2 Obstacles on the Path to Personalized Medicine

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Aims

1. Introduce 2 senses of PM.
2. Describe 2 obstacles to achieving PM.
3. Offer exhortation to "U.S." bioethicists & pose question to "H.K." bioethicists.

2 Senses *Personalized Medicine*

1. Tailored *to* persons' genomes
   - assumes clinical utility of WGS data
2. Shows respect *for* persons
   - in US, assumes informed consent
     - persons seen *as individuals*

2 Obstacles

1. Increasing awareness of complexity, & limited current clinical utility, of data

2. Increasing pressures to abandon traditional informed consent

Sense 1
(tailored to)
&
Obstacle 1
(increasing complexity)

The Original Vision

- Genome as "book of life"
  - Francis Collins, 2000
    - "instruction book," "blueprint," "grail"
- Key to diagnosis, treatment, prevention
  - rare **and** common diseases

Big Successes

- E.g., definitive diagnoses rare diseases
  - Progressive Spastic Paraplegia → L-dopa
- E.g., new meds targeted to rare diseases
  - Chronic Myelogenous Leukemia → Gleevec
- E.g., drug-prescription decisions based on kg of genomic variants
  - Rare CYP2D6 variant → avoid codeine

Disappointment, So Far

- **Common** diseases
  - medical "and" psychiatric have resisted clinically useful genomic explication
  - candidate studies failed replication
  - GWAS replications, but:
    - small effect sizes
    - small increase *absolute* risk

"An elephant for a nickel is a bargain,
if you have a nickel and need an elephant."

--James Evans,
Author, PSP article
Editor-in-Chief, *Genetics in Medicine*

- limited health-care nickels
- gigantic data not always clinically useful
  - irrational exuberance can be costly

Sense 2
(respect for persons)
&
Obstacle 2
(increasing pressure to abandon traditional informed consent)

Traditional IC

- Response to ½ century eugenic thinking
  - forced "research" participation
  - "fitter families"
- Shows respect for persons *as* individuals
  - not *as* members of families / communities
- Honors individual variation:
  - different people, different psychologies
  - same person, different attitudes:
    - toward different kinds of genetic info
    - at different life stages

New Reality

- Early days genetic counseling
  - focused on limited info, # serious conditions
- Today, gigantic amount of data

  medically serious ---- not medically serious

  actionable ---- not actionable

  certain ---- uncertain significance

  early ---- late onset
- Serious question:
  - is traditional IC practicable anymore?

Signs of drift away from traditional IC

- Invocation of survey data
  - "people want it all"
    - tacit question: Why use IC re: some bits?
- 2013 ACMG recommendation
  - adults & children should get actionable data
    - de facto mandating return of some findings
- 2013 NIH grants to explore WGS in NBC
  - these researchers care deeply about IC
    - where's "drifting" ?

Newborn Context

- Since 60s: *exception* to traditional IC
  - mandated testing for treatable conditions
    - *direct benefit to individual child*
- 2005: ACMG recommends expanding list
  - now includes 2° disorders found incidentally
- Today: expanding conception of benefit
  - end "diagnostic odyssey"
    - *in*direct benefit to child: reduce parental anxiety
  - "family planning"
    - highly *in*direct benefit to tested child

Imaginable Question

- If we mandate expanded **newborn** testing, why not **prenatal**?
  - advantages of NBS +
    - *in utero* treatment
- If abandoned traditional IC in prenatal context:
  - look like return to "eugenic" ideas
    - which traditional IC was to combat.

3-Part Exhortation for “US” bioethicists:

a) Remember: traditional IC is one way of showing respect for persons, as individuals

b) Acknowledge: perhaps PM of the future must break with tradition
   - fetishized individual choice?
   - no longer practicable?

c) Accept responsibility for giving reasons
   - Don’t drift on tide of enthusiasm about elephants for nickels !

Question for “HK” Bioethicists

- In age of WGS, how *should* HK health systems show respect for persons?