Systems approach of Respiratory Diseases from Reactive to Pro-active medicine - P4 Medicine

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Inserm1055
Biologie Environnementale et Systémique - BEeSY

European Institute for Systems Biology and Medicine - EISBM

Nantes, 15th December 2014
Contents

- Why we must change?
- What is Systems approach?
- Projects in Rhône-Alpes
  from Lung Transplantation, COPD and Asthma to Wellness
Why changing?

- Uncontrolled increase in health costs, Efficacy & Justice decline
- Burden of respiratory diseases
- Limitations in present treatments and majors problems in new drug registrations

New paradigms irruption

- Exposome & Omics data accumulation
- Specialized versus Systems Medicine
- Reactive versus proactive Medicine?
Uncontrolled increases in health costs

- USA 18% GIP 2009 to 30% by 2030 & last OECD
- France, 12% GIP 2009, life expectancy 81 years in 2009
### Table 1. Cost per Quality-Adjusted Life-Year (QALY) Gained from Selected Clinical Strategies.*

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switch to an aromatase inhibitor for early-stage breast cancer vs. continued tamoxifen⁸</td>
<td>$22,900</td>
</tr>
<tr>
<td>Implant a cardioverter–defibrillator (primary prevention) vs. continued medical management⁹</td>
<td>$37,400 to $77,200</td>
</tr>
<tr>
<td>Perform fusion surgery for degenerative spondylolisthesis with spinal stenosis vs. conservative management¹⁰</td>
<td>$120,000</td>
</tr>
<tr>
<td>Prescribe trastuzumab for metastatic breast cancer vs. standard chemotherapy¹¹</td>
<td>$150,000</td>
</tr>
<tr>
<td>Prescribe erlotinib for advanced pancreatic cancer vs. gemcitabine alone¹²</td>
<td>$370,000 to $500,000</td>
</tr>
<tr>
<td>Perform helical computed tomographic screening for lung cancer in 60-year-old former heavy smokers vs. no screening¹³</td>
<td>$2,300,000</td>
</tr>
</tbody>
</table>

* Values are given in 2008 U.S. dollars, with adjustment for inflation according to the Consumer Price Index. Numbers are the ratios of the added cost per person to the gain in QALYs per person.
NCDs WHO
Table 1. Top 10 Causes of Death, Years of Life Lost from Premature Death, Years Lived with Disability, and Disability-Adjusted Life-Years (DALYs) in the United States, 2010.

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Deaths (N=2664)</th>
<th>Years of Life Lost (N=45,145)</th>
<th>Years Lived with Disability (N=36,689)</th>
<th>DALYs (N=81,835)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rank</td>
<td>No. (%)</td>
<td>Rank</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>1</td>
<td>563 (21.1)</td>
<td>1</td>
<td>7165 (15.9)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>5</td>
<td>154 (5.8)</td>
<td>4</td>
<td>1913 (4.2)</td>
</tr>
<tr>
<td>Low back pain</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cancer of the trachea, bronchus, or lung</td>
<td>3</td>
<td>163 (6.1)</td>
<td>2</td>
<td>2988 (6.6)</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Other musculoskeletal disorders</td>
<td>36</td>
<td>14 (0.5)</td>
<td>37</td>
<td>254 (0.6)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2</td>
<td>172 (6.5)</td>
<td>3</td>
<td>1945 (4.3)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6</td>
<td>86 (3.2)</td>
<td>7</td>
<td>1392 (3.1)</td>
</tr>
<tr>
<td>Road-traffic injury</td>
<td>12</td>
<td>44 (1.7)</td>
<td>5</td>
<td>1873 (4.1)</td>
</tr>
<tr>
<td>Drug-use disorders</td>
<td>27</td>
<td>19 (0.7)</td>
<td>15</td>
<td>841 (1.9)</td>
</tr>
</tbody>
</table>
France

2010 total population: 62 787 427
Income group: High

<table>
<thead>
<tr>
<th>NCD mortality</th>
<th>males</th>
<th>females</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2008 estimates</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total NCD deaths (000s)</td>
<td>233.4</td>
<td>221.0</td>
</tr>
<tr>
<td>NCD deaths under age 60</td>
<td>17.0</td>
<td>9.3</td>
</tr>
<tr>
<td>(percent of all NCD deaths)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age-standardized death rate per 100 000</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All NCDs</td>
<td>419.0</td>
<td>224.8</td>
</tr>
<tr>
<td>Cancers</td>
<td>183.4</td>
<td>93.7</td>
</tr>
<tr>
<td>Chronic respiratory diseases</td>
<td>18.8</td>
<td>7.4</td>
</tr>
<tr>
<td>Cardiovascular diseases and diabetes</td>
<td>128.3</td>
<td>69.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Behavioural risk factors</th>
<th>males</th>
<th>females</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2008 estimated prevalence (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current daily tobacco smoking</td>
<td>27.4</td>
<td>20.1</td>
<td>23.6</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>29.1</td>
<td>36.5</td>
<td>33.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metabolic risk factors</th>
<th>males</th>
<th>females</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2008 estimated prevalence (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raised blood pressure</td>
<td>47.5</td>
<td>38.4</td>
<td>42.7</td>
</tr>
<tr>
<td>Raised blood glucose</td>
<td>8.2</td>
<td>5.5</td>
<td>6.8</td>
</tr>
<tr>
<td>Overweight</td>
<td>56.4</td>
<td>45.4</td>
<td>50.7</td>
</tr>
<tr>
<td>Obesity</td>
<td>19.1</td>
<td>17.4</td>
<td>18.2</td>
</tr>
<tr>
<td>Raised cholesterol</td>
<td>64.9</td>
<td>65.5</td>
<td>65.2</td>
</tr>
</tbody>
</table>

Proportional mortality (% of total deaths, all ages)

- CVD: 30%
- Cancers: 31%
- Diabetes: 2%
- Respiratory diseases: 4%
- Injuries: 7%
- Communicable, maternal, perinatal and nutritional conditions: 6%
- Other NCDs: 20%

NCDs are estimated to account for 87% of all deaths.
5.2 million disability life years lost annually in the EU
300 billions € / year in the EU
Cystic fibrosis 1st genetic lethal disease
Asthma one of the most common chronic diseases in children
COPD 4th cause of death, 2nd cause disability life year by 2008 in USA
Lung cancer 1st cause of death by cancer in men, 2nd in women

No cure for any!
Systems Medicine in Respiratory Diseases

Long-life dimension
repeated measurements to refine phenotypes

Adapted from R. Slama group
Systems Biology to Systems Medicine

Systems Biology

Research strategy in model systems
- Bioinformatics
- Modeling
- Quantitative Data Generation

Medical Systems Biology

Research strategy in humans
- Computational Disease Models
- Animal Models
- Patient Cohorts

Systems Medicine

Clinical implementation
- Clinical Decision Support Systems
What is Systems approach?

- Complexity of biology an diseases

- 3 comprehension levels
  - modules
  - inter-connexions
  - system dynamics

- Informations : 2 types
  - signals: air, exercise, nutrition, sleep, stress, « exposome »
  - digital genomics informations

- From informations to phenotypes: networks et molecular machineries
What is Systems approach?

Challenge
to integrate multi-scale space-time dimensions
Box 1: The car analogy to personalized medicine.

The paradigm shift required to make the change from today’s medical practices to the predictive personalized medical care is revolutionary, but by no means unprecedented. A metaphor for this is how radically automobile “healthcare” has been digitally transformed over the past five decades by Moore’s Law. In the late 1950s and 1960s, you took your car to the mechanic when you heard loud thumps or saw smoke come out of the engine. When you went in with such a “symptom,” you invariably were told: “This is going to cost you,” since you had burned up some key part of the mechanical or electrical systems. Cars in those days had limited lifetimes and typically “died of a chronic failure” before you reached 100,000 miles.
As microprocessors, flash memory, and sensors exponentially decreased in cost, car manufacturers could afford to put more electronic devices into cars to measure moment-by-moment functioning of every key subsystem. Rather than wait until you have a costly “symptom,” you now take your car into a service facility every 10,000 miles for “preventive maintenance,” during which the car’s measurements are digitally read out and compared with a database of all other cars of the same model. Should the data be out of range of the “norm,” then you get “personalized car service,” which involves a repair on a specific set of items determined by the sensor readings. The end result is that your car at 200,000 miles runs just as well as the day you bought it.
Systems Medicine Methods

- Environmental « Tracking » 5 pillars
  Air, Nutrition, Exercise, Sleep, Stress (cf. Table)

- Internal « Tracking » Blood
  supplements, syst. hemat., glucose, hormones, liver, kidney, cardio-vascular, inflammation

- Genomics
  - complete human sequence 1000 $
  - gut meta genome
  - lung meta genome

- Personal Omics
CNRS-EISBM EU Projects in Rhône-Alps

Structuring Effect on Regional and European Levels

Unbiased BIOMarkers for the Prediction of Respiratory Disease outcomes
- 40 partners
- Including 10 big pharma
  - IMI exemplar project

**HIGHLIGHT -3 M€- (2012-2016)**
Highlighting EU-funded Health research results via TV media and the Internet
- 6 media partners

**SysPatho -3 M€- (2011-2014)**
Inserm Systems Biology of Hepatitis C infection
- 11 partners (9 academics, 2 SMEs)

**eTRIKS -24 M€- (2012-2017)**
Developing and Deploying a European Translation Information & Knowledge Management Service Infrastructure
- 6 partners (academics+SMEs) +10 big pharma EFPIA
  - Deliver Knowledge Management Platform
  - Structuring effect for IMI, FP7 and Horizon 2020

**MeDALL -14 M€- (2010-2014)**
Mechanisms of the Development of ALLergy
- 23 partners (academics + SMEs)

**AirPROM -16 M€- (2011-2016)**
Airway Disease PRedicting Outcomes through Patient Specific Computational Modelling
- 33 partners (academics + SMEs)

**SysCLAD -4 M€- (2012-2014)**
Systems prediction of Chronic Lung Allograft Dysfunction
- 8 partners (4 academics, 4 SMEs)
  - Based on existing lung transplantation cohort

**Synergy-COPD -5 M€- (2011-2016)**
Modelling and simulation environment for systems medicine (Chronic obstructive pulmonary disease -COPD- as a use case)
- 8 partners (academics + SMEs)

**CASyM -4 M€- (2012-2016)**
Coordinated road map to implement Systems Medicine across Europe
- 23 partners (academics, SME, industry, hospitals, government, patient org)

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**Lyonbiopole-EISBM**
Information and Knowledge Management Services (TRI Bioaster ICT platform)

**Network of Systems Medicine Centres**
(Horizon 2020)

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**Microbiome**
TRI (Bioaster experimental platforms)

**Strengthen involvement of clinicians and SMEs in Systems Medicine**
(HCL, CHU Grenoble)

**Bioenergetics Exercise**

**CENS Nutrition**
Achilles' tendons in Lung Transplantation

- Shortage of grafts, Primary Graft Dysfunction

- Chronic Lung Allograft Dysfunction - CLAD
  - BOS in 50% at 5 years
  - different patterns
  - 30% cause of death > 1 year
  - median survival 1.5 years, if early onset

-15%, 3 months
-4% / year
Editorial

Prediction of chronic lung allograft dysfunction: a systems medicine challenge

Christophe Pison, Antoine Magnan, Karine Botturi, Michel Sève, Sophie Brouard, Benjamin J. Marsland, Florian Ernst, Tobias Paprotka, Kevin Deplanché, Andreas Fritz, Valérie Siroux, Jean-Pierre Boissel, Paul A. Corris, Charles Auffray, Laurent P. Nicod and the SysCLAD consortium

Eur Respir J 2014
Fingers and Hand prints to predict CLAD

1. Complete recipient genome sequencing
2. Plasma proteome
3. Immuno-monitoring, PBMC, HLA, DSA
4. Clinicome 1st year
5. Pollution by geolocilsation
6. Transcriptome and miRNA
7. Lung microbiote and macrophage polarization
**TABLE 1. PATIENTS’ CHARACTERISTICS**

<table>
<thead>
<tr>
<th></th>
<th>All Subjects (n = 213)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>63.6 ± 7.0</td>
</tr>
<tr>
<td>Male, %</td>
<td>59</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.2 ± 5.1</td>
</tr>
<tr>
<td>FFMI, kg/m²</td>
<td>17.0 ± 2.4</td>
</tr>
<tr>
<td>mMRC dyspnea grade</td>
<td>2.1 ± 1.09</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>28</td>
</tr>
<tr>
<td>Pack-years</td>
<td>46 ± 26</td>
</tr>
<tr>
<td>Long-term oxygen therapy, %</td>
<td>17</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>1.40 ± 0.54</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>51.2 ± 16.9</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>0.40 ± 0.11</td>
</tr>
<tr>
<td>ITGV, % predicted</td>
<td>148 ± 33</td>
</tr>
<tr>
<td>TLCO, % predicted</td>
<td>56 ± 17</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>470 ± 106</td>
</tr>
<tr>
<td>SGRQ, total score</td>
<td>51.3 ± 17.5</td>
</tr>
<tr>
<td>Updated BODE score</td>
<td>2.9 ± 2.5</td>
</tr>
<tr>
<td>Framingham 10-yr risk, %</td>
<td>9.4 ± 6.7</td>
</tr>
</tbody>
</table>
New taxonomy in COPD

![Bar chart showing frequency of comorbidities per patient](image-url)

- Number of comorbidities per patient:
  - 0: 2.3%
  - 1: 7.0%
  - 2: 17.8%
  - 3: 19.2%
  - 4: 24.9%
  - 5: 17.8%
  - 6: 8.0%
  - 7: 2.3%
  - 8: 0.5%
# New taxonomy in COPD

## TABLE 2. DETAILED DESCRIPTION OF THE FIVE CLUSTERS IN TERMS OF THE NUMBER OF COMORBIDITIES AND THE PREVALENCE OF EACH COMORBIDITY

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Cluster 1: Less Comorbidity</th>
<th>Cluster 2: Cardiovascular</th>
<th>Cluster 3: Cachectic</th>
<th>Cluster 4: Metabolic</th>
<th>Cluster 5: Psychological</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>67</td>
<td>49</td>
<td>44</td>
<td>33</td>
<td>20</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>2.5 ± 1.4*</td>
<td>3.8 ± 1.7</td>
<td>4.2 ± 1.4†</td>
<td>4.4 ± 1.1†</td>
<td>4.1 ± 1.8</td>
</tr>
<tr>
<td>Renal impairment, %</td>
<td>16</td>
<td>24</td>
<td>45†</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Anemia, %</td>
<td>9</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>3*</td>
<td>98†</td>
<td>43</td>
<td>100†</td>
<td>5*</td>
</tr>
<tr>
<td>Obesity, %</td>
<td>30</td>
<td>14</td>
<td>0*</td>
<td>61†</td>
<td>15</td>
</tr>
<tr>
<td>Underweight, %</td>
<td>0*</td>
<td>0*</td>
<td>66†</td>
<td>3*</td>
<td>0</td>
</tr>
<tr>
<td>Muscle wasting, %</td>
<td>12*</td>
<td>10*</td>
<td>98†</td>
<td>0*</td>
<td>20</td>
</tr>
<tr>
<td>Hyperglycemia, %</td>
<td>52</td>
<td>41†</td>
<td>43</td>
<td>91†</td>
<td>60</td>
</tr>
<tr>
<td>Dyslipidemia, %</td>
<td>42</td>
<td>16†</td>
<td>25</td>
<td>67†</td>
<td>40</td>
</tr>
<tr>
<td>Osteoporosis, %</td>
<td>27</td>
<td>37</td>
<td>52†</td>
<td>0*</td>
<td>35</td>
</tr>
<tr>
<td>Anxiety, %</td>
<td>5*</td>
<td>28</td>
<td>26</td>
<td>0*</td>
<td>84†</td>
</tr>
<tr>
<td>Depression, %</td>
<td>6*</td>
<td>23</td>
<td>7</td>
<td>6</td>
<td>68†</td>
</tr>
<tr>
<td>Atherosclerosis, %</td>
<td>56</td>
<td>67†</td>
<td>12*</td>
<td>81†</td>
<td>53</td>
</tr>
<tr>
<td>Myocardial infarction, %</td>
<td>2*</td>
<td>11</td>
<td>7</td>
<td>13</td>
<td>32†</td>
</tr>
</tbody>
</table>

Summary variables are presented as mean ± standard deviation for quantitative variables, and percentage for discrete variables.

*Less prevalent compared with the whole study sample (95% confidence interval).

† More prevalent compared with the whole study sample (95% confidence interval).
New taxonomy in COPD

The pulmonologist view of comorbidities

Moving towards a Copernican view of COPD

Courtesy of Alvar Agusti, Barcelona, 2014
Systems Medicine Methods

**Development of Disease**

- Baseline Risk
- Earliest Molecular Detection
- Earliest Clinical Detection
- Typical Current Intervention

**Time**

- Initial Events

**Personalized Medicine Tools**

- Quantify Baseline Risk
- Monitor Progression
- Refine Risk Prediction
- Define Disease
- Monitor Progression
- Refine Disease Definition
- Personalize Therapy

**Disease Burden**

**Cost**

1/reversibility

Common mechanisms linked to environmental insults

*miRNA, epigenetic, Warburg effect, ..*

Common patients, common tools, systems approach

Reactive Medicine
University Hospital

Cost-effectiveness - Sustainability
Pro-active Medicine
Community Wellness
Wellness
4P Medicine

Chronic Respiratory Failure
Lung Cancer
Chronic Respiratory Diseases

Clinique Universitaire de Pneumologie
Pôle Thorax et Vaisseaux
CHU - Université Grenoble Alpes
Personal omics profiling reveals dynamic molecular and medical phenotypes
Proposed Wellness Project

• 100,000 patients
• 10-year longitudinal analyses (at least)
• Complete genome sequences
• Blood—transcriptomics, proteomics, metabolomics, WBC analyses
• Stool—gut metabolomics
• Traditional clinical data—histories
• Quantized self data
• ISB wellness assays
• Data analytics—integration and graphical presentation to patients
• Creation of a wellness data base that can be mined for the wellness assay and strategies of the future

Courtesy form Leroy Hood, Institute of Systems Biology, Seattle, 2014
Wellness Assays

Examples that are ready to go

1. **Organ-specific blood proteins** Mass-spec based detection of defined organ specific proteins to monitor global organ health

2. **Circulating non-coding RNAs** Sequencing / nCounter based detection of circulating non-coding RNAs to monitor changes in systemic regulation (regulome)

3. **Actionable Genetics/Genomics** Genome analysis and detection of genetic variants that, if identified, can improve health and wellness

4. **Gut (and other) Microbiome**
   Sequencing and culture based detection of changes in levels of good and bad gut microbes that have been directly linked to human health – including obesity, inflammation, IBD and cancer (36% in bloodstream)

5. **Origene Protein-Chip** Cheap and fast analysis of an individual’s autoimmune responses towards 12,000 human proteins

6. **Quantified self** Social networks have been created that use digital devices to capture personal information on sleep, emotion, exercise, etc. We will integrate this information with conventional medical data and our new wellness assays

*Courtesy from Leroy Hood, Institute of Systems Biology, Seattle, 2014*
**PROTOCOLE DE RECHERCHE BIOMEDICALE**

<table>
<thead>
<tr>
<th>Titre de la recherche</th>
<th>Les Pionniers du projet Santé et Bien-Etre en France / Pioneers of the French Health and Wellness Project</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acronyme</td>
<td>Vistera</td>
</tr>
<tr>
<td>Investigateur principal</td>
<td>Pr Christophe Pison, Clinique Universitaire de Pneumologie, Pôle Thorax et Vaisseaux, CHU de Grenoble, 38043 Grenoble Cedex 9 ; Université Grenoble Alpes ; Inserm1055, Grenoble ; Institut Européen de Biologie et Médecine Systémiques IEBMS (European Institute for Systems Biology and Medicine - EISBM), Paris, Lyon, France. Tel : +33 (0)4.76.76.54.53 ; Fax : +33 (0)4.76.76.56.17</td>
</tr>
<tr>
<td>Code promoteur</td>
<td>RCB 2014-A01037-40</td>
</tr>
<tr>
<td>Promoteur</td>
<td>Institut Européen de Biologie et Médecine Systémiques – IEBMS (European Institute for Systems Biology and Medicine - EISBM), Siège social : Hôpital St Louis 1, avenue Claude Vellefaux 75010 Paris ; Bureaux : 50, avenue Tony Garnier, 69007 Lyon, France. Tel : +33(0)4.37.28.74.80 ; Fax : +33(0)4.37.28.74.54 Dr Charles Auffray, Président ; Pr Dominique Charron, Pr Christophe Pison, Vice-Présidents</td>
</tr>
</tbody>
</table>
Les Pionniers de la Santé et du Bien-Etre en France

- Whole-genome
- Blood samples
- Only one time

DNA sequencing

- Blood chemistry
- Blood samples
- Every three months

Biochemistries

- Gut microbiome
- Stool samples
- Every three months

Microbiome

**Monitoring**
- Physical activities
- Sleep patterns
- Blood pressure
- Biosensor
- Daily

**Biomarkers**
- Organ-specific blood markers
- Blood samples
- Every three months

**n=1**
P4 Medicine

• Predictive
  • Probabilistic health history
  • DNA sequence & Regular multi-parameter (blood) measurements

• Preventive
  • Design of therapeutic and preventive drugs/vaccines via systems approaches
  • Wellness

• Personalized
  • Unique individual human genetic variation mandates individual treatment
  • Patient will be their own control for longitudinal (lifelong) data analyses

• Participatory
  • Patient-driven social networks for disease and wellness will be a driving force in P4 medicine
  • Society must access patient data and make it available to biologists for pioneering predictive medicine of the future
  • How does one educate patients, physicians and the healthcare community about P4?
  • IT for healthcare

Courtesy from Leroy Hood, Institute of Systems Biology, Seattle, 2014
Conceptual Themes of P4 Medicine

P4 Medicine
- Predictive
- Preventive
- Personalized
- Participatory

Wellness Quantified

Disease Demystified

Courtesy from Leroy Hood, Institute of Systems Biology, Seattle, 2014
Messages

- Clinicians to be involved ASAP
- Holistic changes, with new Curriculum for health professionals
- Moving from centred Deliver Systems to Health in the Community
- Moving from Reactive to Proactive Medicine
- 10% Health related to Intrinsic biological factors
- Doing better with cost containment is feasible
- Demonstrators needed