# About OMICS Group

OMICS Group International is an amalgamation of Open Access publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 400 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 300 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

# About OMICS Group Conferences

OMICS Group International is a pioneer and leading science event organizer, which publishes around 400 open access journals and conducts over 300 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

# Personalizing drug treatment using pharmacometabonomic approach

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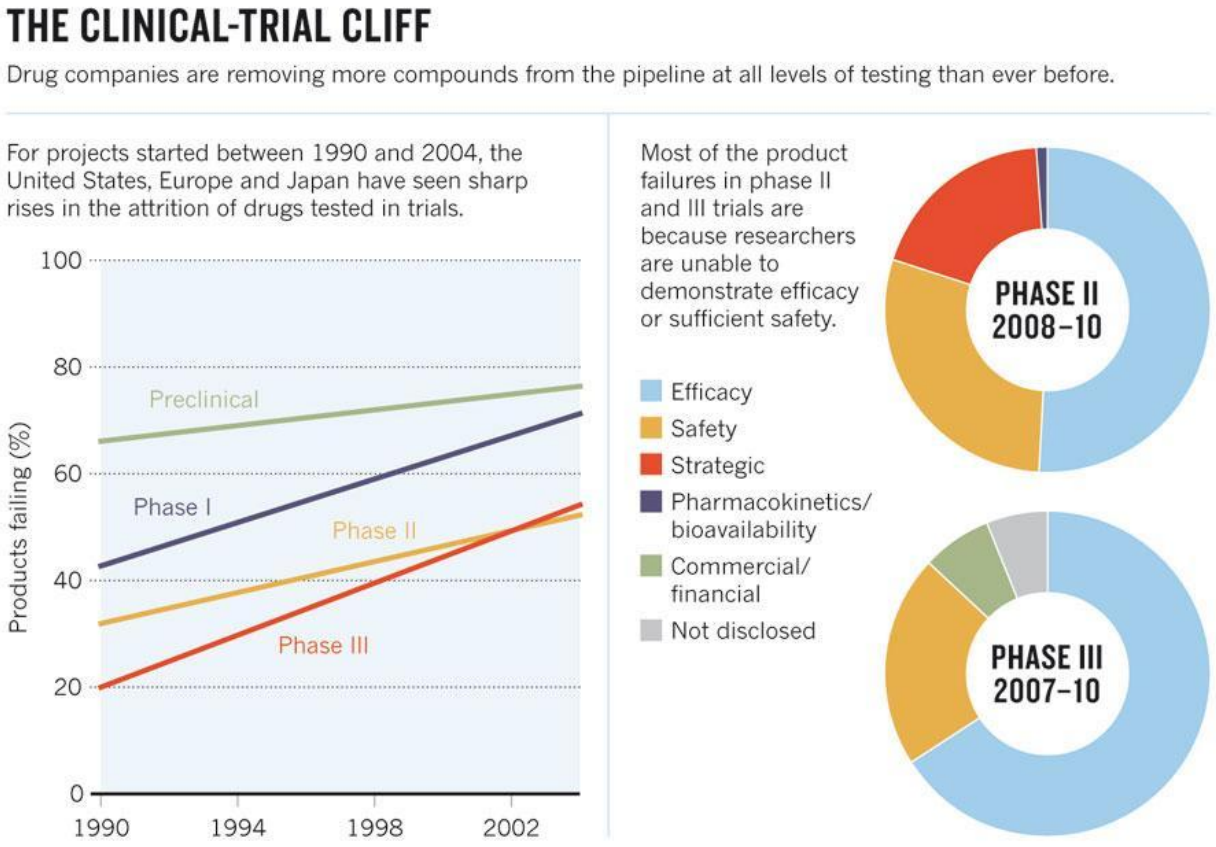
# Current treatment approach

- Based on large cohort studies – blockbuster medicine
- One-size-fits-all model - Do not account for individual differences
- Increased cost and safety concern (without proven efficacy)
- The response rates on drugs is still unsatisfactory, varying widely from 20% to 75% depending on the drug and the disease

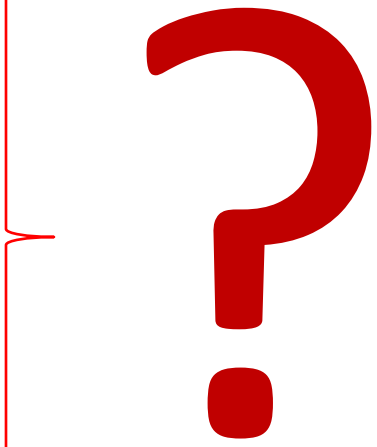

• Diagnostics 2009. Moving towards personalised medicine. PricewaterhouseCoopers LLP. http://pwchealth.com/ Accessed November 10, 2011.
• Agency for Health Care Research and Quality (AHRQ). Reducing and preventing adverse drug events to decrease hospital costs. *Research in Action*, Issue 1. Rockville, Md. Available at: www.ahrq.gov/ Accessed May 29, 2010.

# Drug development failure




Source: Ledford H. Nature 2011.

- Right medication,
- Right dose,
- **Right patient**,
- Right time and
- Right route



# Personalized medicine

## What is personalized medicine?

• Use of patient's characteristics including demographics, histories and **molecular information (genetic, protein and metabolic profile)** to better define therapies

• Integration of diagnostics and therapeutics – known as theranostics (a diagnostic therapy that identifies patients most likely to be helped by a new medication, and targets drug therapy based on the test results).

• Philosophy - every patient has a unique biology and pathophysiology that should be reflected in the choice of pharmacotherapy, thus resulting in an improved treatment outcome


• Personalized Medicine Coalition www.personalizedmedicinecoalition.org/sciencepolicy/personalmed-101_overview.php.
• Lester. DS. Will Personalized Medicine Help in 'Transforming' the Business of Healthcare? Personalized Medicine. 2009;6(5):555-565.

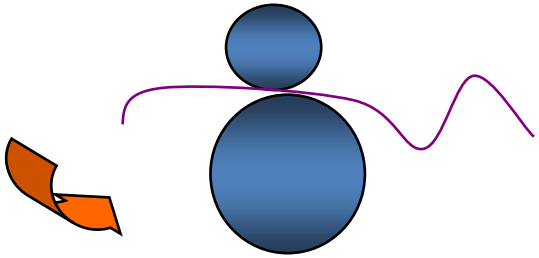
# Personalized medicine

## Why is PM better than the current approach?

- Treat the patient, **NOT** just the disease
- Provide for individual differences – a tailored approach
- Predict susceptibility and risk factors, pre-empt disease progression, target intervention, avoid ineffective treatments and prevent adverse reactions.
- Reduce costs in the long term
- Stratify, genotype and phenotype diseases

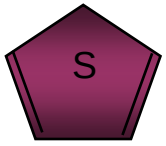
# Omics genotype and phenotype

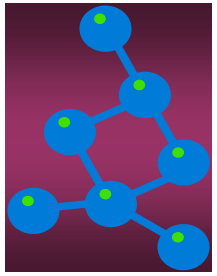
Genomics – study of genes



Transcriptomics – study of mRNA

Proteomics – study of proteins



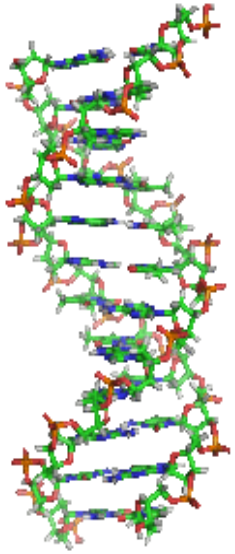



Metabolomics – study of metabolites

# Pharmacogenomics

- Pharmacogenomics - study that examines the impact of genetic variation on the response to medications

- Drug metabolizing enzymes, transporters and receptors are encoded by several hundred genes, playing a pervasive role in ADME and drug targeting



• Shastry BS (2006). "Pharmacogenetics and the concept of individualized medicine". *Pharmacogenomics J.* **6** (1): 16–21

# Pharmacogenomics

## Limitations

• A major factor underlying inter-individual variation in drug effects is variation in metabolic phenotype, which is influenced not only by genotype but also by environmental factors such as nutritional status, the gut microbiota, age, disease and the co- or pre-administration of other drugs which modulate drug pharmacokinetic (ADME), efficacy and toxicity

• Thus, although genetic variation is clearly important, it seems unlikely that personalised drug therapy will be enabled for a wide range of major diseases using genomic knowledge alone


• Sadee W, Dai Z. (2005), *Pharmacogenetics/genomics and personalized medicine*, Hum Mol Genet. 2005 October 15;14 Spec No. 2:R207-14.
•TA Clayton, JC Lindon, O Cloarec, H Antti, C Charuel, G Hanton, J Provost, J Net, D Baker, RJ Walley, JR Everett, JK Nicholson. Pharmaco-metabonomic phenotyping and personalized drug treatment. Nature April 2006; 440(20)

# Pharmacoproteomics

HercepTest

HER2 protein


Trastuzumab

EGFR pharmDX Kit

EGFR protein


Cetuximab


MY GENOME MADE ME DO IT!
STAYSKAL 2000 TAMPA TRIBUNE

# Pharmacometabonomics

• Pharmacometabonomics - the prediction of the outcome (for example, efficacy or toxicity) of a drug or xenobiotic intervention in an individual based on a mathematical model of pre-intervention metabolite signatures

• One of the major factors influencing a patient's response to any medication is drug pharmacokinetic (ADME). Differences in the balance of pharmacokinetic leading to detoxification vs. toxicity are the difference between a treatment being safe and effective or causing an adverse drug reaction

•TAClayton, JC Lindon, O Cloarec, H Antti, C Charuel, G Hanton, J Provost, J Net, D Baker, RJ Walley, JR Everett, JK Nicholson. Pharmaco-metabonomic phenotyping and personalized drug treatment. Nature April 2006; 440(20)
• Ian D. Wilson1 . Drugs, bugs, and personalized medicine: Pharmacometabonomics enters the ring. PNAS August 2009; 106(34):14187–14188

# Pharmacometabonomics

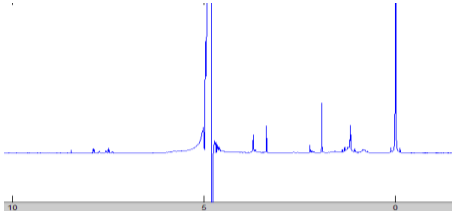
Advantages of metabolomics approach:-

- affected by both genes and environment
- closer to phenotype
- simple and non-invasive
- relatively ease of analysis
- potential to identify novel biochemical pathways

# Pharmacometabonomics

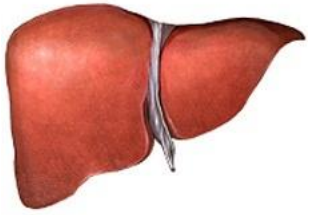
Urine samples of 10 rats


NMR

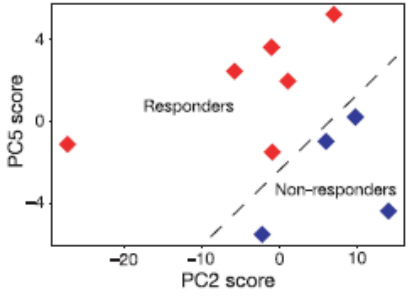


NMR spectra

Inject galactosamine hydrochloride



Liver bioassay

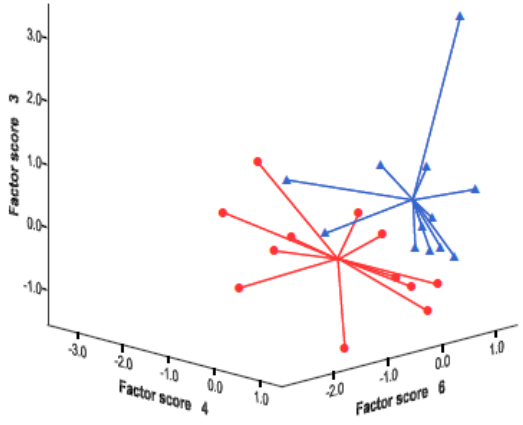



PCA

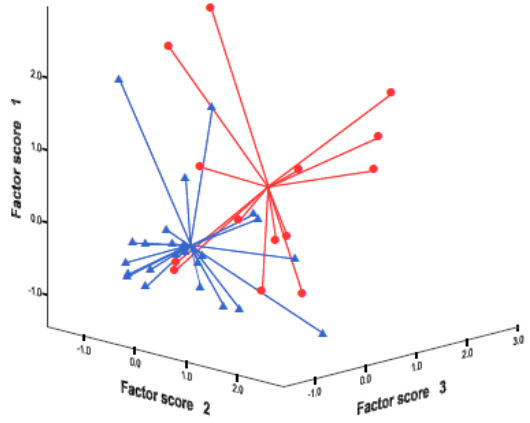
•TA Clayton, JC Lindon, O Cloarec, H Antti, C Charuel, G Hanton, J Provost, J Net, D Baker, RJ Walley, JR Everett, JK Nicholson. Pharmaco-metabonomic phenotyping and personalized drug treatment. Nature April 2006; 440(20)

# Inhaled steroid use

Scatterplots of the discriminating principal components, blue triangles show subjects on ICS




Asthma study




COPD study

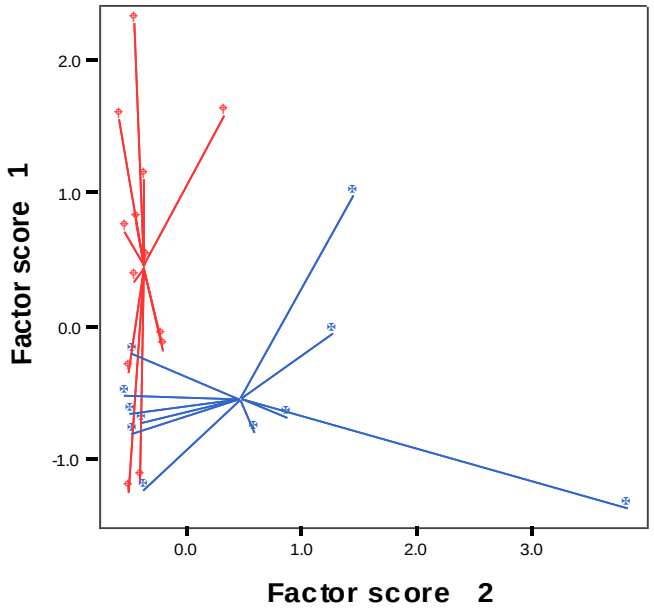

• **Ibrahim B**, Basanta M, Cadden P, Singh D, Douce D, Woodcock A, Fowler SJ. (2011). Non-invasive phenotyping using exhaled volatile organic compounds in asthma. **Thorax** 2011;66:804-809.

• M Basanta, **B Ibrahim**, R Dockry, D Douce, M Morris, D Singh, A Woodcock and SJ Fowler. Exhaled volatile organic compounds for phenotyping chronic obstructive pulmonary disease; a cross-sectional study. **Respiratory Research** 2012;13(1);72

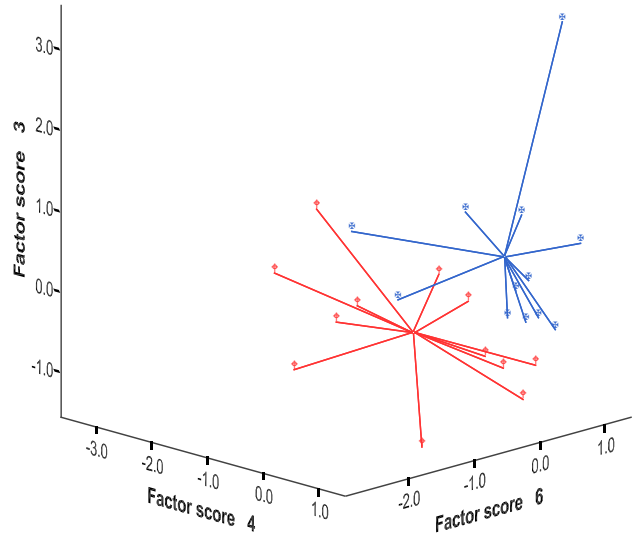
# Eosinophils and neutrophils

Scatterplots of the discriminating PCs derived from the models, blue triangles show: a) sputum eosinophils ≥ 2%; b) sputum neutrophils ≥ median

a

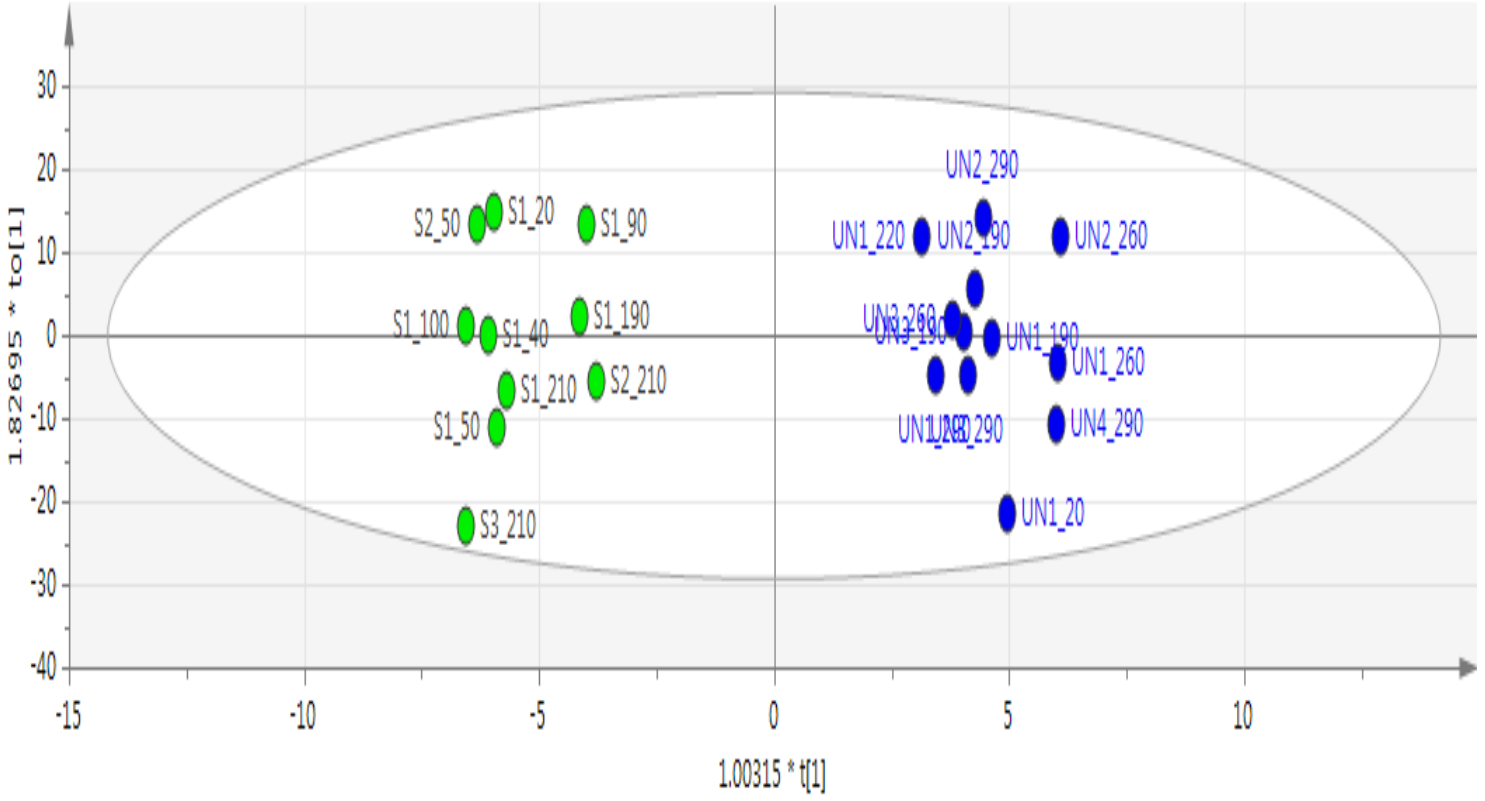



b




M Basanta, **B Ibrahim**, R Dockry, D Douce, M Morris, D Singh, A Woodcock and SJ Fowler. Exhaled volatile organic compounds for phenotyping chronic obstructive pulmonary disease; a cross-sectional study. **Respiratory Research** 2012;13(1);72

# Warfarin use




Stable

Unstable

# Conclusion

- If we can say genetic contribute to a disease, of course it can also contribute to drug response.
- Limitations of pharmacogenomics lead to the new approach known as pharmacometabonomics.
- This method as high potential to personalize drug treatment as it looks at the contribution of both genetics and environmental factors to the drug effects.


www.harunyahya.org
THANK YOU

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www.metabolomicsconference.com