomics

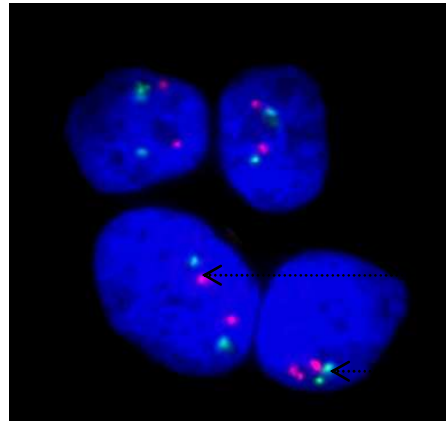
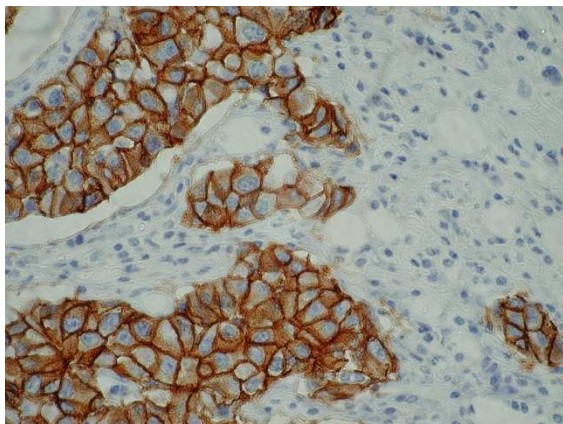
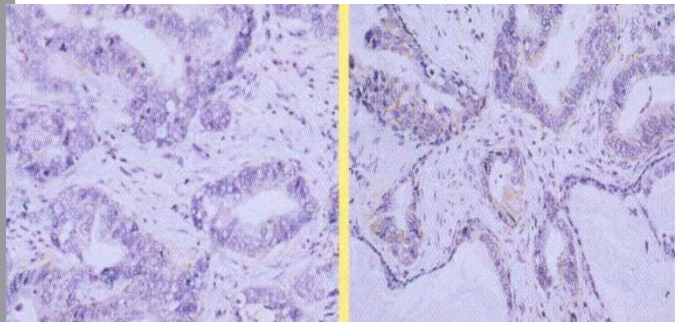
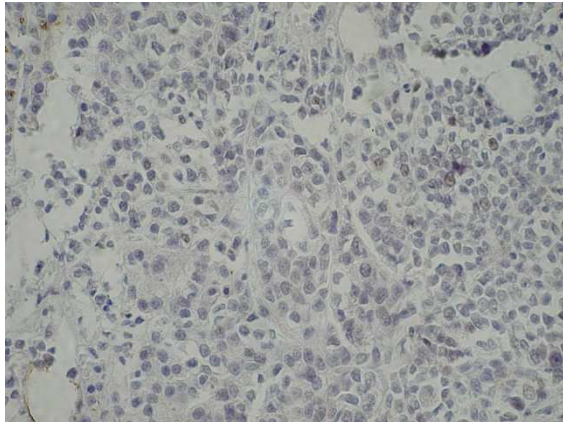


Research Program #2- Biomarkers (Zdenek Kolar& Jiri Drabek)

- Identification of diagnostic, prognostic and predictive biomarkers
- Biobanking, specialized collections
- Validation of biomarkers in clinical trials
- Genomics, Proteomics, Metabolomics
- Regulatory affairs and quality assurance
- Development of diagnostic kits and reagents



Specialized Molecular Diagnostics of Cancers

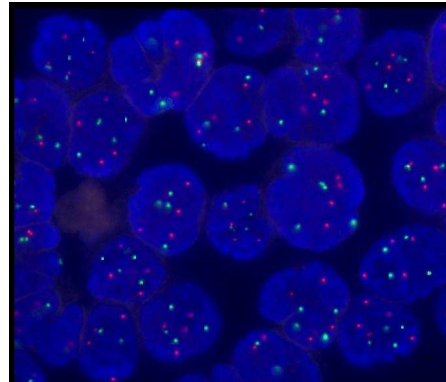


IHC: 0

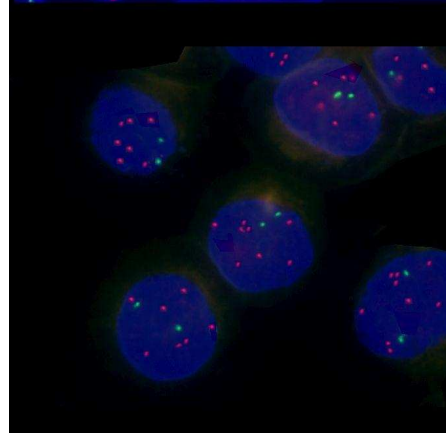
FISH: normal

Her-2/neu

CEP 17



IHC: 1+ to 2+



IHC: 3+

FISH: amplification

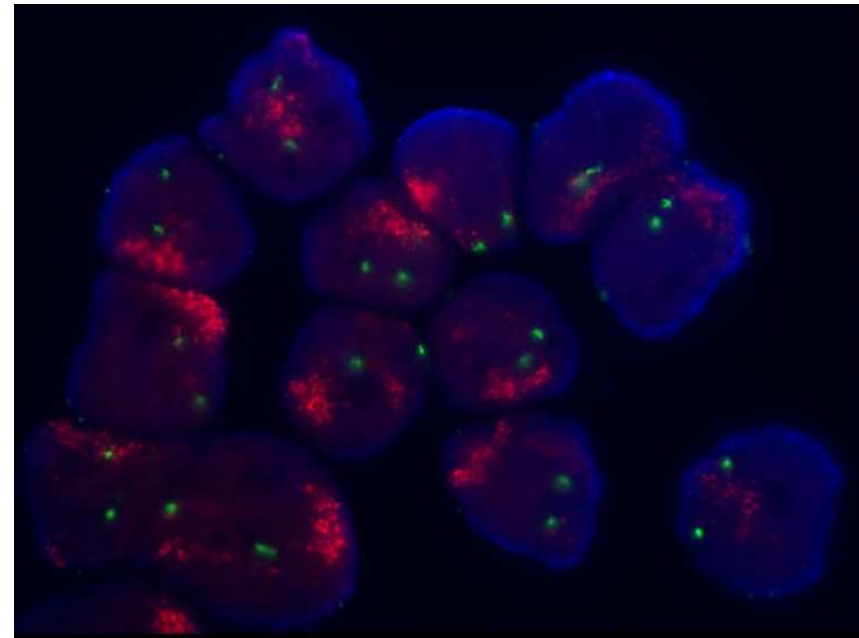
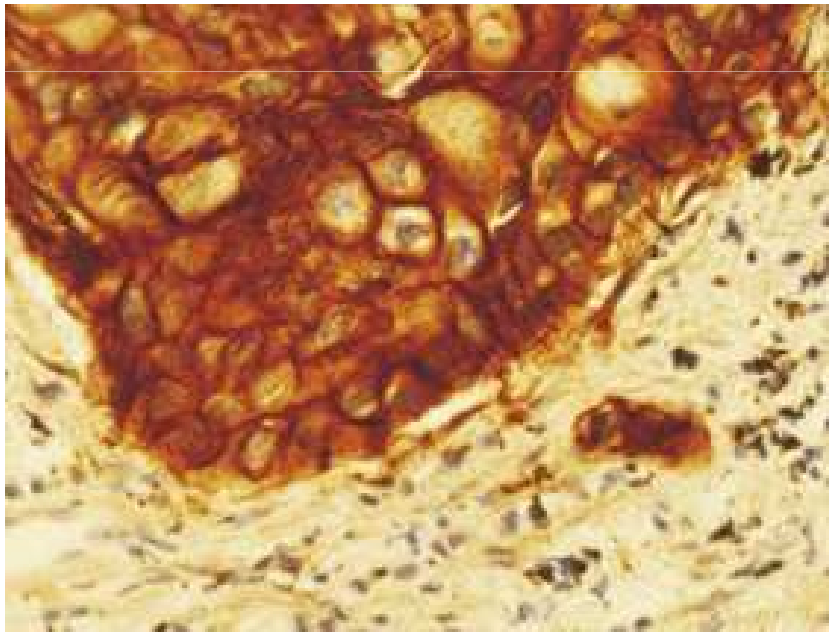
Laboratory/Institute holds accreditation
decision according to CSN ISO/IEC 17025
to meet European diagnostic standards
(www.cia.cz)



Development of new molecular diagnostics

Diagnostic systems for evaluation of molecular biomarkers in human cancers:

- Antibodies for immunohistochemistry
- Genetic diagnostics using FISH
- Mutation status of oncogenes/tumour suppressors



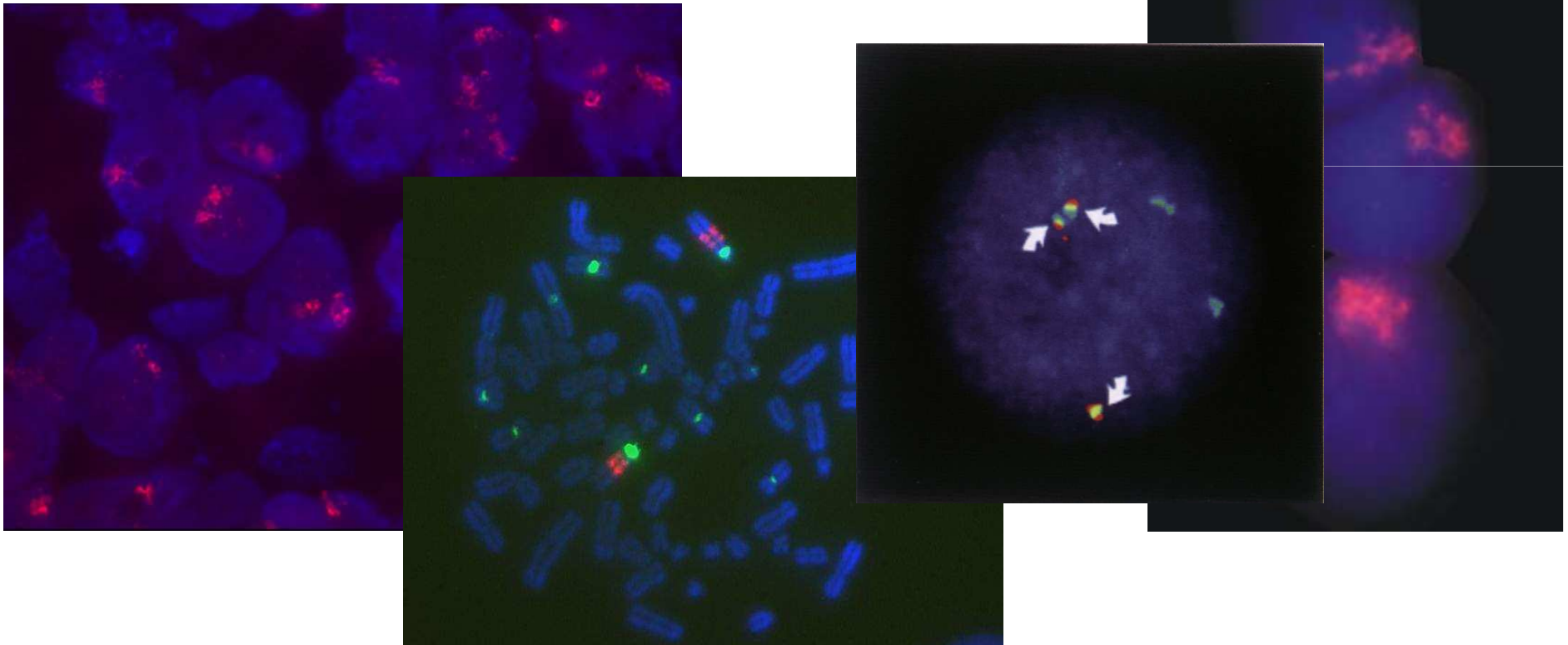
Diagnostic kits are produced and distributed by Institute of Applied Biotechnologies, a.s. (www.iab.cz) and IntellMed. a.s. (www.intellmed.cz)



Development of new molecular diagnostics

Diagnostic systems for evaluation of C-MYC, N-MYC, TP53, TOP2A, EGFR1, CDDN1 and others in human cancers:

- Genetic diagnostic using FISH



Diagnostic kits are produced and distributed by IntellMed s.r.o., University spin-off company

Biomarkers - Implication for clinical oncology

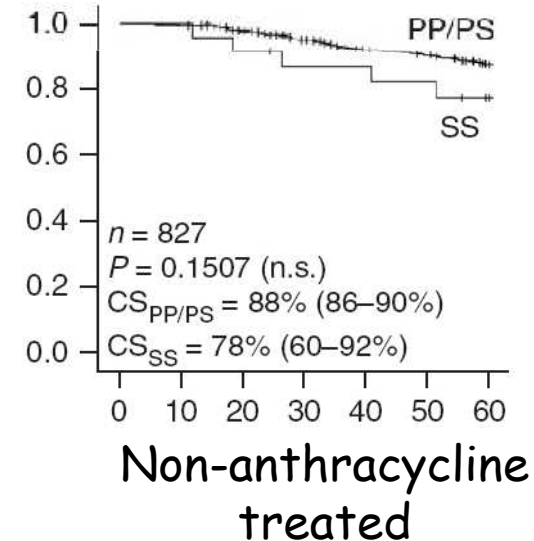
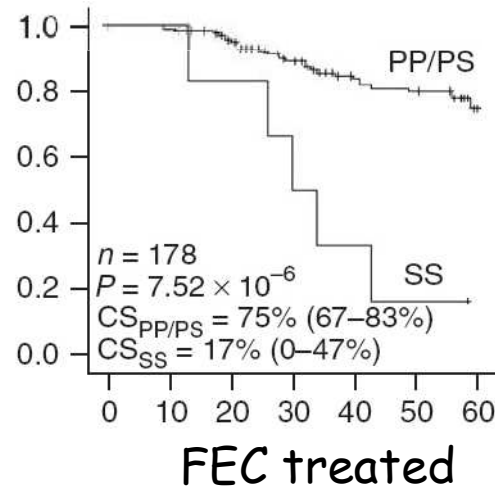
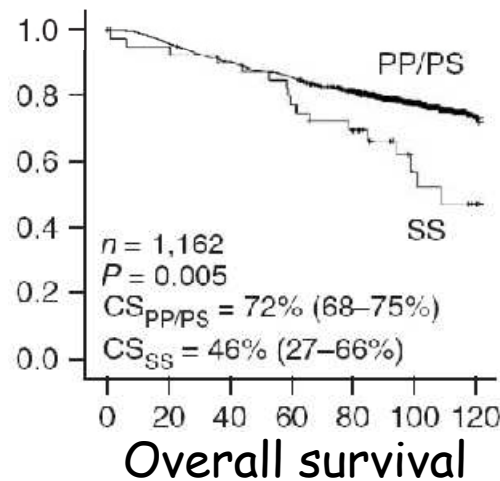
Example: NQO1 status in breast cancer therapy

Mutation in NQO1 (P187S) is a strong prognostic and predictive factor in breast cancer

PP = NQO1 WT/WT

PS = NQO1 WT/ Δ or WT/0

SS = NQO1 0/ Δ or Δ/Δ



Fagerholm et al., Nat. Genet., 2008

FEC = 5-fluorouracil, epirubicin, cyclophosphamide



Research Program #3- Medicinal Chemistry (Vladimir Kral & Jan Hlavac)

- To purchase, collect and establish chemical library of small molecules (100-500.000 compounds) covering the current chemical space, including unique structures synthesized by project partners.
- To analyze structure – activity relationship (chemoinformatics) and optimize hits to leads.
- Introduce and utilize combinatorial chemistry approaches
- Up-scale synthesis of candidate molecules for validation test
- Regulatory affairs and quality assurance
- Development of novel drugs, active foods and therapies



Current joined projects (IOCB/UPOL/ICT)

- MDP analogues – immunomodulatory molecules, vaccine adjuvants, anticancer agents
- Carboranes – antiviral, antibacterial and anticancer properties
- Nucleotide and nucleoside analogues – anticancer and antiviral activities
- Terpenoid compounds – antiviral, immunomodulatory and anticancer activities
- Antimicrobial peptides
- Targeted biological therapies – transport systems
- New biomarkers – new diagnostic tools



Research Program #4- Chemical biology & Experimental Therapeutics

(Marian Hajduch & Peter Dzubak)

Research Program #5- Pharmacology & Toxicology

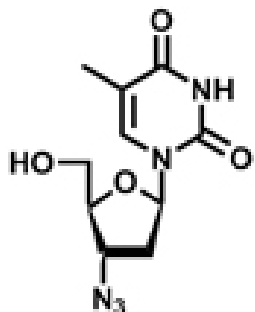
(Pavel Anzenbacher & Jitka Ulrichova)

- Identification of biologically active small molecules and biologics
- Biological assays in uHTS format
- BL3 level
- Pharmacology and toxicology of compounds
- In vitro and in vivo validation tests
- Regulatory affairs and quality assurance
- Development of novel drugs, active foods and therapies

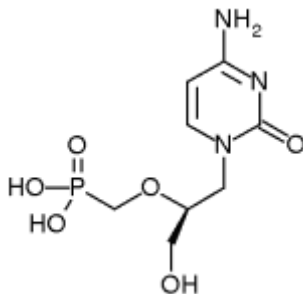


Antiviral acyclic nucleotides

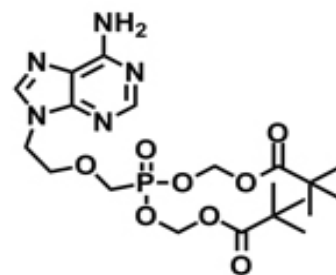
PI: Prof. Antonin Holy, Prof. Hocek IOCHB Prague and
Gilead Sciences, Inc.



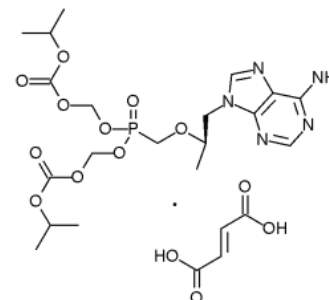
Azidothymidine
HIV infection



cidofovir (Vistide)
CMV infection



adefovir (Hepsera)
Hepatitis B infection



tenofovir (Viread)
HIV infection



tenofovir, emtricitabine
HIV infection



tenofovir, emtricitabine,
efavirenz
HIV infection

Betulinic acid derivatives

Chemistry: Dr. Sarek, Faculty of Sciences, UP



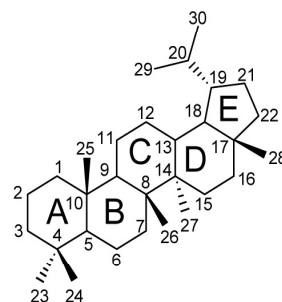
Anticancer

Antibicrobial

Antiinflammatory

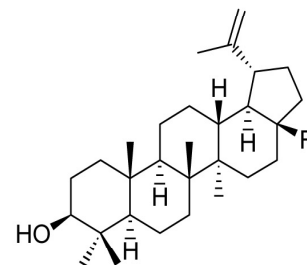
Aniviral (HIV – maturation inhibitors)

Formal skeleton



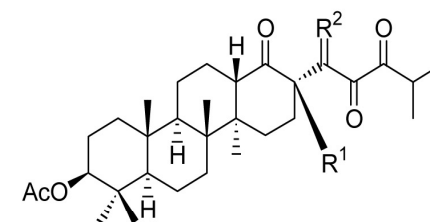
Lupane skeleton

Lead structures
for derivatization



Betulin, R = CH₂OH
Betulinic acid, R = COOH

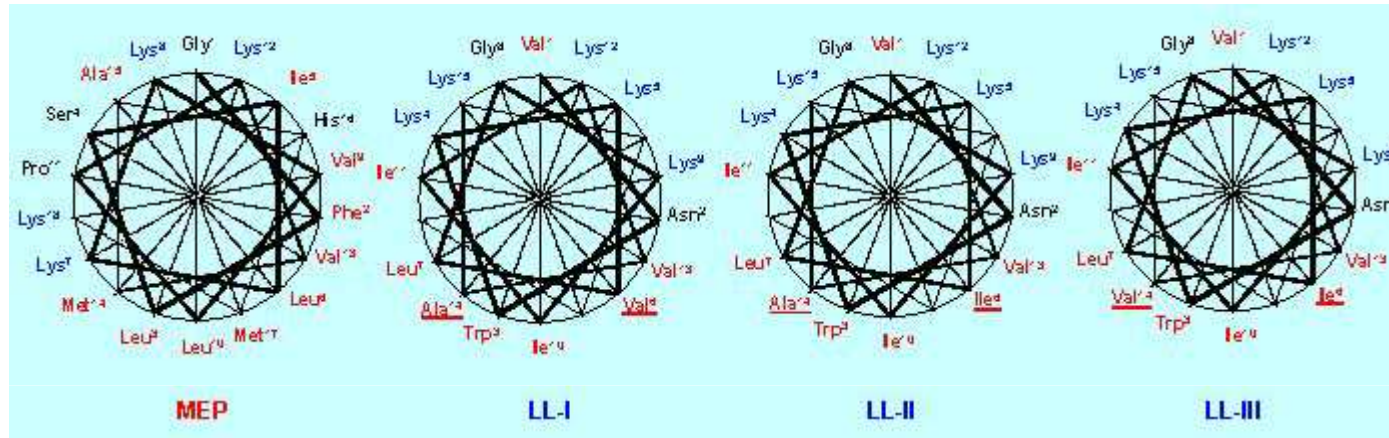
Example of new
structure(s) with
pro-apoptotic activity



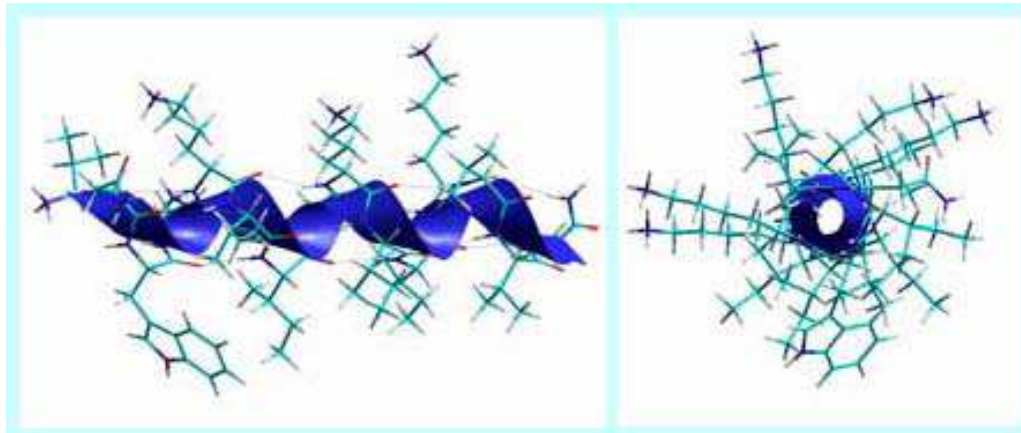
Highly oxygenated 18,19-secolupane type;
R¹ is CH₂OAc or CO₂R³, R² is O or H,H
and R³ is ester group

Bee venom antimicrobial peptides (PI: Dr. Cerovsky, IOCHB)

Peptide sequence



NMR based structure





Bee venom antimicrobial peptides (PI: Dr. Cerovsky, IOCHB)

Antimicrobial activity (bactericidal)
→ **development** as a topical antibiotics

Sample code	Minimal inhibitory concentration ($\mu\text{mol/l}$)							
	<i>Enterococcus faecalis</i> CCM 4224	<i>Staphylococcus aureus</i> CCM 3953	<i>Escherichia coli</i> CCM 3954	<i>Pseudomonas aeruginosa</i> CCM 3955	<i>Staphylococcus aureus</i> 4591 methicillin resistant	<i>Staphylococcus haemolyticus</i> 16568 fluoroquinolone resistant	<i>Escherichia coli</i> 16702 fluoroquinolone resistant	<i>Pseudomonas aeruginosa</i> 16575 fluoroquinolone resistant
LL 8/12	11,4	14,5	0,83	0,61	7,5	0,58	0,62	1,17

Hemolytic activity $>200 \mu\text{mol/l}$
Human fibroblast cytotoxicity $>100 \mu\text{mol/l}$
Solubility in water based formulations $>5\text{mM}$
Without skin and eye toxicity
High stability, apyrogenic





Discovery of metallacarborane inhibitors: from carbon to boron! (PI: Dr. Gruner, IACH and Prof. Kral, ICT Prague)

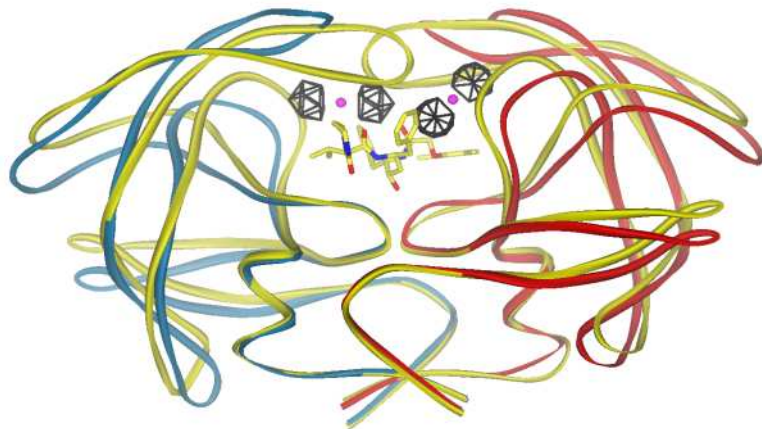
- there is a continuing need for the design of new inhibitors with broad specificity against resistant HIV mutants
- nonpeptidic and unnatural structures are most promising
- in this work, screening of various unnatural structural motifs led to the discovery of completely new core for inhibitors:

icosahedral metallacarborane clusters

- already parental purely inorganic compounds inhibit HIV protease
 - *exo*-skeletal modifications dramatically improve the inhibition efficacy and selectivity



Discovery of metallocarborane inhibitors: from carbon to boron! (PI: Dr. Gruner, IACH and Prof. Kral, ICT Prague)

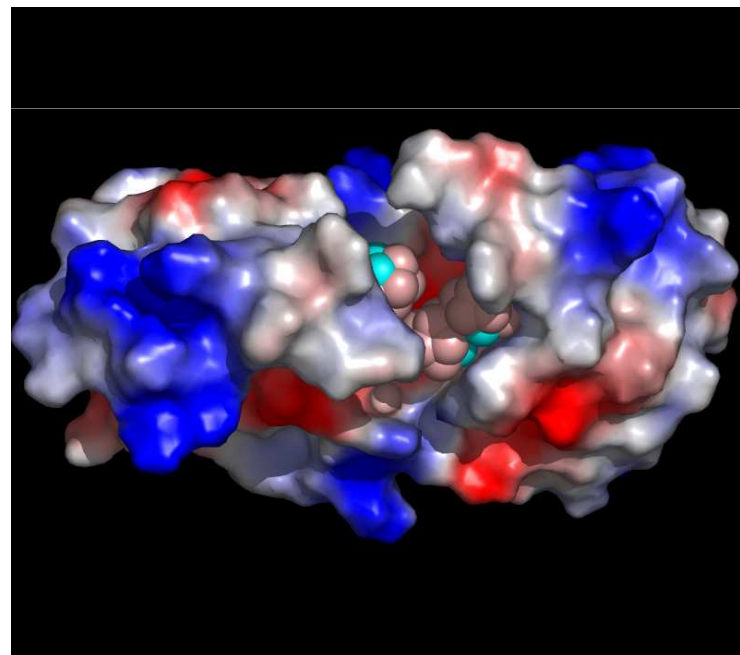


Unique binding mode

- two molecules of parent compounds bind to the hydrophobic pockets
- block of flap closure

X-RAY STRUCTURE

- first carborane-protein complex structure determined
- refinement resolution 2.15 Å



Cigler, P.; Kozisek, M.; Rezacova, P.; Brynda, J.; Otwinowski, Z.; Pokorna, J.; Plesek, J.; Gruener, B.; Doleckova, L.; Masa, M.; Sedlacek, J.; Bodem, J.; Kraeusslich, H.-G.; Kral, V.; Konvalinka, J. *PNAS* 2005, *102*, 15394-15399.

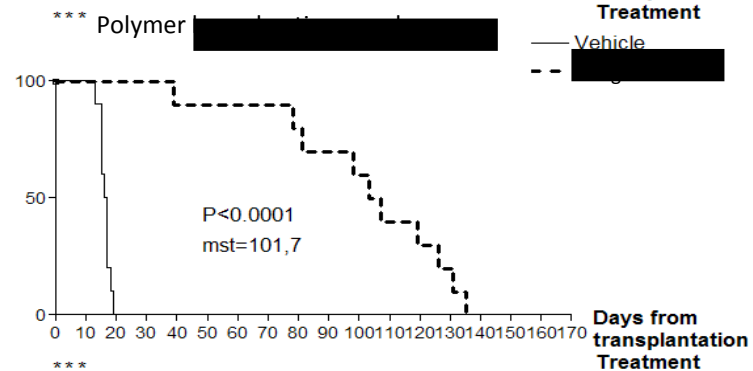
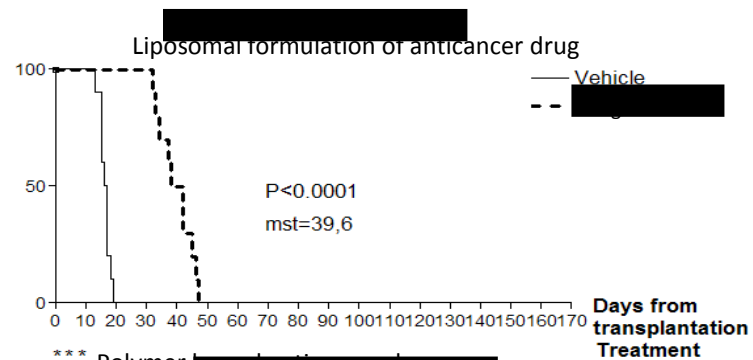
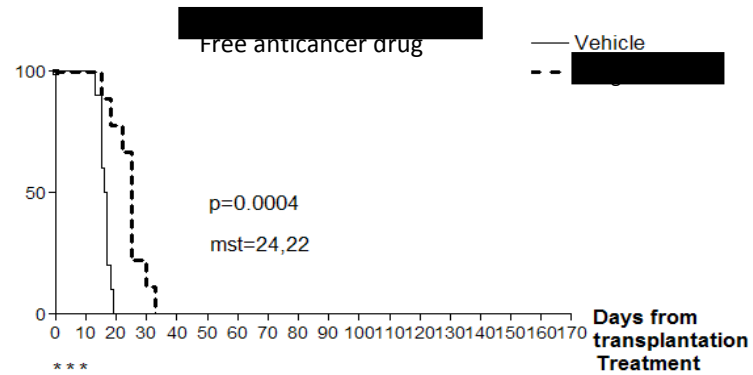
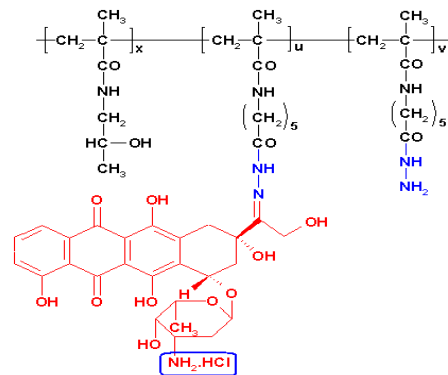
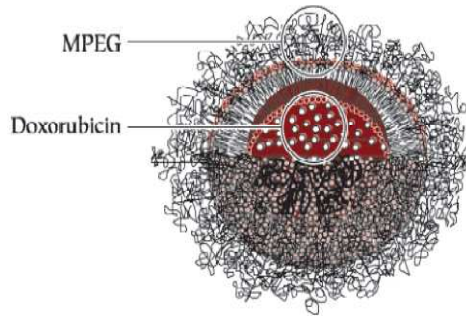
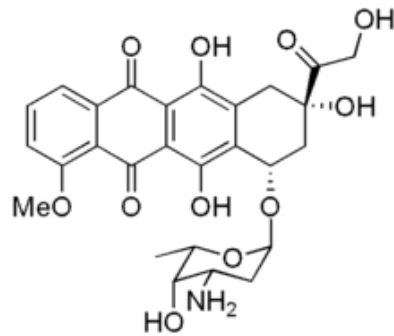


Polymeric anticancer drugs and diagnostics (PI: Prof. Ulbrich, IMCH AS CR) Polymeric Gd MRI contrast agent – blood pool





Polymeric anticancer drugs and diagnostics IN VIVO efficacy (P388D1 leukemia model)





Research Program #6- Translational Medicine

(Jiri Ehrmann & Vladimir Mihal)

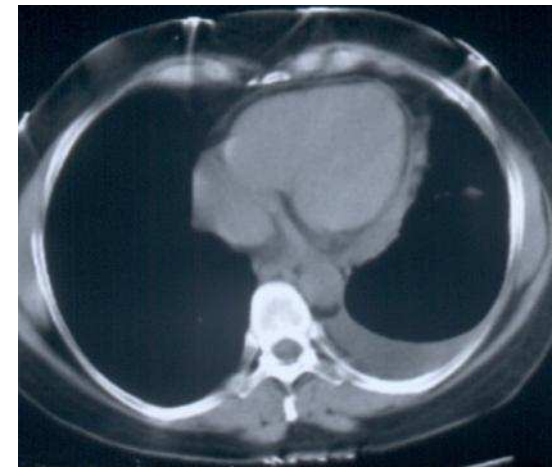
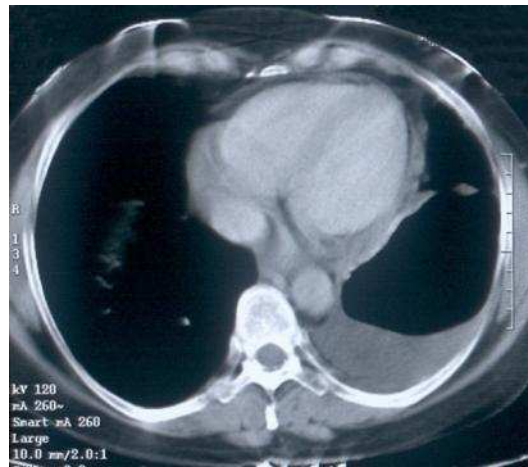
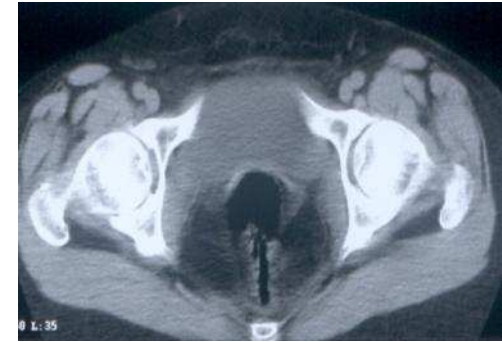
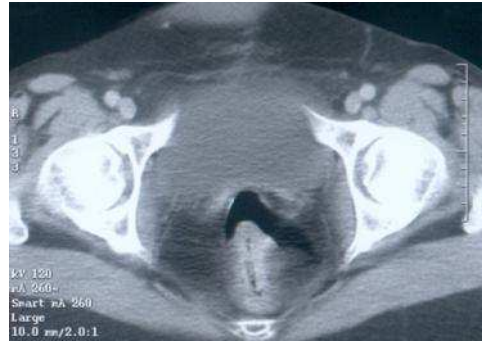
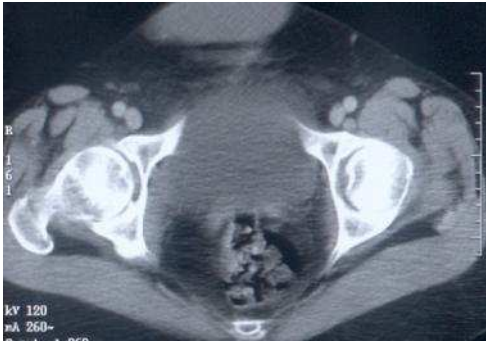
- To translate basic knowledge to clinical practice
- To define clinical needs and translate them into research programmes
- Collect and analyze clinical data
- Perform early clinical trials
- Regulatory affairs and quality assurance
- Development of novel biomarkers, drugs, active foods and therapies

Clinical efficacy of Protaxel therapy in ovarian carcinoma patient – Phase I trial Biophysica Fnd. and Interpharma Praha, a.s.

before treatment

after 3 cycles

after 5 cycles



CA-125: 1400

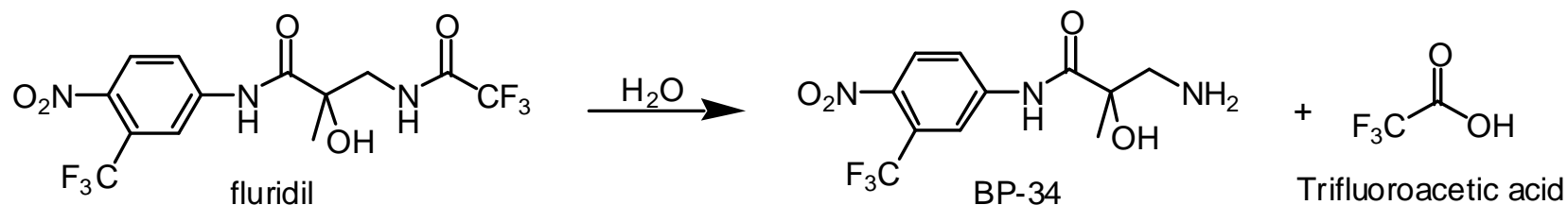
640

106 ng/ml



Fluridil – topical antiandrogen Interpharma Praha, a.s.

- Originally developed for hormonal therapy of prostate cancer
- Blockage of androgen receptor (AR) in hair follicle
- hydrophobic property
- hydrolytic instability-quick disintegration of fragments, systemic tolerance and rapid excretion





Fluridil – topical antiandrogen
Interpharma Praha, a.s.

Survey of pictures of thatches

0



12 months





Fluridil - Eucapil



DIRECTIONS FOR USE - PLEASE READ CAREFULLY.

EUCAPIL®
Fluridil

COMPOSITION
One ampoule contains 2, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290, 300, 310, 320, 330, 340, 350, 360, 370, 380, 390, 400, 410, 420, 430, 440, 450, 460, 470, 480, 490, 500, 510, 520, 530, 540, 550, 560, 570, 580, 590, 600, 610, 620, 630, 640, 650, 660, 670, 680, 690, 700, 710, 720, 730, 740, 750, 760, 770, 780, 790, 800, 810, 820, 830, 840, 850, 860, 870, 880, 890, 900, 910, 920, 930, 940, 950, 960, 970, 980, 990, 1000, 1010, 1020, 1030, 1040, 1050, 1060, 1070, 1080, 1090, 1100, 1110, 1120, 1130, 1140, 1150, 1160, 1170, 1180, 1190, 1200, 1210, 1220, 1230, 1240, 1250, 1260, 1270, 1280, 1290, 1300, 1310, 1320, 1330, 1340, 1350, 1360, 1370, 1380, 1390, 1400, 1410, 1420, 1430, 1440, 1450, 1460, 1470, 1480, 1490, 1500, 1510, 1520, 1530, 1540, 1550, 1560, 1570, 1580, 1590, 1600, 1610, 1620, 1630, 1640, 1650, 1660, 1670, 1680, 1690, 1700, 1710, 1720, 1730, 1740, 1750, 1760, 1770, 1780, 1790, 1800, 1810, 1820, 1830, 1840, 1850, 1860, 1870, 1880, 1890, 1900, 1910, 1920, 1930, 1940, 1950, 1960, 1970, 1980, 1990, 2000, 2010, 2020, 2030, 2040, 2050, 2060, 2070, 2080, 2090, 2100, 2110, 2120, 2130, 2140, 2150, 2160, 2170, 2180, 2190, 2200, 2210, 2220, 2230, 2240, 2250, 2260, 2270, 2280, 2290, 2300, 2310, 2320, 2330, 2340, 2350, 2360, 2370, 2380, 2390, 2400, 2410, 2420, 2430, 2440, 2450, 2460, 2470, 2480, 2490, 2500, 2510, 2520, 2530, 2540, 2550, 2560, 2570, 2580, 2590, 2600, 2610, 2620, 2630, 2640, 2650, 2660, 2670, 2680, 2690, 2700, 2710, 2720, 2730, 2740, 2750, 2760, 2770, 2780, 2790, 2800, 2810, 2820, 2830, 2840, 2850, 2860, 2870, 2880, 2890, 2900, 2910, 2920, 2930, 2940, 2950, 2960, 2970, 2980, 2990, 3000, 3010, 3020, 3030, 3040, 3050, 3060, 3070, 3080, 3090, 3100, 3110, 3120, 3130, 3140, 3150, 3160, 3170, 3180, 3190, 3200, 3210, 3220, 3230, 3240, 3250, 3260, 3270, 3280, 3290, 3300, 3310, 3320, 3330, 3340, 3350, 3360, 3370, 3380, 3390, 3400, 3410, 3420, 3430, 3440, 3450, 3460, 3470, 3480, 3490, 3500, 3510, 3520, 3530, 3540, 3550, 3560, 3570, 3580, 3590, 3600, 3610, 3620, 3630, 3640, 3650, 3660, 3670, 3680, 3690, 3700, 3710, 3720, 3730, 3740, 3750, 3760, 3770, 3780, 3790, 3800, 3810, 3820, 3830, 3840, 3850, 3860, 3870, 3880, 3890, 3900, 3910, 3920, 3930, 3940, 3950, 3960, 3970, 3980, 3990, 4000, 4010, 4020, 4030, 4040, 4050, 4060, 4070, 4080, 4090, 4100, 4110, 4120, 4130, 4140, 4150, 4160, 4170, 4180, 4190, 4200, 4210, 4220, 4230, 4240, 4250, 4260, 4270, 4280, 4290, 4300, 4310, 4320, 4330, 4340, 4350, 4360, 4370, 4380, 4390, 4400, 4410, 4420, 4430, 4440, 4450, 4460, 4470, 4480, 4490, 4500, 4510, 4520, 4530, 4540, 4550, 4560, 4570, 4580, 4590, 4600, 4610, 4620, 4630, 4640, 4650, 4660, 4670, 4680, 4690, 4700, 4710, 4720, 4730, 4740, 4750, 4760, 4770, 4780, 4790, 4800, 4810, 4820, 4830, 4840, 4850, 4860, 4870, 4880, 4890, 4900, 4910, 4920, 4930, 4940, 4950, 4960, 4970, 4980, 4990, 5000, 5010, 5020, 5030, 5040, 5050, 5060, 5070, 5080, 5090, 5100, 5110, 5120, 5130, 5140, 5150, 5160, 5170, 5180, 5190, 5200, 5210, 5220, 5230, 5240, 5250, 5260, 5270, 5280, 5290, 5300, 5310, 5320, 5330, 5340, 5350, 5360, 5370, 5380, 5390, 5400, 5410, 5420, 5430, 5440, 5450, 5460, 5470, 5480, 5490, 5500, 5510, 5520, 5530, 5540, 5550, 5560, 5570, 5580, 5590, 5600, 5610, 5620, 5630, 5640, 5650, 5660, 5670, 5680, 5690, 5700, 5710, 5720, 5730, 5740, 5750, 5760, 5770, 5780, 5790, 5800, 5810, 5820, 5830, 5840, 5850, 5860, 5870, 5880, 5890, 5900, 5910, 5920, 5930, 5940, 5950, 5960, 5970, 5980, 5990, 6000, 6010, 6020, 6030, 6040, 6050, 6060, 6070, 6080, 6090, 6100, 6110, 6120, 6130, 6140, 6150, 6160, 6170, 6180, 6190, 6200, 6210, 6220, 6230, 6240, 6250, 6260, 6270, 6280, 6290, 6300, 6310, 6320, 6330, 6340, 6350, 6360, 6370, 6380, 6390, 6400, 6410, 6420, 6430, 6440, 6450, 6460, 6470, 6480, 6490, 6500, 6510, 6520, 6530, 6540, 6550, 6560, 6570, 6580, 6590, 6600, 6610, 6620, 6630, 6640, 6650, 6660, 6670, 6680, 6690, 6700, 6710, 6720, 6730, 6740, 6750, 6760, 6770, 6780, 6790, 6800, 6810, 6820, 6830, 6840, 6850, 6860, 6870, 6880, 6890, 6900, 6910, 6920, 6930, 6940, 6950, 6960, 6970, 6980, 6990, 7000, 7010, 7020, 7030, 7040, 7050, 7060, 7070, 7080, 7090, 7100, 7110, 7120, 7130, 7140, 7150, 7160, 7170, 7180, 7190, 7200, 7210, 7220, 7230, 7240, 7250, 7260, 7270, 7280, 7290, 7300, 7310, 7320, 7330, 7340, 7350, 7360, 7370, 7380, 7390, 7400, 7410, 7420, 7430, 7440, 7450, 7460, 7470, 7480, 7490, 7500, 7510, 7520, 7530, 7540, 7550, 7560, 7570, 7580, 7590, 7600, 7610, 7620, 7630, 7640, 7650, 7660, 7670, 7680, 7690, 7700, 7710, 7720, 7730, 7740, 7750, 7760, 7770, 7780, 7790, 7800, 7810, 7820, 7830, 7840, 7850, 7860, 7870, 7880, 7890, 7900, 7910, 7920, 7930, 7940, 7950, 7960, 7970, 7980, 7990, 8000, 8010, 8020, 8030, 8040, 8050, 8060, 8070, 8080, 8090, 8100, 8110, 8120, 8130, 8140, 8150, 8160, 8170, 8180, 8190, 8200, 8210, 8220, 8230, 8240, 8250, 8260, 8270, 8280, 8290, 8300, 8310, 8320, 8330, 8340, 8350, 8360, 8370, 8380, 8390, 8400, 8410, 8420, 8430, 8440, 8450, 8460, 8470, 8480, 8490, 8500, 8510, 8520, 8530, 8540, 8550, 8560, 8570, 8580, 8590, 8600, 8610, 8620, 8630, 8640, 8650, 8660, 8670, 8680, 8690, 8700, 8710, 8720, 8730, 8740, 8750, 8760, 8770, 8780, 8790, 8800, 8810, 8820, 8830, 8840, 8850, 8860, 8870, 8880, 8890, 8900, 8910, 8920, 8930, 8940, 8950, 8960, 8970, 8980, 8990, 9000, 9010, 9020, 9030, 9040, 9050, 9060, 9070, 9080, 9090, 9100, 9110, 9120, 9130, 9140, 9150, 9160, 9170, 9180, 9190, 9200, 9210, 9220, 9230, 9240, 9250, 9260, 9270, 9280, 9290, 9300, 9310, 9320, 9330, 9340, 9350, 9360, 9370, 9380, 9390, 9400, 9410, 9420, 9430, 9440, 9450, 9460, 9470, 9480, 9490, 9500, 9510, 9520, 9530, 9540, 9550, 9560, 9570, 9580, 9590, 9600, 9610, 9620, 9630, 9640, 9650, 9660, 9670, 9680, 9690, 9700, 9710, 9720, 9730, 9740, 9750, 9760, 9770, 9780, 9790, 9800, 9810, 9820, 9830, 9840, 9850, 9860, 9870, 9880, 9890, 9900, 9910, 9920, 9930, 9940, 9950, 9960, 9970, 9980, 9990, 10000.

INDICATIONS FOR USE
Eucapil is used for the treatment of acute and chronic inflammation of the respiratory tract, such as acute and chronic bronchitis, acute and chronic sinusitis, acute and chronic otitis media, acute and chronic laryngitis, acute and chronic pharyngitis, acute and chronic tonsillitis, acute and chronic epiglottitis, acute and chronic tracheitis, acute and chronic bronchiolitis, acute and chronic pneumonia, acute and chronic emphysema, acute and chronic asthma, acute and chronic allergic rhinitis, acute and chronic allergic conjunctivitis, acute and chronic allergic dermatitis, acute and chronic allergic urticaria, acute and chronic allergic angioedema, acute and chronic allergic anaphylaxis, acute and chronic allergic shock, acute and chronic allergic death.

CONTRAINDICATIONS
Eucapil is contraindicated in patients with known hypersensitivity to fluridil or any of the excipients.

WARNINGS
Eucapil should be used with caution in patients with severe renal or hepatic impairment.

ADVERSE EFFECTS
The most common side effects are headache, dizziness, and nausea.

DRUG INTERACTIONS
Eucapil may interact with other drugs used for the treatment of the respiratory tract.

PREGNANCY AND LACTATION
Eucapil should be used with caution during pregnancy and lactation.

HOW TO USE EUCAPIL
Eucapil is used by inhalation. The ampoules should be opened and the contents should be inhaled through the applicator.

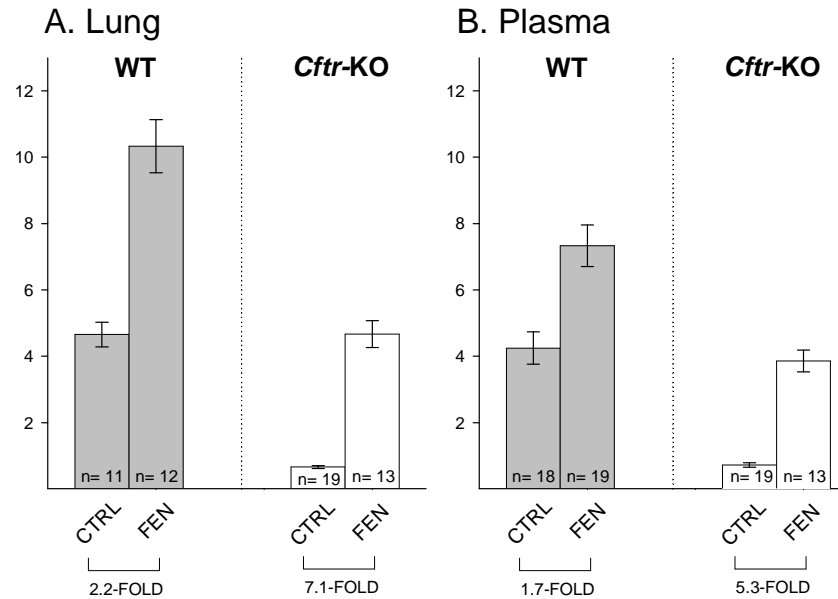
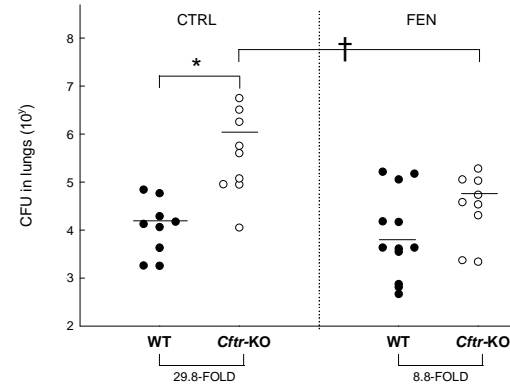
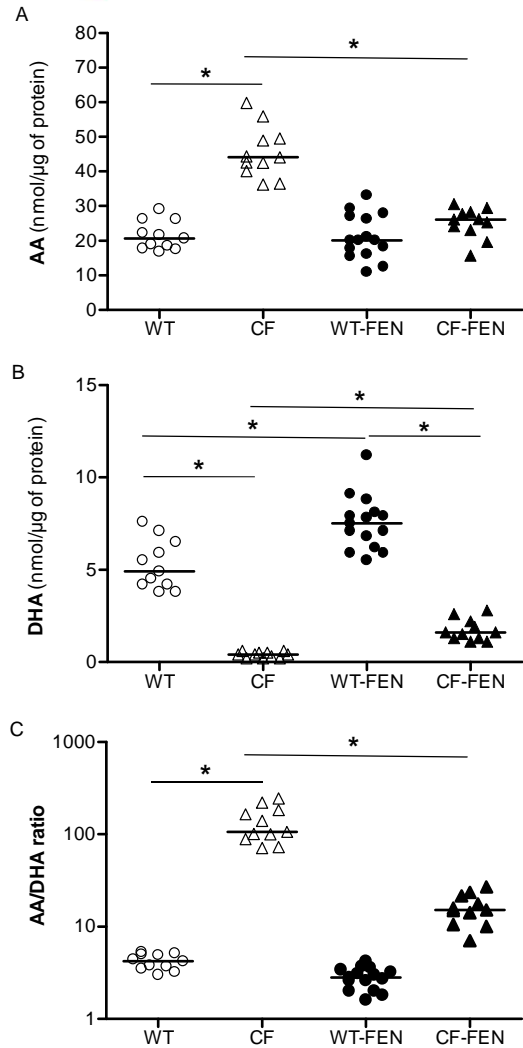
PACKAGING
Eucapil is available in a box containing 30 ampoules and an applicator.





Fenretinide in Cystic Fibrosis

P.I.: Prof. Radzioch, McGill University



Gibault et al. AJRCMB 2009, Wojewodka et al. AJRCMB2009

Fenretinide for colonized CF patients – FDA approval for orphan drug status and clinical trial in 2010



BIOMEDREG/IMTM – Major Milestones

- Start of the Project: January 1, 2008
- Preparatory Phase: January 1, 2008 – March 31, 2010
- Construction Phase: April 1, 2010 – March 31, 2012
- Start-Up Phase: April 1 2012 – March 31, 2013
- Full Operation: Since April 1, 2013

120 scientists and PhD. students, 4700 m² of research space, uHTS facility, BL3 laboratories including animal facility, genomics&proteomics&metabolomics unit, tissue bank, clinical trial unit, GLP, GMP, GCP certified units



BIOMEDREG/IMTM

Selected Monitoring Indicators

(since April 1, 2010)

- 17 publications with IF
(Nature Genetics, Nature Reviews in Cancer, Nature Structural & Molecular Biology, Mol. Cell. Proteomics, Prostate, Oncogene, Cell Cycle, J. Comb. Chem., Tetrahedron Lett., Cytokine, etc.)
- 2 national, 1 US patent
- 10 graduated MSc students
- 8 graduated PhD students
- 1 drug received orphan drug status by FDA and enters clinical trial in cystic fibrosis
- 1 transfer of know-how to spin-off company

BIOMEDREG



INSTITUTE OF MOLECULAR AND
TRANSLATIONAL MEDICINE

Cluster of Medicinal Chemistry and Biochemistry MEDCHEMBIO

OPPI

Project Leader:

Cluster MedChemBio, z.p.o.

Partners:

Academic and Private Institutions

Allocation:

Approx. 0,6 M €

Phase of the Project:

Realization phase started on September 1, 2009

Information:

www.medchembio.cz



- Established in February 2009
- The main field is the area of biomarkers and biologically active substances, i.e. substances that find application in human and veterinary medicine as a medicament.
- Cluster MedChemBio will become a key player in cooperation between academic institutes, small and medium-sized companies (as well as large firms), suppliers, investors, professional and manufacturing enterprises in development, testing and production of medicaments and thereby helps development of medicinal and biological chemistry in the Czech Republic.
- Cluster will enable all participants to assess the existing intellectual property.



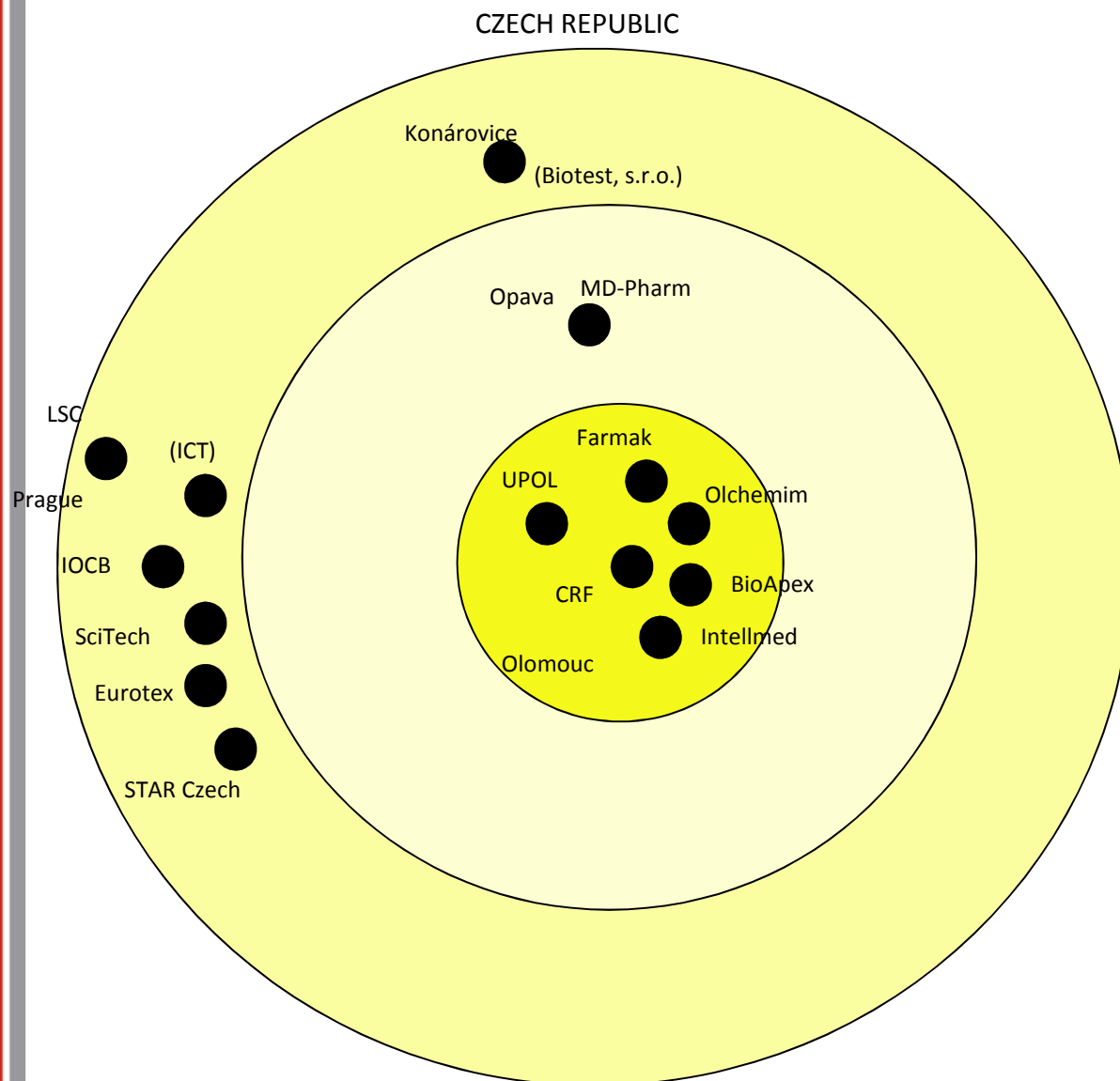
THE MAIN OBJECTIVES:

- Consultancy for Czech scientific workplaces in the field of technology transfer
- The creation of spin-off companies
- Assess of intellectual property
- Organization of substances testing
- Research and development of new predictive or surrogate biomarkers
- Transfer between laboratories and pilot plants
- Certification and legislation
- Investment in is the area of biologically active substances and biomarkers
- Development of the region
- Contacts with foreign commercial partners



STRATEGY:

- The strategy supports the cluster across the sector, which hasn't a common platform for contacts and cooperation in the Czech Republic.
- Cluster is trying to build a structure that provides continuous support to cluster members but also to new subjects, and generally allow the development of new scientific and technical areas in the region
- Cluster MedChemBio wants to support chemistry and biomedicine as well as bring together all stakeholders with an interest in this area.
- Cluster now associates leading academic institutions (Palacky University in Olomouc and Institute of Organic Chemistry and Biochemistry in Prague), major professional societies (Czech Chemical and Czech Society for Biochemistry and Molecular Biology) and a number of primarily small and medium-sized companies engaged in the fields of medicinal and biological chemistry and is open to the accession of other members, including large pharmaceutical concerns.



MEMBERS

- *Academia :*
- Palacky University Olomouc
- Institute of Organic Chemistry and Biochemistry, AS CE, Prague
- Institute of Chemical Technologies, Prague
- *Small and medium size companies :*
- Quinta Analytika, s.r.o., Praha
- LSC, s.r.o., Praha
- STAR Czech s.r.o., Prague
- Olchemim, s.r.o., Olomouc
- MD-Pharm, s.r.o., Opava
- Sci-tech, s.r.o., Prague
- ITA-intertact, s.r.o., Olomouc
- Intellmed s.r.o., Olomouc
- Farmak, a.s., Olomouc
- Circle Line Associates, s.r.o., Prague
- BioApex, s.r.o., Olomouc
- BioPatterns, s.r.o., Olomouc
- (Biotest, s.r.o., Konárovice)
- *Others*
- ČSCH, Prague
- ČSBMB, Prague
- Cancer Research Foundation, Olomouc



COLLABORATIVE PROJECTS:

1. The system for managing research and development projects in medicament regimens GMP, GLP, GCP
2. The center for molecular diagnostics
3. The center for synthesis, isolation and production of chemical compounds
4. Electronic content database and processing system translations



EATRIS-CZ

National Road Map of Large Infrastructures

Project Leader:

Palacký Universty in Olomouci (IMTM)

Partners:

Academic Institutions

Allocation:

Approx. 0,5 M € in Construction Phase

Phase of the Project:

On the Roadmap since March 15, 2010

Information:

www.eatris-cz.cz (under construction)



ESFRI – EATRIS - ERIC

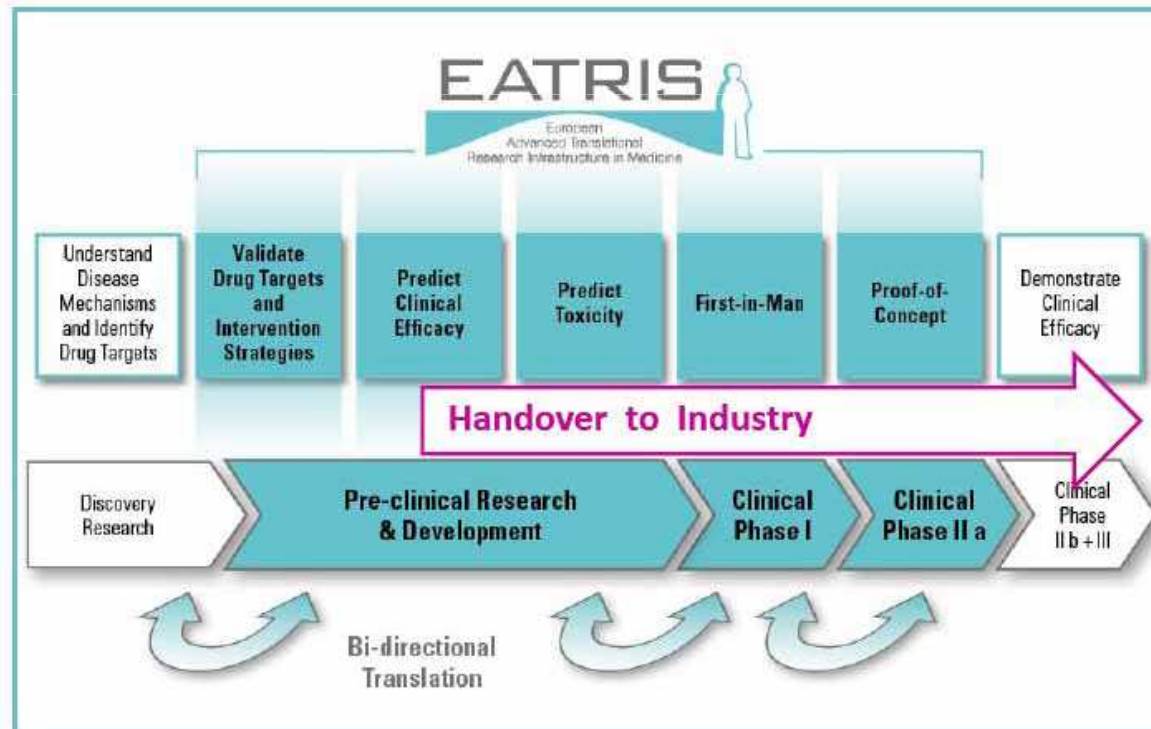
ESFRI - European Strategy Forum on Research Infrastructures

EATRIS - European Advanced Translational Research InfraStructure in Medicine

ERIC - Legal Framework for a European Research Infrastructure Consortium



Infrastructure for Pipeline





EATRIS/EATRIS-CZ: Disease Areas and Products

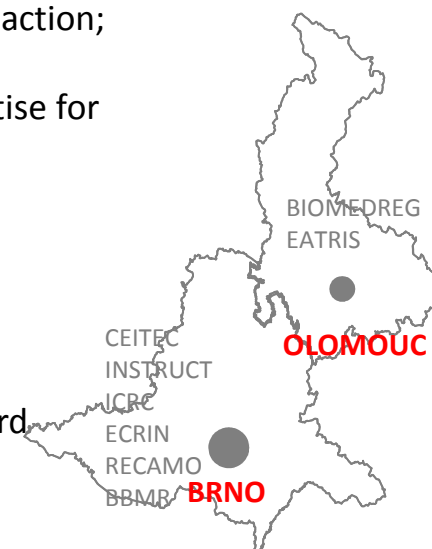
Products	Cancer	Cardio	Infection	Metabolic	Neuro
Vaccines / prevention			DE, ES, NL, NO		
Tracer	DE, DK, IT, NL, ES	NL, IT, DK, ES	ES, NL	SE, ES, NL	IT, NL, NO, FR, ES
Biomarker	DE, FI, IT, NL, CZ	FI, IT, NL	FI, NL, CZ	FI, SE	FI, IT, CZ
Small Molecules (drugs)	DE, FI, IT, NL, CZ	NO, IT, NL	DE, IT, NL, CZ	FI, SE, IT, NL	IT, NO, IT, NL, CZ
Biologics	DE, ES, NL, CZ	ES	DE, NL	SE, ES	FR, ES, CZ
ATMP*	DE, IT, NO, ES, CZ	NL, IT, ES	DE	SE	IT, FR, NO, CZ

* Advanced Therapy Medicinal Products (cellular therapies and regenerative medicine)



EATRIS/EATRIS-CZ: Relationship to other large infrastructures and Collaborative Opportunities

- **BBMRI** – interface: tissue and bio-banks, expertise in human and animal (model) pathology, quality standards, policies, patient data banks, disease-specific data banks;
- **ECRIN** – interface: transfer of projects that successfully passed clinical phase 0, I and IIa studies to progress with late phase II and beyond; use of ECRIN where multi-centre studies are needed even for early phase clinical trials; exchange observations from the clinic back to scientists (reverse translation), expertise in regulatory affairs, common training courses;
- **INFRAFRONTIER** – interface: consultation in choosing the right animal model for pre-clinical studies, characterisation of novel and disease-specific (mouse) models; archiving of such; quality standards and regulatory standards (animal husbandry, animal studies, etc.), training courses;
- **INSTRUCT** – interface: service in /access to specialty infrastructure components in structural biology, e.g. in small molecule characterization, elaboration of a biological mechanism of action;
- **EU-Openscreen** – interface: collaborative use of technology and interdisciplinary expertise for small molecule discovery and development, access to large compound libraries or chemoinformatics, databases;
- **EuroBioImaging** – interface: collaboration on nonstandard/sophisticated problems in biomolecular or biomedical imaging, training possibilities;
- **ELIXIR** (bioinformatics and databases) – interface: exchange on IT management, standard definitions for data collection, storage, utilisation, and on a mid- to long-term basis, agreements on data hosting etc.



BIOMEDREG



INSTITUTE OF MOLECULAR AND
TRANSLATIONAL MEDICINE

THANK YOU FOR ATTENTION

marian.hajduch@fnol.cz

hajduchm@gmail.com

www.lem.ocol.cz

www.medchembio.cz

www.biomedreg.eu



EUROPEAN UNION
EUROPEAN REGIONAL DEVELOPMENT FUND
INVESTING IN YOUR FUTURE



OP Research and
Development for Innovation



BIOMEDREG



INSTITUTE OF MOLECULAR AND
TRANSLATIONAL MEDICINE