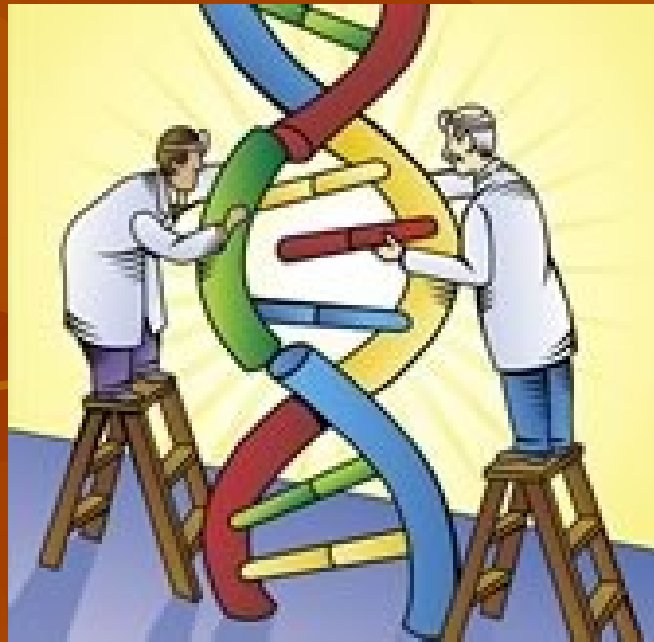


The Future of Practicing Medicine



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What Might it Be Like?

- Clip from GATTACA (1997) 0:22-1:22



- Although we can imagine a world like the sci-fi reality in the movie GATTACA, is this valid or possible in the near future?

What Are the Possibilities?

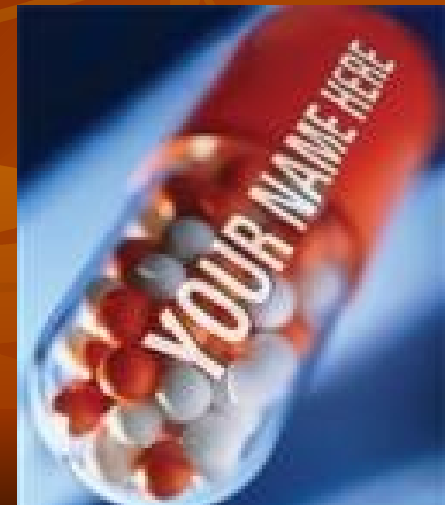
- Personalized Medicine
 - The use of information and data from a patient's genotype, or level of gene expression to stratify disease, select a medication, provide a therapy, or initiate a preventative measure that is particularly suited to that patient at the time of administration. (Wikipedia)
- Renewed Emphasis on Preventive Medicine
 - Evolution of the field of Pediatrics to a more preventive practice.

Personalized Medicine

- “The appropriate drug, at the appropriate dose, to the appropriate patient, at the appropriate time” (Wikipedia).
- Cytochrome P450 (CYP) – family of liver enzymes is responsible for breaking down more than 30 different classes of drugs. (Human Genome Project Information)
 - “DNA variations in genes that code for these enzymes can influence their ability to metabolize certain drugs. Less active or inactive forms of CYP enzymes that are unable to break down and efficiently eliminate drugs from the body can cause drug overdose in patients.” (Human Genome Project Information)

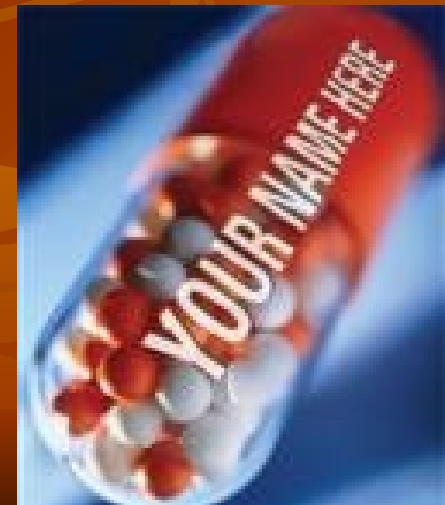
CYP2E1

- CYP2E1 – involved in the metabolism of xenobiotics including acetaminophen (analgesic, antipyretic).
 - A **xenobiotic** is a chemical which is found in an organism but which is not normally produced or expected to be present in it.
 - In rats, this enzyme was found to transcriptionally active one day after birth.
 - The human *CYP2E1* gene is located on chromosome 10 and encodes an mRNA that is 1.6 kb in length. The human CYP2E1 cDNA shares 79% similarity over the coding region with mouse CYP2E1 (Freeman et al., 1992)



CYP2E1 and Acetaminophen

- Cheung C. et al. "The cyp2e1-humanized transgenic mouse: role of cyp2e1 in acetaminophen hepatotoxicity." Drug Metabolism and Disposition. 2005 Mar;33(3):449-57. Epub 2004 Dec 2.
- The study found that rats with a functional CYP2E1 enzyme suffered liver damage at a 400 mg/kg dose of acetaminophen.
- On the other hand, rats that did not have a functional enzyme did not suffer any liver damage because they did not metabolize the drug.



Evolution of the Practice of Pediatrics

- If I can tell the conditions for which my child has a predisposition, why should I wait until disease onset?
 - PKU Newborn Screening (Since mid-1960s)
 - Use Guthrie microbial or other assays on a blood spot from heelprick.
- Two Possibilities
 - New Focus on Early Management of Disease Precursors
 - Like the above case of PKU screening. Use early biomarkers to inform treatment plan.
 - Prevention is better than cure
 - GATTACA world – Why should I wait to see the cards that fate deals me? Why don't I ensure that my child is given the best genome possible and thereby prevent the need for disease predisposition management?

Ethical Considerations for Future Practice of Medicine

- How will knowing the probability of developing a medical condition transform one's quality of life?
 - Contemporary examples of high-risk individuals who do not desire to know their genetic predisposition to diseases such as Huntington's.
- How do we ensure that a statistical probability is not confused with a definitive diagnosis?
- What about self-fulfilling prophecy?
 - Laus – Oedipus's father
- Would there be some beauty lost in by reducing the randomness to life?

References

- Wikipedia
 - http://en.wikipedia.org/wiki/Personalized_medic
- YouTube
 - <http://www.youtube.com/watch?v=48-hnujqpoA&feature>
- Human Genome Project Information
 - http://www.ornl.gov/sci/techresources/Human_
- Drug Metabolism and Disposition
 - <http://dmd.aspetjournals.org/cgi/content>