

泌尿腫瘤的未來醫療 Translational Medicine in Uro-oncology

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A Strategy for Health Care Reform — Toward a Value-Based System by Michael E. Porter, Ph.D.

- To achieve a value-based delivery system, measurement and dissemination of health outcomes should become mandatory for every provider and every medical condition.
- Results data not only will drive providers and health plans to improve outcomes and efficiency but also will help patients and health plans choose the best provider teams for their medical circumstances.

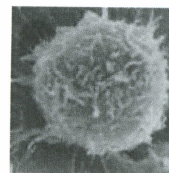
NEJM, July 9, 2009

History

- Radical prostatectomy
- Hormone therapy for prostate cancer
- Transurethral resection of bladder cancer
- BCG therapy in bladder cancer
- LAK cell therapy in kidney cancer
- Nerve sparing radical surgery
- Laparoscopic surgery
- Robotic surgery
- Targeted therapy for metastatic cancer

Challenge in Uro-oncology

- Prostate cancer
- Bladder cancer
- Kidney cancer
- Testicular cancer
- Penile cancer



Surgical Improvement in MIS

- Single port laparoscopy
- Robotic surgery
- N.O.T.E.S.

Overtreatment for Prostate Cancer

- 1 Million additional men being diagnosed and treated for prostate cancer in the States (JNCI, 2009)
- Cryoablation therapy
- HIFU
- Focal therapy

What is translational medicine?

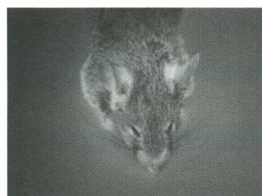
- Philip Pizzo, M.D. (2008): Perhaps the most specific definition is "bench-to-bedside" research wherein a basic laboratory discovery becomes applicable to the diagnosis, treatment or prevention of a specific disease and is brought forth by either a physician-scientist who works at the interface between the research laboratory and patient care or by a team of basic and clinical science investigators.

What is the future of translational medicine in uro-oncology?

- New anti-androgen
- Molecular staging
- Targeted therapy in prostate cancer
- Combination of targeted therapy and/or immunotherapy in kidney cancer

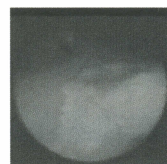
Humanized mouse model

- Engineered human-in-mouse tumors for population based in vivo biomarker development



Imaging biomarker

- Target site occupancy: Emerging generalizations from clinical and preclinical studies. (Sarah Grimwood)



Translational informatics

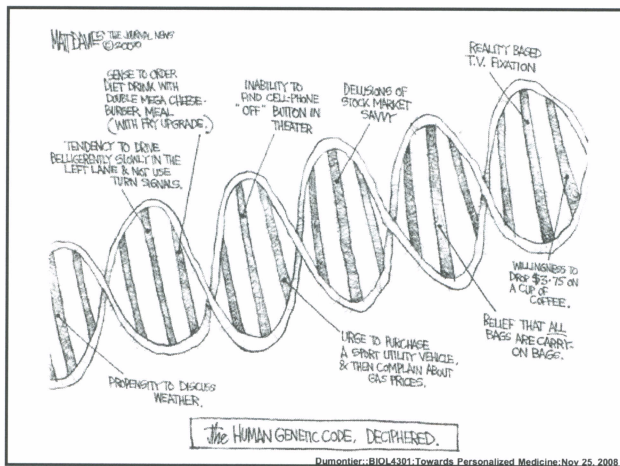
- Omics solutions to diagnostic and prognostic prediction
- Profiling patients to drive biomarker development



"If it were not for the great variability among individuals, medicine might as well be a science and not an art"

Sir William Osler, 1892

Dumontier, BIOL4301: Towards Personalized Medicine, Nov 25, 2008



Dumontier:BIOL4301-Towards Personalized Medicine:Nov 25, 2008

Major sources of variation

- Single Nucleotide Polymorphisms (SNPs)
 - Single base change in DNA
 - AAGCCTA
 - AAGCTTA
 - Average frequency 1/1000bp
 - SNPs arise as a consequence of mistakes during normal DNA replication
- Genomic rearrangements
 - Duplications, insertions, deletions

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Personalized Medicine

The ability to offer

- **The Right Drug**
- **To The Right Patient**
- **For The Right Disease**
- **At The Right Time**
- **With The Right Dosage**

Genetic and metabolic data will allow drugs to be tailored to patient subgroups

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Codine Metabolism

- 5-10% codeine is metabolized into morphine by CYP2D6
 - 7% of caucasians have a nonfunctional CYP2D6 variant
 - <2% are CYP2D6 ultrarapid metabolizers which may suffer from opioid intoxication
- 80% codeine normally converted to glucuronide, eliminated by kidney.
- inhibition of CYP3A4 or rapid metabolic variants of CYP2D6 during renal failure would show toxicity

From: F. Li et al. A white population study of the ultrarapid CYP2D6 genotype. *Pharmacogenetics* 14: 251-254 (2004)

Dumontier:BIOL4301-Towards Personalized Medicine:Nov 25, 2008

Drug-Metabolizing Enzymes

Phase I: modification of functional groups

Phase II: conjugation with endogenous substituents

Most DME have clinically relevant polymorphisms
Those with changes in drug effects are separated from pie.

Pharmacogenomics: Translating Functional Genomics into Rational Therapeutics. *Emerging and Evolving Science*, 2009. Dumontier:BIOL4301-Towards Personalized Medicine:Nov 25, 2008

Benefits of Personalized Medicine

- Better matching patients to drugs instead of "trial and error"
- Customized pharmaceuticals may eliminate life-threatening adverse reactions
- Reduce costs of clinical trials by
 - Quickly identifying total failures
 - Favourable responses for particular backgrounds
- Improved efficacy of drugs

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Personalized Medicine : BiDil

- Combination pill containing two medications for heart failure, cardiovascular disease, and/or diabetes.
- Clinical trials did not show overall benefit across entire population.
- Subgroup of African-descent patients showed benefit
 - BiDil approved for use in African-descent patients.

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Personalized Medicine in Uro-oncology

- Temsirolimus, sunitinib, sorafenib in kidney cancer
- Prognostic factors for targeted therapy
- Combination of targeted therapy
- Novel pathways for targeted therapy
- 3P Uro-oncology

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Thanks for your attention!

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