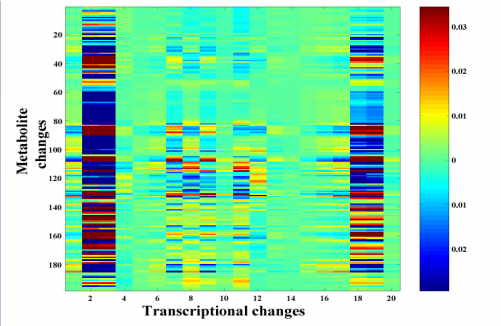


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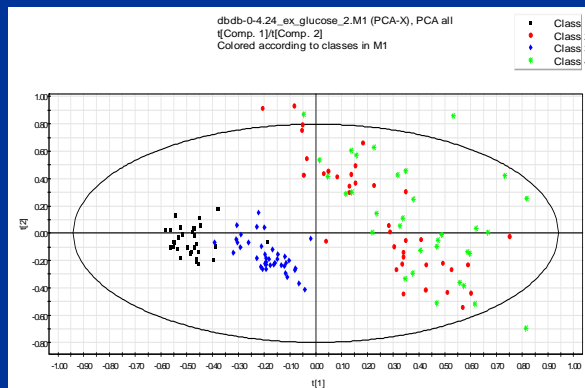
Metabomeeting 2.0: Welcome and Introductions

Jules Griffin, Cambridge

John Haselden, GSK

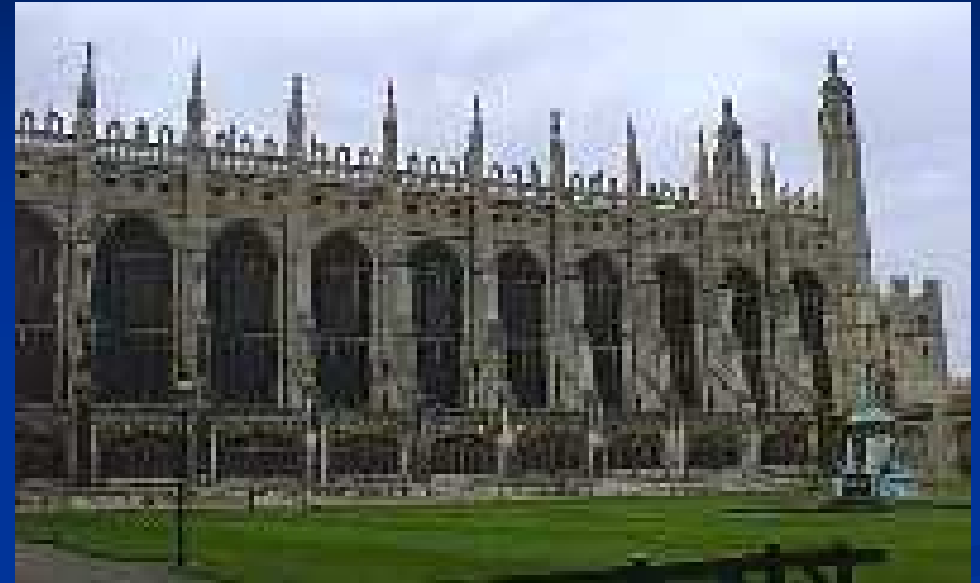
Andrew Nicholls, GSK

Chris Taylor, EBI



Welcome To Cambridge and King's

- A quick tour of the college (with respect to the next two days as well as the past ~550 years)
- King's College (King's College of Our Lady and St. Nicholas) was founded in 1441 by Henry VI
 - But it would take Henry VII and VIII to finally finish the chapel
- Most of the meeting will be focused in the Keynes and Chetwynd rooms
 - The economist Keynes was bursar of the college
 - The lecture theatre seats 150 but we are going to be a tight fit!
 - Coffee and tea will be served in the Chetwynd room but please use the overspill into the bar





- Tonight's dinner will be in the Great Hall
 - Designed by William Wilkins in the 19th Century
 - "The Dining Hall is a major part of college life. In the sombre, sparsely lit Hall, the gowned students would rise as the Fellows entered and walked the length of the Hall to the High Table. After a Latin Grace, intoned by a scholar, the Fellows would wine and dine, while the undergraduates would have to be content with food of indifferent quality, served in the body of the Hall."
 - Drinks and informal discussions will take place in the bar.

- For those of you not staying in hotels breakfast can be bought in the Hall or the Copper Kettle across the road.
- On Tuesday we have a break out session concerning standardisation of reporting metabolomic experiments.
- This will take place in G4 in the Gibbs Building
 - Please ask one of the Griffin group for directions
- One famous former Gibb's resident is Turing
 - mathematician, one of the originators of the computer, wartime cryptographer.



Introductions to the meeting

- This meeting follows on from the highly successful Metabomeeting 1.0 held in July 2005.
 - This aimed to bring together those interested in the description and reporting of metabolomic experiments
- The aims of Metabomeeting 2 are:
 - To provide an informal forum for those involved (or interested) in metabolomics/metabonomics/metabolic profiling to discuss new results, techniques
 - To continue the work began in metabomeeting 1.0
 - To recruit people to the initiative began by the International Society of Metabolomics for standardisation in reporting
 - Provide a friendly forum for student presentations

A Scientific Introduction

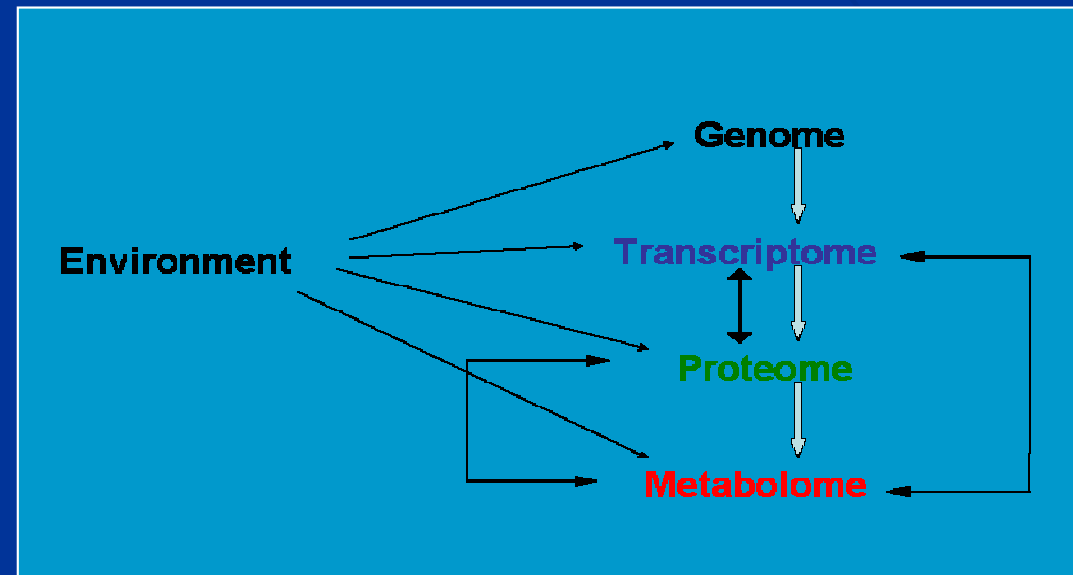
What's in a name?

Metabonomics “...measurement of the dynamic multiparametric metabolic response of living systems to pathophysiological stimuli or genetic modification...” Nicholson *et al.*, 1999

Metabolomics “...the complete set of metabolites/low-molecular-weight intermediates, which are context dependent, varying according to the physiology, developmental or pathological state of the cell, tissue, organ or organism...” Oliver 1999

A Scientific Introduction

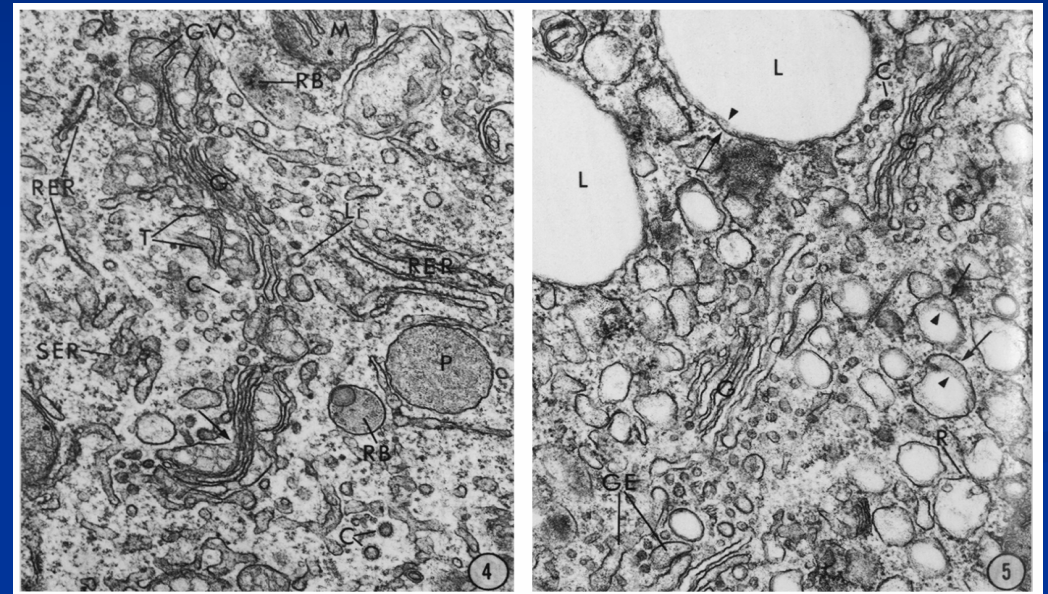
- Genomics
 - Study of genes – the only -ome which is not context dependent
- Transcriptomics
 - All the mRNA in a cell/tissue/organism
- Proteomics
 - All the proteins in a cell/tissue/organism
- Metabonomics/Metabolomics
 - All the metabolites in a cell/tissue/organism



A Brief Cautionary tale

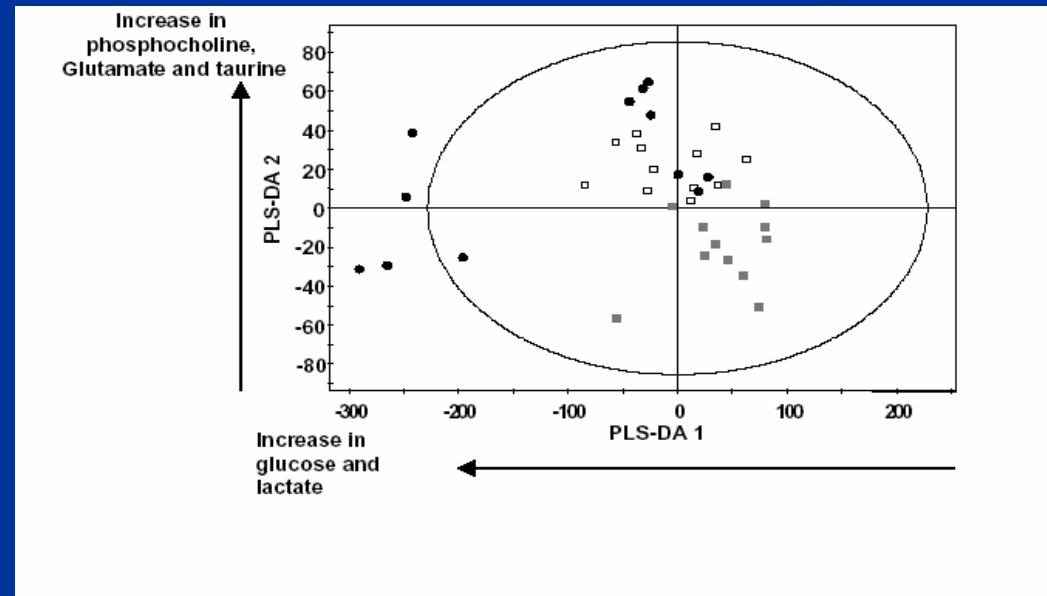
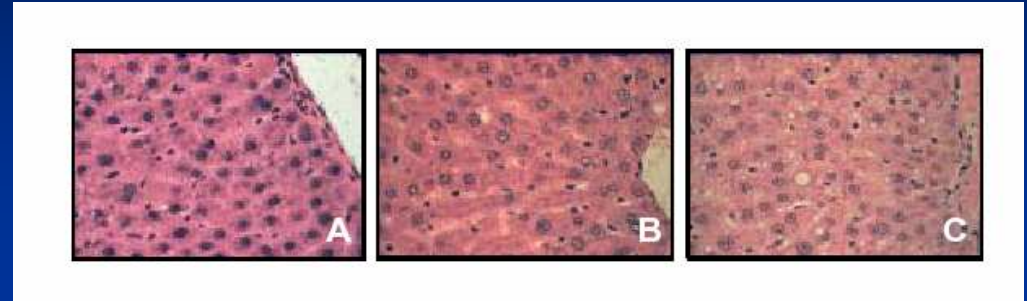
Fatty liver disease

- Non-alcoholic steatohepatitis is a common feature of the Metabolic Syndrome & toxic reactions to pharmacological drugs.
- Orotic acid supplementation induces fatty liver
 - disruption of Apo proteins production?
- Applied a genomic, proteomic and metabolomics approach to the problem



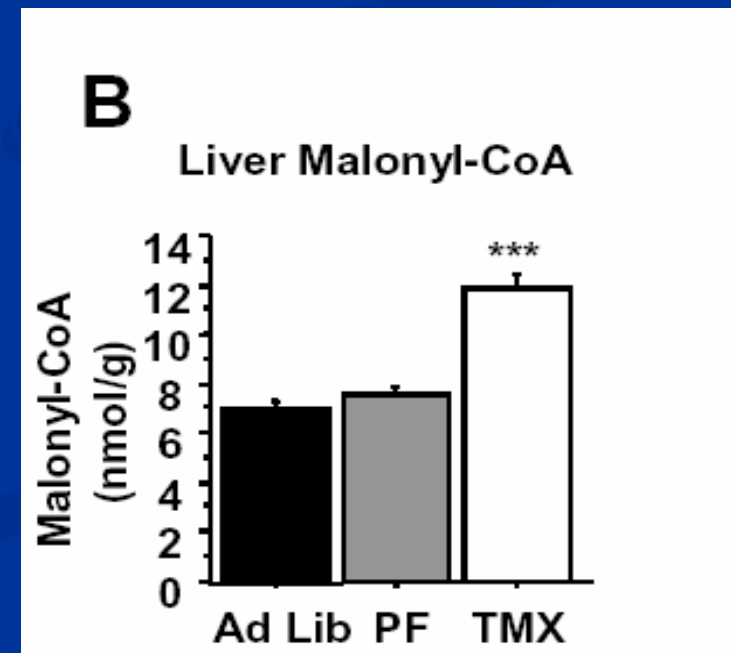
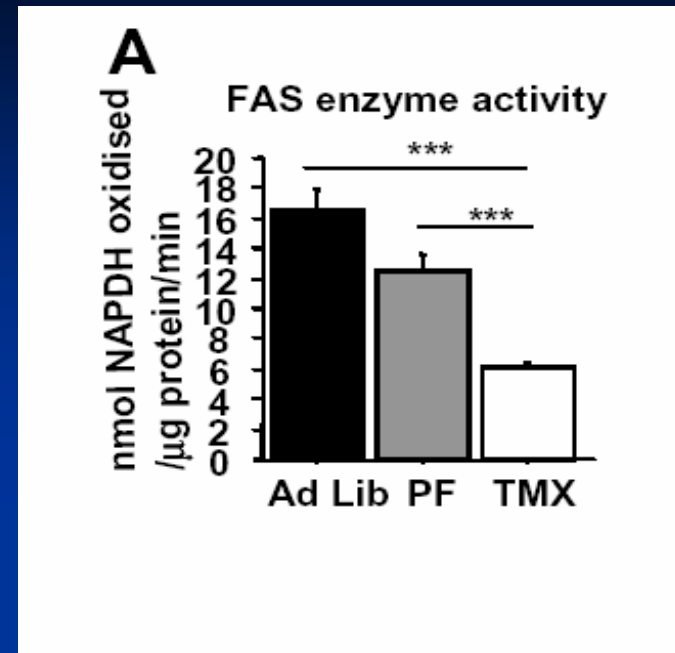
Fatty liver and tamoxifen....

- Tamoxifen, a widely-used anti-breast cancer drug, can induce NASH and changes in plasma cholesterol levels through unclear mechanisms.
- Studied primary actions of TMX using a short term treatment to induce early stages of NASH.
- A pair fed group was vital to this study
 - To avoid the 'usual suspects' being identified



Lelliott et al., Faseb J 2005 (with Toni Vidal-Puig, Clinical Biochemistry)

- Using a transcriptomics & metabolomics:
 - TMX downregulates FAS expression and activity (indicated by the accumulation of malonyl-CoA - known inhibitor of mitochondrial β -oxidation).
 - In the face of a continued supply of exogenous free fatty acid, the blockade of fatty acid oxidation produced by elevated malonyl CoA is likely to be the major factor leading to steatosis.

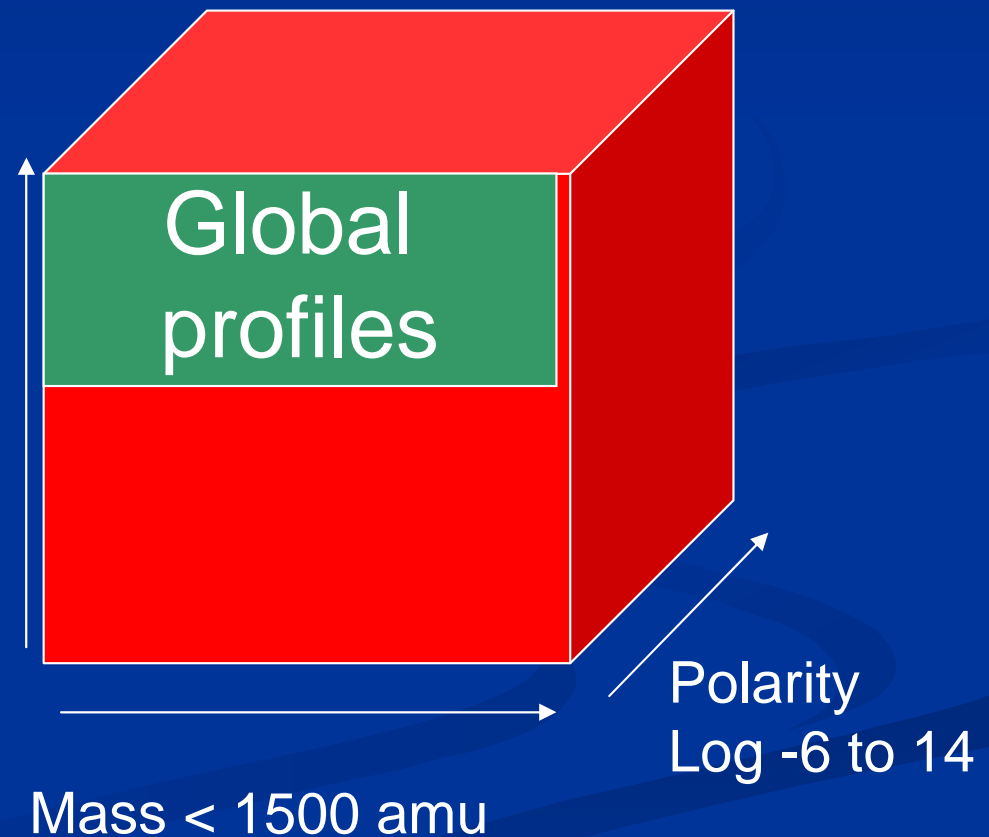


The challenges of metabolomics

- But malonyl CoA was spotted by DNA microarray analysis and not metabolomics!
- We need to improve our dynamic range to compete with the other -omes
- No one analytical tool is likely to give us a complete coverage of the metabolome

Conc. Range 10^9

NMR
GC-MS
LC-MS
Custom assays



“Standing on the shoulders of giants”

- But others have made significant progress in coverage of the metabolome
 - The aim of this forum is to provide an opportunity to exchange some experiences
 - And widen our shopping lists of metabolites



Thank you to...

- BBSRC for supporting this meeting through their E-science development fund
 - And allowing us to include wine as a consumable (twice)
- King's College
 - Especially Sarah Fowell
- GSK
- The Department of Biochemistry
 - The Griffin Group (especially Melanie Gulston for sorting out the accounts)
- The Industrial Sponsors:
 - ACD
 - BlueGnome
 - Bruker
 - Chenomx
 - Scynexis
 - Umetrics
 - Waters
- The speakers
 - But please keep to time!
- The audience
 - At 110 this will be one of the best attended metabolomic meetings in the UK