Prof. Gérard Siest
Gerard.Siest@univ-lorraine.fr

IFCC
And
Personalized Laboratory Medicine

Kuala Lumpur- IFCC General Conference 2012 – IFCC in its 60th Year– November 19, 2012
Personalized Laboratory Medicine

Pharmacogenomics
ESPT

Genetics

Reference Values
Personalized Laboratory Medicine Partners

PLM Partners

- Patients & Citizens
- Clinical Chemists & Clinicians
- Regulatory Agencies & Governments
- Industries & Biotech
- Academic Research Centers

Academic Research Centers
Allowing Birth Of New Paradigm For Disease Management

From
Clinical definition of disease

To
Molecular definition of disease
FIGURE 2

Over the past 30–40 years targeted drugs for the treatment of breast cancer have been developed for yet smaller subgroups of patients.
FIGURE 1

Most diseases are heterogeneous and the use of molecular diagnostics can divide them into biological subgroups each with their targets and drugs.

Near Future

- To conduct specified clinical trials for children and different population
  - Avoid high dosage!
- Help defining biologically different subgroups of diseases
- Organize trials for molecular defined smaller subgroups
- Develop theranostics: genomic, proteomic, metabolic tests
- Help to establish clinical application of PGx in other clinical setting than cancers: Infectious diseases (HIV, CNS illnesses, Crohn’s disease, RA, DM)
- Define a feasible protocol for evaluating the medications side effects in the Real Medical Practice (After phase IV)
Limited and specific genes with approved pharmacogenomical function:
Ex.: Warfarin, Clopidogrel (1-2 genes)

All genes influencing medications effects of a given disease group: Ex. Cardiovascular, Cancers
Using Pre-designed Multiplex Chip (20-25 genes)

Genome wide scans

Exomes

Complete personal genome

The problem of interpretations : Role of Clinical Chemists
THERANOSTICS

150 000 omics publications

100 diagnostic tests
259 drugs – 75 first-in-class and 20 imaging agents – approved between 1999 and 2008, and found that 100 were discovered using a target-based approach and 58 through phenotypic approaches.

Of the 75 first-in-class drugs, 28 were assigned to phenotypic assays and only 17 to target-based approaches « CNS and infectious disease were the therapeutic areas that benefited the most from phenotypic screening ». 
Pharmacogenomics
Patients benefit

1) Deciding the most effective choice of available drugs
2) Avoiding potentially dangerous side effects

The majority of the presented results were obtained on monotherapy. But for cardiovascular diseases, patients are in general on polytherapy and drug interactions are important to be considered.
Search new markers of gene-drug combinations for implementation of PGx in clinical practice i.e. transcription factors

Provide easily-performed, easily-accessible point-of-care (POC) testings

Develop targeted, evaluable educational programs for patients, clinicians and other related health workers

Determine validated reference values (healthy controls)

Define guidelines using Systems Biology, Medicine and PGx
Reference Values
What is missing
What an IFCC Committee could do

1. To introduce more seriously the reference values concept in a general strategy of medical interpretation and health maintenance

2. To write practical recommendations and SOP for all steps involved in the production and use of reference values:
   - Consent form and patient information
   - Health questionnaire
   - Blood upatke
   - Specimen handling
   ...

3. To think about genetic based reference values (not only ethnical ones)
Reference Values
What is missing
What an IFCC Committee could do

4. To define particular reference values (For obese people? For women taking oral contraceptives...)

5. To think more deeply about individual/personal reference values

6. To look at the future for new tissue biomarkers reference values based on laboratory medicine techniques and imaging

G. Siest. Padova October 2010
ANATOMICAL VARIATIONS - SIGNIFICANCE

Stomach, variations in form. From laboratory specimens. The author is deeply indebted to Dr. Barry J. Anson of Northwestern University, who has kindly allowed him to reproduce illustrative material from his valuable *Atlas of Human Anatomy* (W.B. Saunders Co., Philadelphia, Pa., 1951). This illustration is on page 287.

Williams R. J. Biochemical Individuality 1956 – p21
New Biomarkers and Imaging Technology for Reference Values

Virtual Reference Values

Proteins and metabolites in:

- Brain
- Muscle
- Heart
- Liver
- Bone
- Intestin
- Plasma
Incorporate Personalized Laboratory Medicine as particular course in Pharmacy/Medical Schools

Create specific national/European expert centers (Societies/Hospitals) for training Personalized Medicine Specialists

To conduct pilot studies to assess cost-effectiveness of global approach in daily practice

Evaluate Eric Topol philosophy
THE CREATIVE DESTRUCTION OF MEDICINE
Timing of the big 6 major digital advances

Patient driven clinical trials – iPhone
Listen to your body

App: Genome music

This new iPhone app will not only be music to your ears, it will also be music from your ears, as well as your nose, legs, internal organs, in fact, your whole biological being. The GeneGroove app creates a musical melody based on your personal genome data. In total, it produces 11 different tracks based on your inner you. While the app itself is free, you first need to map your genome data via DNA testing company 23andMe (co-founded by Anne Wojcicki, wife of Google’s Sergey Brin: 23andme.com).
Real-Time Clinical Data Capture for Clinical Phenotyping
Science Fiction Turns Reality in 2004
The "George Orwell Perspective"

TRIUM Analysis Online GmbH, Munich, Germany (www.trium.de)
The Future of Pharmacogenomics and Theranostics

Integrated approach

We need to develop one health solution which is an integrated approach combining a drug, a companion diagnostic, a monitoring device and a patient support platform including education material and social networking.

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Not develop one test but one health product
The Eventual Desire: Real Personalized Therapy

Considering:

- **Baseline health status:**
  - Basal Metabolic Rate (BMR) and physiological conditions (endobiotics metabolism)
  - Personal Reference Values

- **Specific disease subgroup (pathways involved)**

- **Environmental effects:**
  - Life style (Diet, Tobacco, Alcohol, ...)
  - Concurrent drug therapy (Drug-drug interaction)

- **Complete Genome profile**

Data Reduction and Interpretation
P4 Strategy

Predictive, Personalized, Preventive, Participatory health / medicine

In conclusion:

The two examples for Personalized Laboratory Medicine:

- Personalized Therapy and Pharmacogenomics
- Reference Values: an unfinished symphony

Focus on biological variability and not only on the analytical aspects.

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Participate more in education and training of patients, clinicians and all health workers
Pharmacogenomics and theranostics in practice
Firenze, Italy

in cooperation with the European Society of Pharmacogenomics and Theranostics
Thank you for your attention!

(Stanislas Square in Nancy, France)
Theranostics is the association of a diagnostic (laboratory) test with a drug treatment.

Companion diagnostics
« The existence in every human being of a vast array of attributes which are potentially measurable (whether by present methods or not), and often uncorrelated mathematically, makes quite tenable the hypothesis that practically every human being is a deviate in some respects. »

Roger J. Williams
### TABLE 1

**Drugs – diagnostic combinations for the treatment of solid tumors. For several of the listed drugs it is a requirement that companion diagnostic testing is performed before they are prescribed to the patient.**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Biomarker</th>
<th>Assay mentioned in prescribing information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoxifen (Nolvadex®, AstraZeneca)</td>
<td>Breast cancer</td>
<td>ER</td>
<td>No</td>
</tr>
<tr>
<td>Aromatase inhibitors:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Letrozole (Femara®, Novartis)</td>
<td>Breast cancer</td>
<td>ER</td>
<td>Yes</td>
</tr>
<tr>
<td>Anastrozole (Arimidex®, AstraZeneca)</td>
<td>Breast cancer</td>
<td>ER</td>
<td>Yes</td>
</tr>
<tr>
<td>Exemestane (Aromasin®, Pfizer)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trastuzumab (Herceptin®, Roche)</td>
<td>Breast cancer, Gastric cancer</td>
<td>HER2/HER2</td>
<td>Yes</td>
</tr>
<tr>
<td>Lapatinib (Tykerb®, GlaxoSmithKline)</td>
<td>Breast cancer</td>
<td>HER2/HER2</td>
<td>Yes</td>
</tr>
<tr>
<td>Epirubicin (Ellence®, Pfizer)</td>
<td>Breast cancer</td>
<td>TOP2A</td>
<td>No</td>
</tr>
<tr>
<td>Doxorubicin (Adriamycin®, Pfizer)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cetuximab (Erbitux®, BMS/Merck)</td>
<td>Colorectal cancer</td>
<td>EGFR/KRAS</td>
<td>Yes</td>
</tr>
<tr>
<td>Panitumumab (Vectibix®, Amgen)</td>
<td>Colorectal cancer</td>
<td>KRAS</td>
<td>Yes</td>
</tr>
<tr>
<td>Imatinib (Glivec®, Novartis)</td>
<td>Gastrointestinal stromal tumor</td>
<td>C-KIT (CD117)</td>
<td>Yes</td>
</tr>
<tr>
<td>Vemurafenib (Zelboraf®, Roche)</td>
<td>Melanoma</td>
<td>BRAF V600E</td>
<td>Yes</td>
</tr>
<tr>
<td>Gefitinib (Iressa®, AstraZeneca)</td>
<td>Non-small-cell lung cancer</td>
<td>EGFR</td>
<td>Yes</td>
</tr>
<tr>
<td>Erlotinib (Tarceva®, Roche)</td>
<td>Non-small-cell lung cancer</td>
<td>EGFR</td>
<td>Yes</td>
</tr>
<tr>
<td>Crizotinib (Xalkori®, Pfizer)</td>
<td>Non-small-cell lung cancer</td>
<td>EML4-ALK</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Stratified pharmacogenomics and therapy

Cancer leads the way

- Infection diseases – HIV, HCV
- Anti-Neurodegenerative drugs
- Cardiovascular drugs
2010

From group Personnalized Therapy

→

Individual Personnalized Therapy
Recent Patents on Theranostics

Following are the highlights of recent theranostics patent applications. Complete review of theranostics related patent searches and data mining are available through Sciclips consultancy services ([http://www.sciclips.com/sciclips/consultancy.do](http://www.sciclips.com/sciclips/consultancy.do))

1. Theranostic classification of basal-like breast cancer tumors
2. Diagnostic therapy method (Theranostics) for Aspergillus fumigates infections
3. Theranostics method for premature birth (PTB)
4. Theranostic chitosan-coated gold/gold sulfide nanoparticles
5. Theranostic compounds for the management of diseases manifesting focal hypoxia
6. PBEF1 gene expression as a theranostic biomarker for HIV-related diseases
7. Theranostic methods for the treatment of cancers using mannose derivatives
8. Preparation of photosensitive ruthenium based aminoacid monomers and oligomers for imaging and theranostics applications
9. A diagnostic therapy (theranostics) method for multiple myeloma patients
10. System for generating image-based patient profiles
11. Method of predicting or identifying response to treatment with a modulator of a reverse cholesterol transport pathway in atherosclerosis patients
12. Biomarkers for the detection of the presence and for the theranostics of unstable atherosclerotic plaques
13. Spectral imaging for medical diagnosis

http://www.linkedin.com/groups/recent-patents-on-Theranostics-3372336.S.9463909...
Disease types

Cancer (16430)
ENT (1468)
Cancer (16430)
Gastrointestinal (678)
Bone and skeletal (204)
Renal (3066)
Pregnancy related (1525)
Metabolic (2376)
Autoimmune (1983)
Liver (1258)
Infectious (1034)
Neurological (3373)
Inflammatory/Allergic (7730)
Neuropsychiatric (3301)
Neurodegenerative (1200)
Skin (167)
Cardiovascular (4459)