

CME Course on

Concepts, Methods and Clinical Implementation in Precision Medicine

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Course Overview and Goals

Precision Medicine comprises customized diagnostic and therapeutic strategies targeting patients with susceptibility to a distinct disease condition based on individualized and family genomic background, environmental effects, lifestyle habits and co-morbidities.

It is an emerging clinical field that integrates broadly validated results from investigations of molecular and genetic basis of diseases with prevention, diagnosis and treatment of the individual patient. It is also a necessary aspiration if we are to achieve a health care delivery system that can provide accessible, high-quality, and cost/effective clinical care.

While it has tremendous potential to contribute to improving outcomes and decreasing cost of treatments, there remain important challenges to its clinical implementation that need attention, including: Education of physicians for successfully transition to using Precision Medicine at their medical practice; Integrating molecular and genetic guidance into routine healthcare delivery; Securing patient engagement and trust; Regulating Laboratory Developed Tests (LDTs) and targeted therapies; Generating the evidentiary support for Precision Medicine; Data-sharing and infrastructure needs; Economics of Precision Medicine and the new business models that simultaneously reduce the cost but improve the quality of care.

On this basis, this course has been mainly designed to meet the educational needs of physicians and other healthcare providers who see patients and have the desire of understanding newest concepts, methods and procedures of Precision Medicine, its cost-effectiveness and its distinct business model, commercialization channels and reimbursement.

Learning Objectives

Upon completion of this course, participants should be better able to adopt Precision Medicine in their clinical practice supported by a broad understanding on:

- **The Precision Medicine model of healthcare.**
- **How molecular composition and gene expression patterns are controlling pathogenic and pathophysiological mechanisms of cancer and non-cancer diseases and are teaching us on what is specific and targetable in each patient's disease.**
- **Clinical use and interpretation of newest laboratory developed tests (LDTs) for enhanced diagnosis and therapeutic management of patients.**
- **Laboratory and information technologies and their regulatory environments during Precision Medicine practice.**
- **The Precision Medicine Business model, company's landscape, marketing strategies, commercialization channels and reimbursement.**
- **Ethical, legal, economic, social and operational issues around how molecular biomarkers, genomic data, aggregated clinical data, and patient-reported data are being brought to bear on refining diagnoses and personalizing treatments, and on predicting susceptibility in patients with major immune-inflammatory, endocrine-metabolic, and neurodegenerative disorders.**
- **The interpretation of molecular and genomic data from developing malignant tumors and tumor microenvironments in combination with pathophysiological data from the patient to refine diagnosis and personalize cancer therapy.**

Disclaimer

The information provided in this Course is for medical education and informational purposes only. It should not be construed as personal medical advice and is not meant to substitute for the independent medical judgment of a physician regarding diagnosis and treatment of a specific patient's medical condition. The opinions expressed in this educational course are those of the faculty and do not necessarily represent the views of organizers of the Course. For any question or concern about a medical matter, participants at the course should consult healthcare provider and refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

SYLLABUS

1. Background and New Trends in Precision Medicine Development

Recent biotechnological advances have led to an explosion of disease-relevant molecular information, with the potential for greatly advancing patient care. However, the success of Precision Medicine depends on establishing frameworks for interpreting the influx of information that can keep pace with rapid scientific developments.

In this session we provide solutions on how physicians can successfully transition to using knowledge and methods of Precision Medicine in the most efficient and effective way for their daily practice.

Particular attention is paid on the clinical development of Laboratory diagnostic tests (LDTs); and on enhancing knowledge for the application of existing and developing complementary and companion diagnostic tests in tailoring diagnostic information and therapeutic effects to each patient's disease.

Topics/Lectures

1. Concepts and Methods of Molecular Medicine.

- a. Clinical value of genes and molecules identified in the mechanism of disease: How the molecular composition and gene expression patterns are controlling pathogenic and pathophysiological mechanisms of disease and are teaching us on what is specific and targetable in each patient's disease.
- b. Converting genomic and molecular datasets into healthcare improvement: molecular and genomic biomarkers and therapeutic targets; genomic and molecular data interpretation and translation into the clinical practice.

2. Laboratory technologies for Precision Medicine: Signature genes and molecules to each patient's mechanism of disease and of response to environmental factors, food and drugs.

- a. Genome-wide association studies based on SNP analyses.
- b. Multiplex gene and protein expression high/low density arrays.
- c. Developing a personal omics picture by connecting genomic, transcriptomic, proteomic, metabolomic, and autoantibody profiles.

3. Transforming genomic and molecular data into healthcare improvements: How to integrate Precision Medicine into clinical practice.

- a. Laboratory diagnostic tests (LDTs) and its regulatory structure.
- b. Molecular Targets for therapy and Drug response biomarkers.
- c. Pharmacogenomics of drug targets, of drug effects and of drug responses.

4. Tailoring diagnosis and therapy to each patient's disease.

- a. Clinical development and application of complementary diagnostic tests.
- b. Clinical development and application of companion diagnostic tests.

2. Precision Medicine Adoption, Regulation and Outcome's Monitoring

In this session we introduce systems approach to improving healthcare and achieving a greater understanding of the complexities of human health and disease. We discuss the clinical use and interpretation of datasets generated by functional genomics and proteomics, and to developing pathways for molecular and genetic guidance integration into medical practice. Finally, we analyze the contribution of IT and digital healthcare to Precision Medicine and the existing evidences on Precision Medicine's effects on outcomes.

Topics/Lectures

1. Healthcare organization models of Precision Medicine, cost-effectiveness, diagnostic accuracy and metrics.
 - a. How to prepare for the Precision Medicine model of care and key disease indications: Strengthening engagement and trust of the patients; overcoming barriers for Precision Medicine services to be adopted; and proper planning in the delivery of Precision Medicine.
 - b. Developing evidences of Precision Medicine's effects on outcomes: provider and patient adoption of Precision Medicine; and regulatory approval of technologies and procedures for Precision Medicine.
 - c. Designing national and international strategies in Precision Medicine, with an appropriate planning that guarantees equal access of all citizens to best clinical and laboratory practices, without violating the rights of patients and healthcare provider and jeopardizing healthcare system budget.
 - d. Environmental Precision Medicine and Precision Public Health.
2. Human resources, technologies and infrastructures for integrating molecular/genetic guidance into routine healthcare delivery.
 - a. Adopting patient's "omics" guidance as foundational information for healthcare.
 - b. Digitalization of clinical and analytical exams and medical records. Patients' data sharing and main ethical, social and legal issues.
 - c. Developing comprehensive knowledge networks encompassing clinical and molecular/genetic data.
 - d. The role of molecular geneticists, clinical geneticists, and genetic counselors.
3. Contribution of Computer Sciences and digital healthcare to Precision Medicine's effects on outcomes.
 - a. Bioinformatics and healthcare Big data analytics. Predictive models. Patient similarity algorithms.
 - b. Digital biomarkers: Collecting real-time data on patient's pathophysiological parameters and getting healthcare targeted to individual characteristics.
 - c. Radiogenomics, radiomics and multimodal molecular imaging.
4. Artificial intelligence, interactive simulation and point of care technologies in Precision Medicine.

- a. Artificial intelligence and supervised machine learning techniques for diagnosis and prediction.
- b. Modeling and interactive simulation in precision diagnosis and patient subtyping.
- c. Point of care technologies: wearable devices and real-time non-invasive biosensors.
- d. Multiplex electrochemical immune-sensing devices.

3. Economics and Business Models of Precision Medicine Services

Precision Medicine is changing the way patients are classified and therapies are being developed. In addition, trends supporting Precision Medicine, such as clinical integration of molecular and genetic datasets, lower cost of LDTs, and widespread use of electronic medical record are on the rise. Moreover, drug companies are now partnering with diagnostic companies to develop therapies with companion diagnostic tests.

Altogether, new business models are now being developed by small and large-size clinical centers and by industries developing technologies and providing clinical and laboratory services.

In this session, we analyze the current status of emerging industries in Precision Medicine, their economic models and challenges for getting a sustainable and scalable business.

Topics/Lectures

1. Today's global landscape in Precision Medicine business: Companies developing clinical technologies and providing clinical services in Precision Medicine.
 - a. Emerging industries developing technologies and resources.
 - b. Emerging industries outsourcing laboratory services to Precision Medicine providers.
2. Marketing Precision Medicine services and commercialization models.
 - a. Ordering Precision Medicine services online (Direct-to-Consumer, DTC).
 - b. Precision Medicine in comprehensive clinical centers.
 - c. Outsourcing Precision Medicine services.
3. Reimbursement/non-reimbursement markets. Managing clinical innovation-oriented reimbursement.
 - a. Developing economic evidences and appropriate methods of evaluation to support Precision Medicine implementation.
 - b. Reimbursing the value created by the clinical translation of innovative diagnostics tests and therapies.
 - c. Validating cost-effectiveness in Precision Medicine and its potential impact on the overall healthcare budget.
4. The economics of Precision Medicine.
 - a. Developing an economic model for Precision Medicine services.
 - b. Creating a sustainable and scalable business in Precision Medicine.
 - c. Logistic management of Precision Medicine data.

4. Clinical Case Studies in Precision Internal Medicine

A series of clinical case studies is used to illustrate the concepts and main ethical, legal, economic, social and operational issues around how molecular biomarkers, genomic data, aggregated clinical data, and patient-reported data are being brought to bear on refining diagnoses and personalizing treatments, and on predicting disease susceptibility.

Special emphasis is done on those clinical cases tailoring diagnostic information and therapeutic effects to each patient's disease using molecular and genetic LDTs based on specific functional changes occurring at key pathogenic pathways of major immune-inflammatory, endocrine-metabolic, neurodegenerative and neoplastic disorders.

Topics/Lectures

1. Identifying functional changes occurring at key pathogenic pathways of disease for tailoring diagnostic information and therapeutic effects to each patient's disease.
 - a. Clinical cases on chronic inflammatory disorders.
 - b. Clinical cases on endocrine-metabolic disorders.
 - c. Clinical cases on cardiovascular disorders.
 - d. Clinical cases on neurodegenerative disorders.
2. Customized medical research services.
 - a. Clinical cases on the use of LDTs for detecting the occurrence and spread through family members of gene and protein expression patterns representing biomarkers of predisposition to disease, of acquired susceptibility factors or of the disease's status.
 - b. Clinical cases on the use of LDTs for uncovering nutrigenomic information on how genes involved in inflammatory, degenerative and neoplastic disorders respond to the foods we eat, and on how food-related gene changes affect molecular processes that make us healthy or prone to aging and major diseases.

5. Clinical Case Studies in Precision Cancer Medicine

Precision Cancer Medicine focuses on a patient's disease at the clinical, molecular and genetic levels, and seeks for targeted therapies for each patient at each stage of this complex disease, including the earliest stages of asymptomatic tumor development, and the symptomatic stages of tumor growth, invasion and dissemination with the formation of lymph node and organ metastases.

In addition, both genetics of the tumor and of the patient are influential on the course of the disease, and therefore, systemic and local microenvironmental factors affecting the tumor and its genetic and molecular profiling are essential for a Precision Cancer Medicine.

On the one hand, molecular and genomic profiling of suspicious tissue lesions and the genetic background, environmental effects (microbiota, radiation, smoking, etc.), co-morbidities (diabetes, chronic inflammatory diseases, etc.) and lifestyle habits (diet, sports, etc.) of the patients are critical in the accurate diagnosis of cancer risk and therefore, are major targets for Precision Cancer Medicine practice. In addition, certain sensing and defensive organs such as the liver, blood vessels, and cells of the lymphoid and hematopoietic organs undergo early pathophysiological changes whose altered gene expression and secretion of soluble factors can alert us on the occurrence of occult cancer development too. On the other hand, the genetic and growth patterns of the primary, metastatic tumors, circulating tumor cells and tumor DNA, and the specific immune-phenotype and stromal cell compositions of the tumor are all providing relevant information for tumor classification, prognosis and treatment response.

On the basis of this comprehensive approach to Cancer Medicine, a series of clinical case studies, including patients with most prevalent malignancies (lung, colorectal, breast, prostate, melanoma, etc.) is used to show how molecular biomarkers and genomic data from the developing tumor and its tumor microenvironment are associated to aggregated pathophysiological data from the patient to refine diagnosis and personalize treatment.

Topics/Lectures

1. Carcinogenesis Bioscreening.

- a. Clinical cases on the diagnosis and management of occult colorectal cancer in patients.
- b. Clinical cases on the procarcinogenic screening of breast B3-lesions with a high malignant potential

2. Molecular biomarkers defining cancer phenotype and guiding therapy

- a. Clinical cases on the diagnosis and management of prostate and breast cancer cell osteomimicry.
- b. Clinical cases on the diagnosis of inflammation-dependent and independent melanoma and colorectal cancers and their implications for immunotherapy.

3. Prometastatic bioscreening.

- a. Clinical cases on the diagnosis and management of the liver prometastatic reaction in advanced-stage cancers.
- b. Clinical cases on the diagnosis of brain micrometastasis in advanced-stage cancers.

