The Evolving Role of Molecular Imaging in Transforming Reactive to Proactive (P4) Medicine: Predictive, Preventive, Personalized and Participatory

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AIMS

• Explain the Concept of Systems Medicine and P4 Medicine

• Describe P4 Medicine in the Context of Molecular Imaging

• What is the Opportunities and Challenges of P4 Medicine

• Future of Practice and Research in Image Professions Based on This Revolutionary Medicine
<table>
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<th>Medicine of Tomorrow</th>
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<tr>
<td><strong>Evidence Based Medicine</strong></td>
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<tr>
<td>• Symptoms Based</td>
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<tr>
<td>• Disease-Treatment System</td>
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<tr>
<td>• Few Measurements</td>
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<td>• Disease-Centric</td>
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<td>• No Large-Scale Diffusion of Medical Information</td>
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Systems Biology

Systems Biology, with Its Holistic Approach to Figuring out Important Principles in Biology (Complex system), and the Enabling Technologies in Genomics, Proteomics, Single-cell Analysis, Microfluidics and Computational Strategies, Empowers a Comprehensive Approach to Medicine.

Systems View Focuses at Understanding:

• The Complexity of the System
• The Networks Activated in the System
• The Control Methods of the System
• Key Nodes in the System
Health and Complexity

- Health and Disease are Regulated by Complex Interactions of Genes and Proteins, and Impact of Environment, Behavior, Diet, Infection on the Host Response Explain Differences Between People

- The Organization, Dynamics, and Regulation of Genes and Proteins in the Networks Are Critical in Determining Health and Disease
A Systematic Model of Disease Postulates That Disease Arises from Disease-Perturbed Networks

Complex Networks of Direct Relevance to Network Medicine
Construction of the “Diseasome”. The circles represent diseases and the rectangles genes. A disease and a gene are linked if mutations in said gene provoke said disease. The size of the circle is proportional to the number of genes that participate in said disease. Disease Gene Network, DGN: two genes are connected if they are involved in the same disease; Human Disease Network, HDN: two diseases are connected if the same gene is involved in both. Source: Goh K et al. 19 ©2007 by National Academy of Sciences.
Holy Trinity

P4 medicine as the clinical face of systems medicine has two main goals: to quantify wellness and to demystify disease.

Flores et al.; Personalized Medicine (2013) 10(6), 565–576
P4 Medicine Components

- **Predictive**: Molecular mechanisms that define illness AND wellness. Identify risk health → disease.
- **Preventive**: Perturbed biologic networks → disease. Definitive therapies that halt or reverse.
- **Personalized**: Billions of data points → each individual. Each individual is their own ‘control’.
- **Participatory**: Care designs focused on the consumer. Fun, engaging, ‘sticky’ solutions.

Based on Lee Hood presentation with modification, ISB
Driving the Emergence of P4 Medicine

- **Transformation of Biology**
  - Systems Biology is resolving the complexity of human biology
  - The fundamental molecular basis of disease & health is being revealed

- **Digitization of Medicine**
  - “Clouds” of longitudinal health data are emerging around each individual
  - The P4 Medicine “cloud” will be the defining asset in clinical care & translational research

- **Informed, Engaged Consumers**
  - As care passively extends into our daily lives, and the ‘black box’ of biology is demystified…
  - Today’s passive patients will become the informed, engaged owners of their own health

Based on Lee Hood presentation with modification, ISB
The Scientific Progresses and Technological Breakthroughs of the Last Few Decades, Accompanied with the Emergence of the New Science of Complex Systems and Networks, Have Provided the Ground for the Birth and Growth of a New Concept to Deal Diseases: P4 Medicine
10 Emerging Technologies That Will Change Your World

- Wireless Sensor Networks
- Injectable Tissue Engineering
- Nano Solar Cells
- Mechatronics
- Grid Computing
- Molecular Imaging
- Nanoimprint Lithography
- Software Assurance
- Glycomics
- Quantum Cryptography
P4 Medicine Will Transform the Health Care System

• Process Billons of Data for Each Individual

• The Gathering And Analysis of Longitudinal Data for Each Individual.

• The Stratification of Patients Into Disease Groups

• The Feasibility of the Whole Drug Development Process by Detection New Therapeutic Target Hubs.

• Academia and Medical Schools

• Medicine - Diagnostics, Therapy, Prevention, Wellness

The Advance of Methods for Sequencing of Personalized Genomes.

Microfluidic Methods and Analysis of Individual Cells.

Advance New Computational Techniques for the Development of Predictive Models of The Networks and Dynamic Interactions Between the Biological Components Which Is Based on the Incorporation of High-throughput Omics Information.

Teaching the Patients and Physicians about P4 Medicine

New Molecular Imaging Techniques

Predictive

• Predict Biological Aggressiveness/Treatability
• Determine the Best Treatment and Dose Before Starting Therapy
• Predict Side Effects
• Monitor Treatment Response Early and Precisely

Only PET Effected the Management Decisions in 38% of Cases of Cancers.
P4 Medicine in the Context of Molecular Imaging

Personalized

- Data Mining of Quantitative Anatomy and Biology
- Targeted Imaging/Targeted Therapy
- Real Time Monitoring of Treatment Response
- Genome-informed Surveillance to Earlier Disease
Toward a Personalized Treatment of Hodgkin’s Disease
Vincent T. DeVita, Jr., M.D., and José Costa, M.D.

Personalized Medicine: Molecular Imaging Predicts Treatment Success in Many Cancers
Studies show molecular imaging’s benefits in the evaluation and successful treatment planning for a wide spectrum of diseases.

Reston, Va — A series of studies published in the Journal of Nuclear Medicine (JNM) show that molecular imaging plays a critical role in the evaluation and treatment planning for a broad spectrum of cancers, including thyroid cancer and lymphoma.

RSNA: New era of image-guided personalized cancer care dawn

CHICAGO—The opportunities for imaging have never been greater, offered RSNA President Hedvig Hricak, MD, PhD, chair of radiology at Memorial Sloan-Kettering Cancer Center in New York City, during today’s opening session of the annual conference of the Radiological Society of North America (RSNA).

During the president’s address—Oncologic Imaging: A Guiding Hand of Personalized Cancer Care—Hricak stated that the ultimate goal of personalized medicine is preemptive medicine. With cancer incidence projected to increase 45 to 50 percent in the next 20 years, the need to expand personalized medicine is significant.

The good news is that the tools that facilitate personalized medicine, genetics and molecular imaging, continue to emerge and develop. “Imaging has continuously advanced cancer care and paved the road to personalized medicine. The pace at which medicine is transformed will be guided not only by the pace of discovery, but also by the pace at which we educate new physicians, ourselves and our co-workers,” said Hricak.
Schematic Representation: Theranostics for NENs

Digitalised Histopathology Combined with Somatostatin Receptor PET/CT – From Tissue to Molecular Imaging to Therapy

On the Way to Personalized Medicine

Theranostics

Tx Is Now Part of the Concept of PM:
The Right Treatment for the Right Patient at the Right Time at the Right Dose.

Personalized Medicine/Precision Medicine/Genomic Medicine

In NM, Tx is Easy to Apply and to Understand, Because of an Easy Switch of Radionuclide form Dx to Rx on the Same Vector.

The Concept of PM Has Now Been Extended to Personalized Health care (PHC) That Relate to All Health Care Levels (Physicians, Technologists, Drugs, Nurses,..)
Multimodal Theranostics Nanoparticles

Kelkar et al, Bioconjugate Chem. 2011, 22, 1879–1903
Hong et al. Nano Today. 2009 October 1; 4(5): 399–413
P4 Medicine in the Context of Molecular Imaging

Molecular Imaging

- Study Molecular and Cellular Events in Intact Living Animal or Human
- Study More Complex Events e.g. Interaction of Two Intracellular Proteins, Cellular Metabolic Flux, Transcription of Gens
- Study of Simple and Complex Processes with All Molecular Feedback Loops
- Process of Drug Discovery and Validation and Also Predicting and Monitoring Response to Different Kinds of Therapy
P4 Medicine in the Context of Molecular Imaging

Preemptive

- Molecular/Genetic Screening as Well as Intervention (Often Guided by Imaging) Is the Most Efficient Approach to Disease Management
- Diagnose and Treatment to Improve Outcomes
- Transition to Wellness Assessment
- Theranostic Agents Can be Implemented in this Field Either.
P4 Medicine in the Context of Molecular Imaging

Participatory

• Democratization of Medicine
• Patient-Driven Social Networks
• Link Surveillance, Diagnose, Staging, and Treatment in an Efficient, Convenient, Patient Friendly Paradigm
Smart Machines

• Molecular Machines Can Create Works of Astonishing Complexity and Size, Such as the Human Being

• Image Doctors Work on More Complex and Novel Imaging Modalities

• Consultation with Clinicians and Patients

• Value to the Healthcare

• Participation and Leadership

Clay Marsh, OhioStateUMedicalCenter, P4 Medicine: Value Innovation and Consumer-Centered Healthcare
A future application of Cornell's molecular motor research: With the integration of biomolecular motor devices and cell-signalling systems -- by engineering a secondary binding site tailored to a cell's signalling cascade -- researchers plan to use the cell's sensory system to control nanodevices implanted in living cells. Nanoscale Biological Engineering and Transport Group/Cornell University.
Imaging Phenotype to Predict Genotype

Imaging Phenotype to Predict Diagnostic and Therapeutic Events Based Integrative Mechanistic Model.
Modeling Staging Mechanism in Alzheimer's Disease

Schematic Representation of the Proposed Workflow for Translation of Imaging Information into Stage-Specific Disease Maps.

Younesi and Hofmann-Apitius The EPMA Journal 2013, 4:23
Based on Lee Hood presentation with modification, I SB
Convergence of Technologies for Systems Medicine

Information Technology

Biotechnology

Nanotechnology

Molecular Imaging
Innovations

• NGS based –OMIC Studies
• Bioinformatics
• Multiplex Multimodality Imaging (Nanotechnology)
• Smart Machines (Robot, …)
• Hybrid Imaging: PET-MRI
Radiogenomics as an OMIC Study, Is the Integration of in Vivo Imaging with Large Scale Gene Expression Profiles Which Can Show Imaging Heterogeneity Mirroring Biological Heterogeneity.

The Fusion of Imaging Tools With Molecular Techniques Such as Functional Genomic Assays Offers the Potential for Rapid Clinical Translation of Powerful High-Throughput Technology.
Radiogenomics
Creating a Link Between Molecular Diagnostics and Diagnostic Imaging

NEW HORIZONS LECTURE

P4 Medicine is the Future

Public health demand and research advances are pushing medicine into an era of transformation, one of the nation’s most influential radiologists told an audience at the Arie Crown Theater.

Elias A. Zerhouni, M.D., director of the National Institutes of Health (NIH), delivered the Eugene P. Pendergrass New Horizons Lecture, titled "Trends in the Imaging Sciences," on TUESDAY.

Dr. Zerhouni also described the shift he believes will take place as the public demands medicine move away from a curative paradigm to a preemptive model, where physicians have the information to identify patients at risk for diseases.

The population's healthcare needs are changing from acute illnesses to chronic illness, said Dr. Zerhouni.
NEW! PROGRAM FEATURES

NEW! Request for Information about the 3D Nucleome!

The NIH is soliciting feedback from the community on the highest priority areas to pursue to understand and model the relationship between genome organization in the nucleus and regulation of gene expression programs in development and disease.

Provide input on Request for Information (RFI): Challenges and Opportunities for Understanding the 3D Nucleome. Focused discussions will be held on the following topics:

- Chromatin architecture
- Nuclear organization
- Gene expression regulation
- Developmental biology

Bring your ideas and comments to the discussions and help shape future research directions.

Click here to watch the video.
Program Snapshot

The Common Fund’s Molecular Libraries and Imaging program offers biomedical researchers access to the large-scale screening capacity necessary to identify small molecules that can be optimized as chemical probes to study the functions of genes, cells, and biochemical pathways in health and disease. They may also be used by researchers in the public and private sectors to validate new drug targets, which could then move into the drug-development pipeline. Components of the Molecular Libraries program include:

- The Molecular Libraries Probe Production Centers Network (MLPCN)
- PubChem
- Technology Development

Read more...
The Future of Imaging Doctors

Imaging Doctors Must Learn Genetic Pathways and Therapeutically Target Points in New Genetic World Consisting of Genetic, Clinical Data, and Imaging Features.

The Future of Practice and Research Will Require the Network-Connected Interdisciplinary Teams of Image Professions, Clinicians, Specialists Familiar with Integrated Analysis of Both Imaging and Genetic Data Types, as Well as Physiochemists and Molecular Biologists.

In Future, Imaging Doctors' Role Will be Diagnostic Data Manager Coordinator Not Image Interpreter.
Conclusion


Catalyzing a Revolution from Reactive to Proactive Medicine by Imaging and P4 Medicine Workgroup