Managing resources
for biomedical research

Biobanking
in Biomedical Research

Part 6

The European Research Infrastructure for Biobankin and Biomolecular resources (BBMRI)

Kurt Zatloukal, Medical University of Graz, Austria

Siena, June 2009

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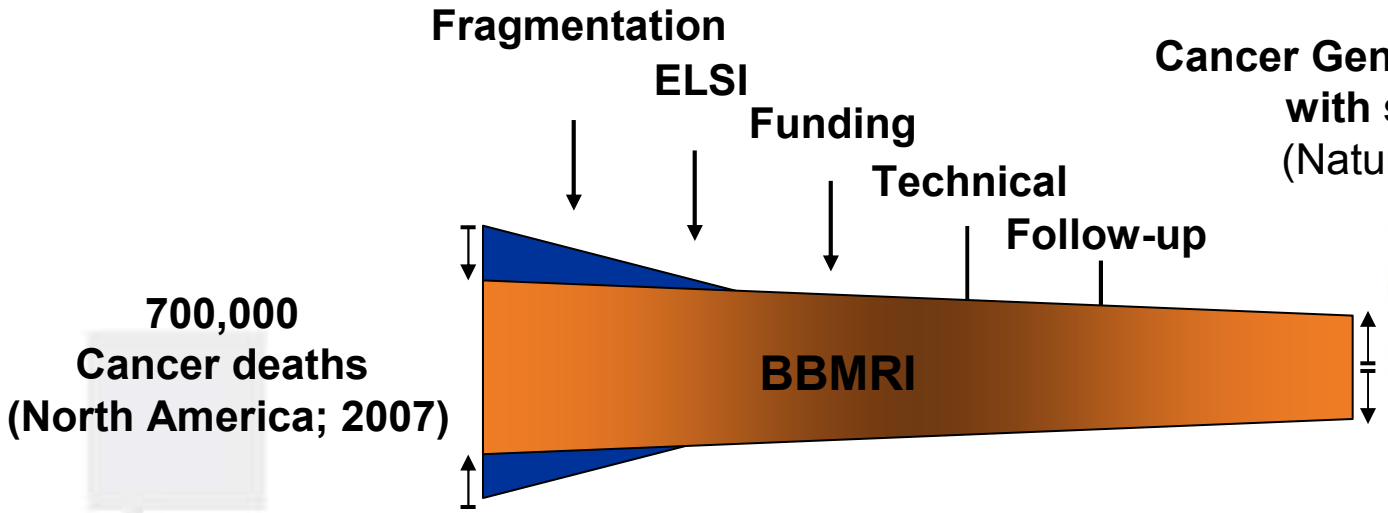
Biobanking and
Biomolecular
Resources Research
Infrastructure

Biobanks in Medical Research



Cancer Genome Project struggels with sample shortage
(Nature Medicine 2007)

Mainframephotographics.com

Long haul: The Lung Cancer Tissue Bank has only 20 of the 500 samples required.

NCI: Biological sampels are #1 roadblock
OECD: Global Biological Resource Centre Network
WHO/IARC: Standards for biological resource centres
ESF: Science Policy Briefing: Need for integration
EU/ESFRI: Research infrastructure for Biobanks and Biomolecular Resources (BBMRI)

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The Next Big Questions

Why are we different?

- **Why remain some healthy until high age?**
- **Why do some develop certain diseases?**
- **Why do some respond to therapy?**
- **Why do some develop adverse drug reactions?**

- 1000 genomes project
- Cancer genome project
- Innovative Medicines Initiative
- Personalized medicine

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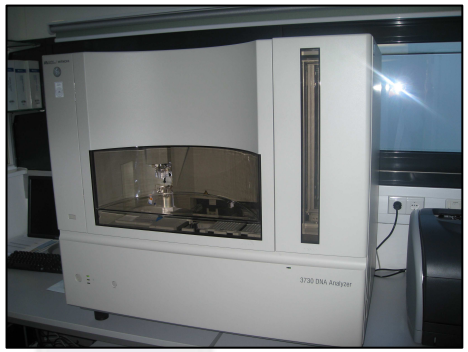
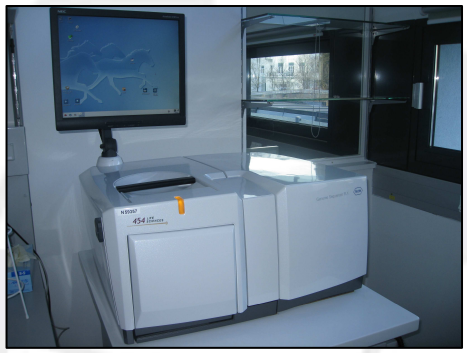
Progress in Sequencing Technologies



Sequencing of the human genome:

2001: Human Genome Project
10 years - 3 bio. USD



2008: Next generation sequencing
10 hrs - 50,000.- USD

Allows new research approaches
Shifts bottleneck to biological samples and data management

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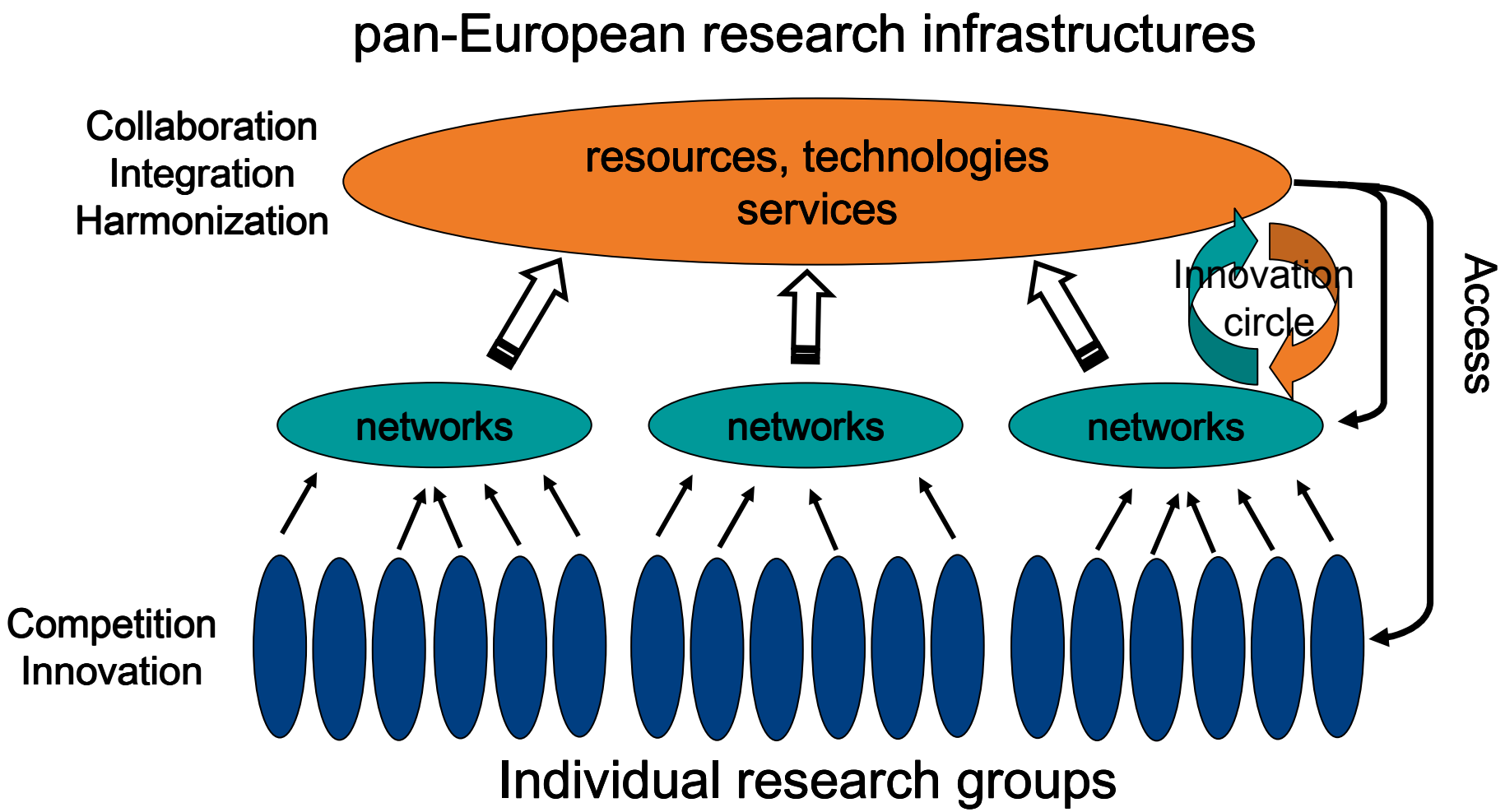
The New Dimension in Life Sciences Research



EUROPEAN ROADMAP FOR RESEARCH INFRASTRUCTURES

Report 2006

The facility

A pan-European and broadly accessible network of existing and de novo biobanks and biomolecular resources. The infrastructure will include samples from patients and healthy persons, molecular genomic resources and bioinformatics tools to optimally exploit this resource for global biomedical research.

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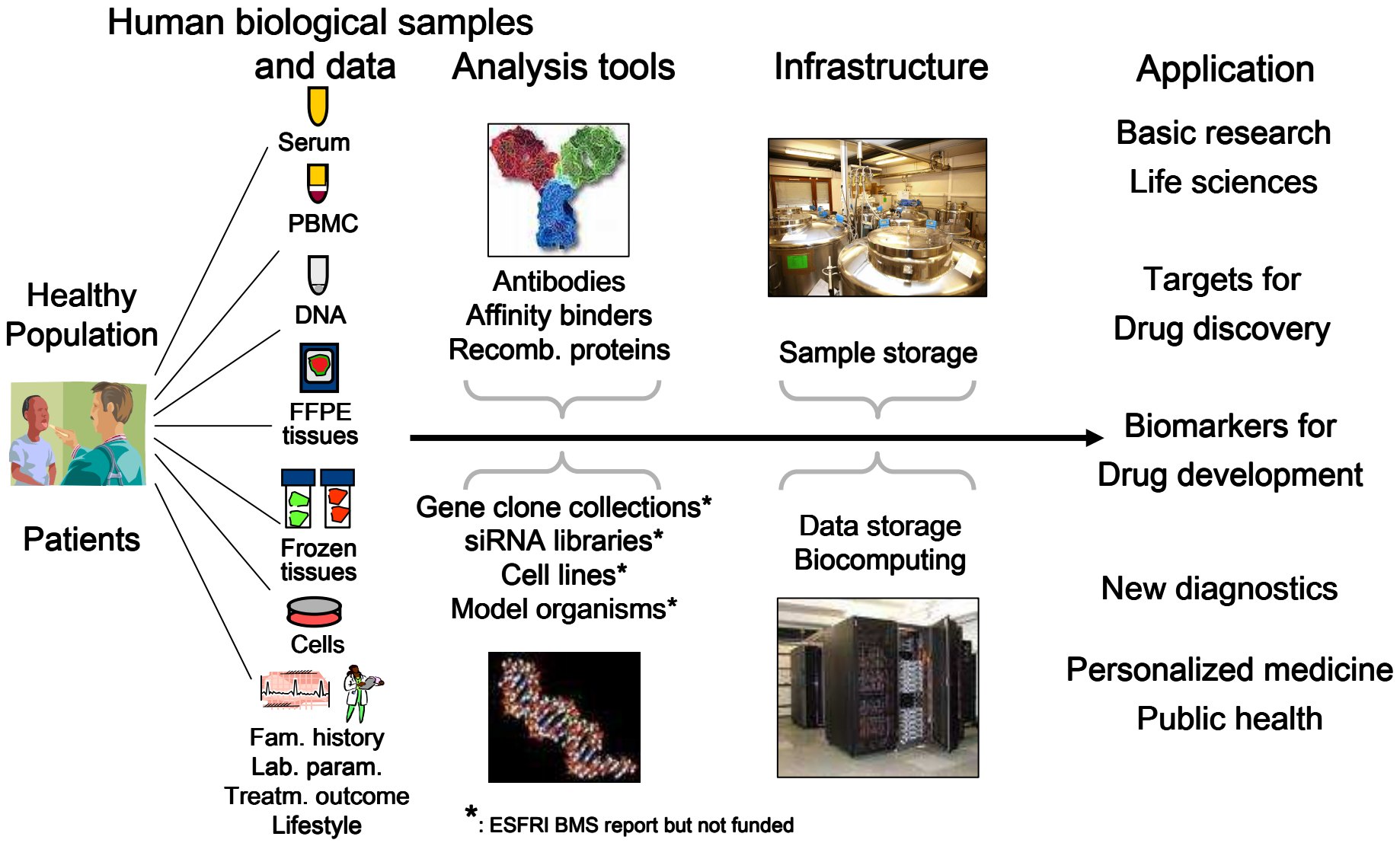
Key Components of BBMRI



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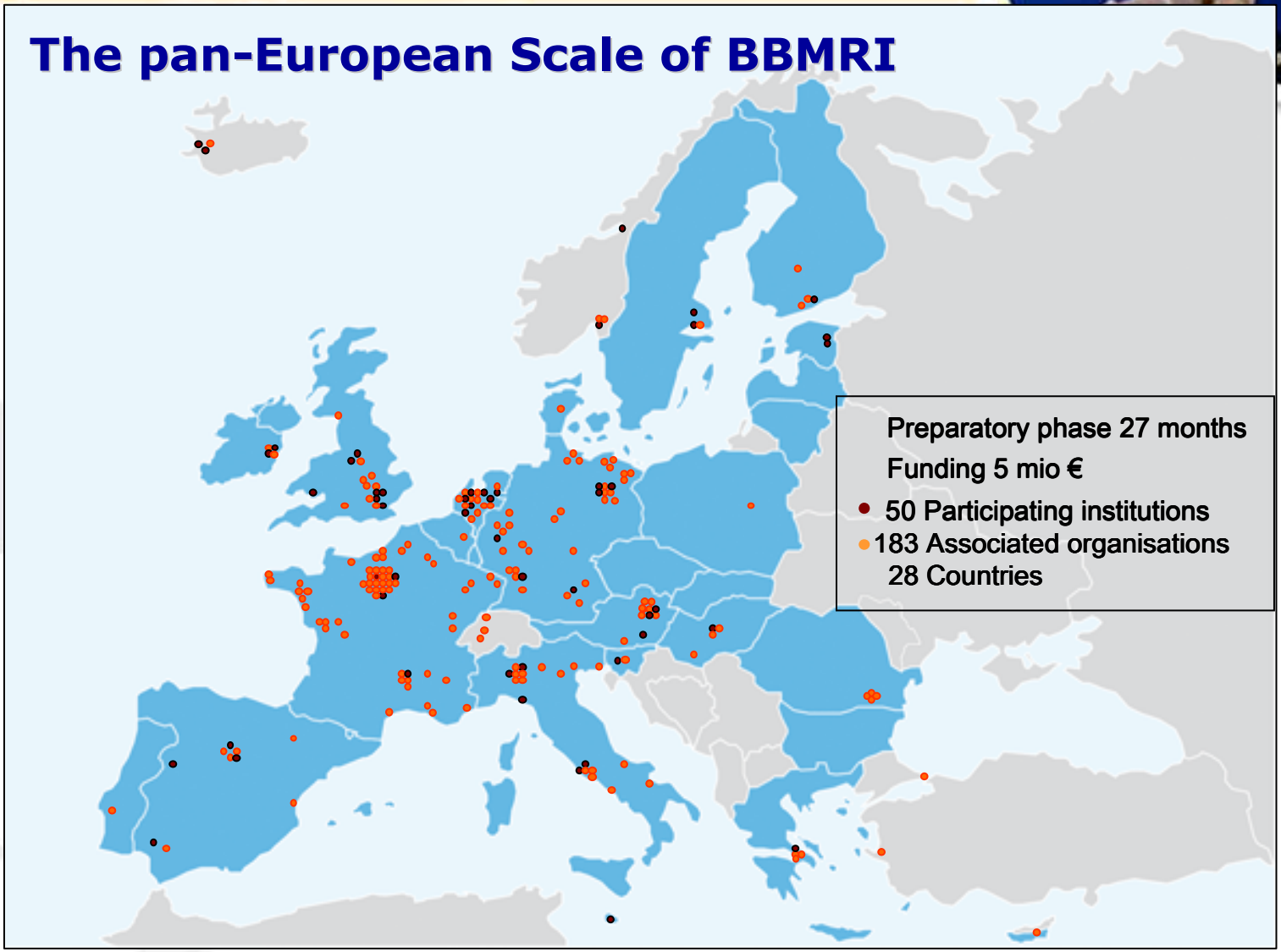
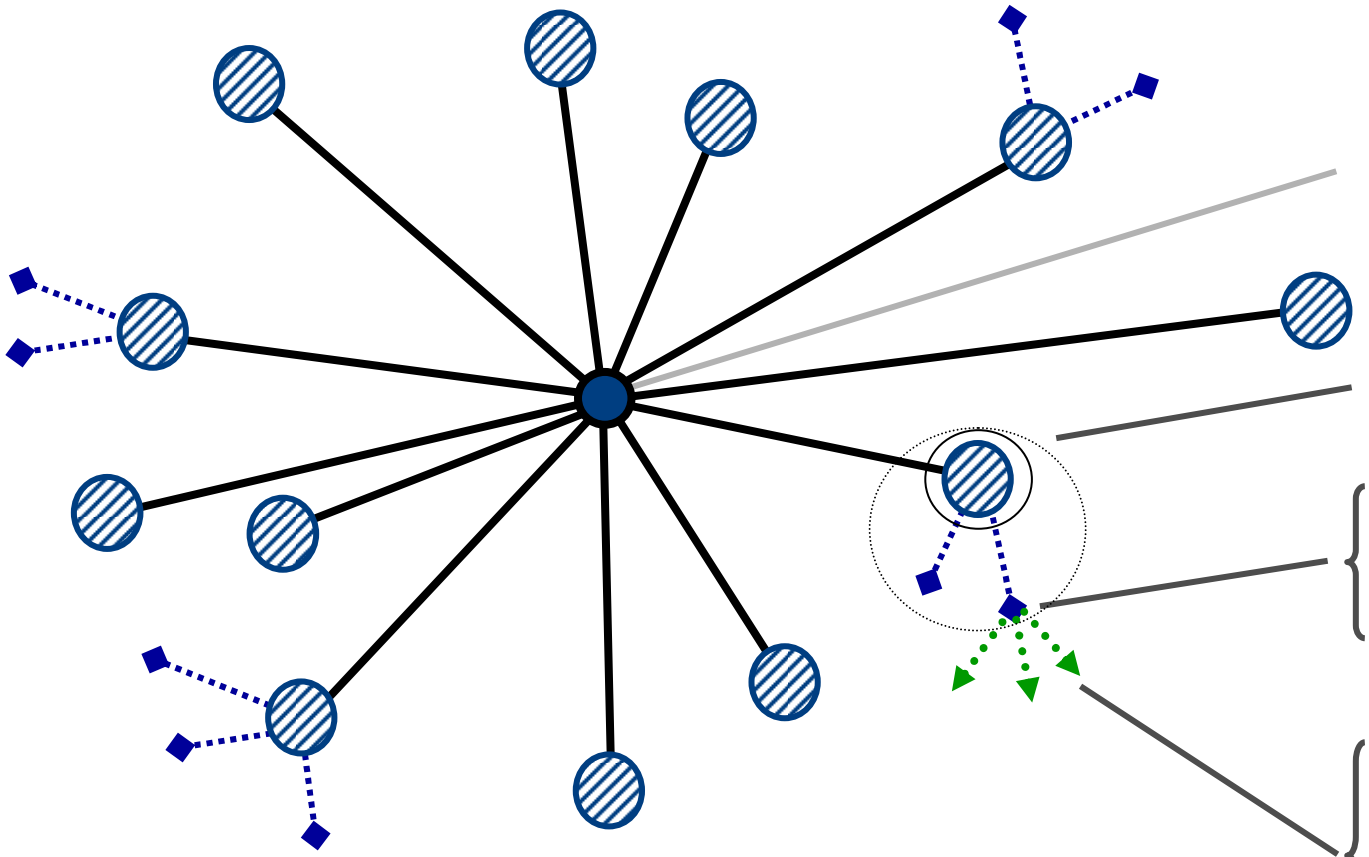
The pan-European Scale of BBMRI



Possible Legal Structure of BBMRI (ERIC)

Distributed hub and spoke structure



Secretariat
(statutory seat)

National members

Biobanks
Biomolecular res.
Technology centers

Associated partners
Hospitals
Universities
Service providers …

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Organization (prep phase)

Strategic

Science
Industry
ELSI

Advisory board → **Governance council** (participants, ass. organizations) ← **Stakeholder forum**

Funders
Patients
Clinicians
Industry
Partners
Users

Executive

Coordination board (external projects)

Steering committee (WP leaders, chairs)

Participants — **Project Management WP1** — **Executive Management** — **Funding Financing WP7** — **Participants**

Operative

Population-based Biobanks WP2

Disease-oriented Biobanks WP3

Biomolecular resources Technologies WP4

Data bases Biocomputing WP5

E L S I WP6

Participants | **Participants** | **Participants** | **Participants** | **Participants**

The Challenges

- Harmonized processes (evidence-based standards)
- Incentives for contributors
- Access rules
- Heterogenous European ethical and legal landscape
- Data protection in biobanking
- Sustainable funding

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The Process

- Assessment of existing resources and technologies
- Concept for integration
- Prototype
- Infrastructure

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The Questionnaire

- Evaluation of:
  - Available samples: type, quality, quantity
  - IT infrastructure, database, data protection
  - Governance structure
  - Access rules
  - Pertinent ELSI
  - Funding

⇒ Inventory
  - Identify candidates for prototype and demonstration project
  - Identify candidates for future members
  - Basis for construction and operation plan

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Inventory on Existing Disease-Oriented Biobanks

- BBMRI questionnaires have been developed jointly by all WPs and P^{3}G
- were sent to European biobanks via the national coordinators
- Collection process is still ongoing
- Meanwhile returned:
  - 38 network questionnaires,
  - 185 core questionnaires,
  - 216 collection questionnaires and
  - 185 supplementary questionnaires
- Stored in a relational database system

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Country	Network	Core	Collection	Supplements
Austria	2	12		2
Belgium		1		1
France	5	23	50	50
Germany	12	30	31	37
Greece		2	1	
Hungary	1	11	32	
Iceland	1	3		
Ireland		1		3
Israel	1	2		6
Italy	4	30	39	62
Portugal		1	34	
Romania		2		6
Spain	5	13	11	11
Sweden		1		
Switzerland	1	3		
The Netherlands	5	47	18	6
United Kingdom	1	3		1
TOTAL:	**38**	**185**	**216**	**185**

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Web-based Overview Catalogue

Erich Wichmann (WP3), Klaus Kuhn (WP5)

Basic requirements:

- Clearly presented key data of the individual biobanks (Background, objectives, number of samples etc.) with links to homepages
- Overview of existing samples, sorted by disease group
- Overview of biobanks that are part of the inventory
- Descriptive statistics of key questions (histograms etc.)
- Search function and possibility to sort
- Online entry of new biobanks with web-based forms and online update of data already stored in the database
- Comparison tables
- User administration

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The Prototype

Aims

- The prototype should fulfil the role of proof-of principle for BBMRI. After being implemented under the final legal entity of BBMRI the prototype should be scaled up to the fully working infrastructure in the construction phase of BBMRI.

- Since the construction of a prototype of BBMRI is not part of the BBMRI PP, no funding from the BBMRI PP project is available and all activities along these lines have to be on a voluntary basis.

- All activities should be well coordinated with the BBMRI-PP and results should be made available for the construction of BBMRI

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Key Features of the Prototype

- The prototype should reflect the distributed hub and spoke architecture of BBMRI.
- Procedures for efficient transnational exchange of samples and data that properly consider the applicable ethical and legal requirements should be established.
- The OECD best practice guidelines and the WHO/IARC guidelines for biological resource centres the should be considered.
- There should be only one BBMRI prototype. Consortia working on a prototype hub should well coordinate their activities with other consortia and the leader of the corresponding BBMRI workpackages.

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Recommendations

It is recommended that biobanks participating in the prototype activity will address the following issues:

Evaluation of compatibility of:

- Sample & data quality
- Data formats (web interfaces, access)
- ELSI (applicable data protection legislation, requirements for REC approval, rules for access, etc.)

It should be explored whether the competent national authority for research infrastructures requests approval for participation in the prototype activity.

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Some Expected Outcomes

- Standard Operating Procedures for collaboration including approved MTA, CDA, IC, assess rules
- Realisation of the quality criteria which are being developed in BBMRI
- Development of concept of BBMRI hubs including the options of a decentralized as well as a partially centralized repository
- To provide common access via the web site of the prototype

All established procedures should be suited to become integrated into the operational concept of BBMRI.

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Prototype Hub for Disease-Oriented Biobanks

Partners

The BBMRI WP3 Prototype is open for disease-oriented biobanks. In the first stage the following partners will collaborate:

- BB-MUG:Medical University of Graz (Austria)
- PSI: The String of Pearls initiative (The Netherlands)
- BNADN: Spanish National DNA Bank (Spain)
- NetGerBB-Pilot: Network of German Biobanks – Pilot (Germany)
- Genethon: Genethon Network of Rare Diseases (France)

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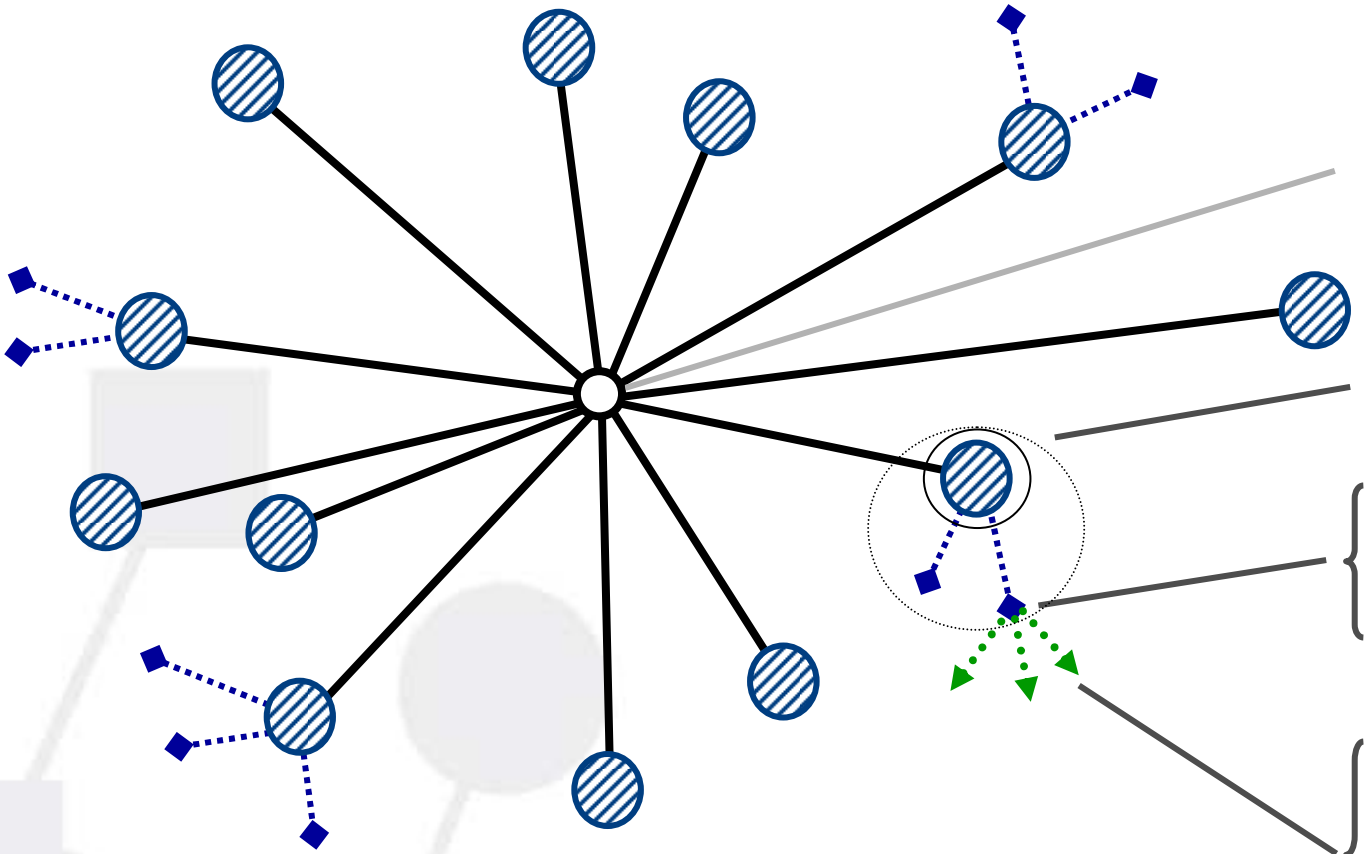
Distributed hub and spoke structure



Secretariat
(statutory seat)

National members

Biobanks
Biomolecular res.
Technology centers

Associated partners
Hospitals
Universities
Service providers …

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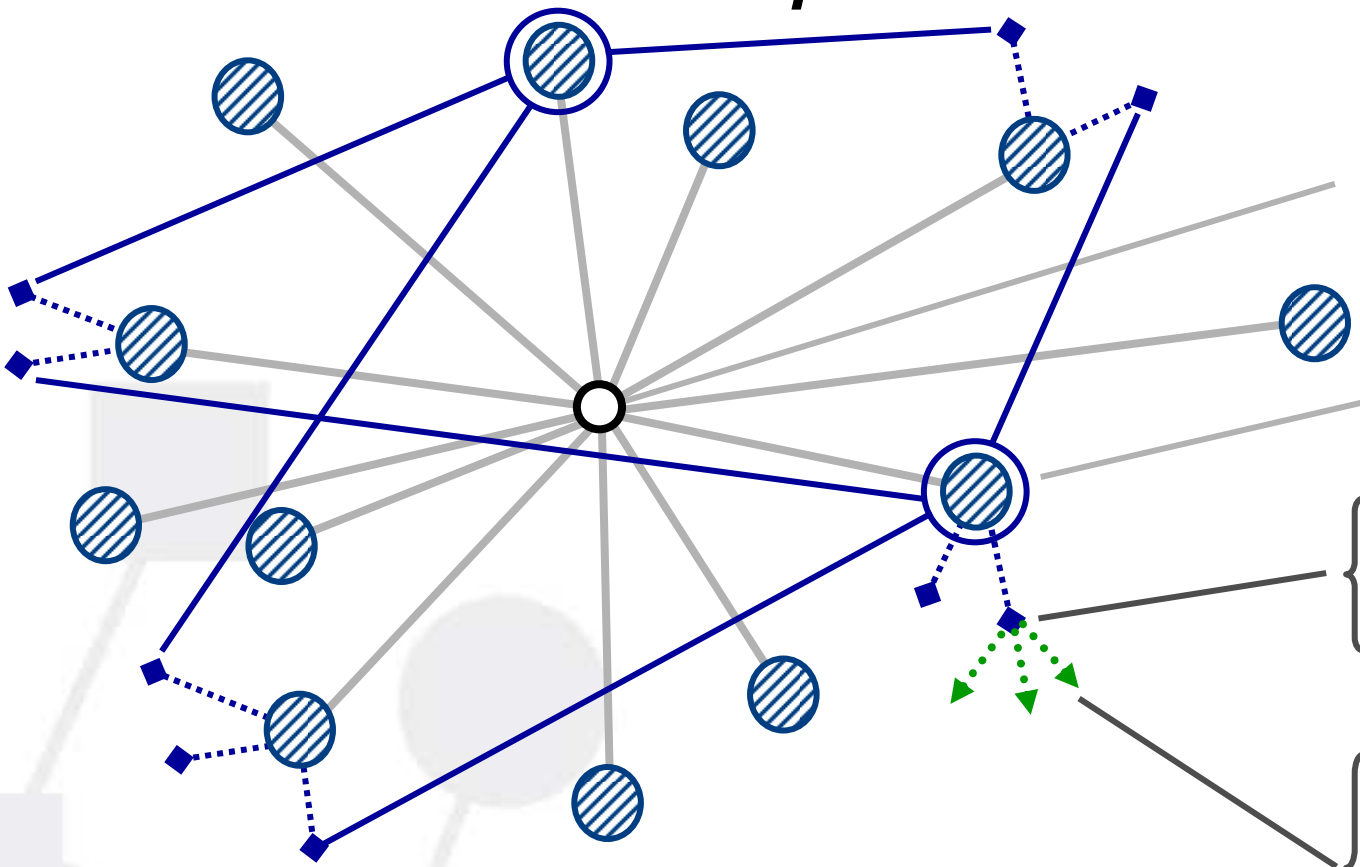
Distributed hub and spoke structure



Secretariat
(statutory seat)

Domain Hub

Biobanks
Biomolecular res.
Technology centers

Associated partners
Hospitals
Universities
Service providers …

Table 1. Disease categories and topics of the involved biobanks.

DISEASES	BB-MUG	PSI	BN-ADN	Net-GerBB-Pilot	Gene-thon
Certain infectious and parasitic diseases	X			X	
Neoplasm	X	X	X	X	
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	X		X		
Endocrine, nutritional and metabolic diseases	X	X	X		
Mental and behavioural disorders		X	X	X	
Diseases of the nervous system	X	X	X	X	
Diseases of the eye and adnexa	X				
Diseases of the ear and mastoid process	X				
Diseases of the circulatory system	X	X	X	X	
Diseases of the respiratory system	X				
Diseases of the digestive system	X	X			
Diseases of the skin and subcutaneous tissue	X				
Diseases of the musculoskeletal system and connective tissue	X	X	X		
Diseases of genitourinary system	X	X			
Pregnancy, childbirth and the puerperium	X				
Certain conditions originating in the perinatal period	X				
Congenital malformations, deformations and chromosomal abnormalities	X				
Other	X				

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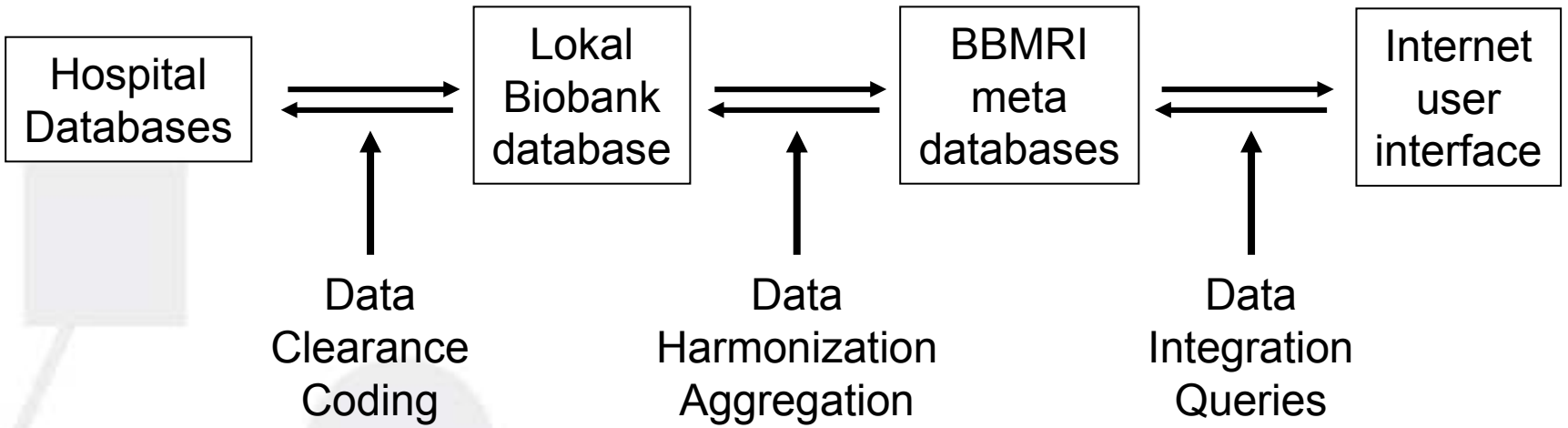
Different Levels of Data Processing



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IT Requirements of BBMRI

- Great flexibility of data integration (communication adaptor)
- Ethical filter for different ethical and legal requirements of Member States and authorization of users
- Flexible query tools

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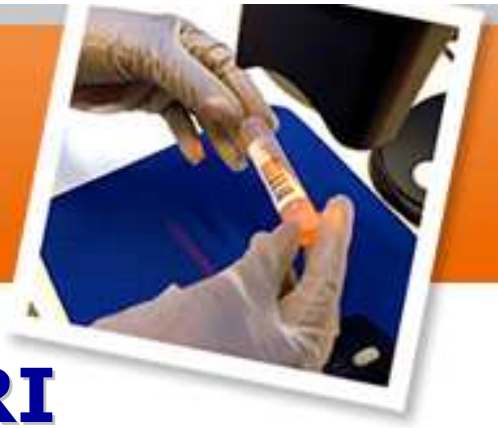

The Adaptor Approach of BBMRI

- Define criteria
  - Which samples and data can be combined?
  - Evidence-based standards
- Develop tools
  - Data exchange
  - Sample intl. transfer

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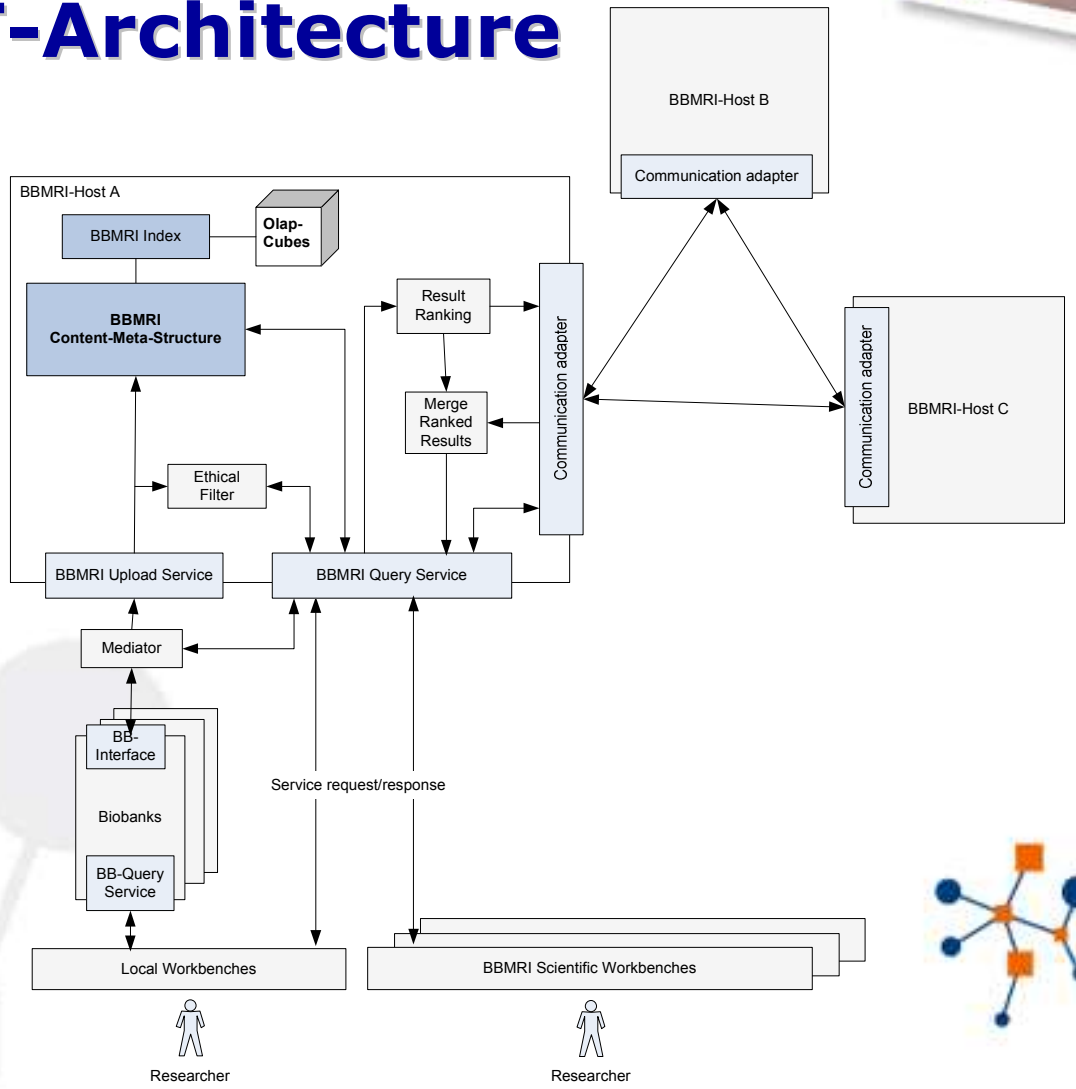
BBMRI IT-Architecture



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Involvement of the Biobanking Community

- ESF workshop, Amsterdam Dec. 06
- Establishment of FIBO, Paris, Dec. 06
- Stakeholder meeting Vienna, Feb. 07
- Presentation at EU Parliament , May 08
- Joint workshop DG Research, BBMRI, PHOEBE; Brussels, November 08
- Joint conference, Brussels, March 09
- Secretariat for OECD GBRCN, Mid 09

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Involvement of Patients

- 1st Stakeholder meeting: Brussels, March 20th 09 (Chair: M. Griffith)
  - European Cancer Coalition (H. Sundseth)
  - Heart EU (M. Livingston)
  - Europ. Fed. of Crohn's and Ulcerative Colitis Associations (R. Mitchell)
  - EURORDIS (V. Bottarelli)
  - Internatl. Alliance of Patients' Organizations (S. McMahon)
  - Europ. Genetic Alliance Network (A. Kent)
- 2nd Stakeholder meeting:
  Brussels, September 16th 09

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Involvement of Industry

- Specific issues
  - QA/QC
  - Access
  - Financing
- Projects
- Strategic issues
  - Long-term strategy for PPP (EFIPA, EDMA)
    - Joint analyses centers
    - Biomarker centers
    - Biobanking service

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Access by the Industry

Surgeons
Pathologists
Radiologists
Oncologists
Lab medicine
etc.

Patient
Sample
Med. data

Samples
Med. data

Industry

Cost recovery

Problem if no scientific collaboration is possible since cost recovery is no reasonable incentive for contributors

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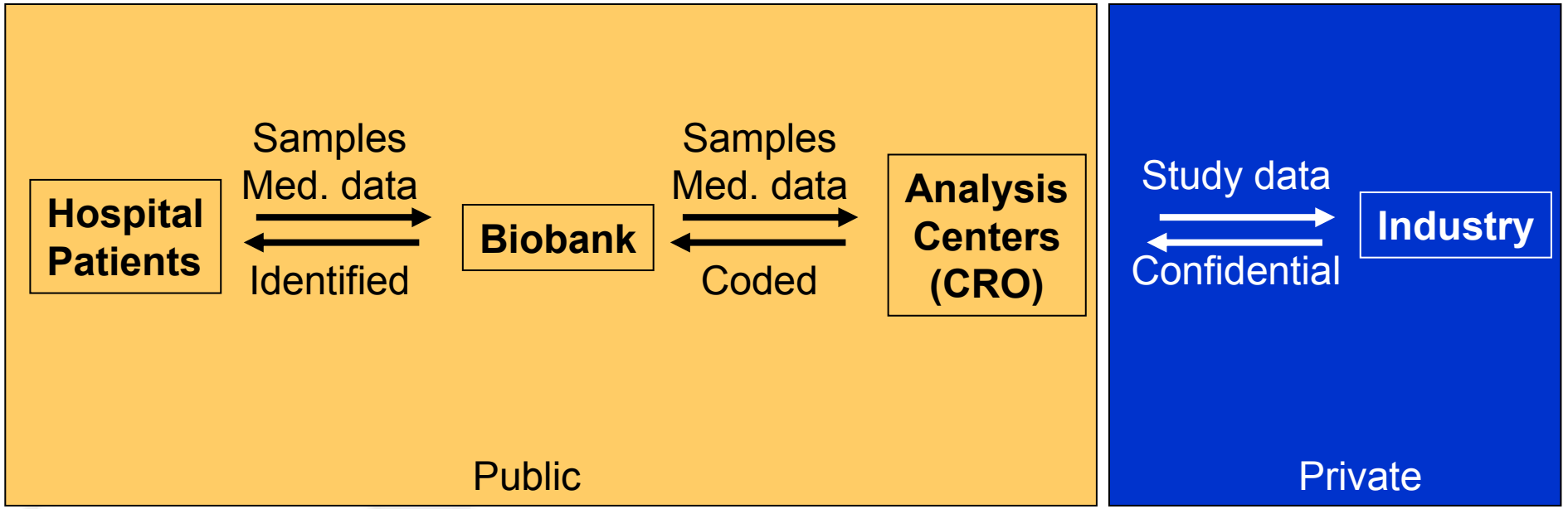
A New Model of PPP for Efficient Access of Industry



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Analysis Centers

- Specifications defined together with industry
- Industry participates in QM
- Participation in ring trials
- Certification
- Projects performed like CRO
- Financing by using EIB loans and structural funds

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Expected Impact of BBMRI

- BBMRI should provide a pan-European framework to foster excellence in biomedical research
  - Better projects, faster, cheaper
- Access to high quality resources, technologies, services, education and training
- Partner for academia and industry
  - SMEs: Strategic partner, customer
  - Pharma: Biomarker and drug development
- Incubator for regional development
  - Start-up packages

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Opportunities for Regional Development

- Biological resources are the essential raw material for future health-related economies
- Biological resource centers may act as nucleus for the establishment of biotech and pharma clusters
- Opportunities for joint-ventures with industry
- Co-financing by structural funds and EIB loans

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BBMRI and Publics

- Socio-economic impact study
  (impact on research, industry, health care)
- Public perception (focus groups and Eurobarometer)
- Coordinated communication strategy of all BMS research infrastructures (joint task force)
- White paper for European Parliament

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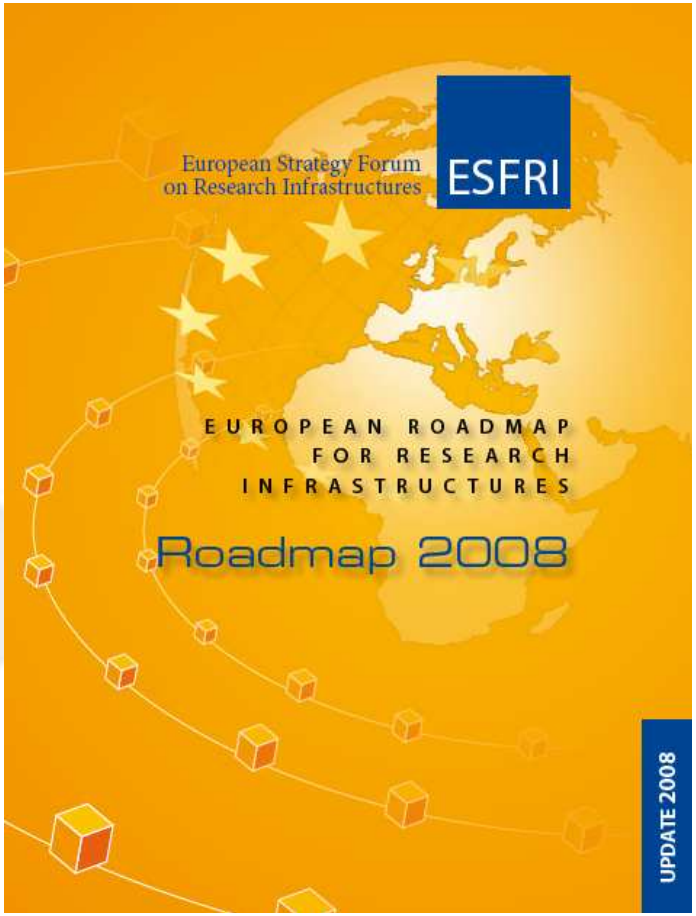
1st Update of the ESFRI Roadmap



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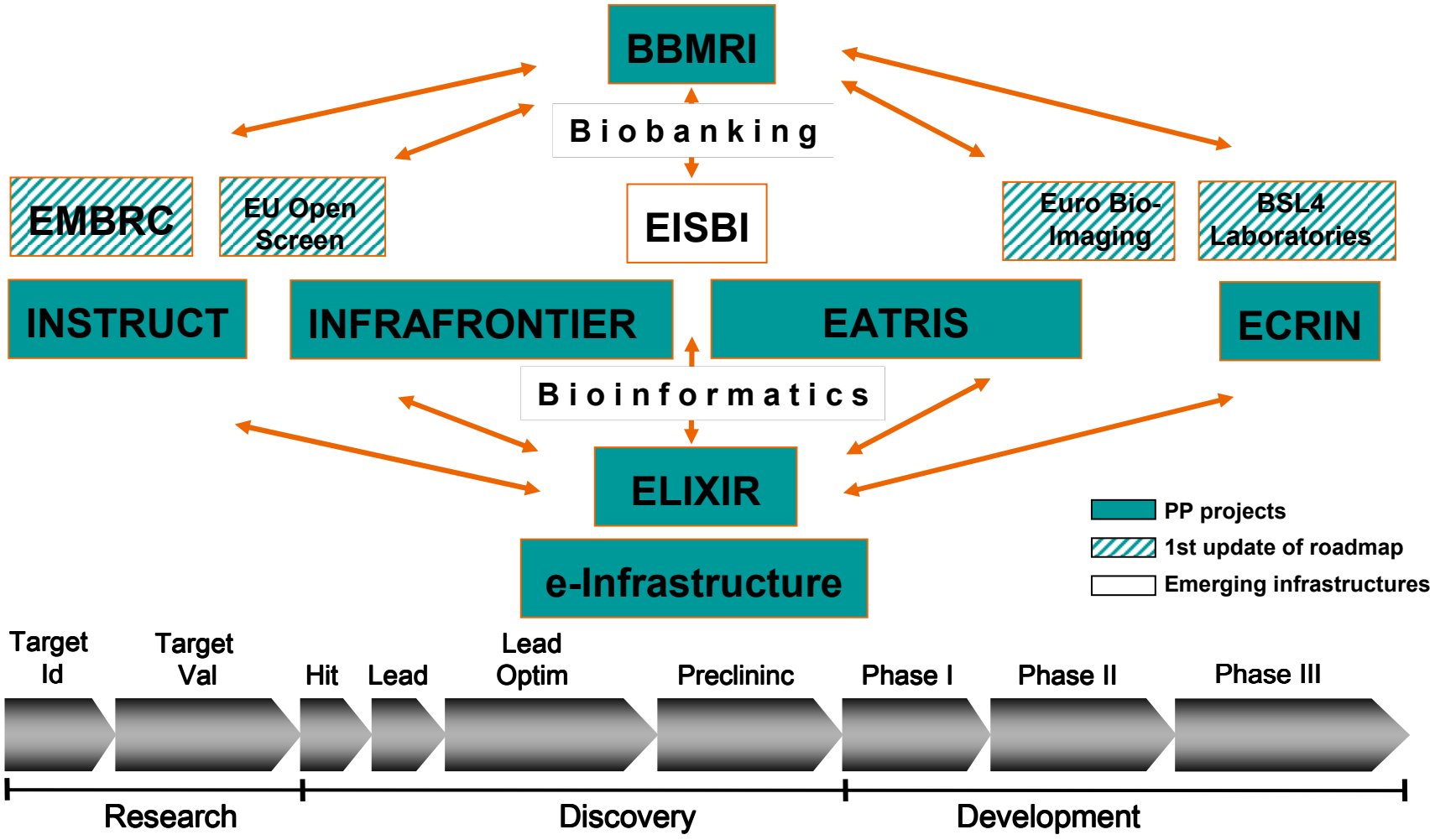
Synergies of BMS Research Infrastructures



How to Capitalize?

- Health-related economies are the potential next driver of global economy
- ESFRI BMS infrastructures together generate an enormous momentum and unique opportunity for European science, industry and society
- Value generating chain without gaps
- Implementation of the ERA in the life sciences
- Co-ordinated commucication strategy

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Communication Strategy: Content

- Expected impact of European BMS RIs on science, industry and society
  - Major impact on European life sciences, health care and economy
  - Unique opportunity for Europe
  - Implementation of ERA concept
  - Public curiosity about the secrets of the living world

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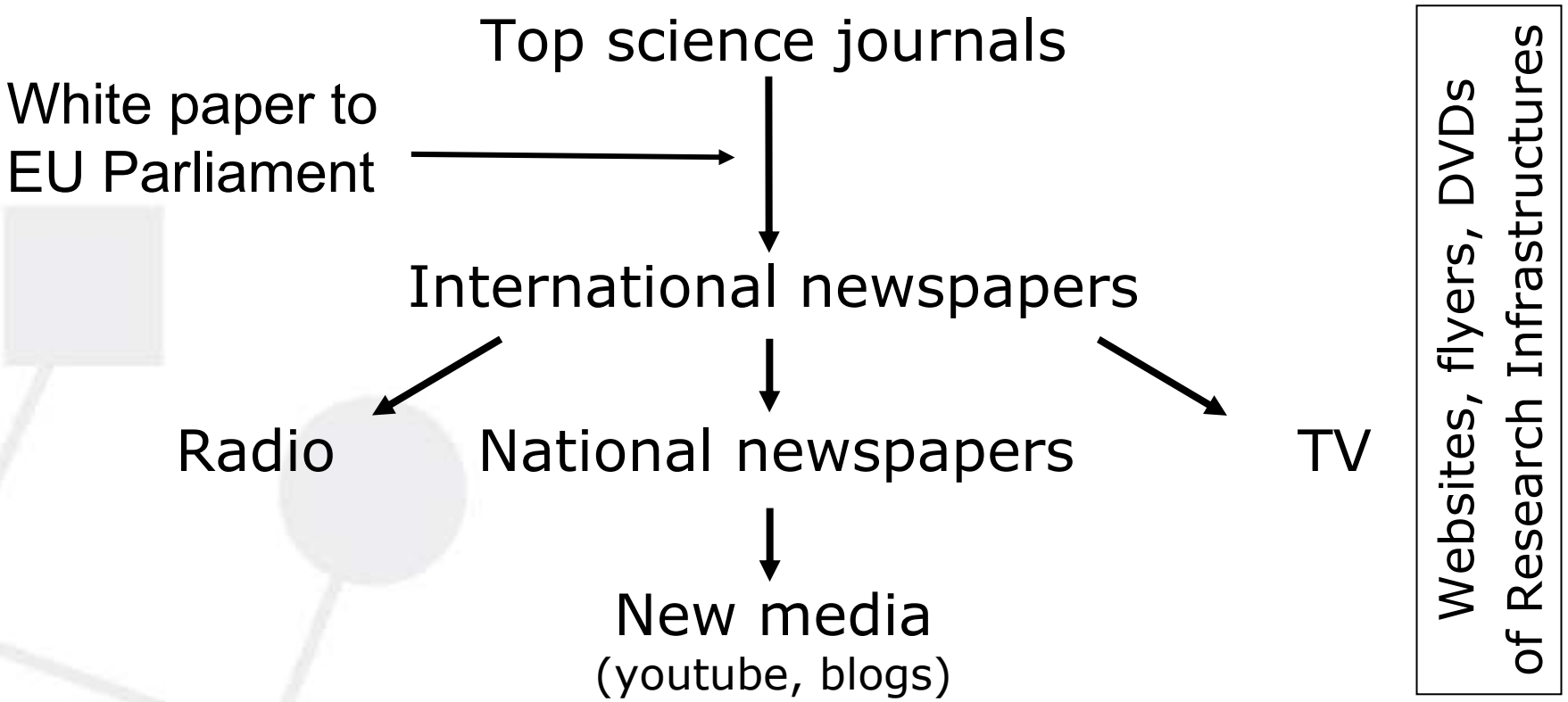
Communication Strategy: Process



The BBMRI Team: WP Leaders and Chairs

Coordination/Executive Mgmnt.	**K. Zatloukal, AT; E. Vuorio, FI**
	M. Yuille, UK; M Pasterk, FR
Population-based Biobanks:	**L. Peltonen, FI/UK; A. Metspalu,EE**
Disease-oriented Biobanks:	**E. Wichmann, GER, T Meitinger, GER**
Biomolecular Resources:	**U. Landegren, SE; M. Taussig, UK**
Databases & Biocomputing:	**J-E Litton, SE**
Ethical, Legal and Societal Issues:	**A. Cambon-Thomsen, FR**
Funding and Financing:	**G. Dagher, FR; J. Ridder, NL**
	C. Brechot, FR;
Governance Council Chair:	**L. Peltonen, FI**
Advisory Board Chair:	**G-J van Ommen, NL**
Coordination Board Chair:	**K. Zatloukal, AT**
Stakeholder Forum Chair:	**M. Griffith, IR**

50 Participants (6 Ministries, 18 Funding Organizations)

183 Associated Organizations 28 Countries

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Further information

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M. Yuille et al. *Briefing in Bioinformatics* 9: 14-24 (2008)

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