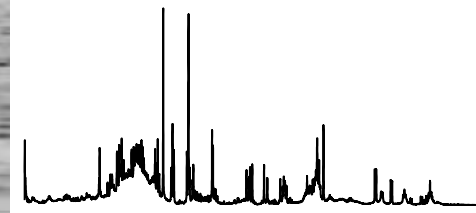
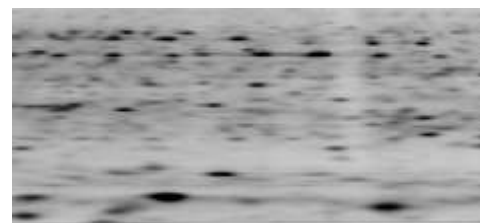
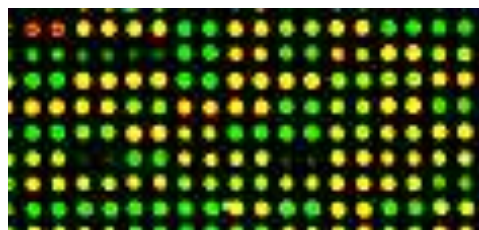
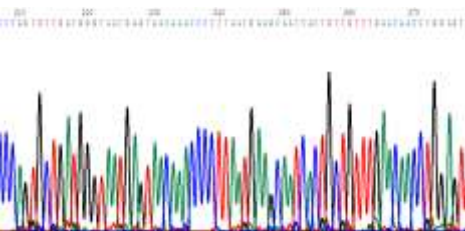
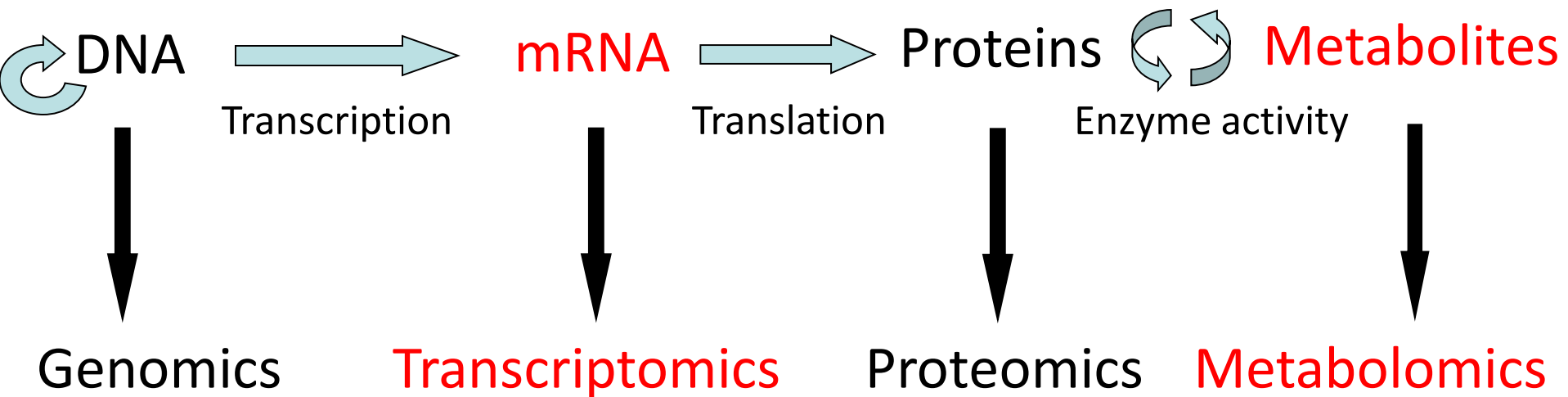
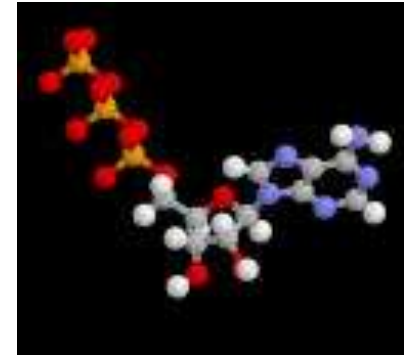
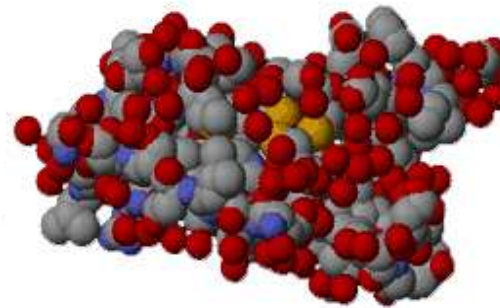
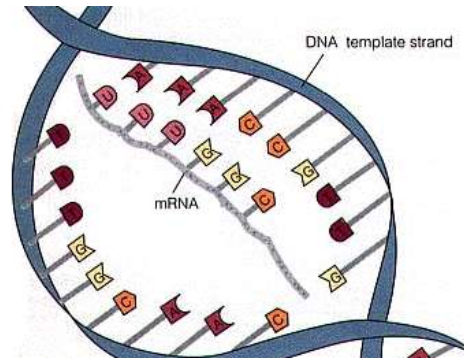
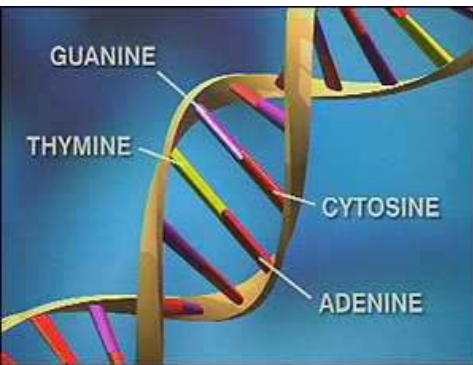


# Transcriptomic and metabolomic approaches to discover biomarkers of exposure and effect (ESR11)

Supervisors: Profs Kevin Chipman and Mark Viant

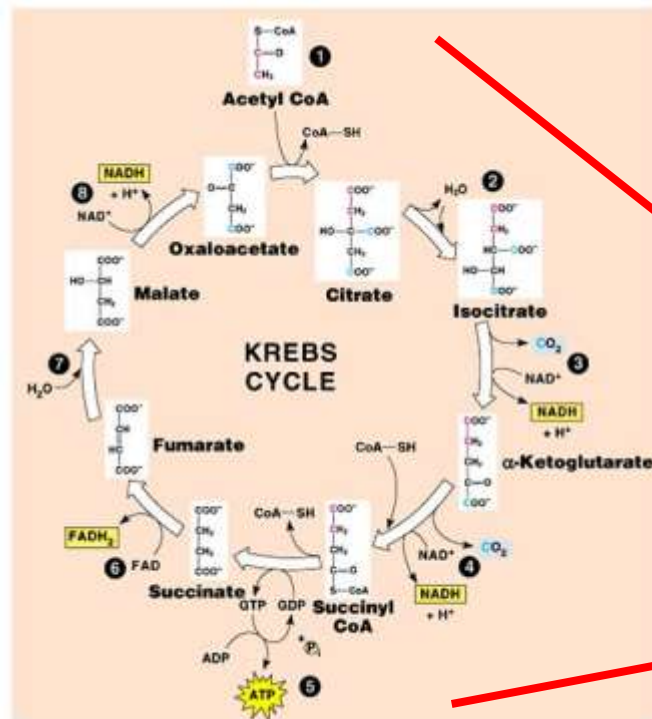
UNIVERSITY OF  
BIRMINGHAM

- Overall project goal: *to elucidate the molecular mechanisms via which FRs exert toxicity*
- Effects of FR-contaminated air and dust exposures will be studied using *in vitro* and *in vivo* models
- Exploit “omics” technologies (transcriptomics and metabolomics) and bioinformatics, and validate findings using targeted analyses

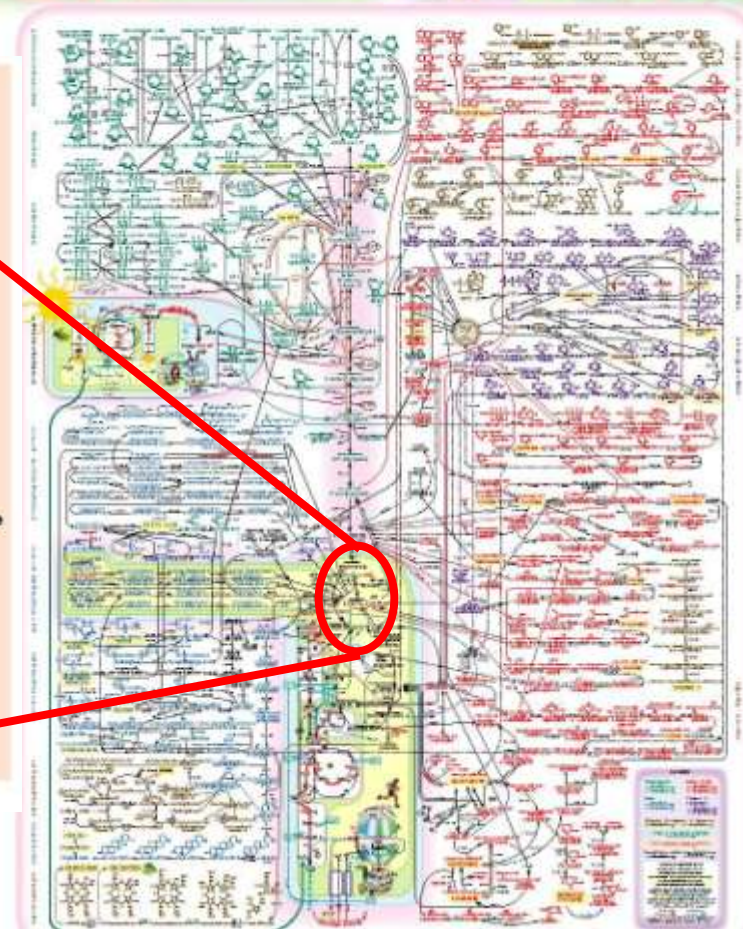


----- Non-targeted analysis -----

# Transcriptional and metabolic pathways (networks)



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# Linking Transcripts and Metabolites

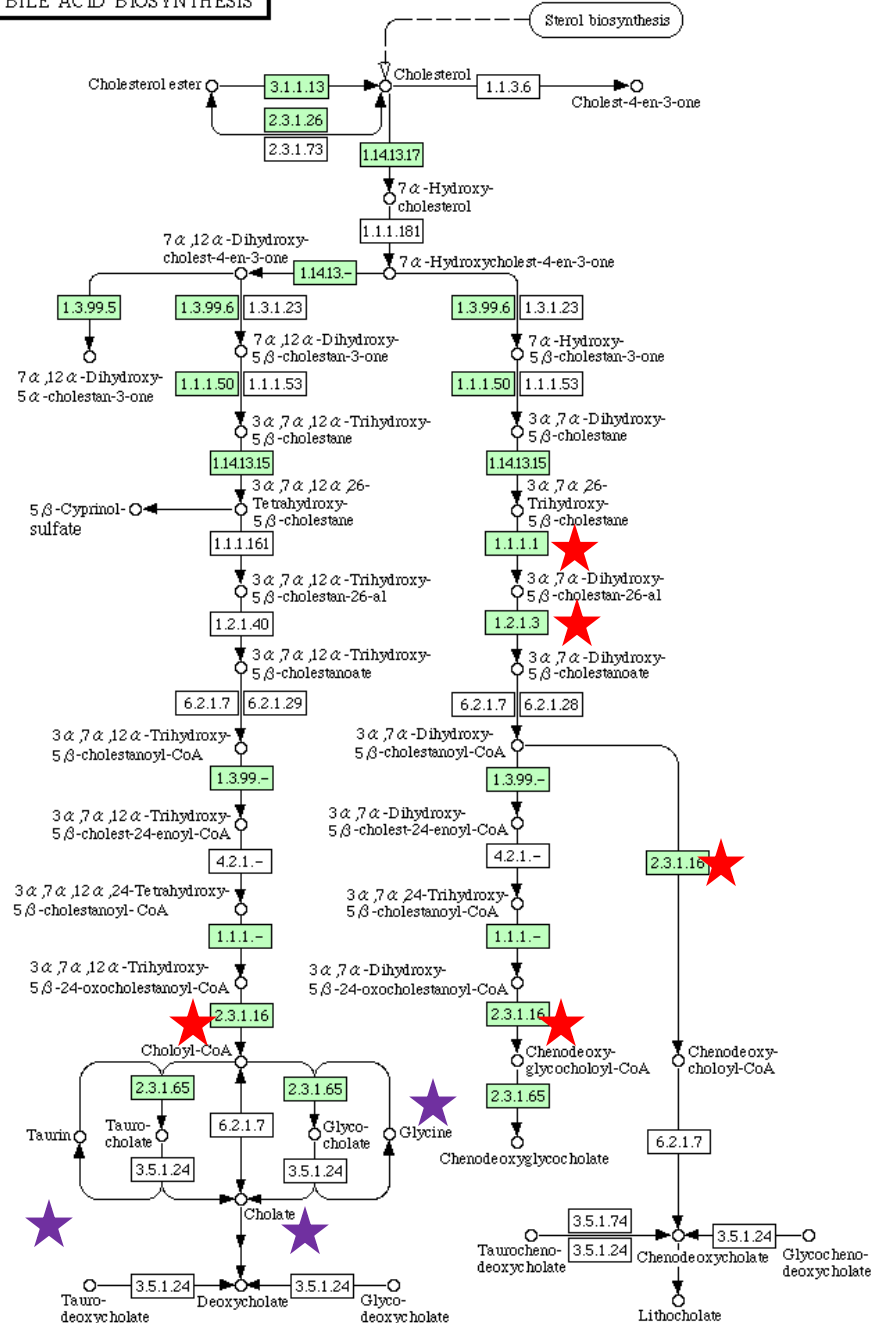


e.g. Bile acid biosynthesis

★ Red star = enzyme encoded by 1<sup>st</sup> neighbour gene

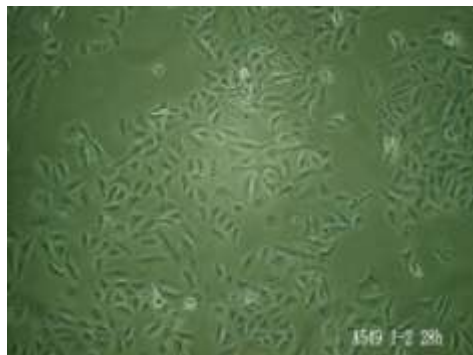
★ Purple star = metabolite identified

## BILE ACID BIOSYNTHESIS





# From discovery to targeted analyses



cell culture


“Omics” – Non-targeted discovery  
phase of research

1. Characterise molecular responses to FRs
2. Discover adverse effect pathways



Application of knowledge –  
targeted analysis of specific  
biomarkers

Transcripts: qRT-PCR  
Metabolites: LC-MS/MS



## ESR11 - Project

- Elucidate molecular mechanisms via which FRs exert toxicity
- Flame retardants
  - Informed by studies in WP1
  - Procured by collaboration with Stuart (UB)
- *In vitro* exposures
  - Cell lines, collaboration with UA (ESR10)
  - Cell lines, also at Birmingham (A549?)
- *In vivo* exposures
  - Murine asthma model, in collaboration with UvA (ESR12)
- Transcriptomics / FT-ICR MS metabolomics / bioinformatics
  - Oxidative stress, energetics, endocrine disruption, inflammation...
- Reveal mechanism; discover biomarker signatures
- Targeted analyses (qRT-PCR, LC-MS/MS)
  - Collaboration with UA to further develop LC-MS



## **ESR11 - Recruitment**

- Advertised since November 2010
- Considerable interest (1-2 potential applicants per week)
- Interviewed, but one appointable candidate took another post
- Advertising on-going
- Expect to interview again late February