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UPCOMING TRENDS IN PERSONALIZED MEDICINE, GENOMIC SEQUENCING TECHNOLOGIES AND PUBLIC HEALTH EDUCATION

PRESENTATION AT THE
INSTITUTE FOR GENOMIC BIOLOGY
University of Illinois at Urbana-Champaign,
Illinois

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Upcoming trends in Personalized medicine

- Quite systematically, the Human genome Sequencing project which was accomplished by March 25, 2003 has begun transformation of clinical medicine and health education of the public.
- The relevant genomic technologies for personalized medicine were developed

INNOVATIVE DEVICES FOR PERSONALIZED MEDICINE

- The application of these devices in personalized medicine will continue to save lives and significantly reduce medical errors that culminate in the unnecessary death of patients nationwide
- Personalized medicine will eventually reinforce the integrity and confidence in primary care physicians, medical interns and specialists
- Personalized medicine can drastically reduce the exorbitant cost of medical malpractice suits.

Leading Causes of Death(2011)

Source.CDC.gov, 2014

Advances in medical science and improved longevity

- According to the former director of the National Institutes of Health, Elias Zerhouni(2007), Over 60% in mortality for cardiovascular diseases and stroke dropped in 2004 and life expectancy has risen to 78 years.
- Between 1974 and 1978, a gain in life expectancy of 6years have occurred.

Genomic Technologies in Personalized Medicine

- The discovery of the structure of the DNA by Watson and Crick laid the foundation upon which other scientists , such as J. Craig Venter and others gleaned their ingenuity regarding the sequencing of human genome(The shot Gun Method)
- Human genome sequencing now involve numerous scientists worldwide

Technologies applied to enhance Personalized medical care

- The 454 gene sequencers manufactured by Roche Diagnostics Corp(Branford, CT).
- Chromatography and electrophoresis, gene amplification, capillary analysis, PCR test, microarray sequencing, and iso-electric focusing

Multi-level sequencing

- NNA-level Research
- De novo sequencing and re-sequencing
- Whole genome
- Exome /Target Region
- SNP Genotyping
- Genotyping-by-sequencing
- Epigenome sequencing
- Ch1 sequencing and others
- There are RNA-level research sequencing and protein-level research sequencing

Combined impact of innovative sequencing and Bioinformatics science

- These innovations have the potential to facilitate significant insights into disease manifestation in individual patients and their clinical differences at molecular levels
- Knowledge derived from these scientific processes will enable physicians to customize treatment to the exact needs of patients

DNA VISION(Charleroi, Belgium)

DNA vision recently created an increased technological platform using a next-generation sequence FLX system(Roche) for genome shotgun sequencing, genome resequencing, transcriptome and metatranscriptomics. A comprehensive list of the state of the art technologies required to improve the dissemination of personalized medicine was compiled by Ebomoyi and Srinivasan(2011).

Pharmacogenomics in the personalized care of patients with CVD

- Pharmacogenomics is defined as the science that investigates how individuals react to medications. The United States Department of Energy (DOE, 2003) explained pharmacogenomics as moving away from “one size fits all” therapeutics. The cogent rationale pertains to the need for medical scientists and clinical epidemiologists to begin to correlate DNA variants with individual patient’s responses to medical treatment and identify drugs customized for a specific cohort of patients

Pharmacogenomics

- Pharmacogenomics is defined as the discipline that blends pharmacology with the genomic characteristics or capabilities of patients
- By March 25, 2003 after the accomplishment of the Human Genome Sequencing Project, The U.S Department of Energy, and the National Institutes of Health (Bethesda, MD) continue to use available clinical data to caution medical practitioners about avoidable disasters

Personalized Medicine can prevent unnecessary death among Patients

- NIH and USDOE reported that 100,000 people die each year due to adverse responses to medication that may be beneficial to other patients
- Another 2.2million patients experience serious reactions while others fail to respond to a similar medication

Specific Clinical Applications of Personalized Medicine

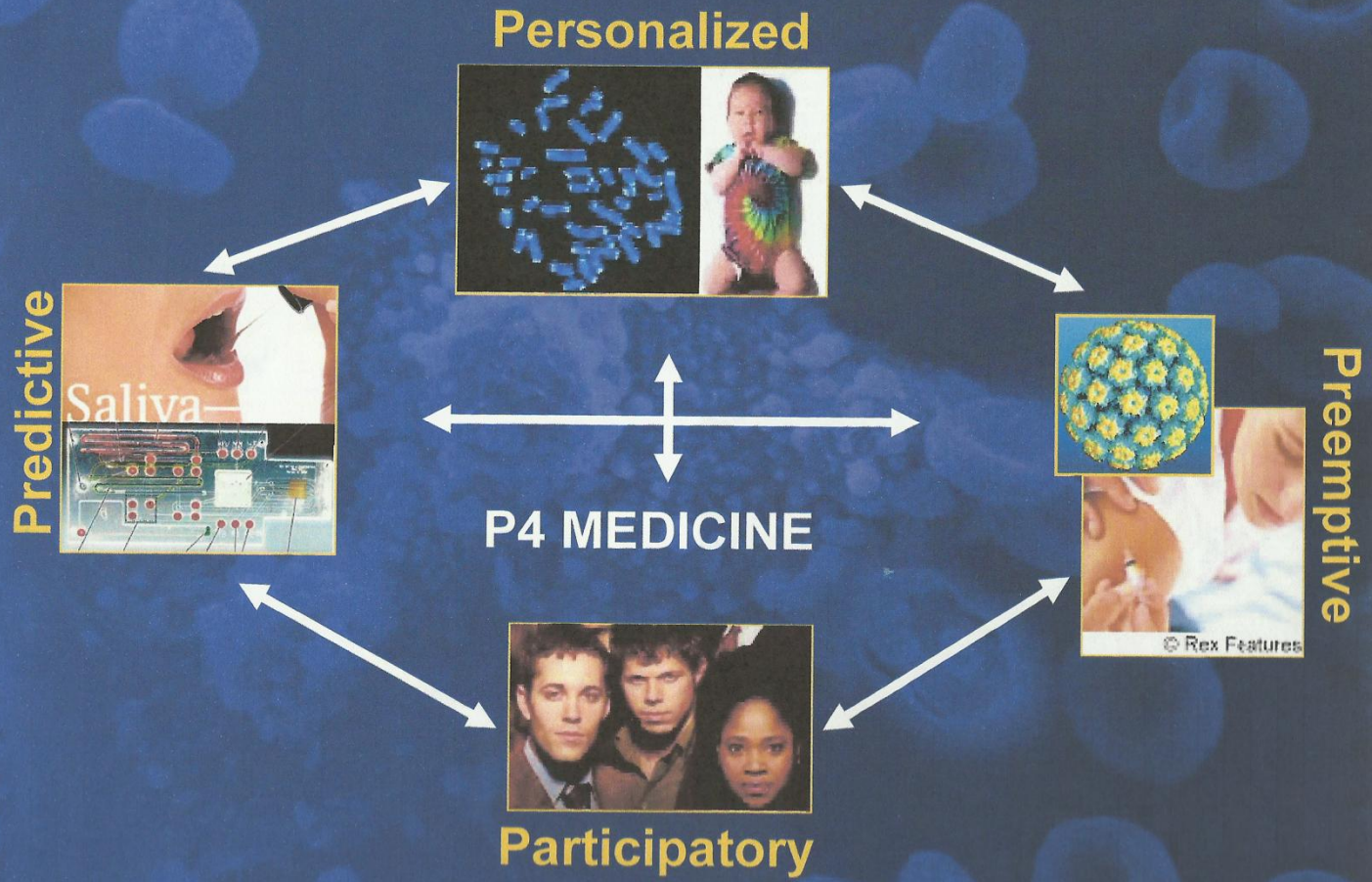
- Recently the scientific knowledge acquired from genomics has revealed the DNA variants present in genes, biochemically in drug metabolism, play a significant role in a patient's response to specific drug, particularly the cytochrome P450 multigene family.
- Besides, enzymes encoded by these genes are linked to the metabolism of most drugs for treating cardiovascular diseases, psychiatric and neurological problems

Knowledge Derived from Personalized Medicine

- DNA variants present in genes biochemically in drug metabolism play a significant role in patients' response to specific drug, particularly the cytochrome P450 multi-genes family
- Enzymes encoded by these genes are linked to the metabolism of most drugs for the treatment of cardiovascular diseases, psychiatric and neurological problems
- The American Heart Association has underscored the relevance of genomics for the prevention and treatment of cardiovascular disease

The Future Paradigm: The 4 P's

Transform Medicine from Curative to Preemptive



Factors that will facilitate Personalized Medicine in United states

- Advances in Sequencing Technologies
- Public Health Education
- Ability to participate in one's medical care
- Uniqueness of Demographic characteristics and responses to specific drugs
- Globalization of genomic science
- Investment in genomic science

Personalized Medicine and Treatment of Patients to Prevent Thromboembolic Events

- Personalized medicine was developed from the commitment of a team of physicians, medical scientists, geneticists, pharmacists, epidemiologists and biologists, and bio-informatics experts involved in laboratory analyses and clinical practice.
- The team reviewed literature to derive the pharmacokinetics, pharmacokinetic profile of numerous drugs. They also genotyped existing genes involved in drug metabolism that influence drug response

Treatment of CVD Patients

- Currently, drug management in personalized medicine can now be carried out from a comprehensive patient profile made available to health care providers
- In an effort to enhance patients' treatment nationwide, there are several institutes at NIH, and US Department of Energy currently working on comprehensive clinical data from several hospitals

Common Data Elements

- There are about 22 federal(NIH) institutes working on the task of CDE. These are comprehensive phenotypical and genotypical data set.
- There are several hospitals involved in this project
- These comprehensive data compiled from the participating hospital across the nation have access to patients continuous and discrete data set with are cross-classified with the CDV profile to assess response to intervention.

Patient Population Outcome Measures

- There are clinical data involving Cardiovascular diseases at many of the participating hospitals. These are phenotypic and genotypic data-continuous and discrete data sets.
- There are specific categorical data, such as ethnicity, education level, smoking status how many packs per week, alcohol use behavior, drug use behaviors etc
- There are challenges with identification of key data elements in terms of terminologies and the handling of missing data at some institutions. This is a synopsis of federal efforts to enhance personalized medicine.

WARFARIN sodium (Brand name Coumadin, (Bristol-Myers Squibb, New York, NY))

- Coumadin is the most commonly prescribed anticoagulant for the prevention and management of thromboembolic disease
- This drug which has been prescribed to well over 30 million patients had mixed therapeutic benefits
- The intended uses were to prevent deep venous thrombosis, pulmonary embolism, blood clots associated with heart arrhythmia (atrial fibrillation).

HGS and Pharmacogenomics

- As a result of the scientific breakthrough in HGS, medical scientists are able to titrate a patient's specific warfarin dosage on the basis of the International Normalized Level (INR)
- The normal range is between 2 and 3
- From clinical data and other patients' genomic profiles, the dosage can be adjusted upward to enhance efficacy. Pharmacogenomics intervention is used to determine the correct dose

Health Education Implications

- An increasing number of patients now attend Coumadin clinic to help prevent clotting
- The drug must be taken as directed by one's physician
- Vitamin K facilitates blood clots; thus patients need to monitor the amount of Vitamin K-rich foods they consume
- Several oil, alcohol, and green tea influence the efficacy of warfarin in the body

Foods rich in Vitamin K

Eats



#8 Parsley >> 65.59%
Among its many nutrients, it's high in folic acid, which helps lower blood pressure



#9 Romaine lettuce >> 63.48%
A plant source of omega-3s, for heart health, plus hydrating water



#10 Collard green >> 62.49%
High in fiber, which can help keep LDL cholesterol levels down



#11 Turnip green >> 62.12%
Dense with vitamin A, which may help avoid age-related ocular disease



#12 Mustard green >> 61.39%
Full of vitamin K for boosting bone density and overall brain health



#13 Endive >> 60.44%
Filled with vitamin A and beta-carotene for mucus membranes, skin and eyes



#14 Chive >> 54.80%
Known to have a mild anti-inflammatory effect, which may relieve rheumatoid arthritis



#15 Kale >> 49.07%
Brimming with vitamin K, it may help reduce heart disease, especially when eaten raw



#16 Dandelion green >> 46.34%
Rich in vitamin K, which, among other assets, may help limit neuronal damage in the brain

#17 Red pepper >> 41.26%

Lots of lutein, which may slow development of cataracts and macular degeneration



#18 Arugula >> 37.65%
Another source for vitamin K, which makes it part of the bone and brain health arsenal



#19 Broccoli >> 34.89%
A source of fiber, aiding in the fight to keep cholesterol from building up in your body



#20 Pumpkin >> 33.82%
Carotids make them orange, and help with premature aging and cardio disease



#32 Winter squash (all varieties)
>> 13.89%



#33 Orange
>> 12.91%



#34 Lime
>> 12.23%



#35 Grapefruit (pink and red)
>> 11.64%



#36 Rutabaga
>> 11.58%



#37 Turnip
>> 11.43%



#38 Blackberry
>> 11.39%



#39 Leek
>> 10.69%



#40 Sweet potato
>> 10.51%



#41 Grapefruit (white)
>> 10.47%

Table 1

Table 1-Food rich in Vitamin K

Asparagus	Cauliflower	Kale	Sauerkraut
Avocado	Coleslaw	Lentils	Soybeans
Broccoli	Collard greens	Lettuce	Spinach
Brussels sprouts	Endive	Liver	Swiss chard
Cabbage	Garbanzo beans	Mustard greens	Turnip greens

Integration of Genomic Medicine

- The integration of genomic medicine into the practice of conventional medicine or patient care in American hospitals must be implemented by evolution rather than revolution
- The former process requires the involvement of hospital administrators, physicians, other providers and stakeholder

Impact of Genomic Medicine

- It will provide comprehensive and multidimensional treatment and management strategies based on the science emerging from genomics.
- Genomics medicine can restore patients confidence in the health care system.
- Medical school curriculum will need to be modified

Innovative Medical School Curriculum

- IMSC will include Mendelian genetics
- Dysmorphology, chromosome disorders
- Inherited metabolic diseases
- Multifactorial basis of complex diseases
- In-depth epidemiological science
- Pharmacogenetics, bio-informatics, ethics and phenomenology

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Parkinson's
Glaucoma
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New genetic tests can point to risks —
but not always a cure

BY BONNIE ROCHMAN

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