

Personalized Medicine – Is There a Future?

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Personalized Medicine

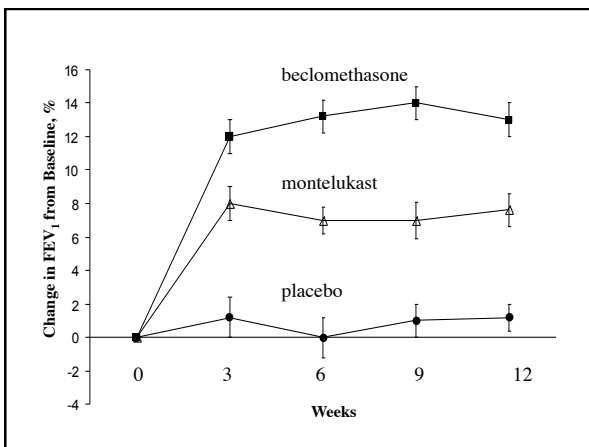
Practicing medicine using additional information from “omics”-based technologies such that a greater refinement in care is provided than would otherwise be possible.

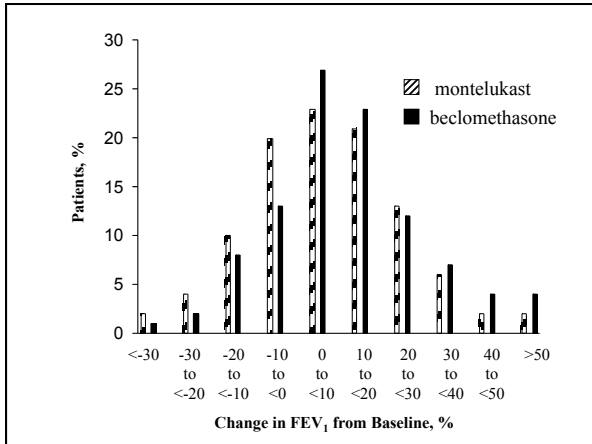
“omics”-based technologies

- **genomics**
 - polymorphisms: noncoding, coding (synonymous, nonsynonymous)
 - copy number variation
 - mRNA expression
 - splice variants
 - methylation
- **metabolomics**
- **proteomics**

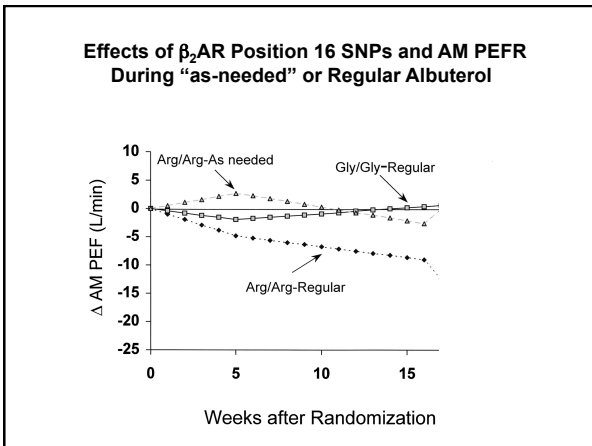
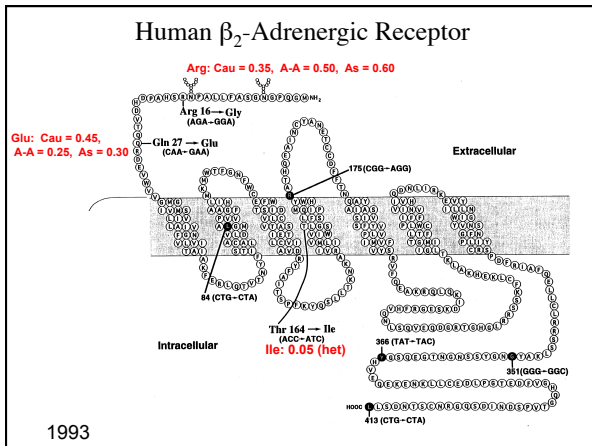
Potential “Direct” Application of Omics-based Clinical Data

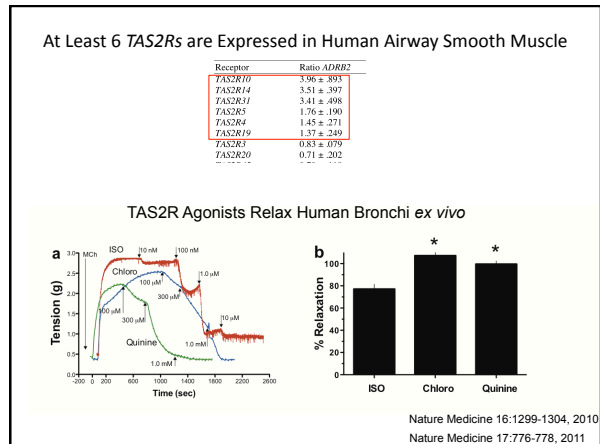
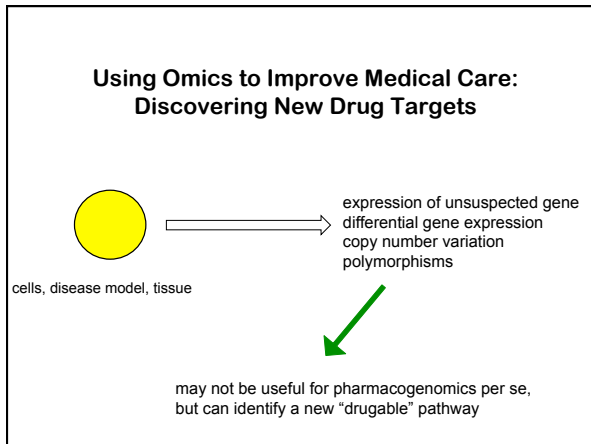
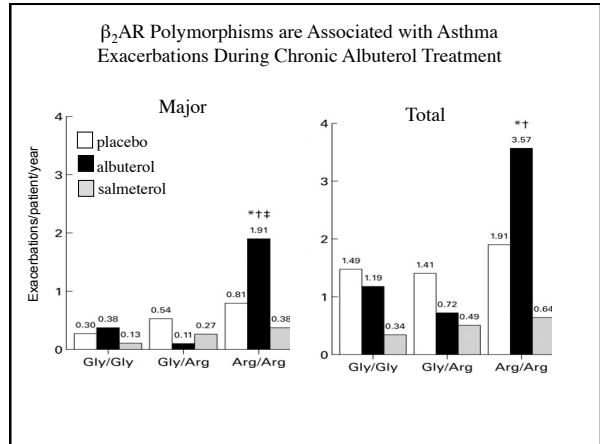
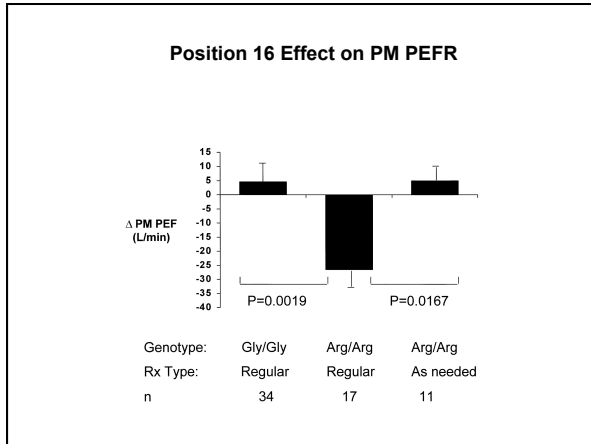
- **Diagnosis/risk**
- **Prognosis**
- **Define clinical subsets**
- **Response to therapy (pharmacogenetics or pharmacogenomics)**
 - Identify those patients most likely to have a response
 - Identify those patients most likely to have a highly responsive phenotype
 - Identify those patients who are likely to have a severe adverse effect

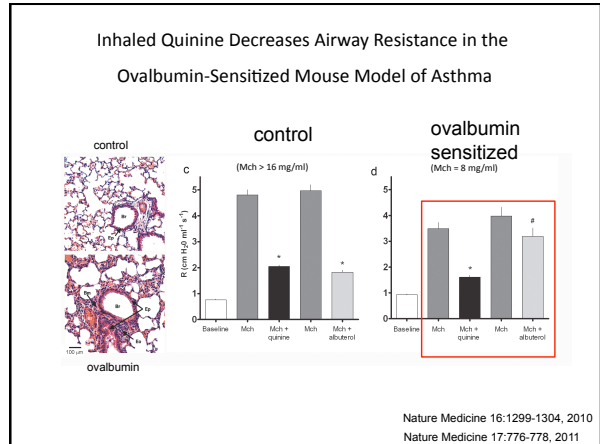
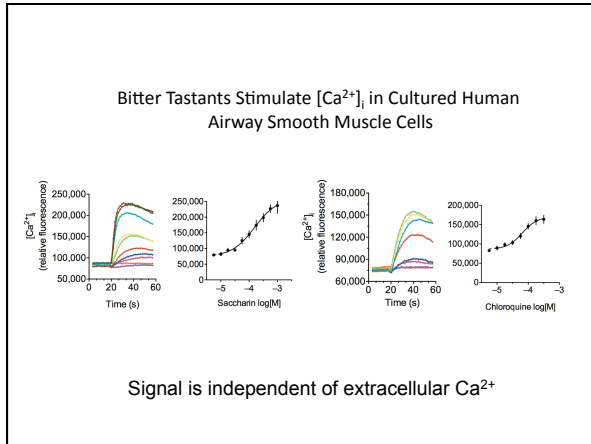




- ### Some Problems with Polymorphism Association Studies
- Underpowered
 - Lack of control for other clinical parameters
 - Lack of correction for population stratification (i.e., ethnic differences in polymorphism frequency)
 - Lack of correction for multiple comparisons
 - Poor (or no) reproducibility by other investigative groups
 - Unidentified clinical subset in first report?
 - Spurious association in first report?
 - Different experimental conditions (LABA vs. SABA)







What About the Genomics of the Pathogen?

- Human rhinovirus (HRV) infection causes ~50% of all asthma exacerbations
- There are >100 HRV serotypes; "pan-HRV" therapeutics have not been successful
- Can differences in HRV genomes define exacerbation subsets, for which conventional (early steroids?) or new therapy can be considered?
- Can HRV genomes be determined quickly?
- Is it necessary to sequence the entire HRV genome to gain prognostic/pharmacogenomic information?

International Rhinovirus Consortium
<http://international-rhinovirus-consortium.org>

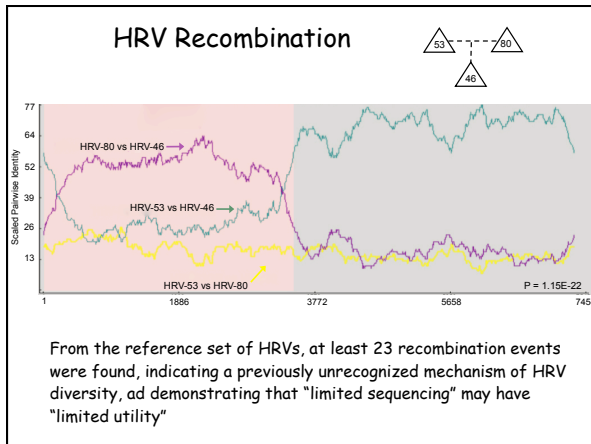
Human Rhinovirus (cont'd)

Single stranded RNA virus

Genome: ~650b 5'UTR, ~6500b ORF, ~50b 3'UTR

ORF encodes a single protein that is subsequently cleaved to form 11 mature viral proteins

- 8 HRV complete genomes were known when study began
- Goal: sequence the complete genomes of all known HRVs



Summary

- Personalized medicine tools based on omics-technology have been applied to asthma
- Variability in patient genomes have been shown to identify:
 - Persons at risk
 - Clinical phenotypes
 - Response to therapy
- Reproducibility, effect size, and usefulness at point of care are issues that need to be addressed
- Omics-based technologies have identified new targets for asthma treatment
- Variability in pathogen (HRV) genome may provide actionable data during virus-promoted exacerbations