

Genetics and Personalized Medicine

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Taxonomy and Nosology of “Disease”

- The oldest profession
- Creating order
- “Lumpers and splitters”
- Implications for “phenotype” and “phenocopies”
 - Genomics is changing how we view the underlying causes of “diseases”, and how we treat them

All Genetic “Diseases” Are Not The Same

- Too rare
- Too poor or minority
 - Ethnicity
- New mutations and epigenetic modification
- Mild vs severe
- Intervention or not
- Inexplicable
- Implications for how approach scientifically, medically, ethically

Determinative vs Contributory

- **Necessary vs sufficient**
- **Overt “disease”, “syndrome”**
 - “simple” Mendelian
- **Most human diseases are multi-factorial**
 - Interactions of multiple genes and environment
 - Redundancy of systems necessary for survival
 - Susceptibility/resilience
- **Penetrance**
- **Epistasis**
- **Gene-environment interactions**

Pharmacogenetics

- Processes focused on “external milieu”
- Evolutionary benefit to population diversity
 - BUT, for therapeutics may lead to “one person’s cure is another’s poison”
- Asking very focused questions using pharmacogenomics
 - Selection of right drug for right condition
 - Targeted therapy
 - Selection of right dose for right patient

Human Heterogeneity and Comparative Effectiveness

- Human heterogeneity in drug kinetics, efficacy, and side effects is a given
 - Only question is can we wisely tap into genomic and other markers of heterogeneity to improve patient outcomes
- In the face of heterogeneity, can standard comparative effectiveness studies based on population average responses tell us which drug is best for an individual patient?
 - DRUG OF CHOICE FOR WHOM?
 - Can we “marry” comparative effectiveness and genomic approaches to get the best answer

Pharmacogenetic/Personalized Medicine Examples

- From “evidence-based” to individualized therapeutics
- Cancer
- Hypertension
 - Ethnicity vs. individual
- Warfarin
 - And life in Korea
- Adverse Drug Reaction Markers
 - Ethnicity vs. individual
 - Necessary vs sufficient
 - Qualification as Dx test

Ethical Implications

- **If it's not good science, it's not ethical**
- **We all are different**
 - **Ethnicity may alter odds and be more or less important for certain conditions**
 - **BUT, it still comes down to the individual**
- **“Diseases” are complex, and “cures” likely to be similarly complex - multiple drugs and environmental modifications**
- **Respect for persons, and distributive justice in clinical trials and patient care**