

What can we learn from USA practices: Technology Transfer at the National Institutes of Health (NIH OTT)

TransMedRI

**Workshop on Entrepreneurship in Life Sciences
Rijeka, 25 April 2013.**

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Research and Technology Transfer Office
University of Zagreb School of Medicine
Zagreb, Croatia

Discussion Points for Today:

- NIH OTT
- NIH TT case studies
- NIH NCATS / TRND
- NIH collaborations
- CTCR Zagreb
- Research and Technology Transfer Office

International Mentoring Program at NIH OTT

August 22 – September 23, 2011

NIH

National Institutes of Health

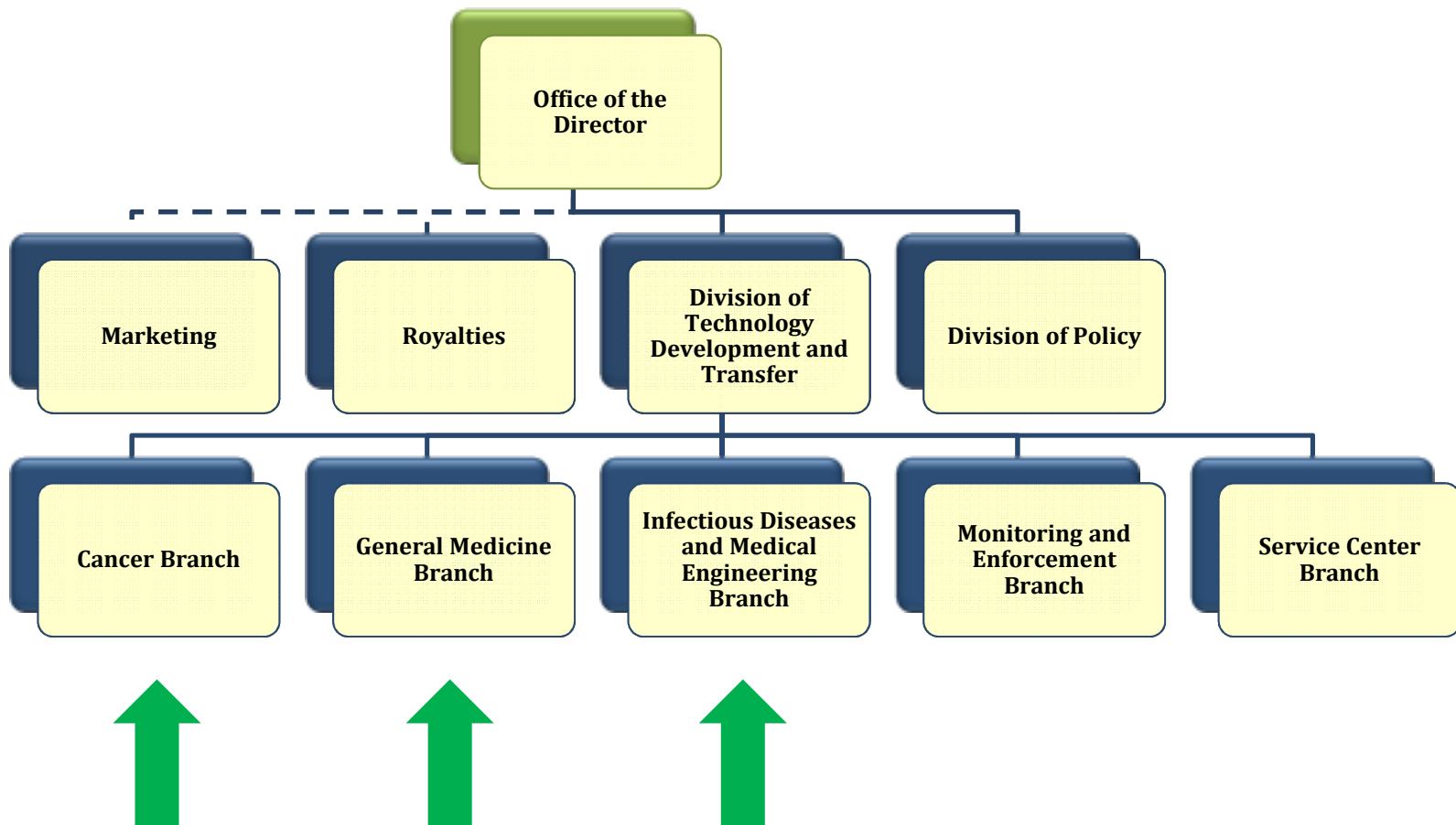
- Unique place for research in the biomedical field – „translational” from the beginning
- 27 institutes and centers
- 30 billion \$ yearly budget, 10% intramural (6000 scientists), 80% extramural (325000 scientists)
- Emphasis on “high-risk, high-reward” research



NATIONAL[®]
CANCER
INSTITUTE



Organizational Structure



Courtesy: Tara Kirby

TRANSMEDRI, Rijeka, 25 April 2013.



Science. Ideas.
Breakthroughs.

Centralized Technology Transfer



Courtesy: Tara Kirby

TRANSMEDRI, Rijeka, 25 April 2013.



Science. Ideas.
Breakthroughs.

Statistics NIH OTT (NIH and FDA)

ACTIVITY	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010
Invention Disclosures	400	403	388	367	419	402	353	340
New U.S. Patent Applications Filed	196	199	186	173	178	176	156	147
Total U.S. Patent Applications Filed	382	396	347	309	354	343	300	304
Issued U.S. Patents	86	122	66	93	117	88	110	134
Executed Licenses	209	276	313	254	264	259	215	226
Royalties (\$ in millions)	\$53.7	\$56.3	\$98.2	\$82.7	\$87.7	\$97.2	\$91.2	\$91.6
Waivers							58	73
Executed CRADAs (NIH Only)								
Standard	84	87	80	51	44	72	77	66
Material	36	43	39	22	23	33	33	39
	48	44	41	29	21	39	44	27

Visits outside of NIH OTT

- NCI and NIAID policies and procedures
- JHU Tech Transfer policies and differences from government
- NIH Clinical Center, NLM, Fogarty Center
- Translational Research Center (now: NCATS)
- MD Biotech Center
- TEDCO
- FDA
- Small Biotechs – Lentigen, Emergent Biosolutions, 20/20
GeneSystems
- My presentation at NIAID on Scientific Programs at University of Zagreb School of Medicine



The Highlights

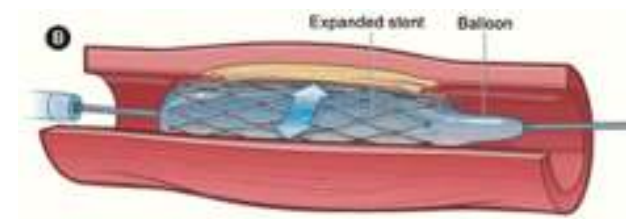
- Research tools patenting policy
- Importance of development plan in license agreements
- Value of monitoring
- Valuation of technologies
- Case studies, successful examples
- Specificities of biotech start-ups
- MD - biotech state, benefits for start-ups and interaction with federal laboratories

Policy and Implementation

- **Public Policy Issues (the Big Picture) – what do you want?**
 - Benefit the public health
 - Attract new R&D resources
 - Obtain return on public investment
 - Stimulate economic development
 - Avoid inhibiting competition
 - Research Tool Policy – limit patenting, non-exclusive license...

TAXUS[®] drug-eluting stent

- National Institute on Aging (NIA)
- Licensed to Angiotech Pharmaceuticals
- Prevents restenosis (narrowing of a blood vessel) after angioplasty to treat a blockage
- Localized release of paclitaxel (taxol), which inhibits mitosis



<http://www.ott.nih.gov/pdfs/TaxusCS.pdf>

Ocuvite® Preservision Nutritional Supplement

- National Eye Institute (NEI)
- Licensed to Bausch and Lomb
- Over-the-counter nutritional supplement to treat macular degeneration



Study details at

http://en.wikipedia.org/wiki/Age-Related_Eye_Disease_Study

Age-Related Eye Disease Study

- The **Age-Related Eye Disease Study** was a **clinical trial sponsored by the National Eye Institute**, one of the National Institutes of Health in the United States. The study was designed to:
 - investigate the natural history and risk factors of age-related macular degeneration (AMD) and cataracts, and
 - evaluate the effects of high doses of antioxidants and zinc on the progression of the two conditions in those with AMD
- The study of 3600 individuals for an average of 6.3 years concluded that high levels of antioxidants and zinc can reduce some people's risk of developing advanced AMD by about 25 percent. Those that benefited from the dietary supplements included those with intermediate-stage AMD and those with advanced AMD in one eye only. The supplements had no significant effect on the development or progression of cataracts. "High levels" in this case were defined to be:
 - 500 milligrams of vitamin C;
 - 400 international units of vitamin E;
 - 15 milligrams of beta-carotene (or 25,000 international units of vitamin A);
 - 80 milligrams of the dietary mineral zinc, in the form of zinc oxide; and
 - two milligrams of copper as cupric oxide, added to prevent copper deficiency anemia, a condition associated with high levels of zinc intake.
- The results were reported in the October 2001 issue of Archives of Ophthalmology.
- Bausch & Lomb was a collaborator in the study and provides vitamins pre-packaged with this formulation, sold commercially as OcuVite PreserVision antioxidant vitamin and mineral supplement, as do other suppliers, for example, Viteyes AREDS formula eye vitamins.

Patents aren't everything

LAD2 mast cell line

- National Institute of Allergy and Infectious Disease (NIAID)
- Not patented, per NIH policy on research tools
- Derived from human mast cell leukemia tissue
- Unique for studies of allergy and inflammation
- 45 executed BMLs to date, to companies around the world
- Hundreds of MTAs (through IC tech transfer office)
- Technology transfer award

Synagis

- A monoclonal antibody used for the prevention and treatment of serious lower respiratory tract disease by respiratory syncytial virus (RSV). RSV is the most common cause of pneumonia and bronchiolitis in infancy and early childhood. **Synagis** is the world's first monoclonal antibody licensed by the FDA for any infectious disease (1998).
- Synagis is a prime example of how government-industry **partnerships benefit the public**. The **NIAID researchers** derived a novel antibody that could prevent RSV infection in cotton rats. However, without the additional research and development conducted by **MedImmune, Inc.**, the therapeutic potential of the antibody for humans would not have been realized. Thus, linking **federal laboratories with private corporations** allow for the introduction of innovative products to the market place that can be used to improve the public health.
- <http://www.otc.nih.gov/productpipeline/default.aspx>

Commercial licensing of HIV -1 protease

Commercial Licensing of HIV-1 Protease: Applications of the NIH Research Tools Policy
 George H. Keller and Steven M. Ferguson, *www.biolawbusiness.com*, vol.12, number4, 2009
<http://www.ott.nih.gov/pdfs/Ferguson-Journal-of-Biolaw-Business-12-4-pp-1-4-2009.pdf>

Table 5 Principles of the NIH Research Tools Policy	
<i>Principle One</i>	Ensure academic freedom and publication.
<i>Principle Two</i>	Promote commercialization consistent with the Bayh-Dole Act.
<i>Principle Three</i>	Minimize administrative impediments to support research.
<i>Principle Four</i>	Ensure dissemination of NIH-funded tools.

Table 6 Typical Royalties for HIV-1 Protease Research Reagent Product Sales	
License Execution Royalty	\$ 2,500
Minimum Annual Royalty	\$ 400
Earned Royalty on Sales	7%

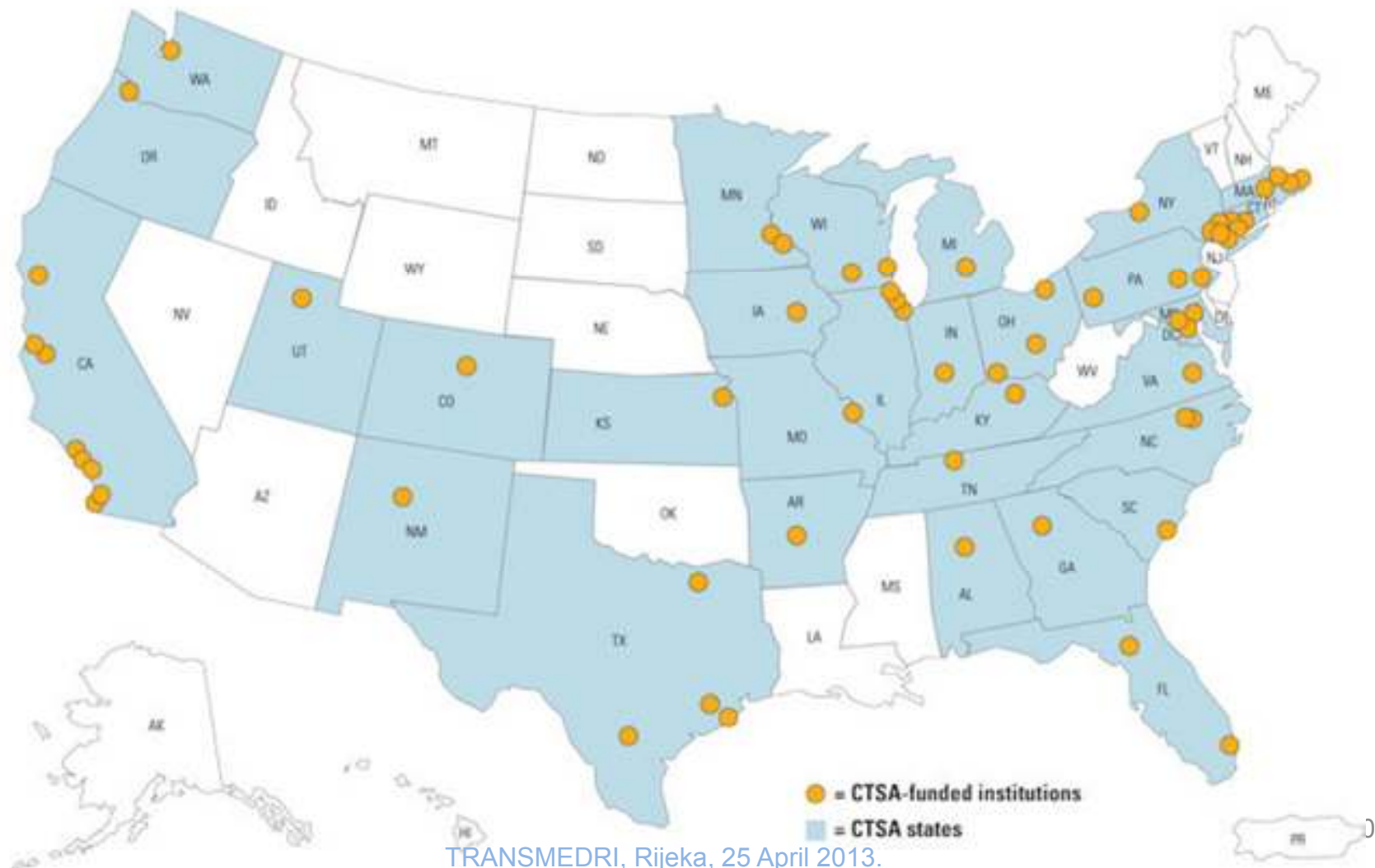
Table 7 Typical Royalties for HIV-1 Protease Diagnostic Product Sales	
License Execution Royalty	\$ 10,000
Minimum Annual Royalty	\$ 10,000
Earned Royalty on Sales	2%

Table 8 Typical Royalties for Internal Use of HIV-1 Protease by Pharmaceutical Companies (By Stage of Inhibitor Development)			
Stage of Inhibitor Development	Execution Royalty	Minimum Annual Royalty	Single Payment Paid-Up License
Pre-Clinical R&D	\$ 50,000	\$ 50,000	\$ 150,000
Clinical Trials	\$ 150,000	\$ 50,000	\$ 250,000
FDA Approved	\$ 250,000	\$ 50,000	\$ 450,000

Table 9 Results of NIH HIV-1 Protease Licensing Program	
Type of Licensee	Number of Licensees
Research Reagent Sales	5
Diagnostic Product Sales	3
Pharmaceutical Internal Use	10
Total (additional agreements pending)	18
Licensing Revenue To Date: over \$10 million	



Translational science reduces the time it takes for laboratory discoveries to become treatments for patients, and to engage communities in clinical research efforts

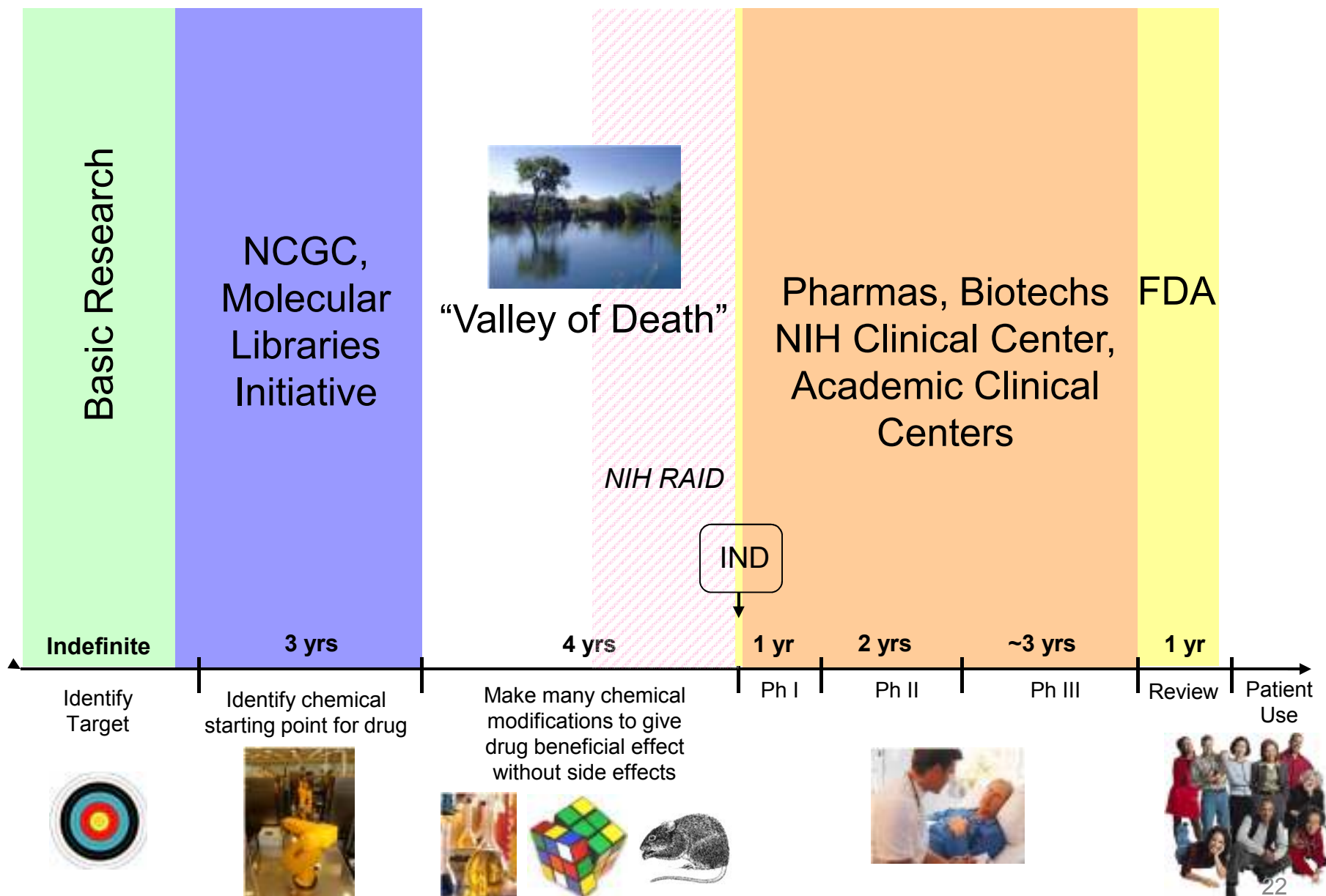


The Problem of Rare and Neglected Diseases

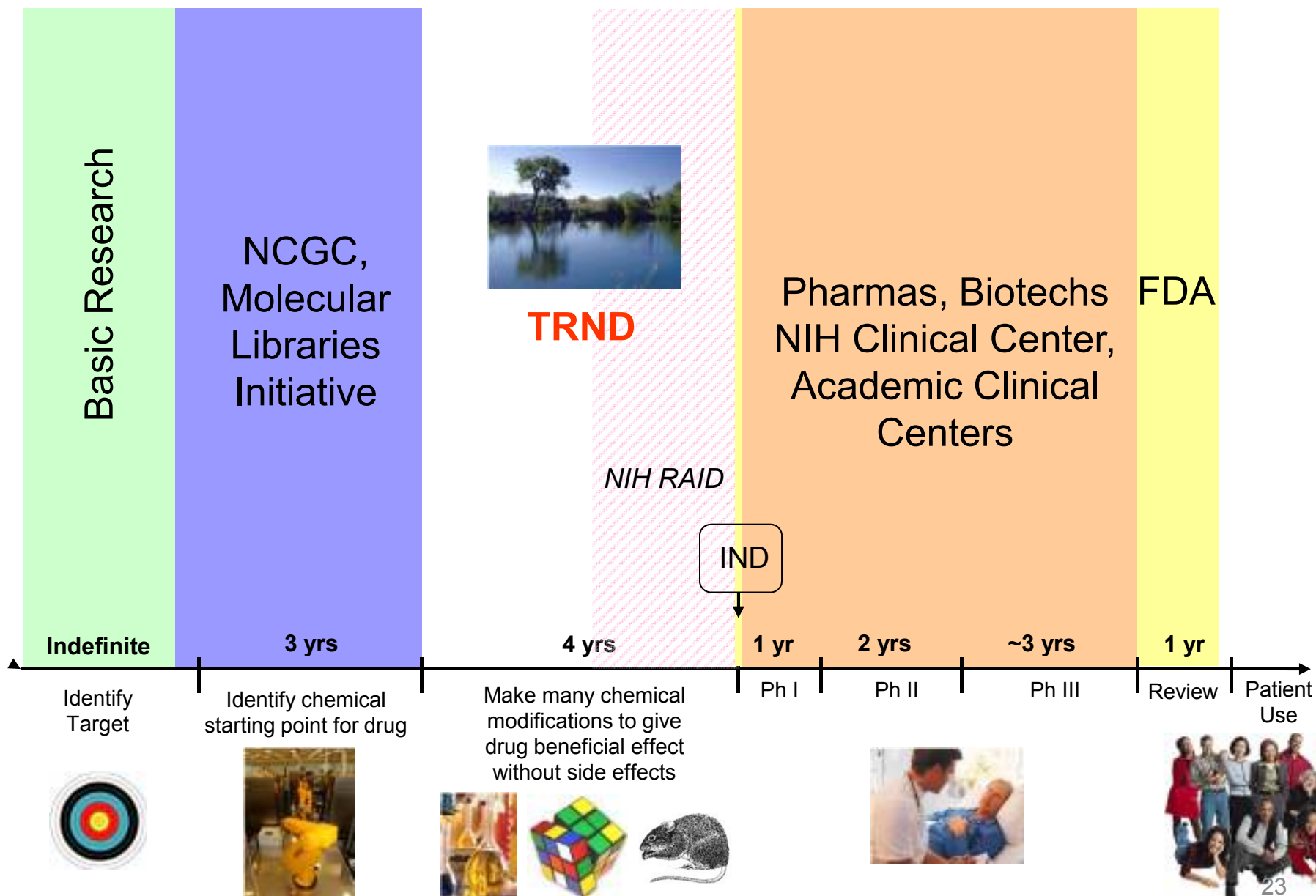
- ~7,000 diseases affect humankind – but only a small fraction support commercial development of therapeutic agents
- Two types of neglected diseases:
 - Low prevalence, i.e., “rare” (<200,000 prevalence in U.S.)
 - There are >6000 rare (orphan) diseases
 - Cumulative prevalence in U.S. ~ 25 – 30 million
 - Most are single gene diseases
 - <200 have any pharmacotherapy available
 - High prevalence but “neglected”
 - Occur chiefly among impoverished and marginalized populations in developing nations (treatment costs prohibitive)
 - Most are infectious



The long pathway to drug development



The long pathway to drug development



NIH Therapeutics for Rare and Neglected Diseases (TRND) Program

Creating a Drug Development Pipeline at NIH

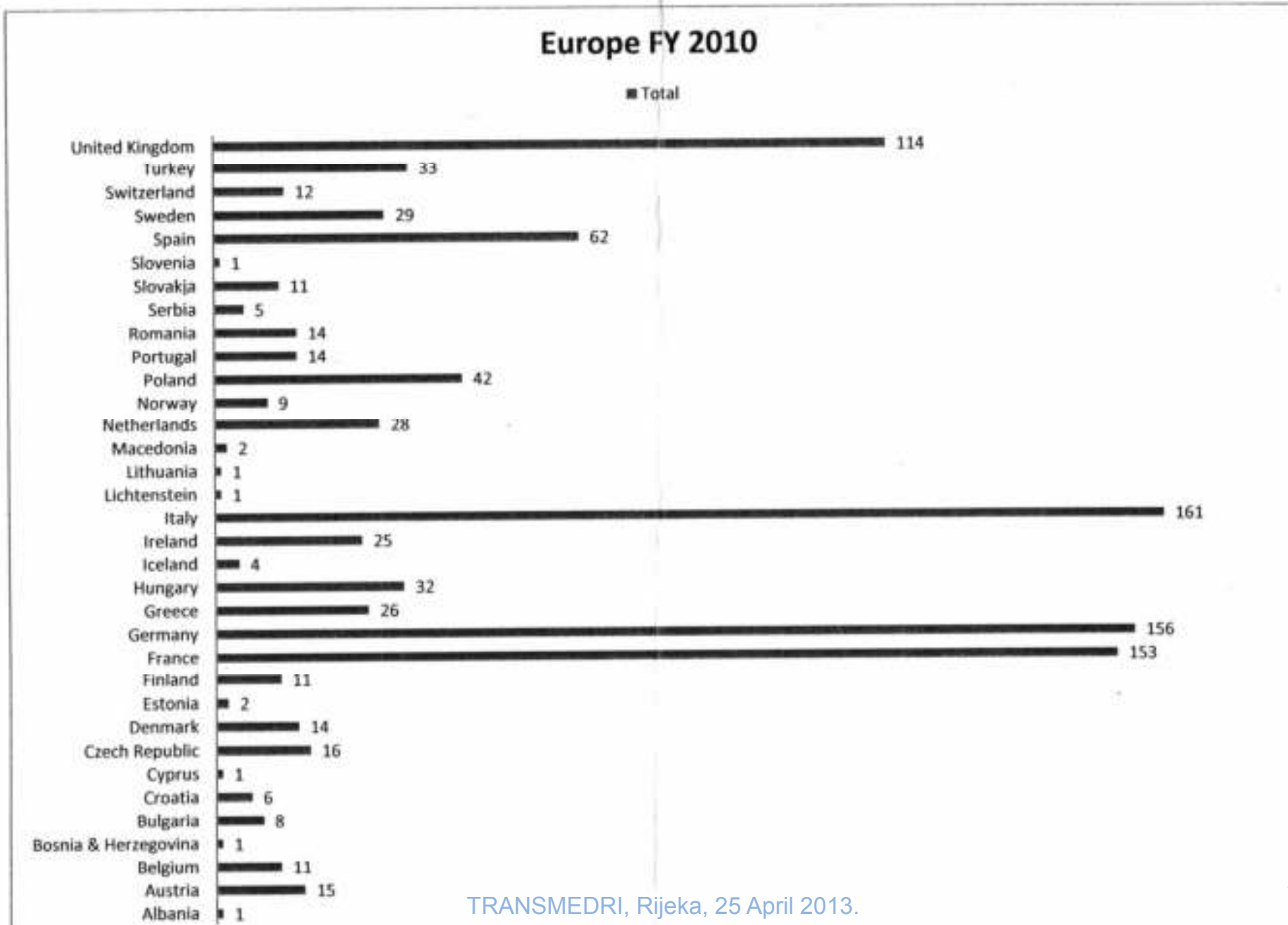
- Congressionally-mandated effort to speed development of new drugs for rare and neglected diseases
- Administration and governance at NIH
 - Governance/oversight by Office of Rare Diseases Research
 - Administered by NHGRI
- Operations: collaboration between intramural and extramural labs with appropriate expertise
- Projects will:
 - Enter TRND at a variety of stages of development
 - Be taken to phase needed for external organization to adopt for clinical development

<http://www.ncats.nih.gov/funding-and-notices/open/open.html>

Take home messages

- TT activities cost, usually it is hard to earn money (but there are indirect benefits too)!
- Importance of having defined policies that express and promote wishes and mission of institutions
- Encourage, reward and appreciate participation in the TT activities, but not demand it
- Can be additional resource of money, but, more important, public benefit
- Strengthening the economy
- For the knowledge transfer you should work good (the best) quality science, not necessarily „applied research”

Fogarty International Center



Collaboration opportunities

- <http://projectreporter.nih.gov/reporter.cfm>

The screenshot displays the NIH RePORTER website's Query Form. The browser window title is "Query Form - NIH RePORTER - NIH Research Portfolio Online Reporting Tools Expenditures and Results". The page header includes the U.S. Department of Health & Human Services logo and the NIH RePORTER logo. The main navigation bar contains links for HOME, FREQUENTLY REQUESTED REPORTS, REPORT CATALOG, CATEGORICAL SPENDING, REPORTER, GLOSSARY, TAGS, LINKS, and ABOUT RePORTER. The Query Form itself is divided into two columns of search criteria, each with a "SUBMIT QUERY" button. The left column includes fields for NIH ARRA Projects Only, Text Search (Logit), Project Number, Principal Investigator (Last Name, First Name), Organization, ORIS Number, Department, Educational Institution Type, City, State, Country, and Congressional District. The right column includes Fiscal Year (FY), NIH Spending Category, Agency/Institution/Center, Funding Mechanism, Award Type, Activity Code, Exclude Subprojects, Study Section, RFA/PA, Public Health Relevance, Project Start Date, Project End Date, and Award Notice Date. There are also "CLEAR QUERY" buttons for each column and a "SUBMIT QUERY" button at the bottom.

Scientists As Entrepreneurs - USA

- No economic prosperity based only on scientific knowledge and research alone
- „local heroes of the global village”
- Often entrepreneur is needed to facilitate development of new ideas from research labs
- Motivating legislative background of technology transfer
- Academia - main purpose: to ask questions!
- Industry - main purpose: to answer questions!

Why Have Scientists Succeeded In the U.S. As Entrepreneurs?

- Not due to geographic origin (many not native U.S.).
- More about institution, legal and organizational support for entrepreneurship
- Bayh-Dole Act seen as stimulus for commercializing federally-funded research in U.S.
- Grants - a proven engine for entrepreneurship.
- 25% of NCI grant recipients from 1998-2003 started their own company.

Growing Entrepreneurial Scientists

- New and emerging companies founded by scientist/entrepreneurs have driven the development of innovative products.
- Funding & training scientists (especially at academic research centers) can provide the next wave of innovative small companies in the U.S. or elsewhere.
- Business & entrepreneurial training programs can provide the spark for such developments.

After the training...

- Done:
 - Technology Mapping
 - Search for technology
 - Contact with NIH colleagues
 - Techno- L
 - GLOWBRAIN
- Still needed:
 - Raise interest among researchers
 - Good Web site
 -

Innovations and Croatia



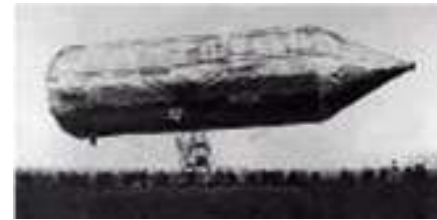
**Homo Volans
(The Parachutist)**
F. Vrančić (1551-1617)



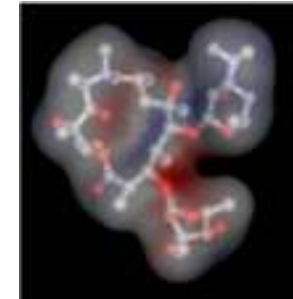
Criminal Fingerprinting
J. Vučetić (1858-1925)



**The Necktie
Era of Luis XIV**
(1635-1650)



Airship (zeppelin)
D. Swartz (1852-1897)



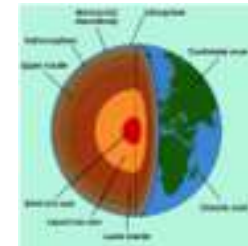
Azithromycin
S. Kobrehel *et al.* (1981)



Torpedo
Ivan Blaz Lupis Vukic



Nikola Tesla (1856-1943)



Moho-Layer, A. Mohorovičić (1858-1936),
seismologist, 'Moho' discontinuity named after him



Technical Pencil, S. Penkala (1871-1922)



First MP3 decoder,
T. Uzelac (1997)



MAG LIGHT A. Maglica

CENTRE FOR TRANSLATIONAL AND CLINICAL RESEARCH OF THE SCHOOL OF MEDICINE AND UNIVERSITY HOSPITAL CENTRE, ZAGREB

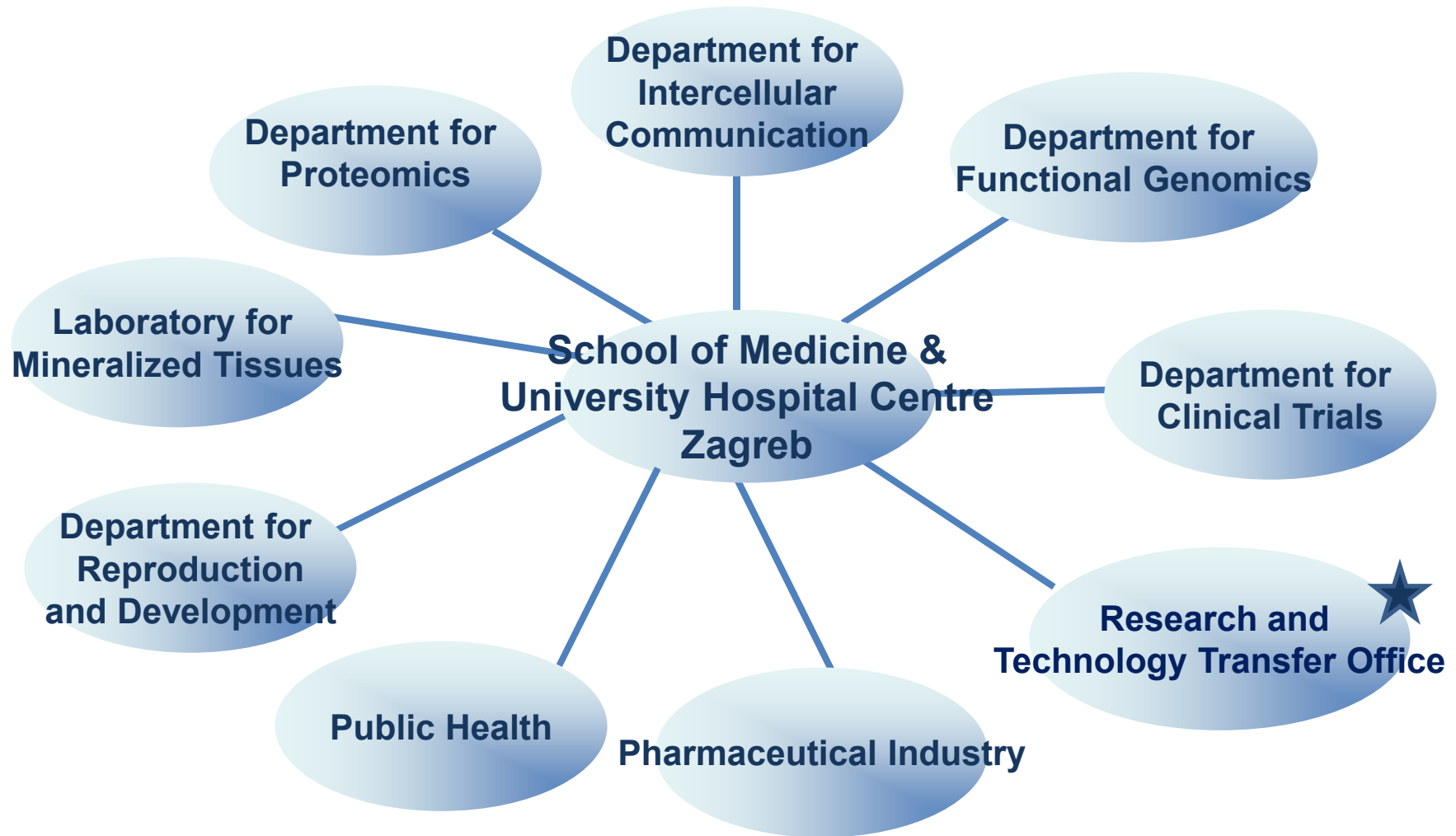
- Established in 2009
- Based on „Strategic Framework for Promotion of Medical Education and Translational Research at Biomedical Centre of University of Zagreb” from 2007. ("STRATEŠKI OKVIR ZA PROMICANJE MEDICINSKE EDUKACIJE I TRANSLACIJSKIH ISTRAŽIVANJA NA BIOMEDICINSKOM SREDIŠTU SVEUČILIŠTA U ZAGREBU,,)
- Collaboration with GlaxoSmithKline/Galapagos/Fidelta
- Transfer of group of people and equipment

BRA-ZAG

- Connect academia, basic research, clinical practice and industry
- Promote translational research
- Promote technology transfer

- Initiate innovation in research, academia and clinical practice
- Biomedical Center – 2002/2003

CENTRE FOR TRANSLATIONAL AND CLINICAL RESEARCH: SCHOOL OF MEDICINE AND UNIVERSITY HOSPITAL CENTRE, ZAGREB



Source: Nada Čikeš

TRANSMEDRI, Rijeka, 25 April 2013.

Research and Technology Transfer Office: Connection between Discovery and Application

Mission:

- Promote the development of inventions toward practical application for public benefit;
 - Identify and promote innovative approaches for rapid transfer to patients and the commercialization of ideas
-
- RTT Office established in April 2009
 - Complementary to University TTO due to specificity of biomedical research

Basic Research / Discovery

Translation/Innovation

Practical Implementation

Barriers to Tech Transfer

- Ideological opposition/ lack of knowledge
- Fear of conflict of interest
- Fear of failure
- Lack of support, insufficient resourcing of TTO's

Research and Technology Transfer Office Activities

- Engage in IP protection and commercialization
- Train others in IP , TT, “self marketing”
 - Doctoral studies
 - Workshops
 - Seminars at Departments
- Collaborate with other TTOs
- Improve research administration to benefit scientists
- Assist in identifying sources of financing
- Assist in international proposal preparation
- Coordinate collaborations with academic / commercial institutions
- Participate in projects

PROJECTS – CTCR - ACTIVE

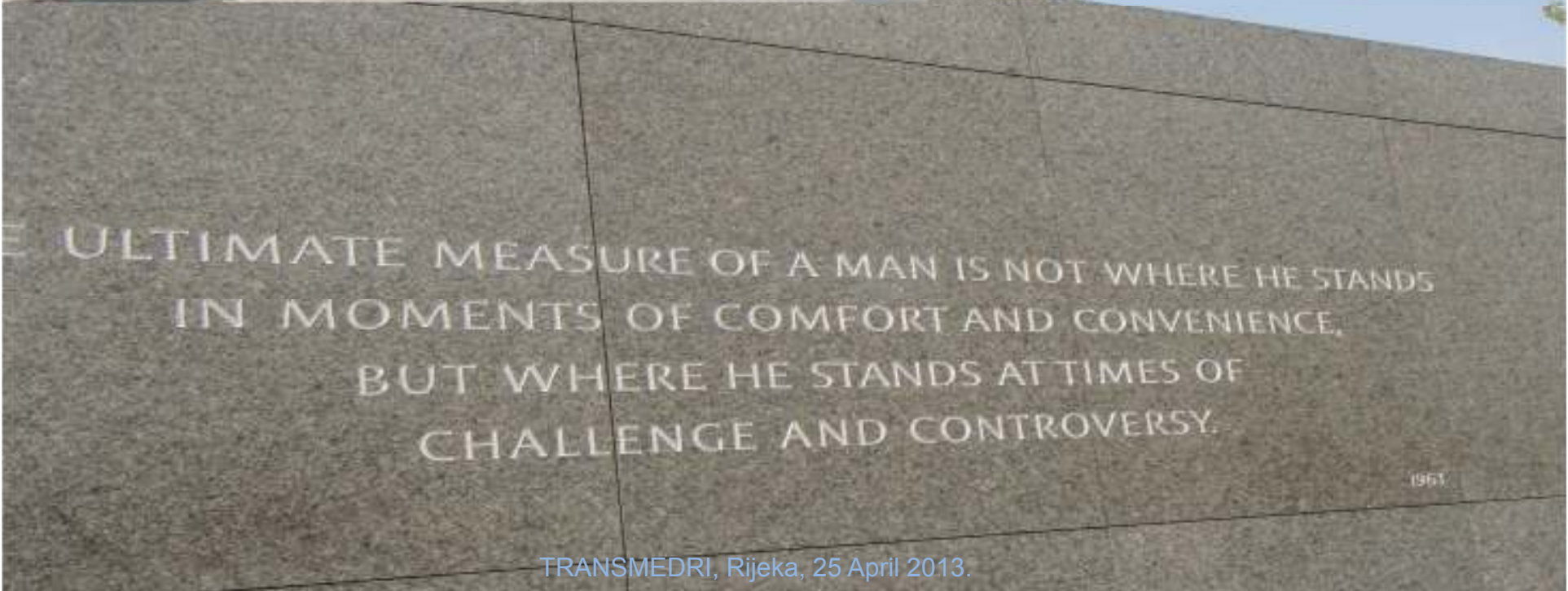
- **OSTEOGROW**, prof. Vukičević coordinator, **FP7 cooperation**, 5,8 mil. EUR (our share 600.000 EUR)
- **GLOWBRAIN**, HIIM, prof. Gajović coordinator, **FP7 REGPOT** (strengthening research capacities); 3,7 mil. EUR
- Molecular profiling and proteomics of urothelial carcinomas (**GENPROCAN**), prof. Jelaković- project leader, **HRZZ**, 200.000 EUR
- A novel anabolic targeted therapy for osteoporosis: (**BONE6-BIS**), prof. Vukičević coordinator, **HRZZ**, 200.00 EUR
- European registry and network for Intoxication type Metabolic Diseases; **E-IMD**, prof. Barić partner, **DG Sanco (EAHC)**, 42.000 EUR
- European network and registry for homocystinurias and methylation defects, **E-HOD**, prof. Barić partner, **DG Sanco (EAHC)**, 27.000 EUR
- Inherited NeuRoMetabolic Diseases Information Network, **InNerMed-I Network**, prof. Barić partner, **DG Sanco (EAHC)**, 76.000 EUR
- The appropriateness of prescribing antibiotics in primary care in Europe with respect to antibiotic resistance (**APRES**), prof Katić, prof. Kalenić partner, **FP7 cooperation**, 94.000 EUR
- Improving quality and safety in the hospital: The link between organisational culture, burnout, and quality of care (**ORCAB**), prof. Mustajbegović partner, **FP7 cooperation**, 110.000 EUR
- Tehnologija za poboljšavanje srčane funkcije nakon preboljelog infarkta miokarda, (**AMI**), prof. Vukičević voditelj, **BICRO** Provjera inovativnog koncepta, 350.000 HRK
- E-modules on HistoPathology: a valuable online tool for students, researchers and professionals - **HIPON**, prof. Seiwerth partner, **Life long learning**, 53.000 EUR

PROJECTS - CTCR

- **Completed:**
- MAGISTER, doc. Jelić, partner, FP7 cooperation, 210.000 EUR (11/2012)
- Cytopathological characterization of the brain in a rat model of sporadic Alzheimer disease, prof. Šalković-Petrišić, **UKF - Crossing border**, 200.000 EUR (7/2012)
- Bone morphogenetic protein-1 isoforms in bone regeneration, prof. Vukičević, **UKF - Crossing border**, 200.000 EUR (7/2012)
- Research Infrastructure for Translational Research and Applied Genomics (**TRANSMED**), prof. Barić partner, **IPA IIIc**
- Technology Mapping of the University of Zagreb, prof. Čikeš, **IPA IIIc**

PROJECTS at evaluation

- UKF (Unity through Knowledge) - 7 submissions
- LLL (Life long learning) 2 submissions
- FP7 Health 1 submission second stage (out of 4)
- FP7 NMP 1 submission
- ERASMUS MUNDUS 1 submission
- TEMPUS 1 submission
- DG Sanco 2 submissions



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President Obama on the Importance of Science

Speaking at the National Academy of Sciences in 2010:

“Science is more essential for our prosperity, our security, our health, our environment and our quality of life than it has ever been before.”

This training was supported by the NIH OTT.

Thanks to:

Dean of the School of Medicine University of Zagreb, prof. Davor Miličić, Prof. Nada Čikeš, Prof. Bojan Jelaković, Prof. Vukičević,
Pfizer, Abbot

And special thanks to Dr. Peter Jackson

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Šalata 2, 10000 Zagreb



TRANSMEDRI, Rijeka, 25 April 2013.

SVETI TRAJAN
PROGRAM