THE ROLE OF GENETICS AND GENOMICS IN THE PRACTICE OF MEDICINE

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GENETICS IN MEDICAL PRACTICE

• The role of genetics in medical practice of medicine has been limited to the diagnosis and management of rare genetic disorders within specialist genetic centers, clinics and academic departments.

• There is a paradigm shift in the medical practice in which genetics and genomics are integrated in the provision of health-care, including primary care.
HUMAN GENOME

Cytosine

Guanine

Adenine

Thymine

DNA
Deoxyribonucleic Acid

Nitrogenous Bases

RNA
Ribonucleic Acid

Nitrogenous Bases

Base Pair

Sugar Phosphate Backbone

ATCG's

AUCG's

Replaces Thymine in RNA
HUMAN GENOME
20,000 to 25,000 gene pairs

DNA
TRANSCRIPTION
RNA
TRANSLATION
PROTEIN
MODIFIED PROTEIN

REPLICATION

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HUMAN GENOME

Figure 2-3 Human Molecular Genetics, 3/e. (© Garland Science 2004)
HUMAN CHROMOSOMES (Male)
DEFINITIONS

• GENETICS: the study of heredity by examining the function and composition of a single gene at one time

• GENETIC DISORDERS: diseases in which genetic factors play an important role in their etiology

• GENOMICS: the study of genes and their function by addressing all genes and their inter-relationship and influence
CLASSIFICATION OF GENETIC DISORDERS

• Chromosomal abnormalities
• Single gene disorders
• Multifactorial disorders

• Genomic disorders
• Simple (Mendelian) disorders
• Complex disorders
TRADITIONAL MEDICAL GENETICS SERVICES

A clinical medical specialty that addresses the diagnosis and treatment of conditions caused by alteration in the genetic material

• Traditional medical genetics
  – Birth defects
  – Metabolic disorders
  – Molecular and cytogenetic testing

• Cancer genetics (familial forms)

• Reproductive genetics
The Human Genome Project Began in 1990

- The Mission of the HGP: The quest to understand the human genome and the role it plays in both health and disease.

“The true payoff from the HGP will be the ability to better diagnose, treat, and prevent disease.”

--- Francis Collins, Director of the HGP and the National Human Genome Research Institute (NHGRI)
GENOMIC MEDICINE

The influencing or basing the clinical care of a patient on the knowledge of the specific genomic variants the patient has

• Whole Exome Sequencing in a child with intractable inflammatory bowel disease

• NT5E mutations and arterial calcifications
GENOMIC MEDICINE

Contribution to the field of pharmaco-genomics

- Carbamazepine (Tegretol) in individuals with *HLA-B*\(^*1502\)  
- The role of the BRAF kinase inhibitor, (vemurafenib) in metastatic melanoma with *BRAF*, p.V600E somatic mutation  
- *CYP2C19* variants and a diminished response to clopidogrel (Plavix)
GENOMIC MEDICINE

Contribution to disease prognosis

• Tumor-gene-expression signature models for several forms of cancer to predict progress and outcome (Breast Cancer)

• Specific B-cell lymphocyte signature distinguishing if a kidney transplant recipient is tolerant to the transplanted kidney and in whom immunosuppression can be discontinued
GENOMIC MEDICINE

Contribution to reproductive genetics

• Prenatal diagnosis relies on molecular karyotyping with shorter turn-around time, no need for cell culture and higher sensitivity and resolution

• Cell-free fetal DNA in maternal blood and non-invasive prenatal diagnosis for chromosomal aneuploidies and even whole genome sequencing of the fetus
PERSONALIZED MEDICINE

• Advances the use of genomic medicine while shifting health care from being reactive to being predictive and preventive

• Integrates unique clinico-pathological, genetic, genomic and environmental information to create an optimized care plan

• Utilizes the molecular knowledge of common diseases to enhance prevention during wellness and begin therapy early
PERSONALIZED MEDICINE

• The development into a comprehensive health-care system that maximizes wellness is influenced by the convergence of deeper understanding of the system biology and the ability to generate and analyze large datasets.

• Precision medicine and P4 medicine (predictive, preventive, personalized and participatory) describe the ultimate proactive health care model.
PREDICTIVE MEDICINE

• Predictive strategies promote the shift of the provision of health-care from being reactive to being preventive
  – Family history
  – Disease model (Framingham study)
  – Computer software based on family history and disease model
  – Genomic (and other omic) information
    • Long QT syndrome
    • \textit{BRCA1} and \textit{BRCA2}
  – Newborn screening
INTEGRATION INTO CLINICAL PRACTICE

- Advance in genomic and computational technologies led to an exponential accumulation of genomic data
- Exposure of the gaps in the infrastructure needed for the implementation of genomic data into clinical practice
  - Paucity of standardization into clinical tests
  - Physicians are unprepared to deliver the information
  - Deficiency in genetics knowledge amongst the average health-care provider
CONCLUSIONS AND RECOMMENDATIONS

• The role of medical genetics has shifted from managing rare disorders to the spectrum of genomic medicine

• Genomic medicine is evolving into personalized medicine that aims at maximizing wellness through prediction, prevention and early treatment

• There is a critical need to educate the health-care providers to incorporate genomic data into the clinical practice

• It is recommended to encourage the legislative bodies for the development of public and regulatory policies and establish acceptable standards
THANK YOU FOR YOUR ATTENTION