

Sustaining the Planet : A call for Interdisciplinary Approaches and Engagement

“Technology and Ethics in the Era Post Genomics”

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The 9th IGCCSI 2017

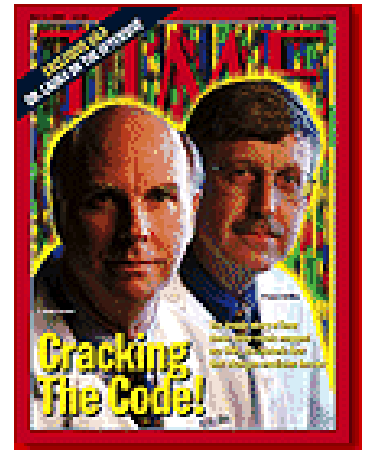
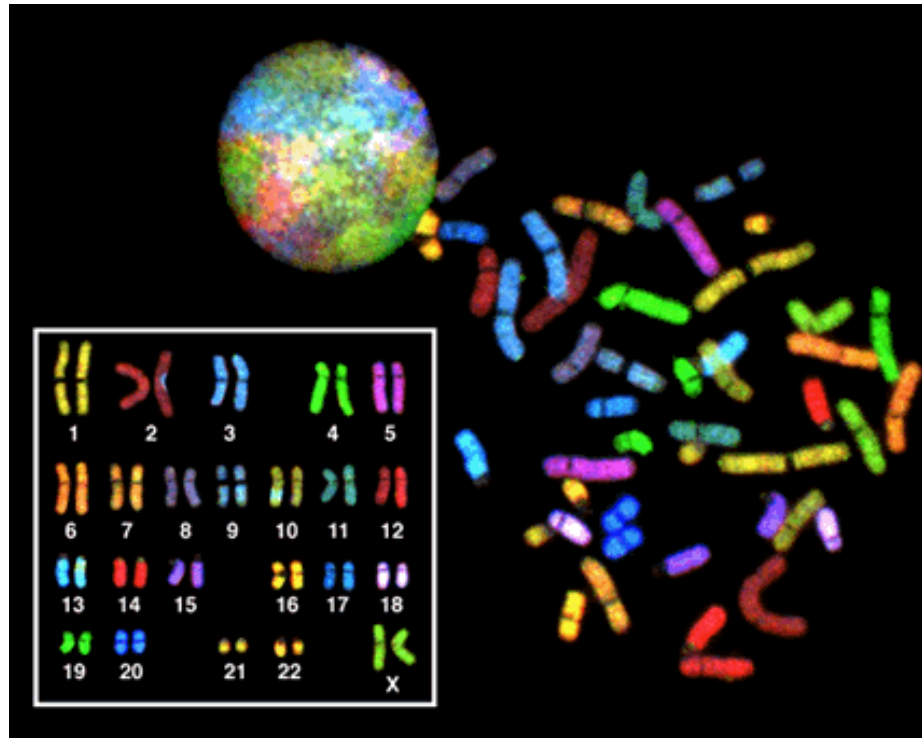
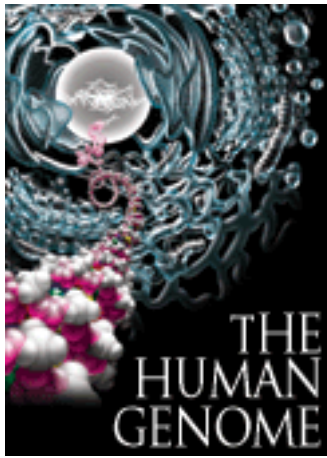
Yogyakarta, 9 - 10 August 2017



Outline of the Presentation

1. Genomic – Post Genomic Era
2. The Future of Health care - Personalized Medicine
3. SDG's targets : sustaining the planet with Ethical Conduct
4. Ethics / Bioethics in Post Genomics' Era
5. Precision Medicine Shaping the Future of Cancer Research through Innovation

Genomic – Proteomic Era



3 billion bases 40,000 genes

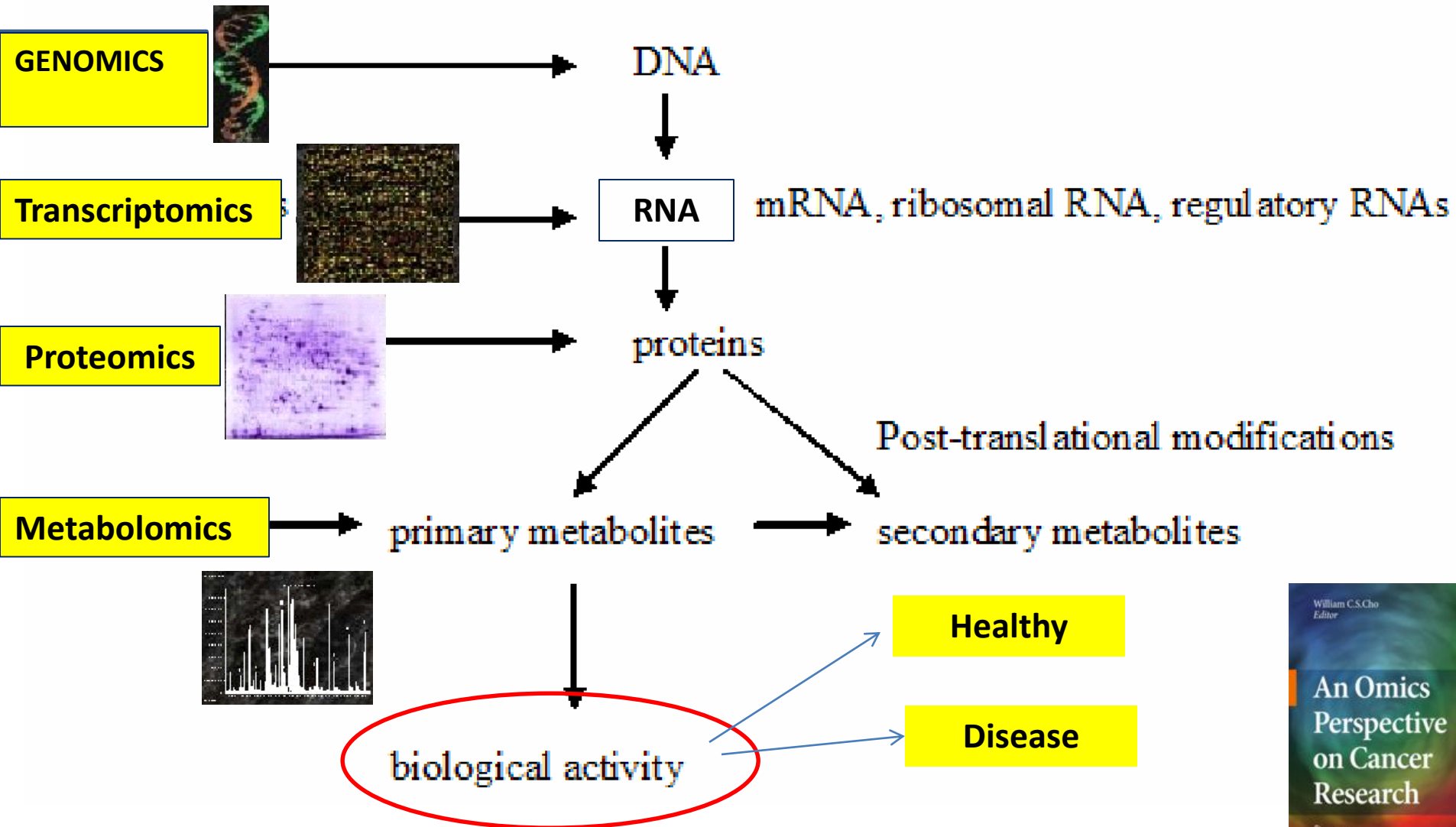
<http://www.genome.gov/>



Personalized medicine in 2010



The 'OMICS'



Post Genomics - Personalized Medicine

1. Utah Pulse.com: The future of personalized medicine : **“From Helix to Healthcare”** Jennifer Logan, 26 March, 2010
2. Stanford , Jan 2011: **The future of medicine** is clear – more and more of our health care will be crafted to **the personal genetics of each patients**, whether **stem cells** or **gene mapping** or disease **biomarkers**.

Personalized medicine

The future of **health care** by utilizing an **improved understanding of genetics** and **molecular biology** to :

- **better diagnosis** ,
- **more precise diagnosis** ,
- **greater predictability** of disease course and
- **improved patient safety** by selecting
 - the right drug for a patient but also
 - proper dosage to reduce adverse effect



USA :
**The Genomics and Personalized
Medicine Act returns to Congress**



The aim of the GPMA is :
To secure the promise of personalized medicine for all Americans by expanding and accelerating genomics research and initiatives to improve the accuracy of disease diagnosis, increase the safety of drugs, and identify novel treatments, and for other purposes.

GPMA 2006 ; GPMA 2010 ; GPMA 2014

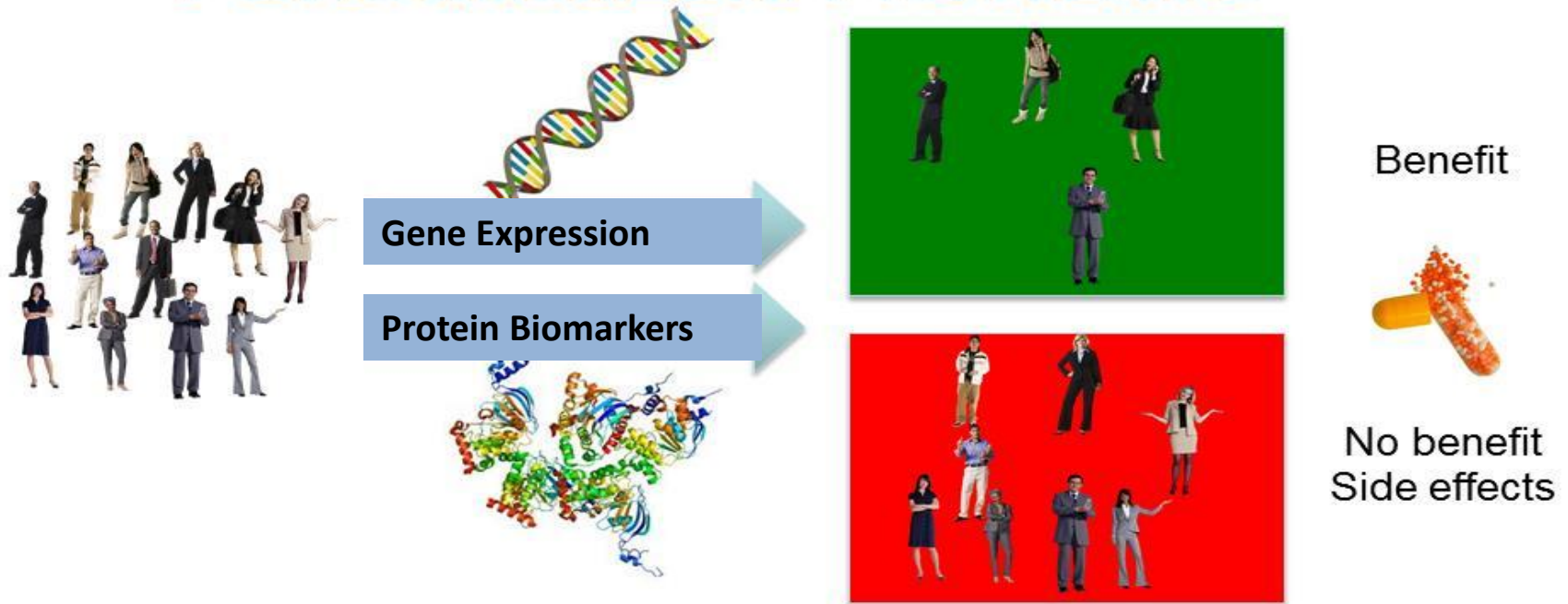
President Bush
President Clinton
President Obama

Indonesia – precision medicine?

- No national genomic bank data
- Biobank - inform consent
- NGS - high throughput genome sequencing
- Need partnership (multicenter - multi /Interdiscipline - ethical code of conduct)
- MoU , MTA, GLP, GCP, GMP
- Health Insurance
- Government Support , Law , Regulations
- **Bioethics Education**

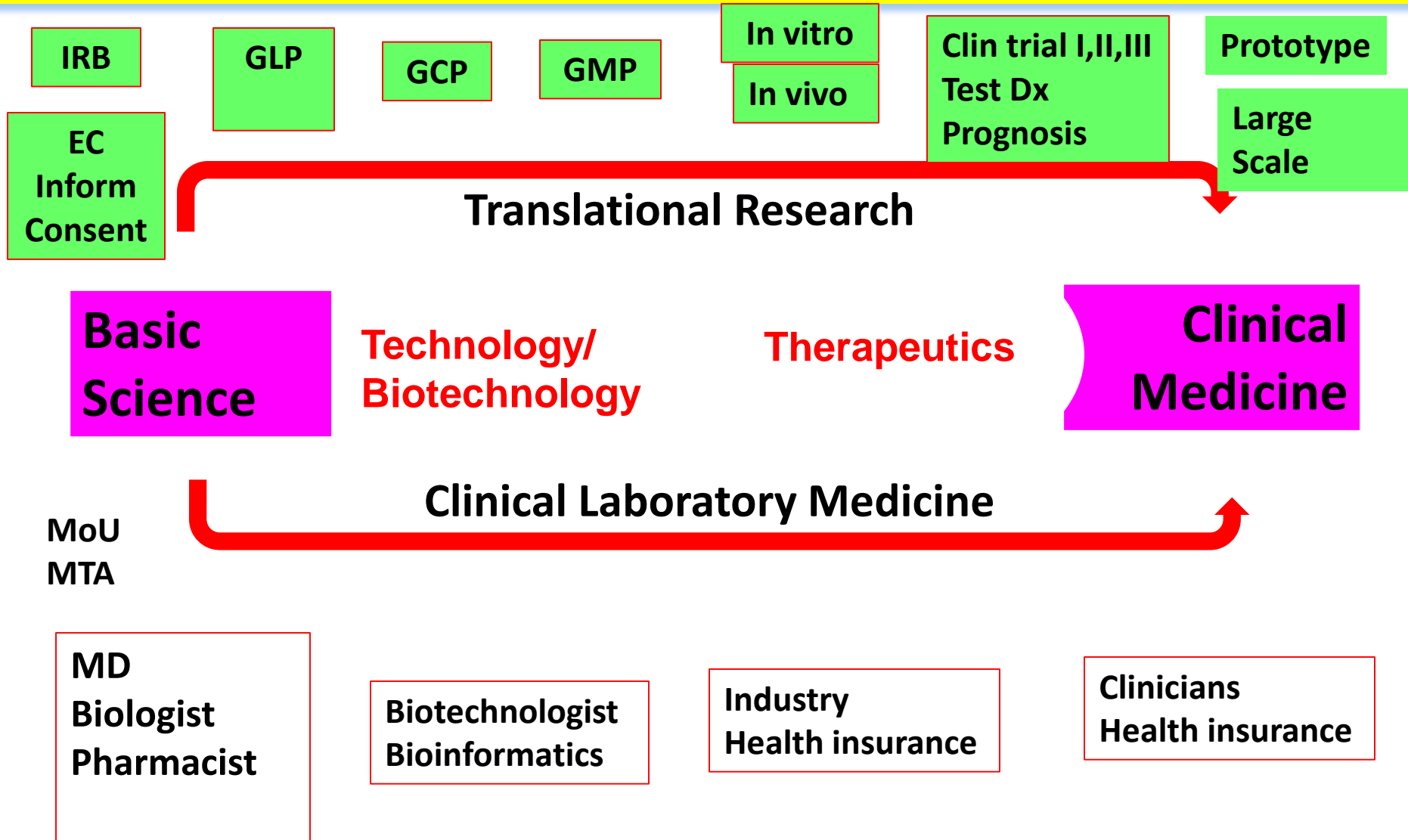
Biotechnology for Better Life ?

Personalized Medicine



- Select most effective therapy without wasting precious time and resources
- Drugs gain approval for specific slice of population
- Early identification of medical condition before acute symptoms occur, while treatment can be most effective
- Using diagnostics to monitor the course of treatment

Technology and Therapeutics as Drivers of Medical Care



Paving the Way for Personalized Medicine

FDA's Role in a New Era of Medical Product Development

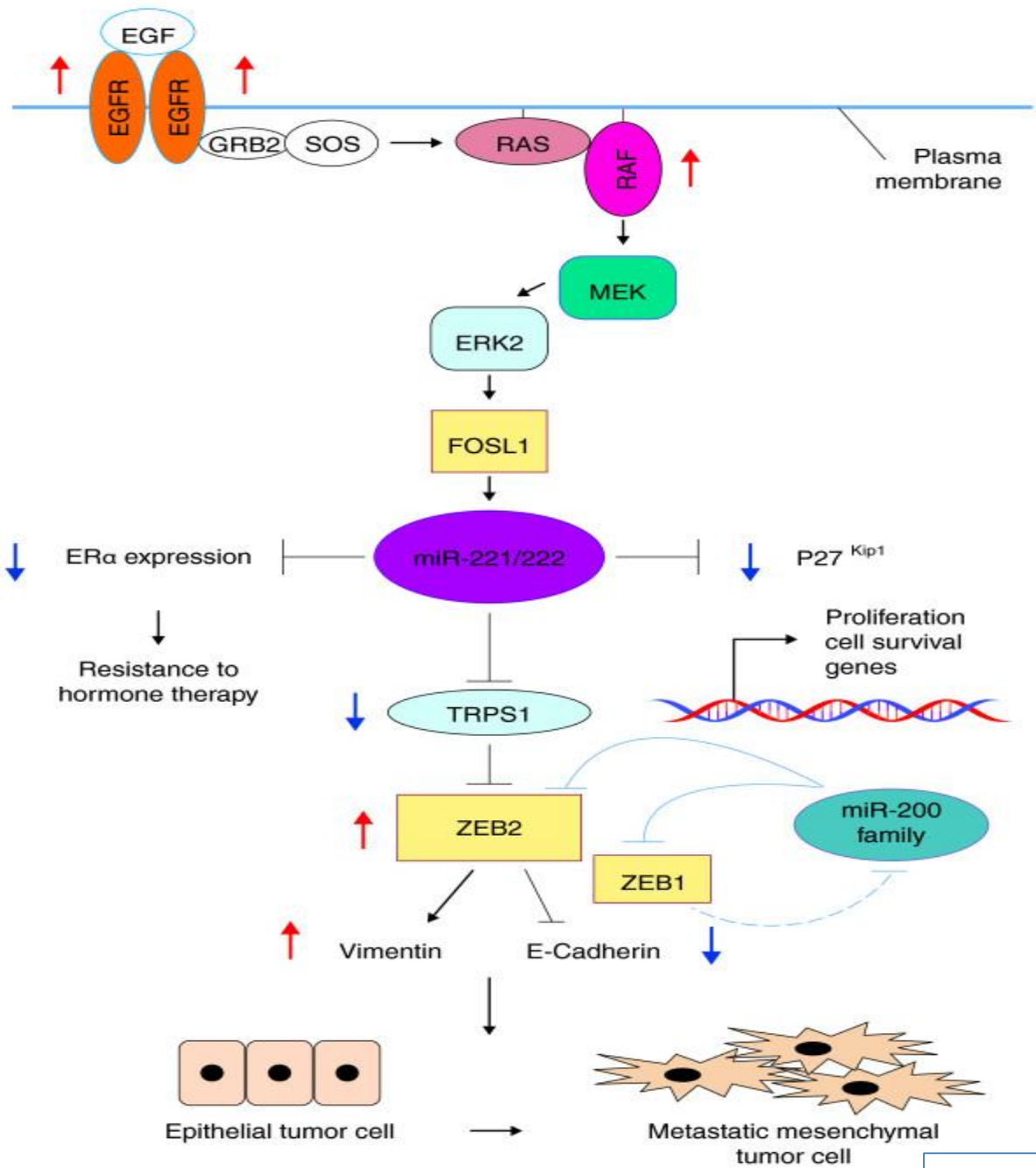


U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
U.S. FOOD AND DRUG ADMINISTRATION

■ Cancer

- Heterogeneous
- Same clinical diagnosis → different response of therapy
- Should be personalized approach

“Precision Medicine Shaping the Future of Cancer Research”



Cancer is Heterogenous

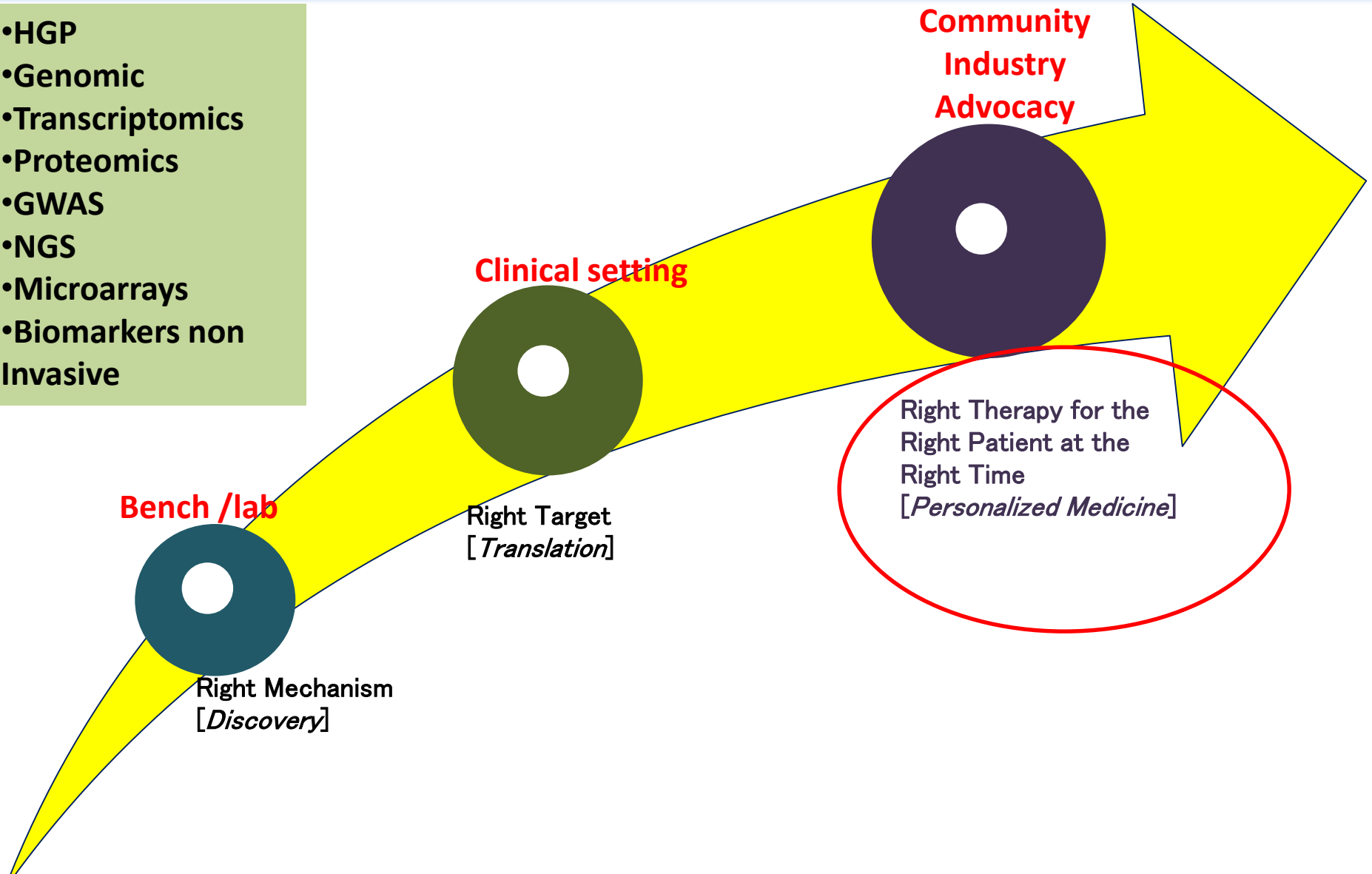
Different signalling pathways

Different response to treatment

Personalized approach

The Future of Health Care Through Innovation and Technology

- HGP
- Genomic
- Transcriptomics
- Proteomics
- GWAS
- NGS
- Microarrays
- Biomarkers non Invasive

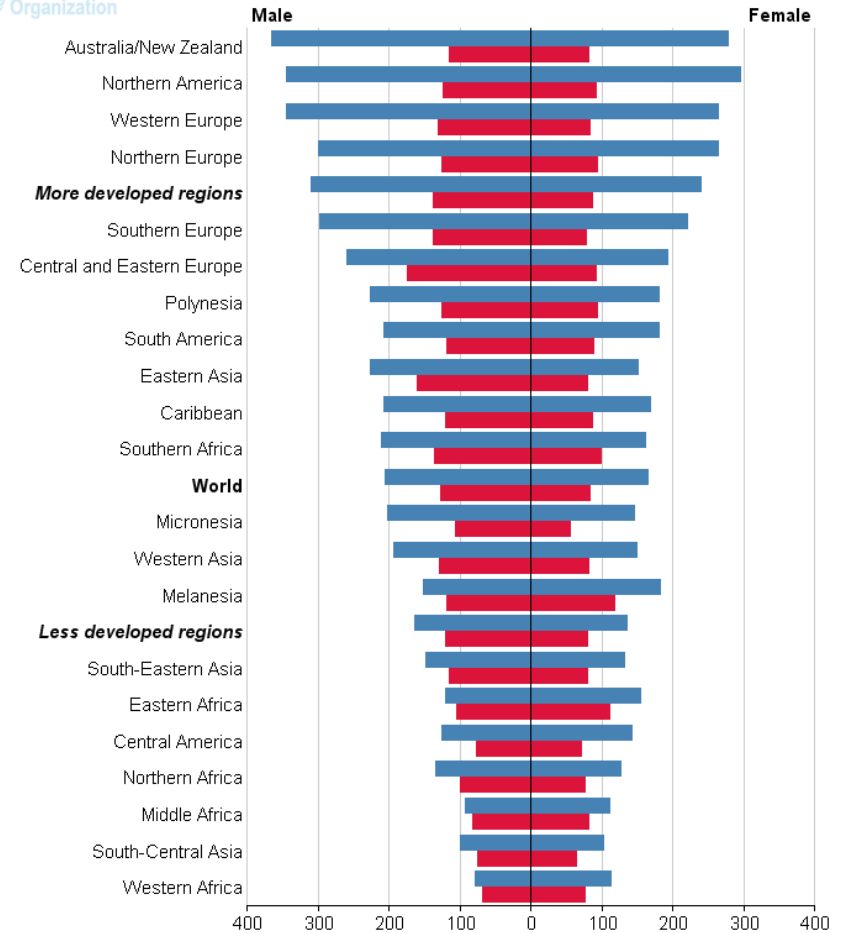


Top 10 Causes of Death, Indonesia

1. Stroke 21%
2. Ischemic Heart Disease 9%
3. Diabetes 7%
4. Lower Respiratory Infections 5%
5. TB 4%
6. Cirrhosis 3%
7. Chronic Obstructive Pulmonary Disease 3%
8. Road Injury 3%
9. Hypertensive Heart Disease 3%
10. Kidney Diseases 3%

Source: [WHO Country Health Profiles 2012: Indonesia](#)

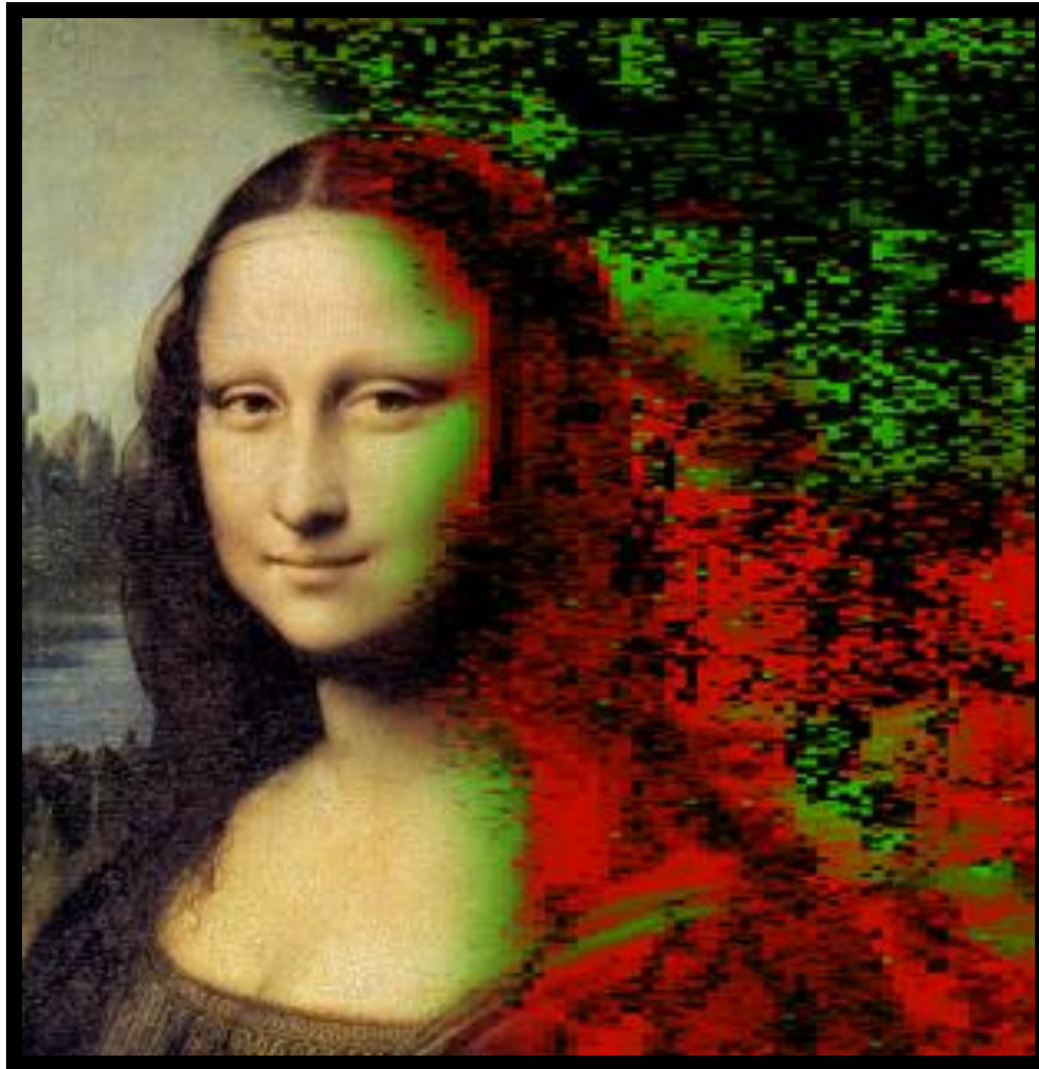
International Agency for Research on Cancer



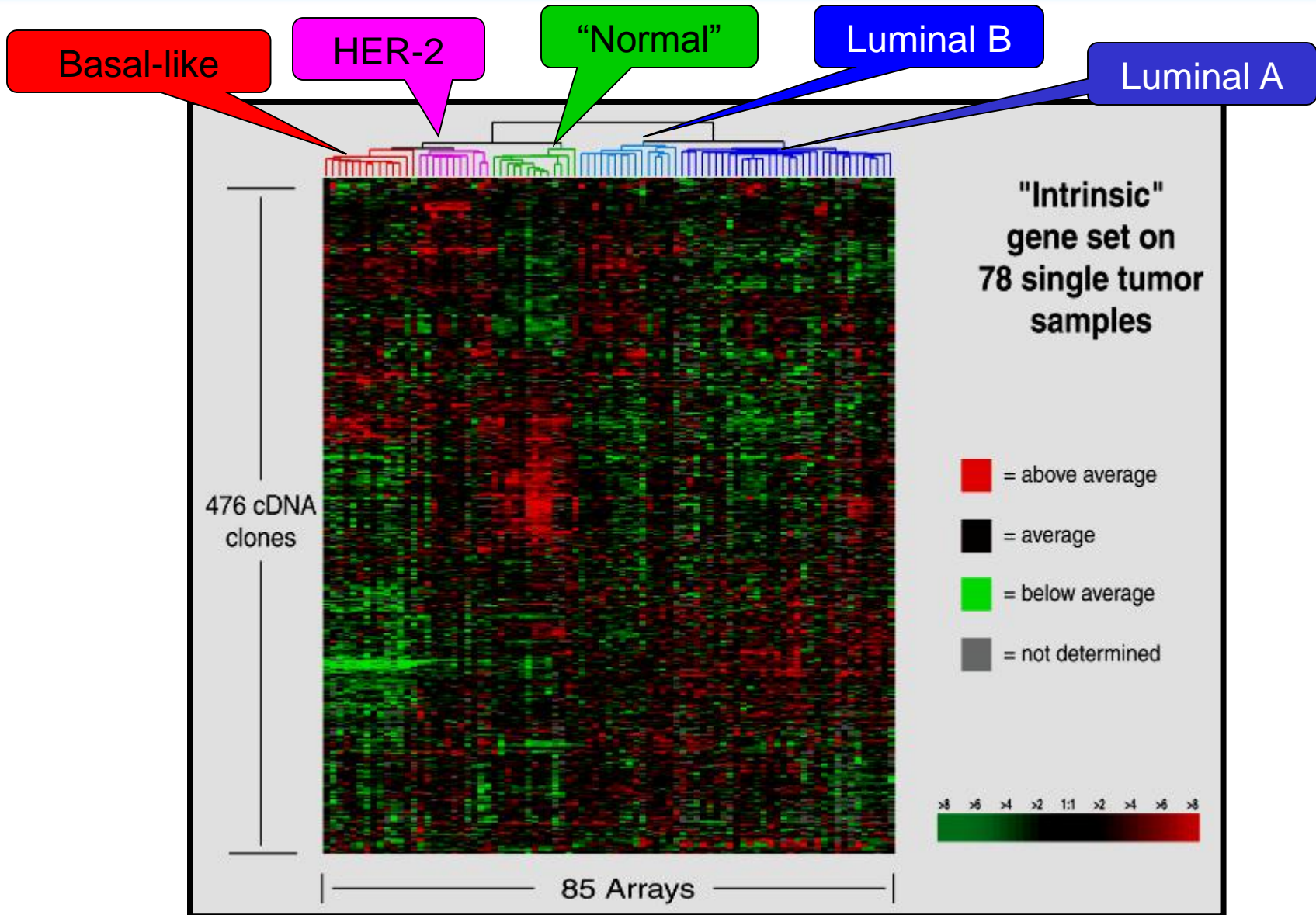
GLOBOCAN 2012 (IARC)

■ Incidence
■ Mortality

Precision Medicine shaping the Future of Cancer Research



Microarray : Molecular Portrait of Breast Cancers



Sorlie T et al, PNAS 2001

Slide courtesy of L. Carey

Example : Breast Cancer HER2 Status

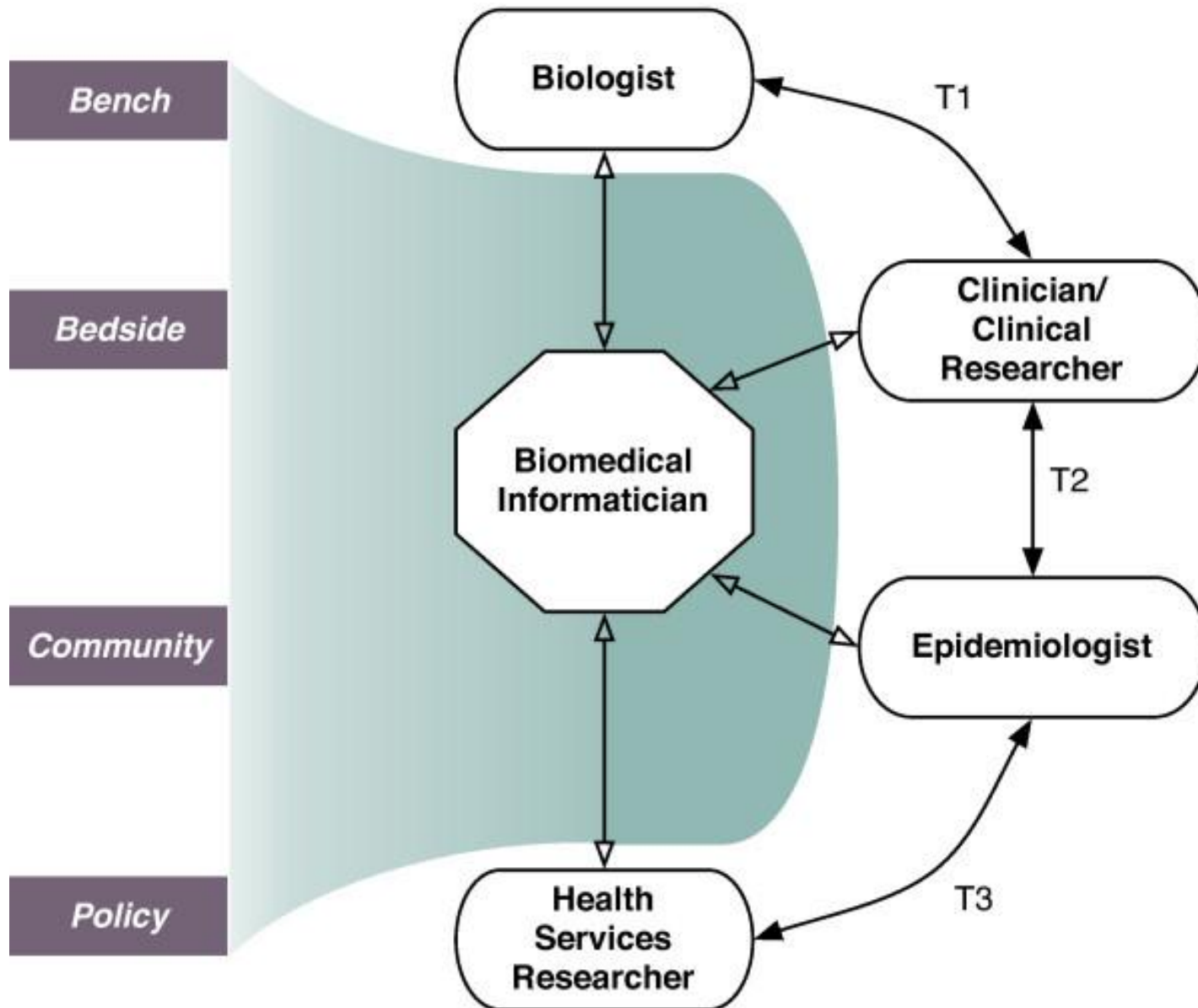
- HER2-positive breast cancers tend to grow and spread faster than other breast cancers.
- **Immunohistochemical stains (IHC)**
- **Fluorescent in situ hybridization (FISH)**
- **chromogenic in situ hybridization (CISH)**

- **Trastuzumab (Herceptin):
(MoAb anti HER2**
- **Pertuzumab (Perjeta)**
- Lapatinib
- Pampanib
- Avatinib

Insurance coverage ?

Equity

The role of the biomedical informatician in a translational medicine team.





SDG's Agenda : The World we want

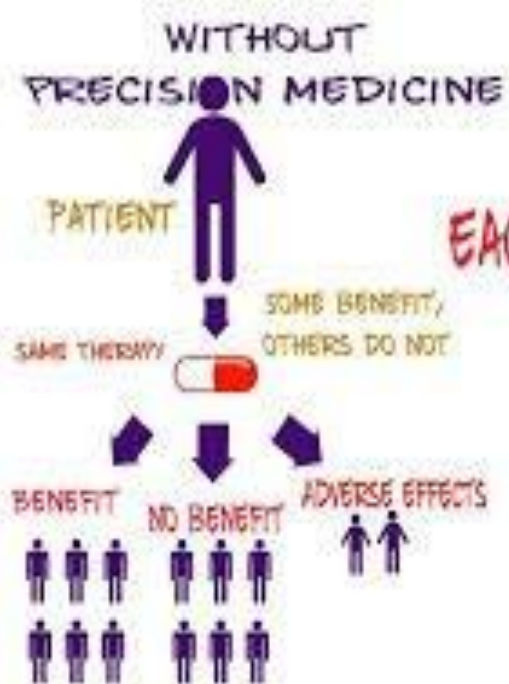
Targets : Poverty (Stunted) , Water, Planet, Transportation
Health - NCD : CV, DM , Cancer , OPCD
CD : Malaria, AI, Dengue, AIDS/HIV, TB, Neglected, E-RE

SDG's Sustaining the Planet and People

Continuation of MDG's → Focus on People , Planet, Peace, Partnership



Personalized Medicine need Biomarkers



BRCA Testing

Determine Your Risk

Stem cell
CM MSC
Gene therapy
Nano
medicine



SDG's target : Non Communicable Disease

- **Genomic → Post Genomic Era**
 1. **NCD** : Cancer , CVD, Metabolic syndrome, Genetic Disease
 2. **CD** : PINERE – M.A.D.A.T., Neglected Disease, new Emerging , Emerging Infectious Disease
- **Post Genomics Era** : need
 - Innovation, Technology and Synergy .
 - Ethical conduct

Sustaining the Planet - SDG's

To make a better world - **17 SDGs Targets**

- Everybody's contribution is needed
- Interdisciplinary approach
- Synergistic engagement
- **Ethical conduct**



**Innovation and Technology in
Personalized Medicine**

Post Genomic's - Ethical Issue

- **Regenerative Medicine : Stem cell ; CM - MSC**
- **Personal Genetic data vs personalized medicine**
- **Biobank for translational / personalized medicine**
- **Nanomedicine/ nano therapy**
- **AbMo recombination**
- **etc**

Ethics is Everybody Business - support SDG's



Emerging ethical dilemmas in science and technology

- the potential privacy issues,
 - how we protect this very personal & private information?
- we headed toward a new era of therapeutic intervention to increase quality of life

1. Personalized genetic tests/personalized medicine

How do we make sure these devices are secure?

11. Genetic Data collection and privacy

2. Hacking into medical devices

10. Human enhancements

3. Driverless Zipcars

9. Ensuring access to wireless and spectrum

Pharmaceutical, surgical, mechanical and neurological enhancements are already available for therapeutic purposes

The ethics of automation and equality of access for people of different income levels

. We now need to have a policy conversation about how to make the most effective use of the precious radio spectrum, and to close the digital access divide for underserved (rural, low-income, developing areas) populations

4. 3-D printing

3-D printers are affordable and patterns abound for products both benign and

Is interspecies research the next frontier in understanding humanity and curing disease, or a slippery slope, rife with ethical dilemmas, toward creating new species?

8. Human-animal hybrids (chimeras)

5. Adaptation to climate change

The differential susceptibility of people around the world to climate change warrants an ethical discussion

7. Autonomous systems

the systems operate without human control and are designed to function and make decisions on their own, the ethical, legal, social and policy implications

6. Low-quality and counterfeit pharmaceuticals

The enormous amount of trade in pharmaceutical intermediaries and active ingredients raise a number of issues, from the technical (improvement in manufacturing practices and analytical capabilities) to the ethical and legal

The Fundamental Ethics Principles

1. **Autonomy** (Respect for People's Right and Dignity)
2. **Beneficence** (Obligation to bring good in all our actions)
3. **Non-maleficence** (Each action must produce >> good than harm)
4. **Justice** (Obligation to treat all people equally, fairly & impartially)

Ethical misconduct?

The most common types of ethical misconduct are :

- conflicts of interest,
- lying to employees and
- abusive behavior.

The result in higher turnover is :

- lower productivity and, ultimately.....
- a diminished reputation and profitability.

Ethical Issues in Biomedical Research

- The Standard of care
- Informed consent
- Community consultation
- Individual control (placebo)
- Community access to research

- The role & responsibility of Ethics Committee
- Compensation for trial injury
- Counseling
- Patient confidentiality
- Locating phase I,II,III trials

Clinical Research needs.....



Bioethical Principles

Ethics of Human Research
Declaration of Helsinki (1996)

Global GCP Guidelines

ICH GCP Guidelines
ICH E6

EU Implementing Directives

Clinical Trials Directive
2001/20/EC

GCP Directive
2005/28/EC

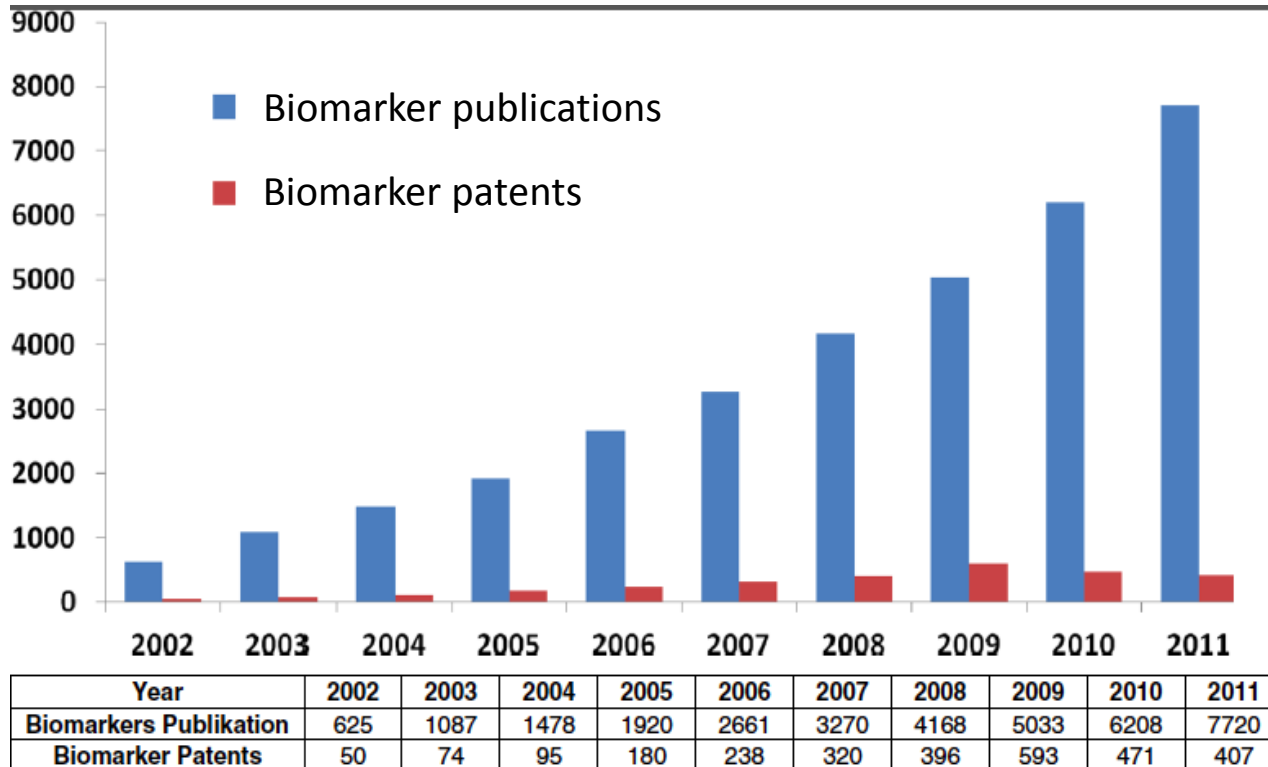
UK Law

The Medicines for Human Use
(Clinical Trials) Regulations
2004
SI 2004/1031

The Medicines for Human Use
(Clinical Trials) Amendments
Regulations 2006
SI 2006/1928

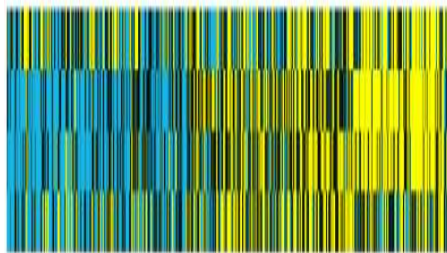
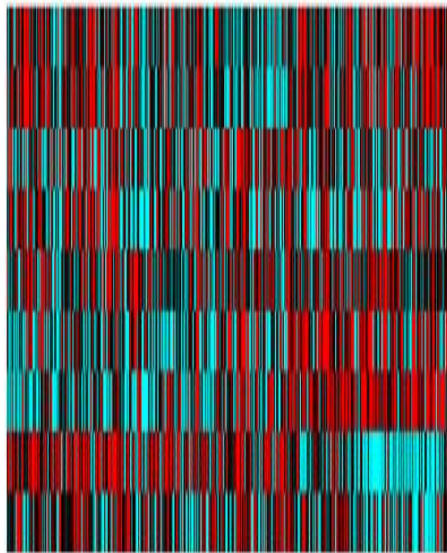
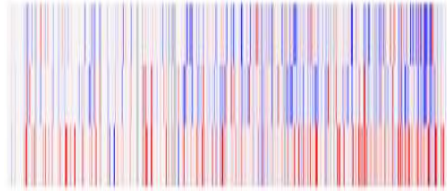
Translational Research??

- Clinical biomarkers need to be highly specific and sensitive
- Majority of the biomarker discoveries do not meet the criteria of high sensitivity and specificity.



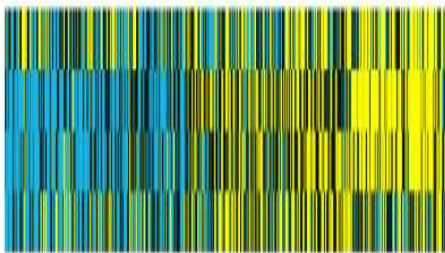
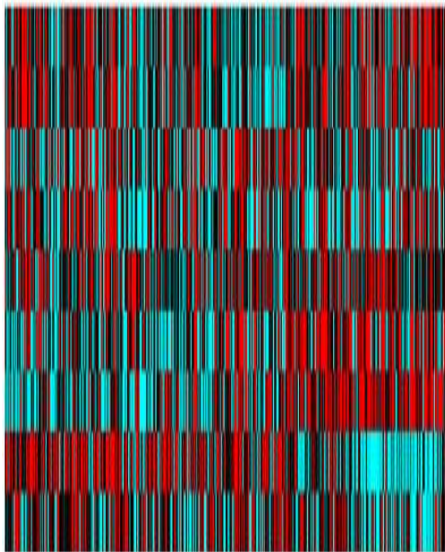
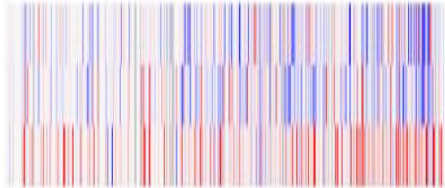
The lack of sensitivity and/or specificity leads to a low number of patent application and, in addition to this, to a low number of successful market applications.

Added Value of Precision Medicine in the Genomic Era for Patient safety, efficacy



- “One-size” does not fit all
- Identifying the right therapy or the right patient
 - Enhance clinical outcomes
 - Increase benefit : risk ratio
 - Accelerate new therapeutic development for breast cancer

Development of Genomic Signatures...

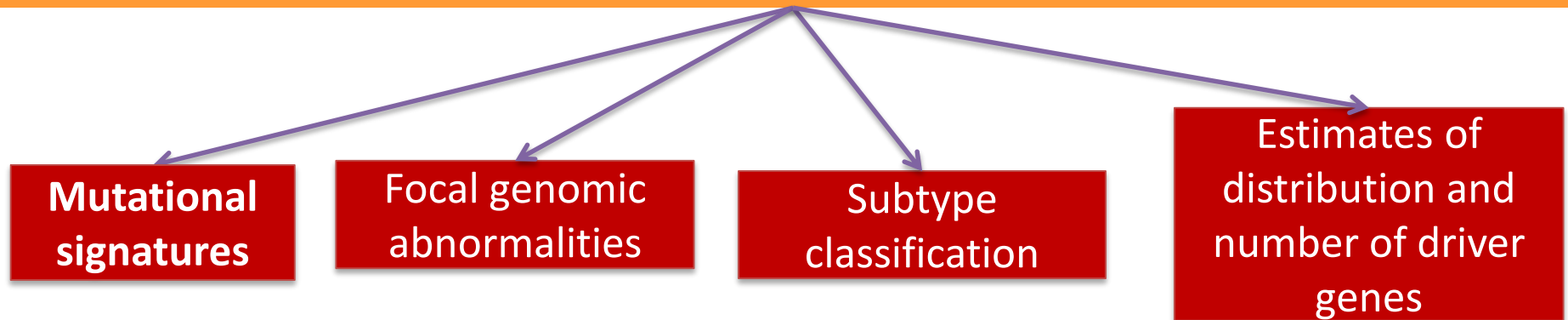


- **Discovery**
 - NGS, RNA seq, proteomics
 - Analytical validation
 - Training sets and validation sets
- **Clinical Validation**
 - Prognostic & Predictive value
 - Retrospective vs Prospective
 - Compared with old therapies
- **Clinical Utility**

Potential of clinical cancer genomics – *Scientists' viewpoint*

Large-scale sequencing projects

International Cancer Genome Consortium (ICGC) and The Cancer Genome Atlas (TCGA).



Ethical Principles Conducts
Era of “cancer biomarker discovery”

Ethics is needed in all aspects

Our world today



Big data

E.g. data mining, risk stratification



Social movements

E.g. patient groups, citizen activists



Social media

E.g. patient forums, blogs



New technologies

E.g. health apps, telecare



Ageing population

E.g. more contact with health services



People-centered care

E.g. personalized services, life-course approach

Clinical res & application Ethics

Biomed Engineering Ethics

Medical Law Ethics

Awareness Ethics

Bioethics is a discipline dealing with the ethical implications of biological research and applications in medicine

BIOETHICS – Everyone's Business

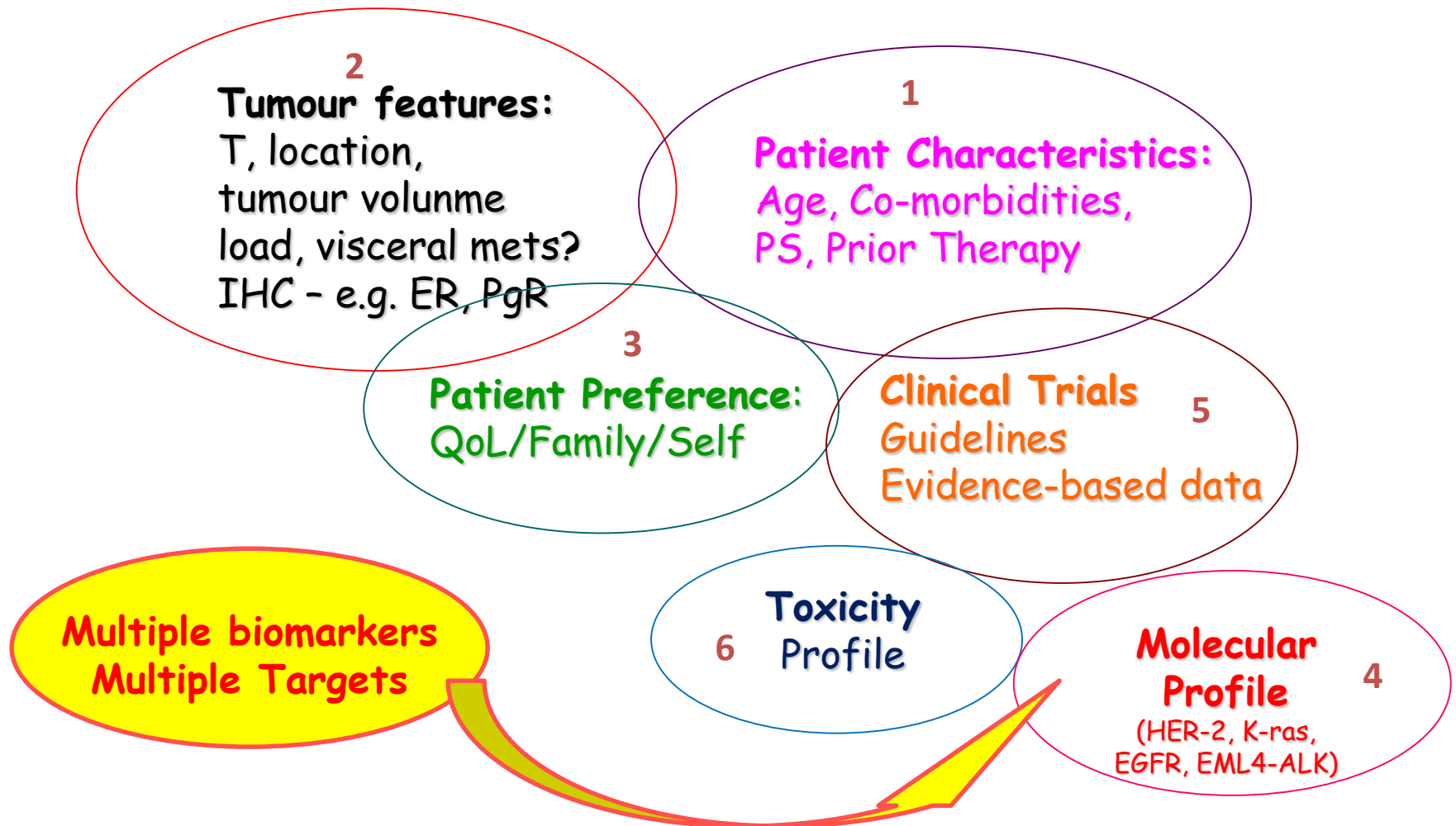
Biotech Ethics

Bioinformatics Ethics

Healthcare Ethics

Health Equipments Ethics

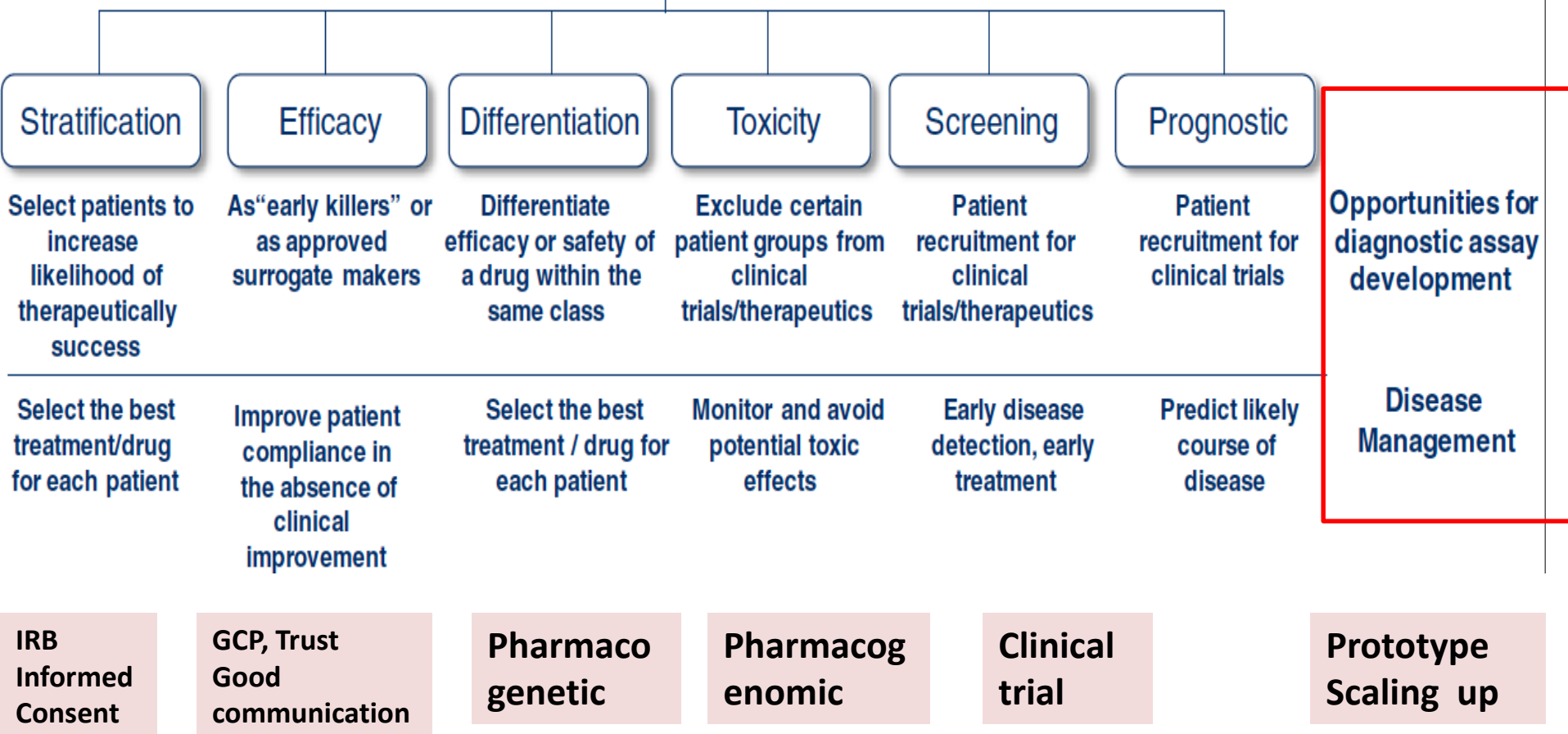
Decision Making in Cancer Treatment



Translational Research – *Clinicians'* viewpoint

Clinical Biomarkers

Molecular Diagnostics (Proteins, Ab, Peptides, Ag, CNAPS, DNA, RNA)



Post Genomic : Multidiscipline and Ethical :

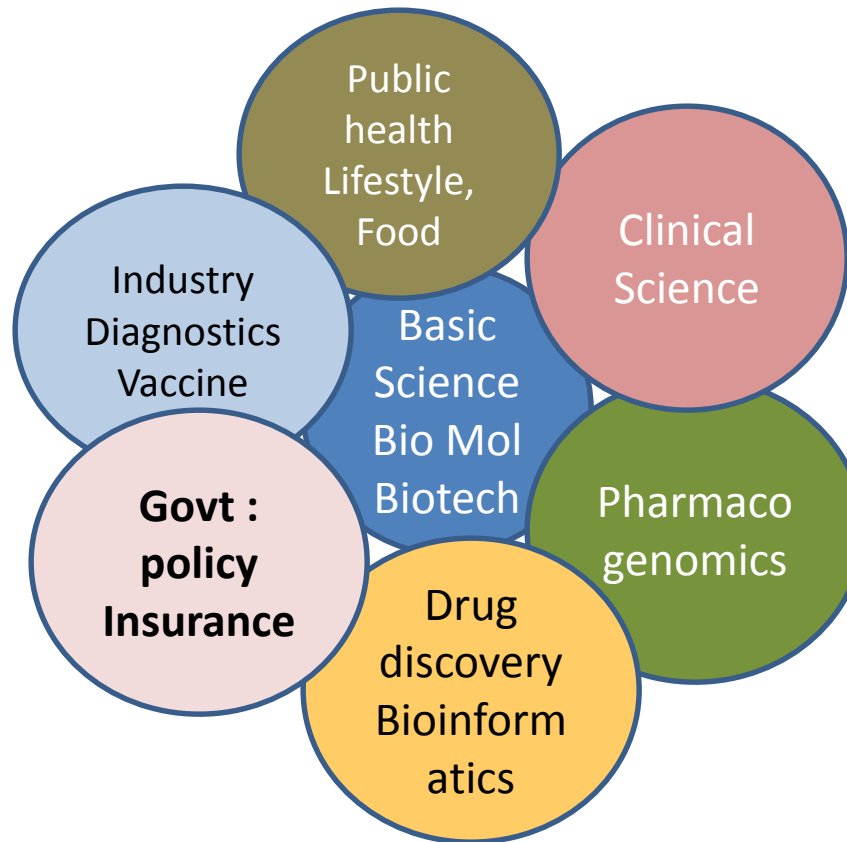
1. **Building Credibility** -The true transformation starts with building credibility at the personal level. The foundation of trust is everybody's credibility
2. **Restore Trust-** the ability to establish, grow, extend, trust among stakeholders is the critical competency of leadership
3. **Passion** - You must have passion. If you don't enjoy what you are doing, then you shouldn't be doing it.
4. **Lead by Example** - in order to be a great leader of others, you must first be a great leader of yourself - to be an effective, inspiring and trusted leader
5. **Goal oriented-** capacity to live up to certain expectations, to deliver on promises, and to achieve clarity on key goals.

Post genomic – Synergy & Ethical :

6. **Reliability** : To be reliable, you need to be dependable, which in turn builds trust from followers.
7. **Social skills** - leaders need to socialize with others
8. **Integrity** - Nothing is Small. As a leader you live under a microscope. The folks you hope to lead watch everything you do and you say. They are watching if it is in integrity with what you say you believe.
9. **Motivate** – for an assignment ,thank the person for taking care of it before it gets done. When it is done tell what excellent job that person did. When you inspire trust and share a common purpose with aligned systems, you empower people
10. **Instill Confidence**- people should feel they really participating in the decision, to retain great people they should feel they are part of the authorship of the strategy and the authorship of the really critical issues.

Lesson learned : translational Research at UGM

Cancer Translational team : NPC, Breast, HCC, Prostate, Ovarian Ca



IRC FERCAP

MTA , MoU

Basic Research : GLP, GCP,
Biosafety, Biosecurity

Clinical Research : GCP,
Informed consent,

Community education and
awareness

Govt : Insurance, Policy

ncRNA – Regulate Gene and Protein Expression



The Nobel Prize in Physiology or Medicine 2006

"for their discovery of RNA interference - gene silencing by double-stranded RNA"

Andrew Z. Fire
Craig C. Mello



Photo: L. Cicero/Stanford



Photo: R. Carlin/UMMAS

Andrew Z. Fire

🏆 1/2 of the prize

USA

Stanford University School
of Medicine
Stanford, CA, USA

Craig C. Mello

🏆 1/2 of the prize

USA

University of
Massachusetts Medical
School
Worcester, MA, USA

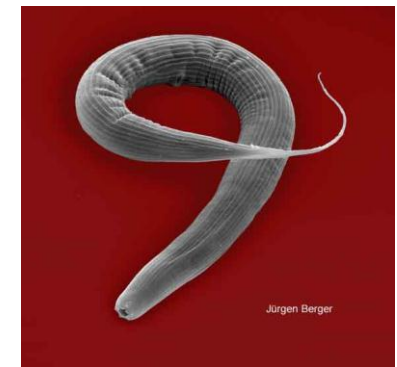
**Potent and specific
genetic interference by
double-stranded RNA in
*Caenorhabditis elegans***

Andrew Fire⁺, SiQun Xu⁺, Mary K. Montgomery⁺,
Steven A. Kostas⁺⁺, Samuel E. Driver[‡] & Craig C. Mello[‡]

NATURE | VOL 391 | 19 FEBRUARY 1998

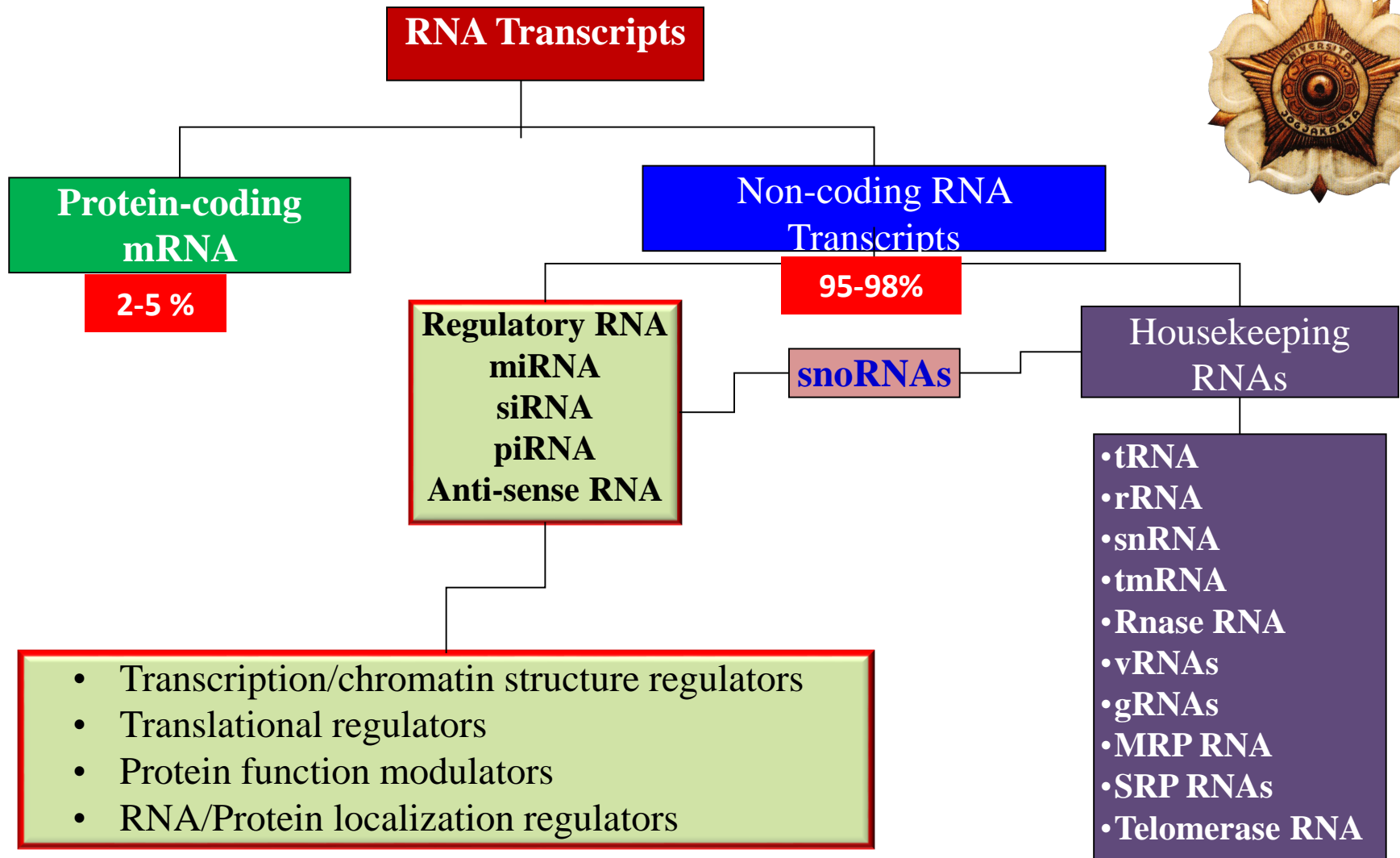
Cho WC. MicroRNAs in cancer - from research to therapy.
Biochim Biophys Acta - Rev Cancer 2010;1805(2):209-217.

C. elegans



Jürgen Berger

Non-coding RNA: the new emerging star in open the Pandora Box



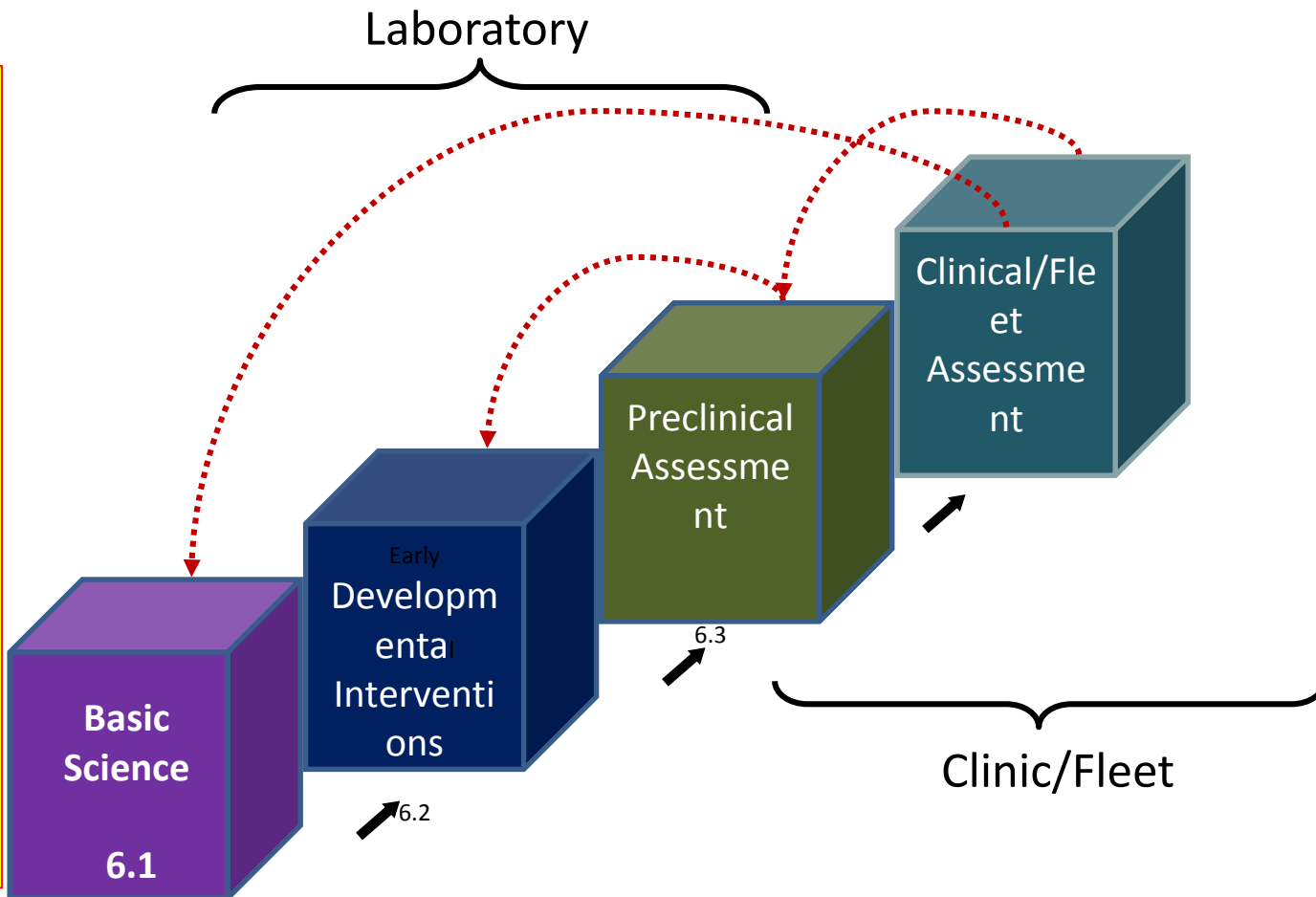
“Bench to Bedside” (and back again) Building Blocks



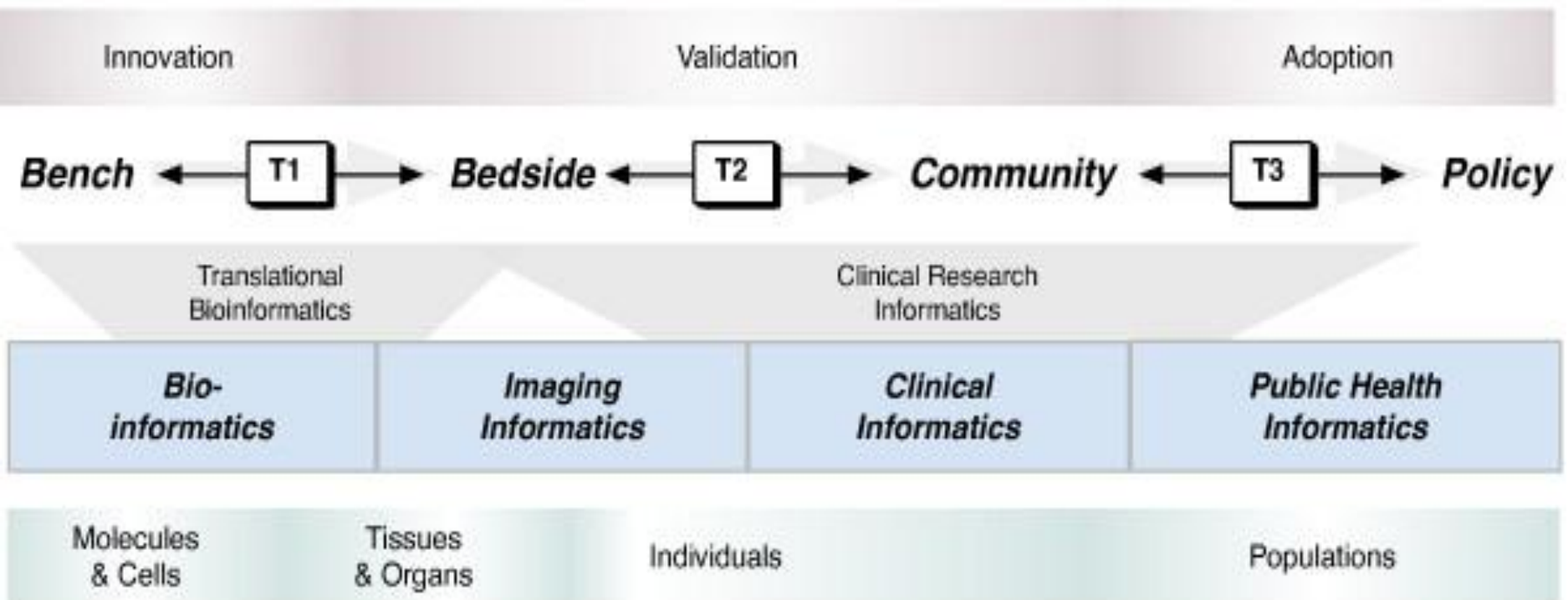
- GCLP
- GCP
- Biosafety
- Biosecurity

- IRB
- Ethical Clearance
- Informed Consent

- Bioethics



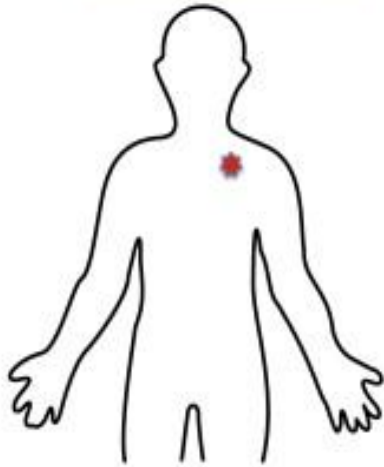
Translational Medicine Continuum



Biomedical Informatics Continuum

miRNA and LncRNA in clinical applications

Diagnosis and prognosis

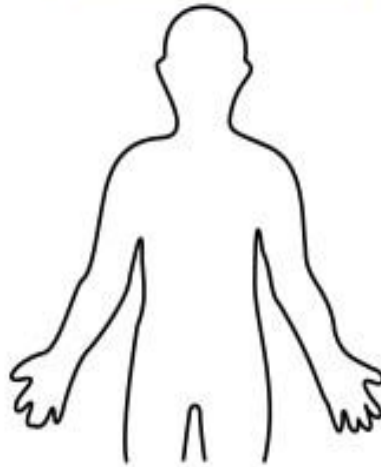


Predictive/prognostic signatures
MicroRNAs delineating subtypes of disease

Prediction of treatment response
e.g. miR-451 in CML

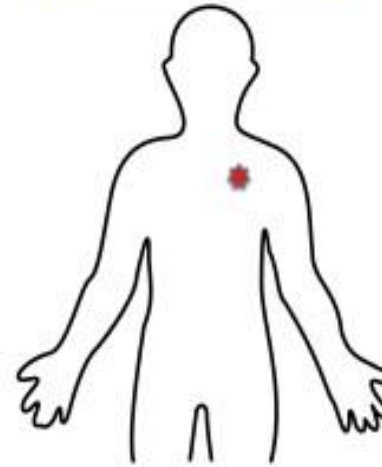
MicroRNA based therapeutics e.g. MRX34

Remission

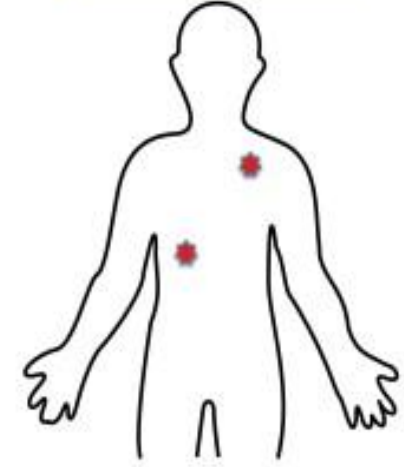


Detection of microRNAs in biological fluids e.g. miR-21
detection in blood in multiple cancers

Relapse



Metastasis



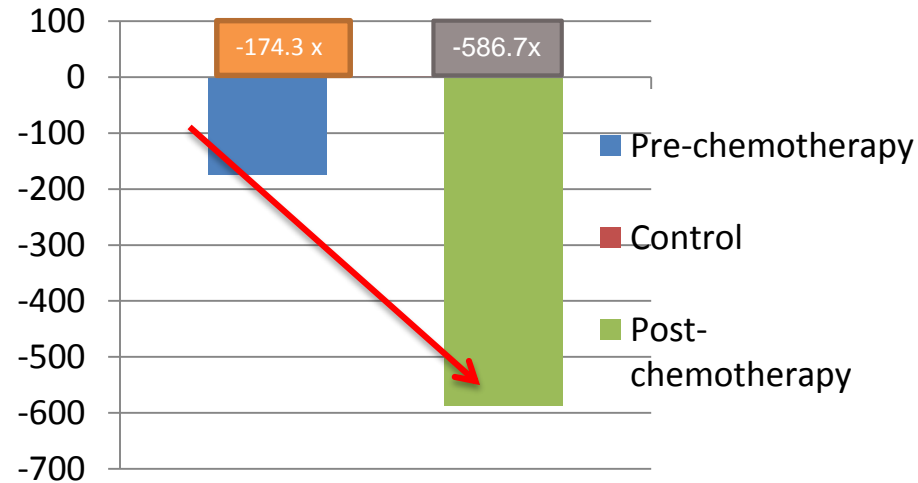
Prediction of metastatic outcomes
e.g. miR-10b in breast cancer

Future applications of microRNAs:

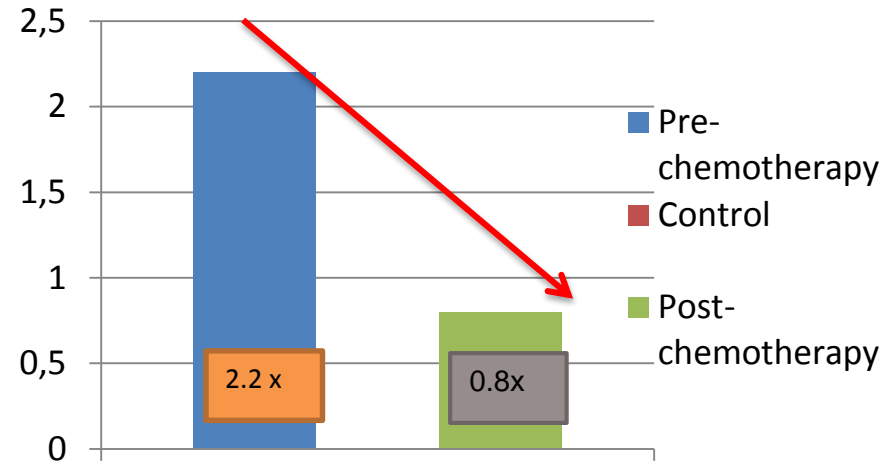
- More accurate detection in bio-fluids – urine, CSF, blood – circulating exosomes
- More precise signatures, tailored to specific therapies
- More therapeutic applications – antisense, therapeutic miR delivery (nanoparticles, cell-based and exosomes), combination therapies

The Expression of miR-21, miR-155 and mRNA PTEN and SOCS1 Pre and Post Chemotherapy Breast cancer

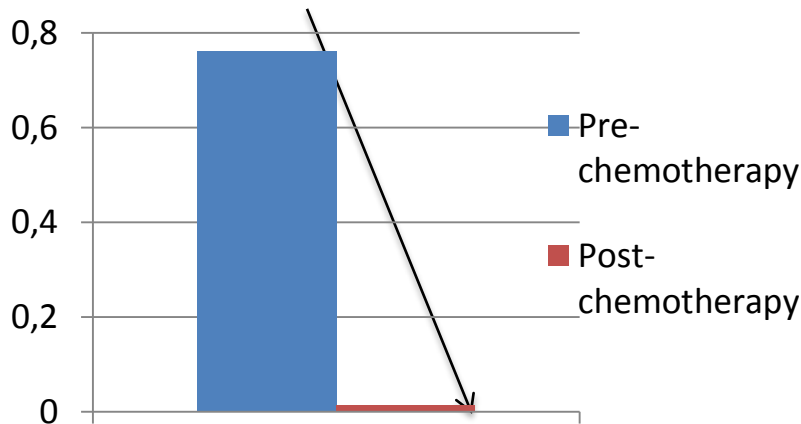
mRNA PTEN – TSG



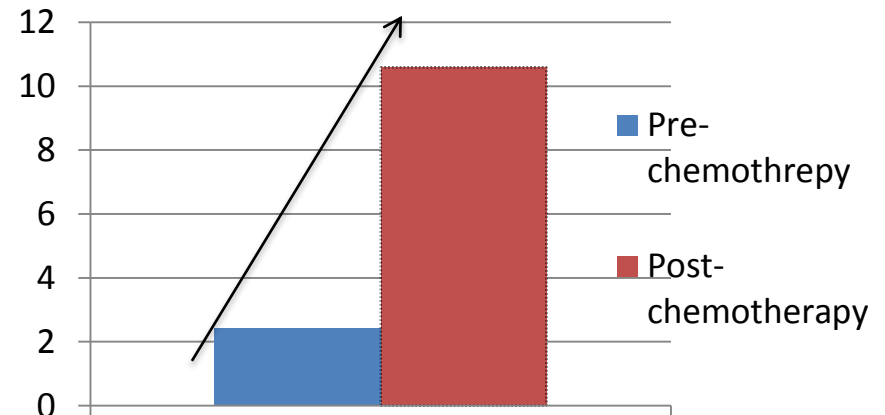
Hsa-miR-21 - OncomiR



mRNA SOCS 1



Hsa-miR -155



**A Continues Ethical Community education
and awareness
in the Era of Post Genomics and
Advancement technology
is needed**

Educations : Public Awareness

- Some people do know the impact of many of the **additives and chemicals** that they come in contact with each day.
- **What are some ethical concerns with food labeling?**
- **Are labels necessary and effective?**



Labelling Requirements

[General labelling requirements](#)

[Carry-over/reverse carry-over additives](#)

[Processing aids/carriers](#)

[Sweeteners](#)

[Food Colourings](#)

[Genetically Modified](#)

[Organisms](#)

[Labelling of additives sold directly to consumers](#)

[Labelling of additives not sold directly to consumers](#)

REGULATION (EU) No 1169/2011
OF THE EUROPEAN PARLIAMENT
AND OF THE COUNCIL of 25
October 2011

CODEX STAN 107-1981 [\[8\]](#)

MANDATORY LABELLING OF PREPACKAGED FOOD ADDITIVES SOLD BY RETAIL

1 DETAILS OF THE FOOD ADDITIVE

2 INSTRUCTIONS ON KEEPING AND USE

3. NET CONTENTS

4 NAME AND ADDRESS

5 COUNTRY OF ORIGIN

6 LOT IDENTIFICATION

MANDATORY LABELLING OF PREPACKAGED FOOD ADDITIVES SOLD OTHER THAN BY RETAIL

1 DETAILS OF THE FOOD ADDITIVE

2 INSTRUCTIONS ON KEEPING AND USE

3 NET CONTENTS

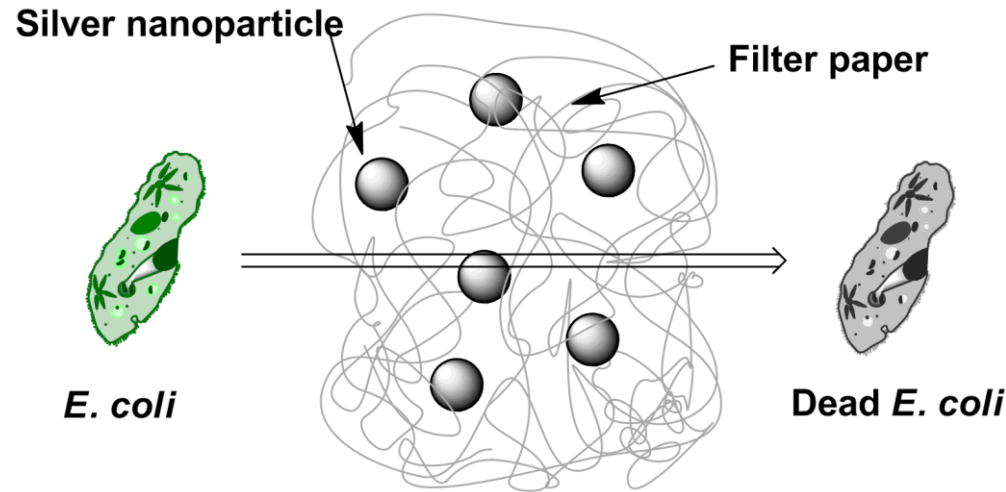
4 NAME AND ADDRESS

5 COUNTRY OF ORIGIN

6 LOT IDENTIFICATION

Nanotechnology

- Field that studies objects 1-100 nm in size (in one direction).
- Silver nanoparticles are naturally antimicrobial and are incorporated into many consumer products.
- **What are some ethical concerns with using silver nanoparticles? Education.....**



Picture courtesy of Environmental Health News

What is Nanofood?

contain engineered nanomaterials (ENMs)
 metal oxide nanoparticles
 man-made nanoparticles such as silver, titanium dioxide,
 zinc oxide, silica, etc.
 used in food supplements and food packaging



<http://www.eantr@11.com/content/uploads/2013/03/Chip-Bags.jpg>



MATERIALS

Nanoparticles

Nano-emulsions

Nanocomposites

Nanostructured Materials

PROCESSING

Heat/Mass Transfer

Reaction Engineering

Biotechnology

Molecular Synthesis

PRODUCT

Controlled Delivery

Formulation

Packaging

PRODUCT SAFETY

Nanosensors

Nanotracers

Genetically Modified Foods

- A genetically modified organism (GMO) is an organism that has foreign DNA inserted into its genome using genetic engineering
- Genetically modified plants were first introduced in the US in 1996
- **Are there any ethical concerns with producing and consuming a GMO?**

Picture courtesy of Monsanto Corp. (used with permission)



Introduction of GMOs in Medicines and Researches

- Since the 1980s, GMOs have emerged as one of the mainstays of biomedical research.
- The use of GMOs in medicine and research has produced a debate that is more philosophical in nature.
- Ethical issues in introducing GMOs as medicines and research include:



Violation of natural organisms' intrinsic values
Tampering with nature by mixing genes among species
Objections to consuming animal genes in plants
Animal rights

Can GMOs HELP PROTECT THE ENVIRONMENT?



THEY ALREADY DO.

Contrary to myths about GMOs hurting the environment, GMOs allow farmers to **preserve the land while doing more with less resources.**

The Environmental CHALLENGE:

20% POPULATION INCREASE BY 2050¹ =

HIGHER DEMAND FOR



FOOD



and **FIBER**



FUEL

2 POTENTIAL PATHS

1

Convert more land, like forests and prairies, into agricultural production

2

Use agricultural technologies like GMOs to increase crop yields on existing farmland

GMOS are ONE SOLUTION

In 2014, GMOs allowed farmers to use

51 MILLION less acres of land

That's equivalent to all the farmland in Iowa and Missouri²



to produce the same amount of food, fuel and fiber crops

Without access to GMOs, farmers would have needed to plant an additional:



22 MILLION acres of corn



19 MILLION acres of soybeans



9 MILLION acres of cotton



1.5 MILLION acres of canola

to keep up with global production levels in 2014³

Need evidences :
community
safety -
basic
ethical
principle

¹World population projected to reach 9.7 billion by 2050 (2015). Retrieved from: <http://www.un.org/en/development/desa/news/population/2015-report.html>.

²Brookes, G. and Barfoot, P. (2016). GM crops: global socio-economic and environmental impacts 1996-2014. Retrieved from <http://www.pgeconomics.co.uk>.

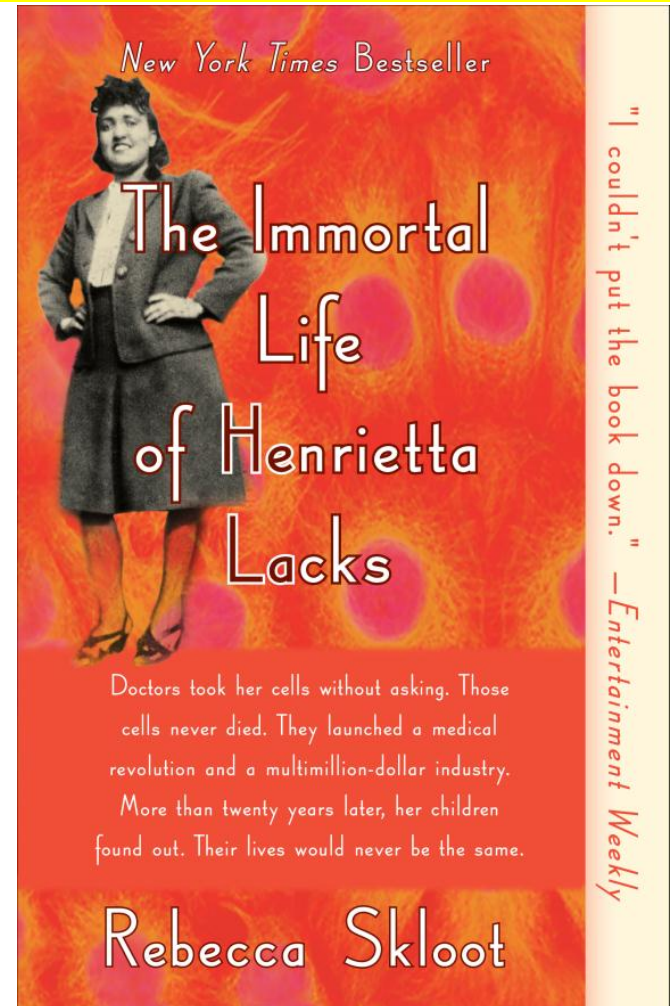
³Brookes, G. and Barfoot, P. (2016). GM crops: global socio-economic and environmental impacts 1996-2014. Retrieved from <http://www.pgeconomics.co.uk>.



Left over tissues? Technology vs Ethics

- After a surgical procedure or biopsy do you own the removed tissue?
- **What are some ethical concerns with the use of collected tissues?**

**HeLa cell lines
Available in the market**



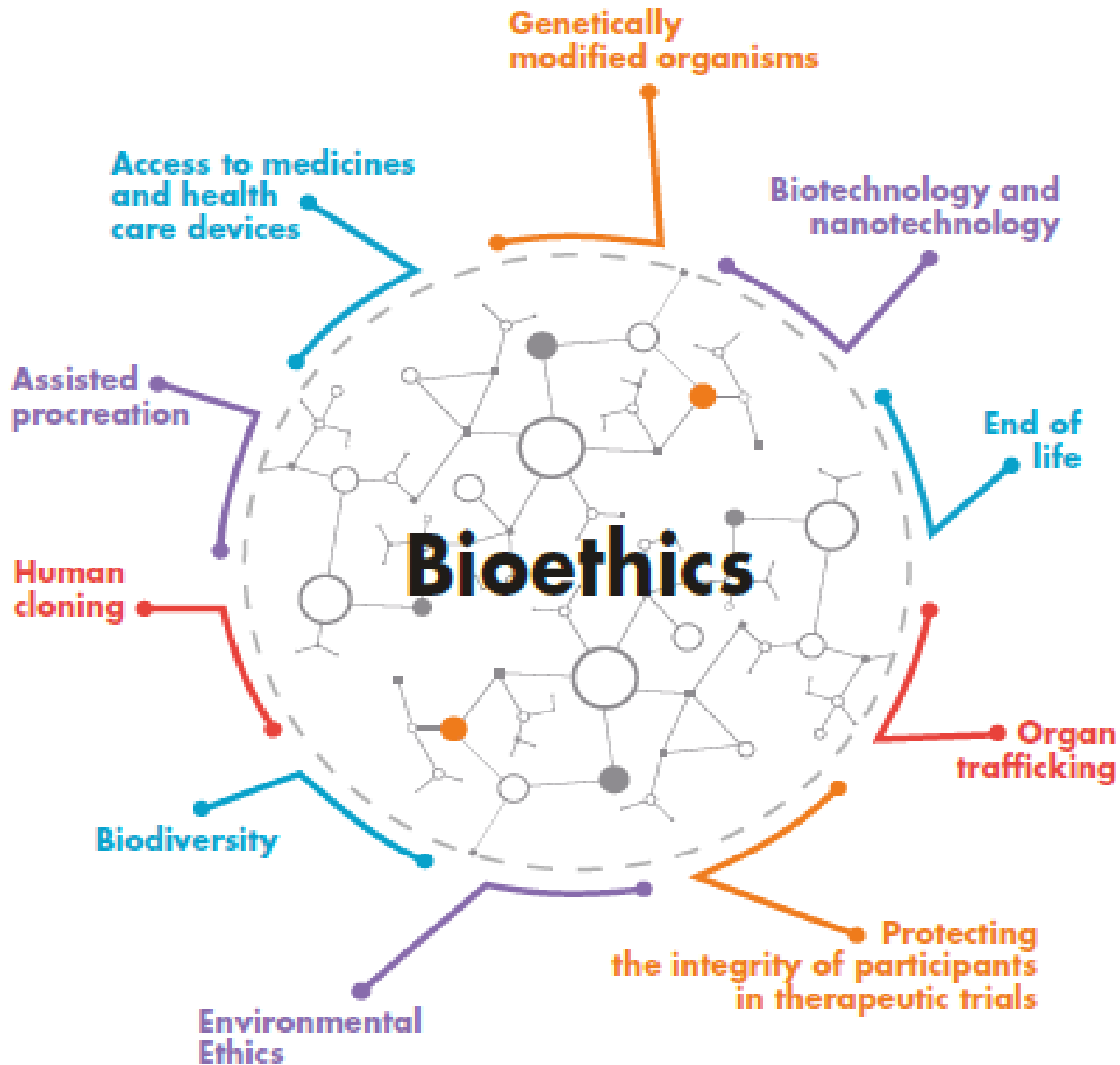
Courtesy of the Lacks Family and Rebecca Skloot.



Engineering Ethics



Medical Technology – Social – Ethical Issues



Tissue is Issue - liquid biopsies



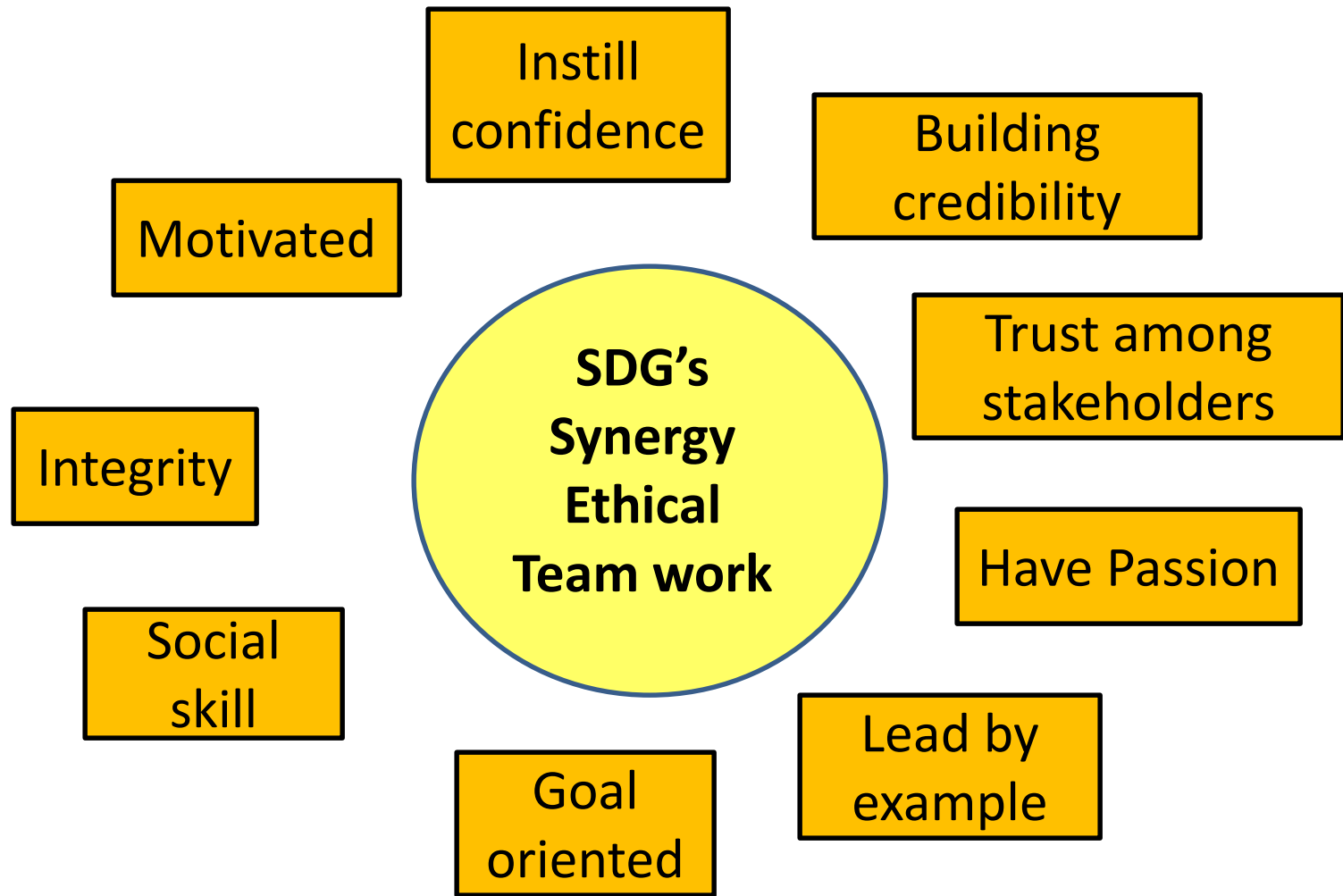
Global Trends

- The applications of science are scrutinizing
- Awareness about bioethics - social responsibility increasing**
- To make the decision citizens need to consider personal and the affect to the society as a whole)

socio-cultural influences

Bioethics Education is a absolutely needed

- To increase respect for life
- To balance the benefits and risks of science and technology
- To understand better the diversity of views of different persons (Macer , 2004)
- **Indonesia – New Sense of Bioethics**
(S. Sastrowijoto, 2014)



Ethical at Workplace

Conclusions

- Post Genomics Era, **bring Innovation and Technology**
- Those need **Ethical and Bioethical Conduct**
- Personalized Medicine – **is the future of Medicine – based on own genetic background**
- SDG's – to sustain **the planet and the people**
- Bioethics education is **absolutely needed**

Thank You