BIOBANKING
a challenge for public / private partnerships

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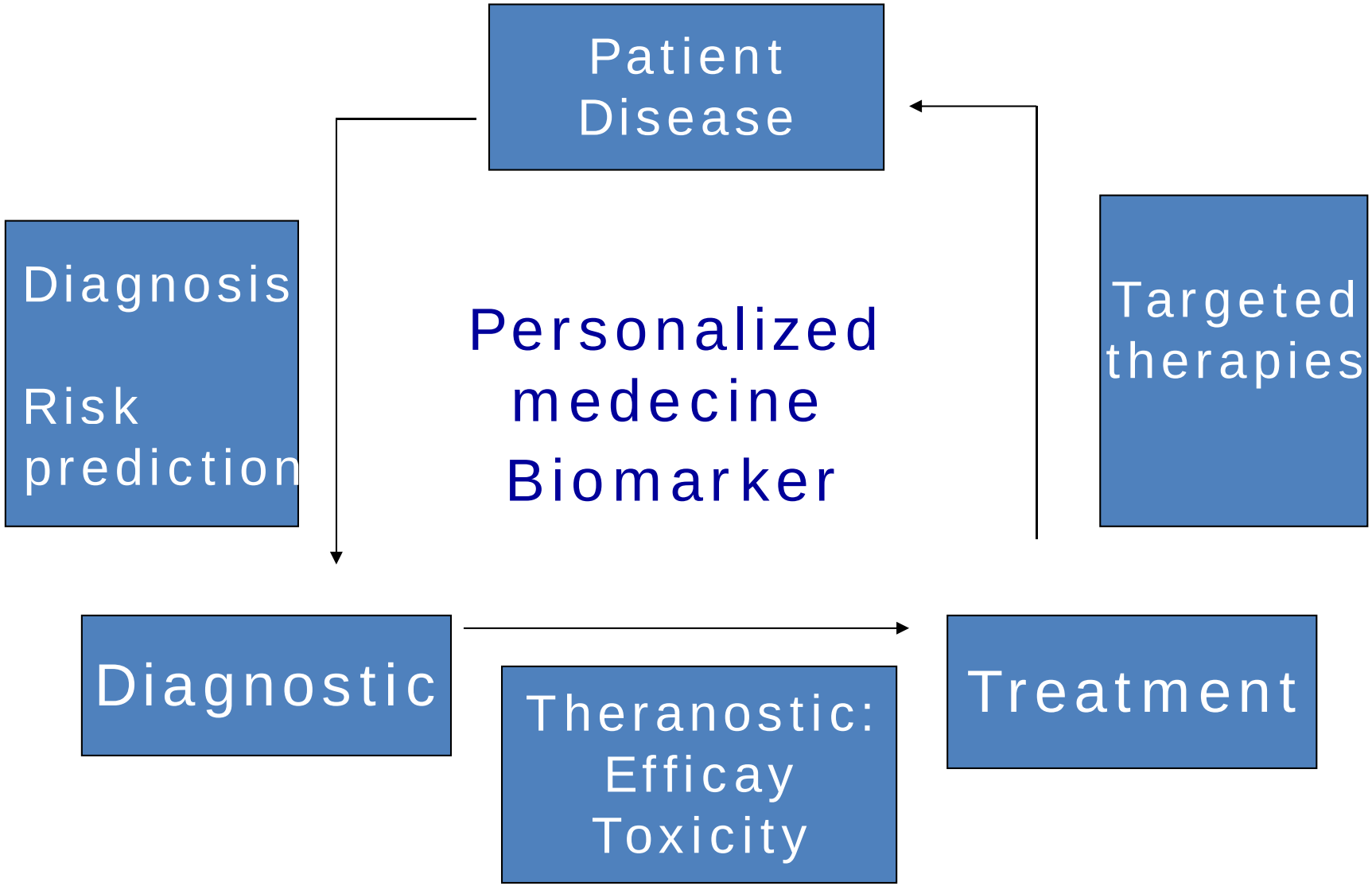
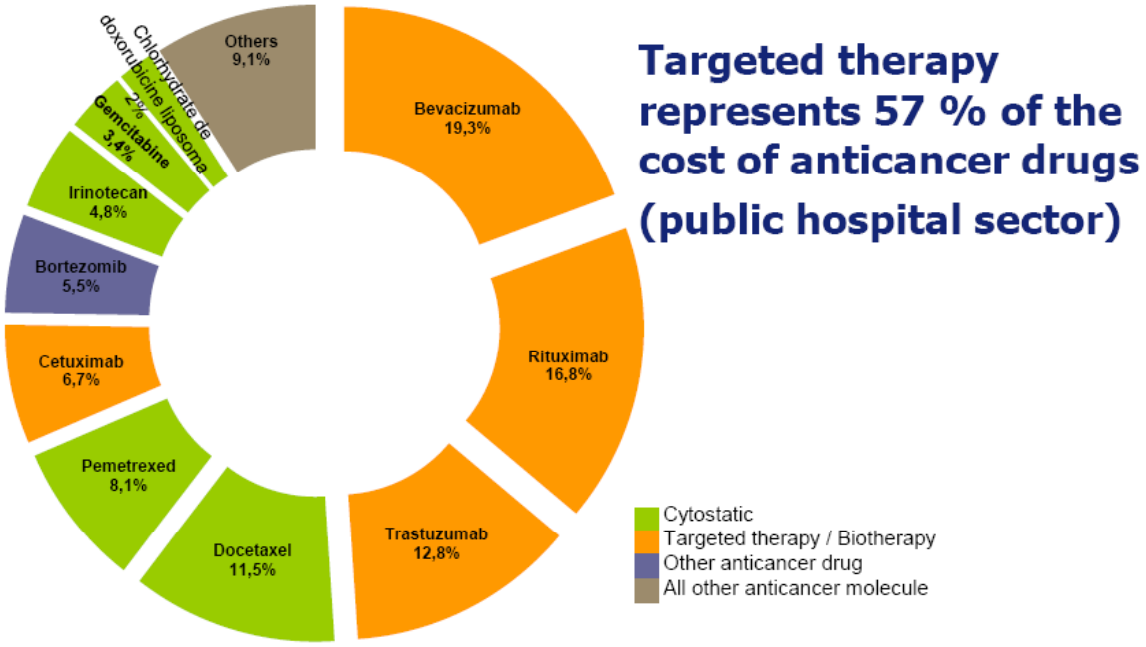
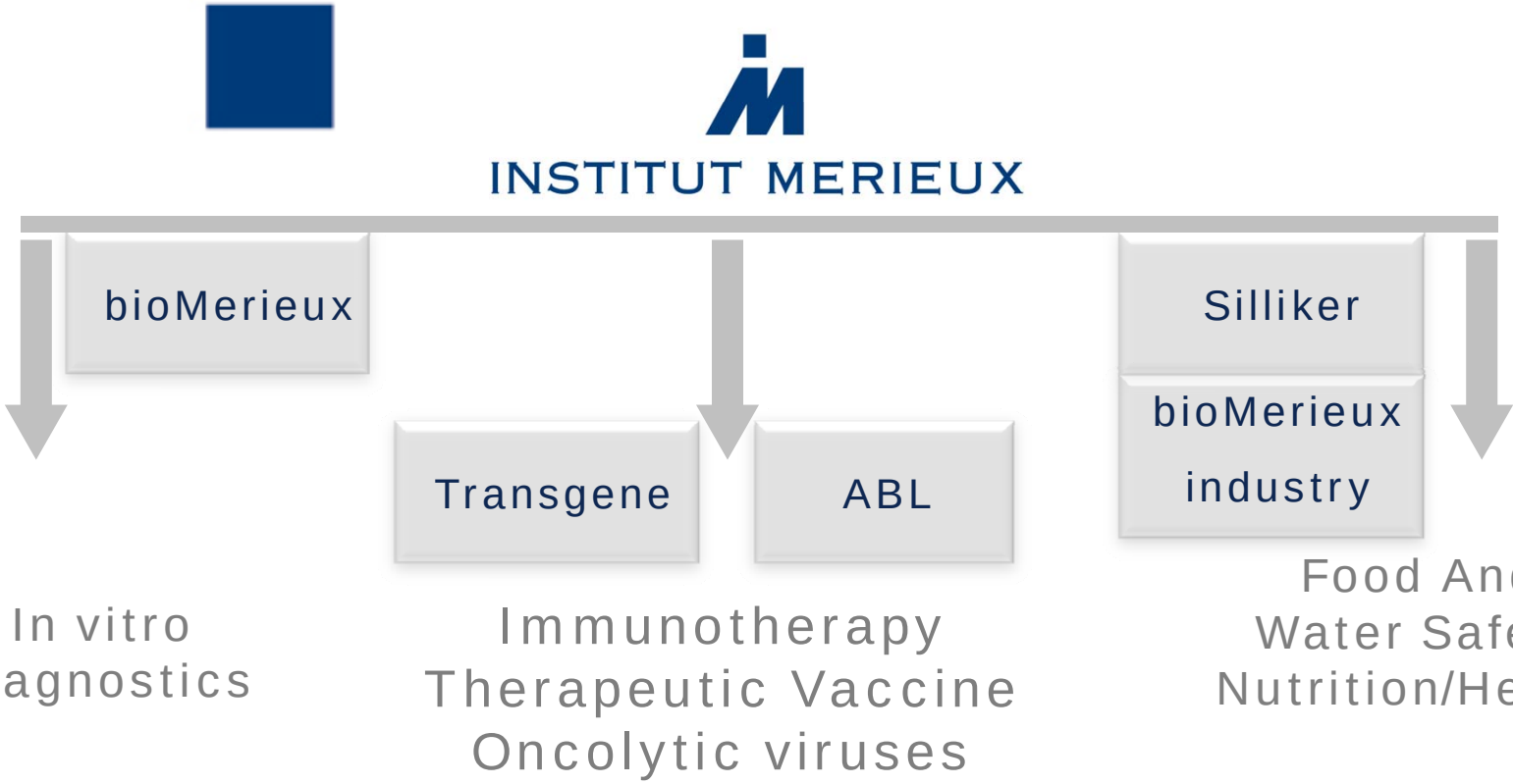

Patient
Disease
Diagnosis
Risk
prediction
Personalized
medecine
Biomarker
Targeted
therapies
Diagnostic
Theranostic:
Efficay
Toxicity
Treatment

BCR-ABL translocation: 1- BCR-ABL detection 2- BCR-ABL quantification 3- ABL mutation	Chronic Myeloïd Leukemia/ Acute Lymphoblastic Leukemia	Imatinib prescription 1- Imatinib prescription 2- Monitoring of minimal residual disease 3- Resistance to Imatinib
KIT and PDGFRA mutations	GIST	Imatinib prescription
HER2 amplification	Breast and gastric cancers	Trastuzumab prescription
KRAS mutations	Colorectal cancer	Panitumumab and cetuximab prescription
EGFR mutations	Lung cancer	Gefitinib and erlotinib prescription
EML4-ALK translocations	Lung cancer	Crizotinib prescription
BRAF mutation V600E	Melanoma	Vemurafenib prescription



Targeted therapy represents 57 % of the cost of anticancer drugs (public hospital sector)

Source : ATIH-PMSI MCO base 2009
F. Calvo, INCa



Biomarkers
(ADNA program)

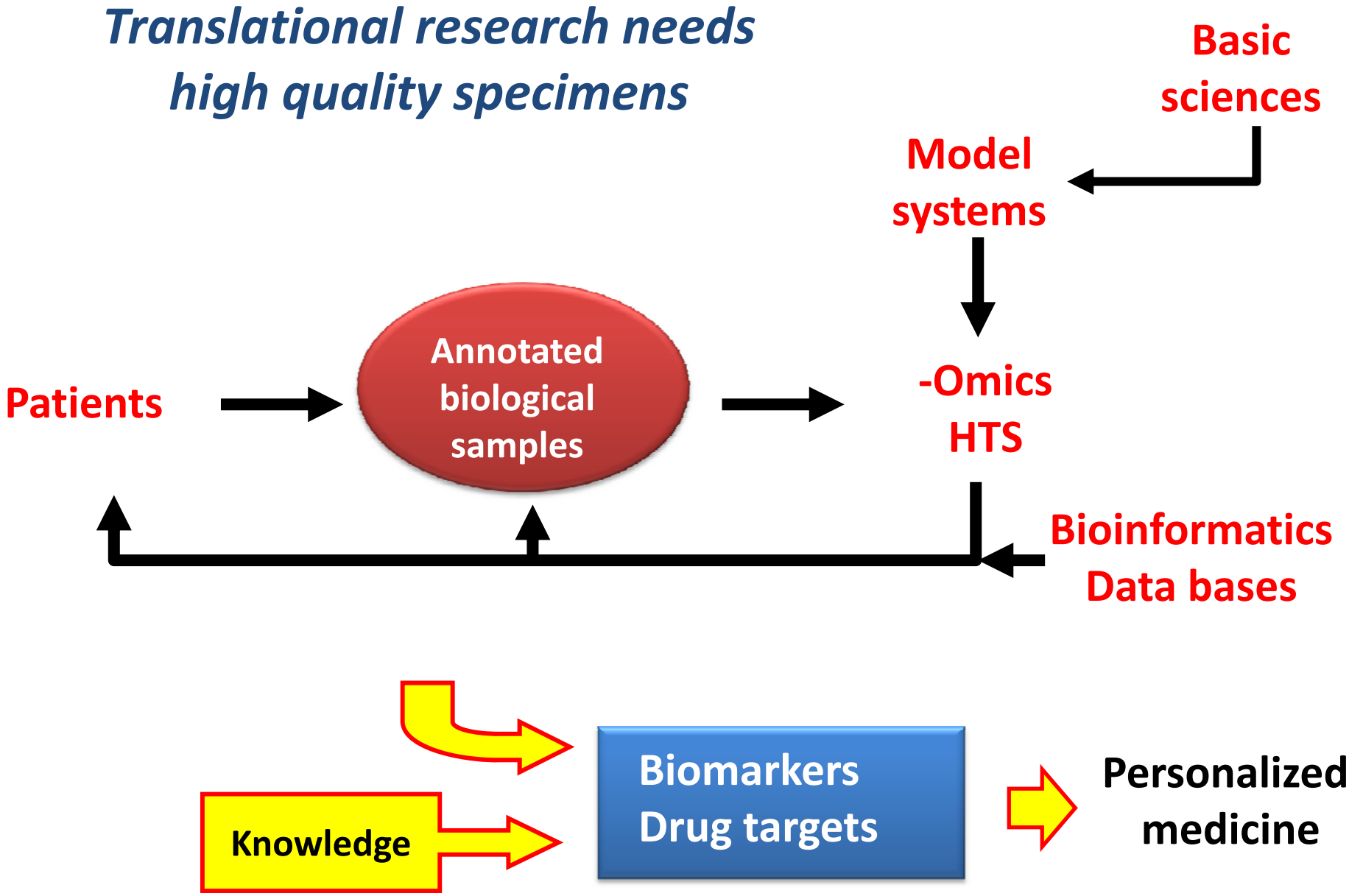

Translational research needs high quality specimens
Basic sciences
Model systems
Patients
Annotated biological samples
-Omics HTS
Bioinformatics Data bases
Knowledge
Biomarkers Drug targets
Personalized medicine

Table 2 Cancer biomarkers that are currently in clinical use.

Tumor marker	Cancer type	Year of discovery and reference	Application based on ASCO and/or NACB recommendations	Reference
Alfa-fetoprotein	Germ-cell hepatoma	1963[5]	Diagnosis Differential diagnosis of NSGCT Staging Detecting recurrence Monitoring therapy	80
Calcitonin	Medullary thyroid carcinoma	1970s[81]	Diagnosis Monitoring therapy	82
CA125	Ovarian	1981[7]	Prognosis Detecting recurrence Monitoring therapy	80
CA15-3	Breast	1984–5[83,84]	Monitoring therapy	77
CA19-9	Pancreatic	1979[85]	Monitoring therapy	86
Carcinoembryonic antigen	Colon	1965[86]	Monitoring therapy Prognosis Detecting recurrence Screening for hepatic metastases	77,80
ER and PgR	Breast	1970s[87]	Select patients for endocrine therapy	77
HER2	Breast	1985–6[88,89]	Select patients for trastuzumab therapy	77
Human chorionic gonadotropin-β	Testicular	1938[90]	Diagnosis Staging Detecting recurrence Monitoring therapy	80
Lactate dehydrogenase	Germ cell	1954[91]	Diagnosis Prognosis Detecting recurrence Monitoring therapy	80
Prostate-specific antigen	Prostate	1979[92]	Screening (with DRE) Diagnosis (with DRE)	80
Thyroglobulin	Thyroid	1956[93]	Monitoring	82

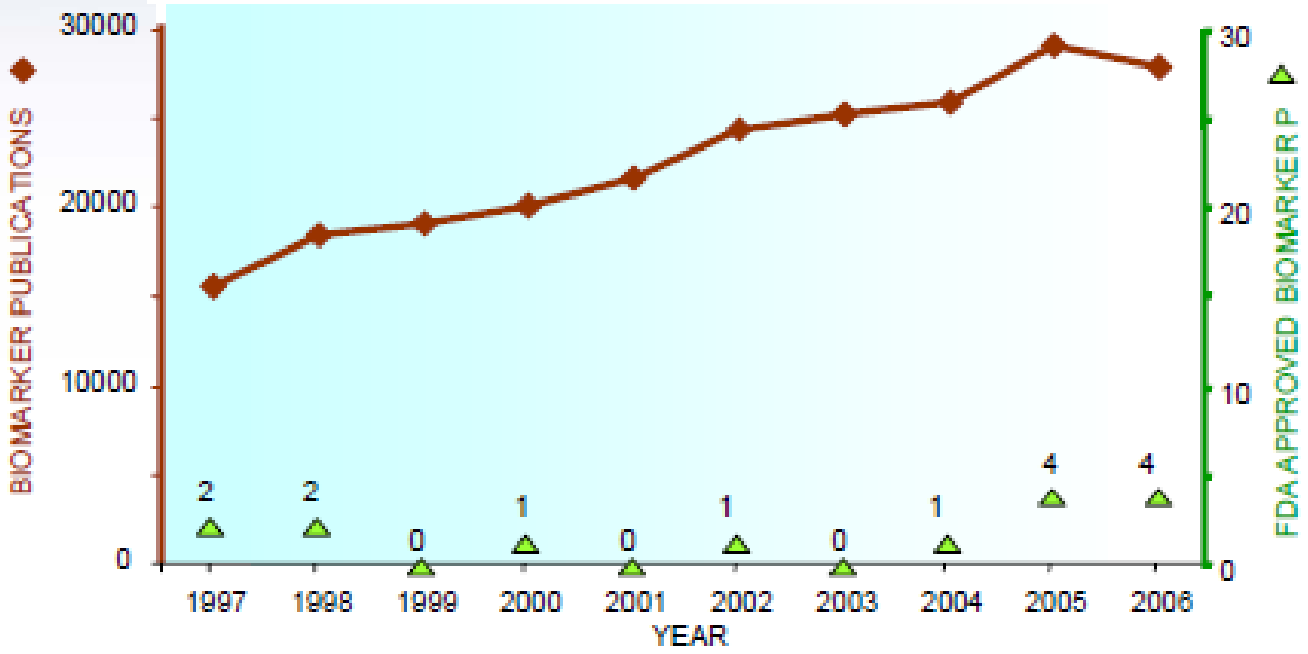
Abbreviations: DRE, digital rectal examination; ER, estrogen receptor; NACB, National Academy of Clinical Biochemistry; NSGCT, nonseminomatous germ cell tumor; PgR, progesterone receptor.

”cancer biomarkers”

n = 11,639

Kulasingam V and Diamandis EP (2008) Strategies for discovering novel cancer biomarkers through utilization of emerging technologies
Nat Clin Pract Oncol doi:10.1038/ncponc1187

Trends of Journal Publication on Biomarkers and FDA Approval of Biomarkers

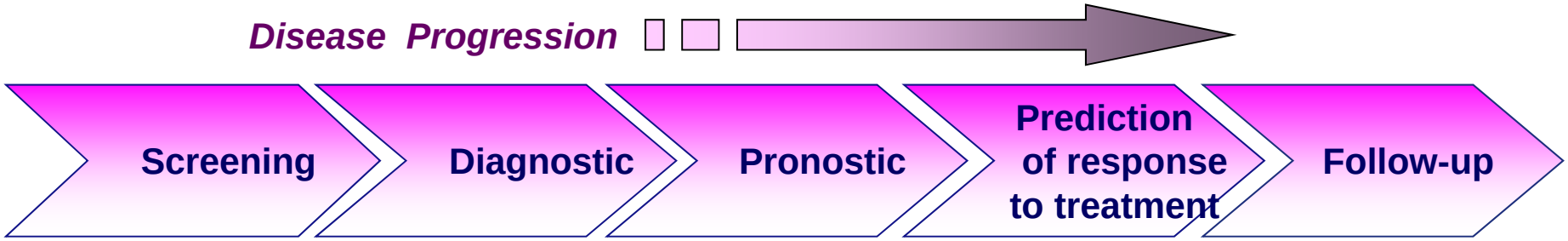


Triangles (green) represent the number of FDA-approved markers per year (data from FDA and Nat Rev Can 2005). Red squares and circles indicate publications under the Medline medical subject heading biomarker

Methodis

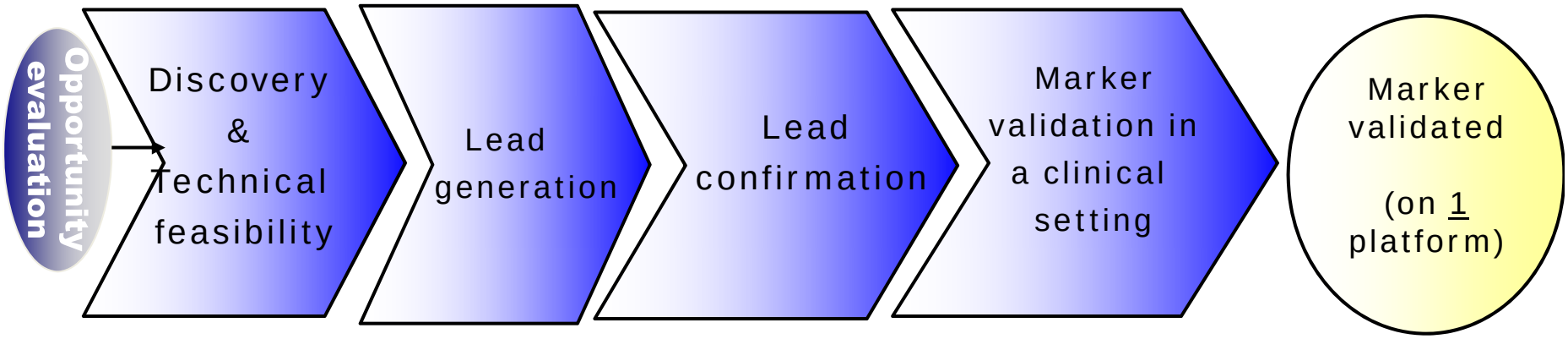
LEADING MEDICINE®

What types of biomarkers do we have ?



1. Screening **(e.g. mammography, fecal occult blood)**
2. Diagnostic **(e.g. cardiac troponin)**
3. Prognosis **(e.g. cytokeratins, estrogen receptors)**
4. Prediction of response to treatment **(e.g. HER2)**
5. Patient follow-up **(e.g. PSA)**

The steps of biomarker discovery and validation



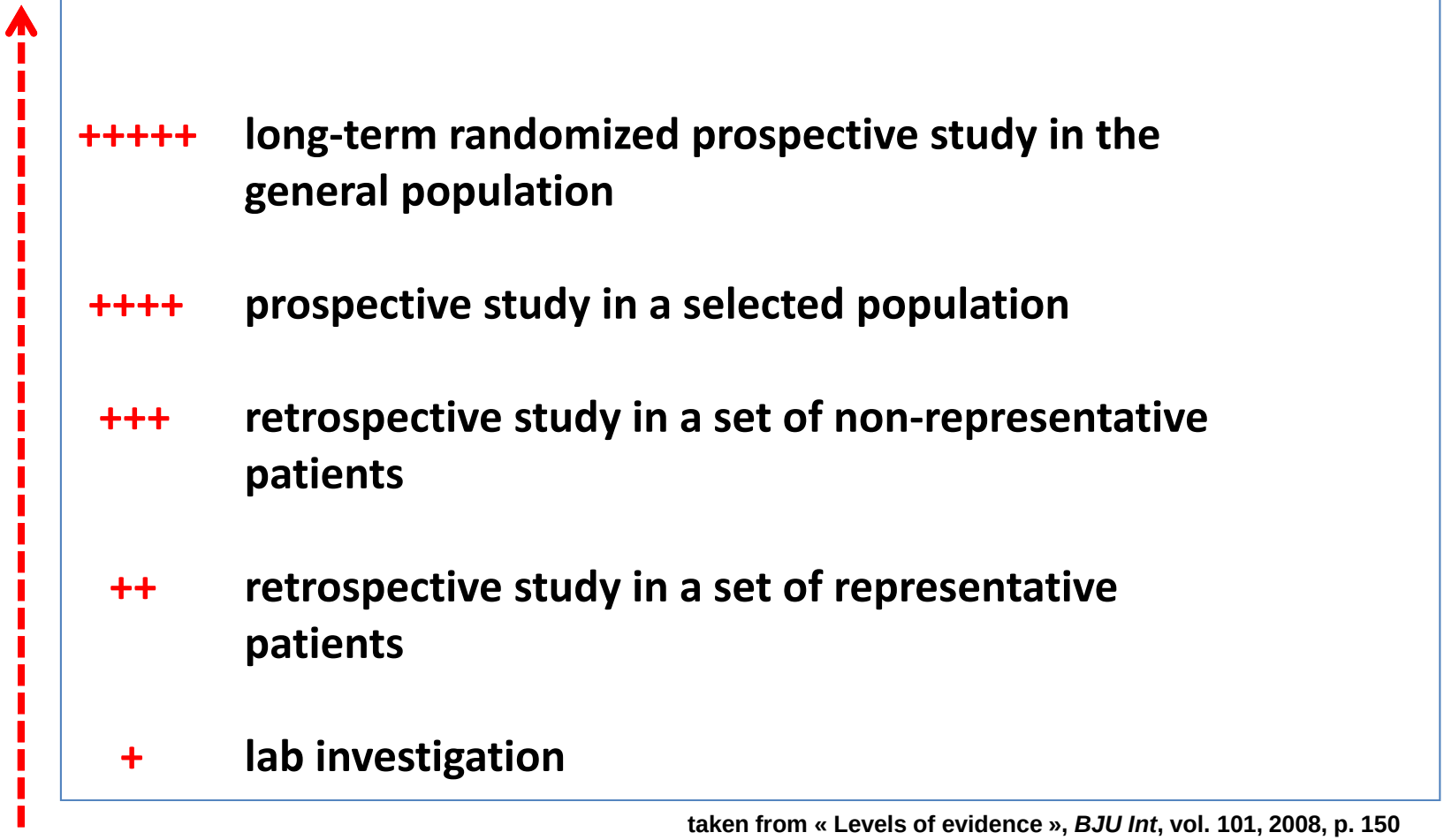
Clinical studies

Sample availability and quality

Quality insurance

Information management

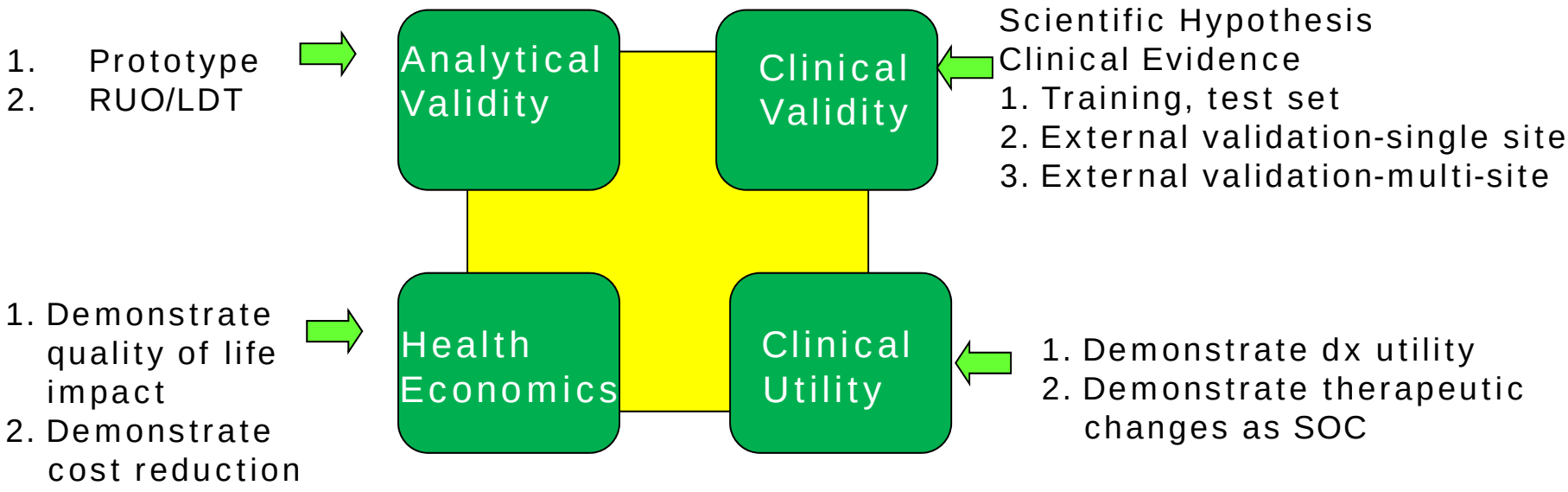
Main challenges in biomarker discovery



taken from « Levels of evidence », *BJU Int*, vol. 101, 2008, p. 150

What Drives Successful Diagnostic Test (DX) Development?

DX regulatory approval drivers



DX reimbursement drivers

For market success, developping a test represents a compelling investment for DX company

...

Main challenges in biomarker discovery

Biological samples

Blood : *plasma, serum*

Tissue ; Cells

Urine ; Stools

Saliva ; Exhaled breath…

Tools

DNA

mRNA, miRNA

Metabolome

Proteome

Glycome

Microbiome

Imaging

Personalised Medecine: Difficulties and challenges

A novel model, based on data integration and validation of biomarkers:

-Technology: **genomics, proteomics, metabolomics**

imaging etc..

-Clinical studies

Different genetic background

Different environmental contexts (life style, nutrition…)

Clinical studies: quality, ethics etc..

- Public health

- Economics: **Cost-benefit, reimbursment etc..**

Personalised Medecine: Difficulties and challenges

A novel model, based on data integration and validation

- A change of paradigm :

- Shift from unique to mutiple, complex, biomarkers
  (multi-parameters = data intégration, bioinformatics, Computational biology, systems biology)

- Intellectual property?.

- Management and transfer of information: **physicians, patients (cell phone, etc…).**

Criteria for success

. Access to biobanks infrastructures, clinical data, standardization (sampling procedures etc.)

A novel paradigm for industrial partners:
Moving to collaboration instead of « isolation »
Refining the intellectual property bases

- Academic environment: Project-driven
- Pharma-Diagnostics companies win-win interactions
- Simplified discussions with regulatory agencies

  Early discussions to define the requirements
  Reimbursements…

- Public-Private Partnerships:

  NCI biomarker network
  FDA

"How long does it take to reach 10,000 cases in a cohort study with 500,000 people?"

Paul Burton, UK BioBank Technical Report 2005

Breast cancer	17 yrs
Colorectal cancer	22 yrs
Prostate cancer	22 yrs
Lung cancer	34 yrs
Stroke	18 yrs
MI and coronary death	8 yrs
Diabetes mellitus	6 yrs
COPD	13 yrs
Hip fracture	21 yrs
Alzheimer's disease	18 yrs
Parkinson's disease	23 yrs

Disease	Consortium	Number of teams	Subjects
• Parkinson	GEO-PD	18	10,000
• Osteoporosis	GENOMOS	10	30,000
• Preterm birth	PREGENIA	10	20,000
• Allergy/Asthma	GA^{2}LEN	50	20,000
• Breast, Lung…K	EPIC	20	500,000
• Lymphoma	INTERLYMPH	15	20,000
• Lung K	ILLCO	30	51,000
• Head & Neck K	INHANCE	13	28,000
• Melanoma	GENOMEL	12	3,000
• Pancreatic K	PACGENE	10	5,000

Thematic network of biobanks

Biobanks => 2 different concepts……

Service

- ✓ Samples + minimum data set
- ✓ One-way service
- ✓ MTA + cash
- ✓ Customer service:
  From nothing to optional

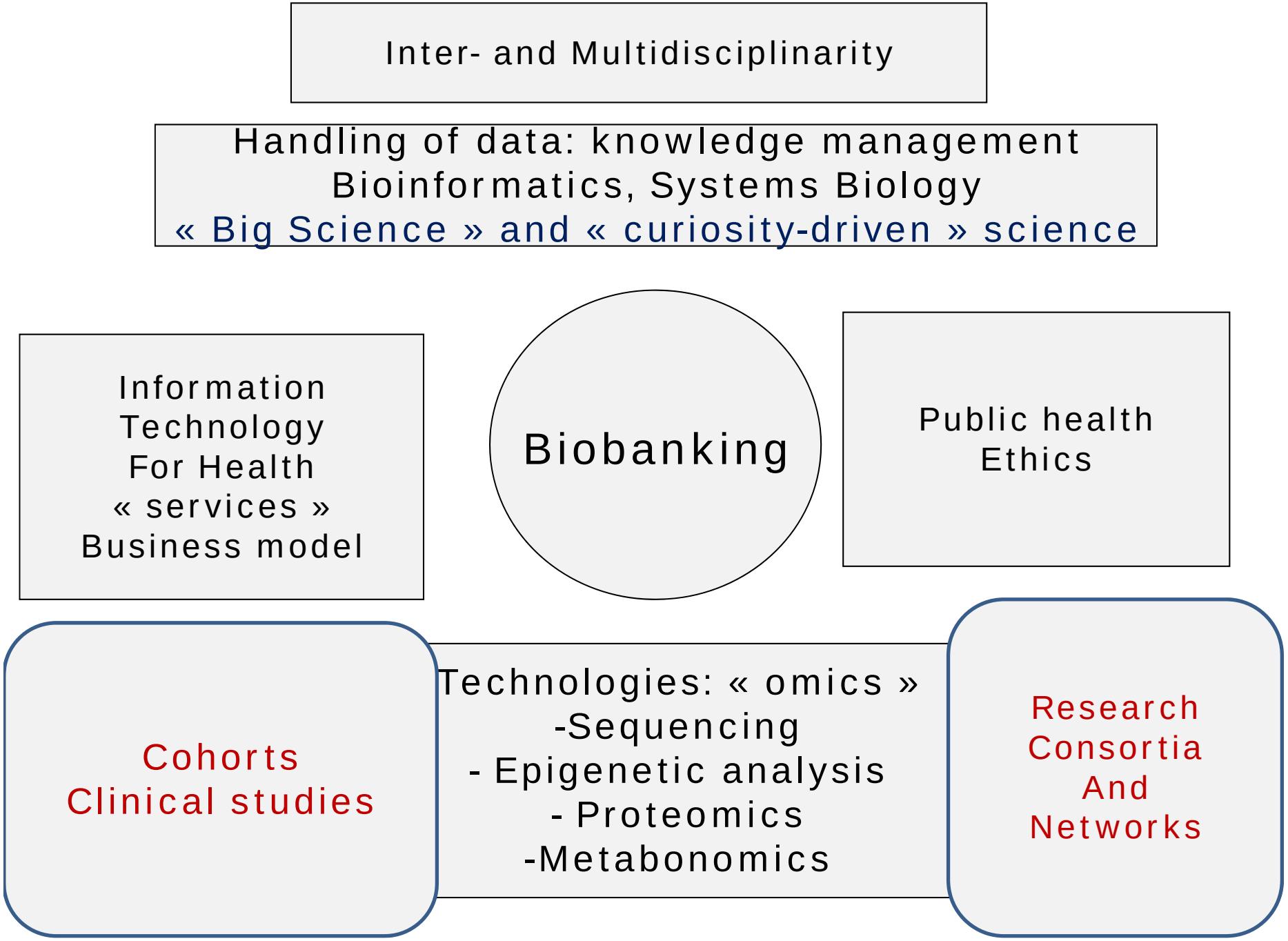
Partnerships

- ✓ Samples + detailed information + outcome of patients + …
- ✓ Bi-directional information
- ✓ MTA, contract ± IPR
- ✓ Customer service:
  Full expertise and advices

How to select a biobank ?

main bottlenecks

- ✓ Quality of both biological samples and linked annotations, based on international standards and guidelines
- ✓ Scientific and medical background
- ✓ Quality of management
- ✓ Well defined access policy
- ✓ Expertise
- ✓ Willingness and reactivity
- ✓ Ethical and regulatory issues


Inter- and Multidisciplinarity
Handling of data: knowledge management
Bioinformatics, Systems Biology
« Big Science » and « curiosity-driven » science
Information
Technology
For Health
« services »
Business model
Biobanking
Public health
Ethics
Cohorts
Clinical studies
Technologies: « omics »
-Sequencing
- Epigenetic analysis
- Proteomics
-Metabonomics
Research
Consortia
And
Networks

Take-home message

- There is a strong need of large cohorts of clinically [well] defined patients with high quality specimens and annotations
- One-stop access to biological samples is a main bottleneck for companies. This should be overcome by the implementation of thematic networks at the European level.
- Top biobanks fit in top science, and *vice et versa*
- Linkage of biobanks with technical platforms in genomics is an added value
- Scientific/medical experts and key opinion leaders should be associated to the biobanking process

Thank you