

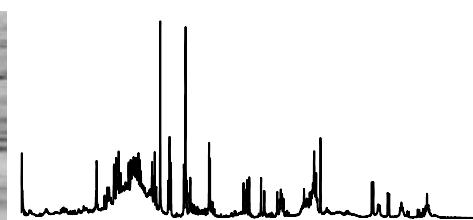
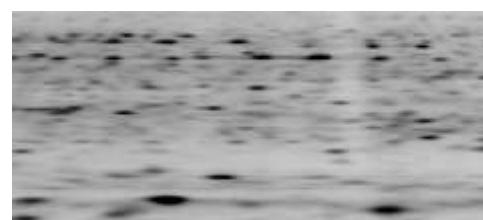
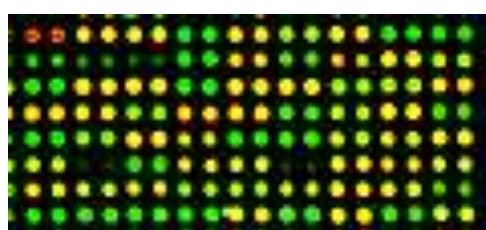
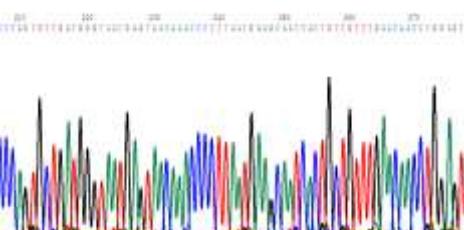
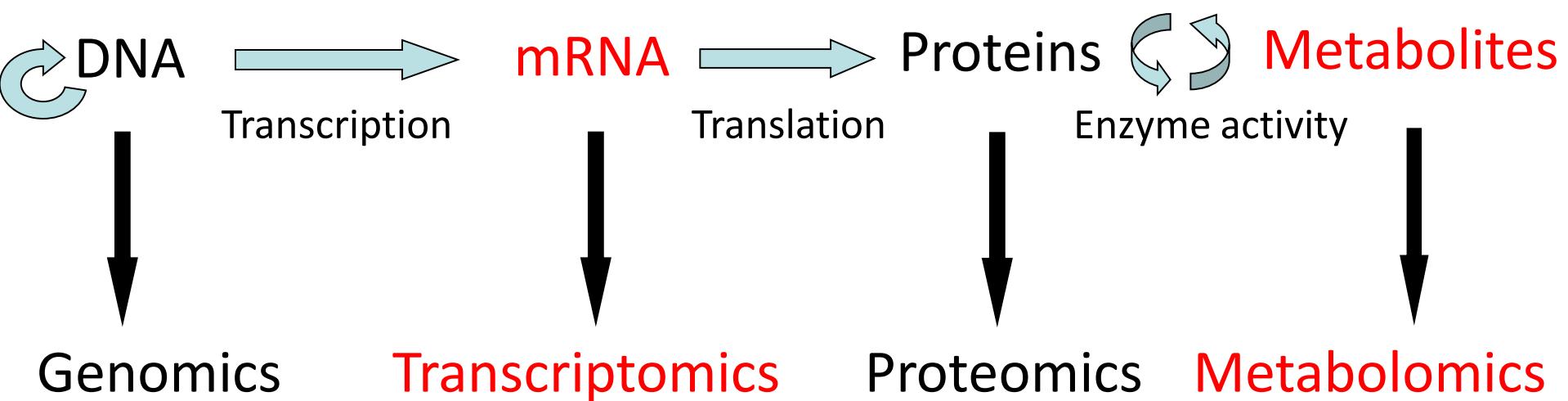
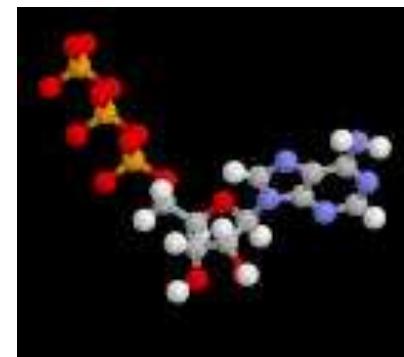
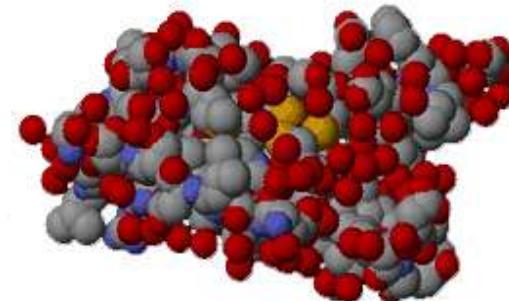
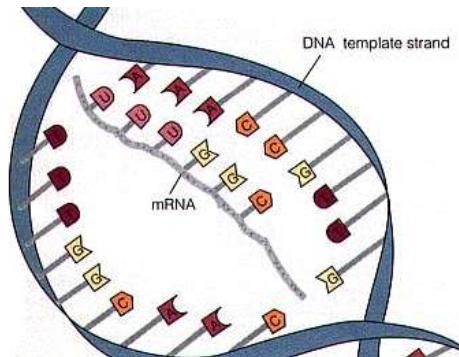
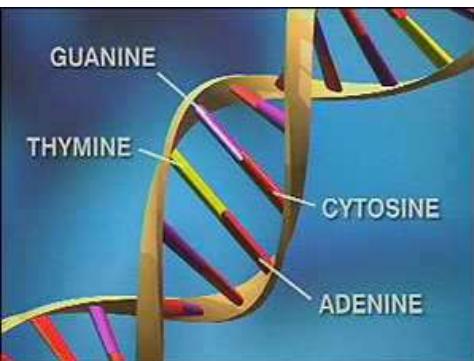


Transcriptomic and metabolomic approaches to discover biomarkers of exposure and effect (ESR11)

Supervisors: Profs Kevin Chipman and Mark Viant

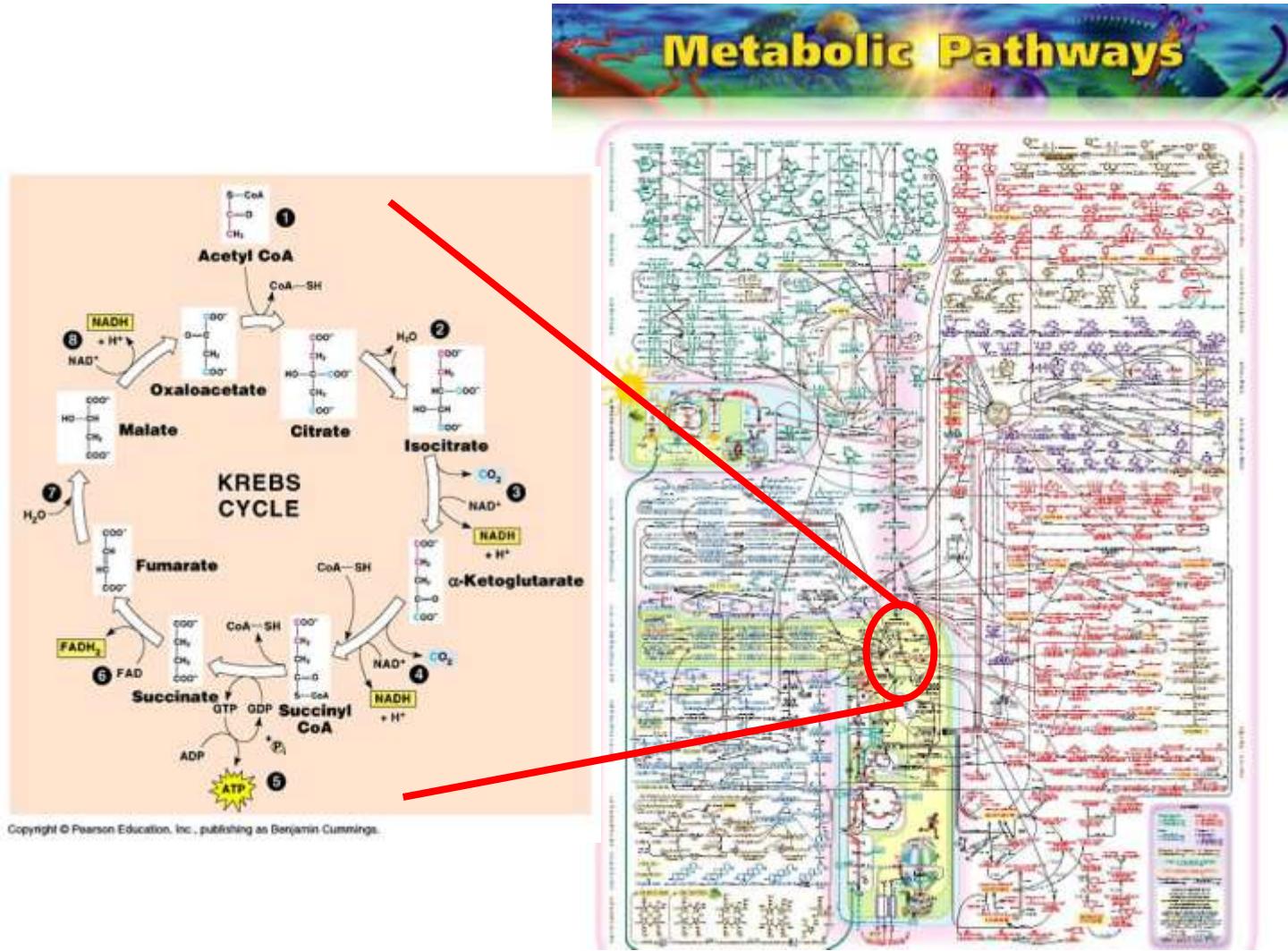
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- Overall project goal: *to elucidate the molecular mechanisms via which FRs exert toxicity*
- Effects of FR-contaminated air and dust exposures will be studied using *in vitro* and *in vivo* models
- Exploit “omics” technologies (transcriptomics and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



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

Transcriptional and metabolic pathways (networks)

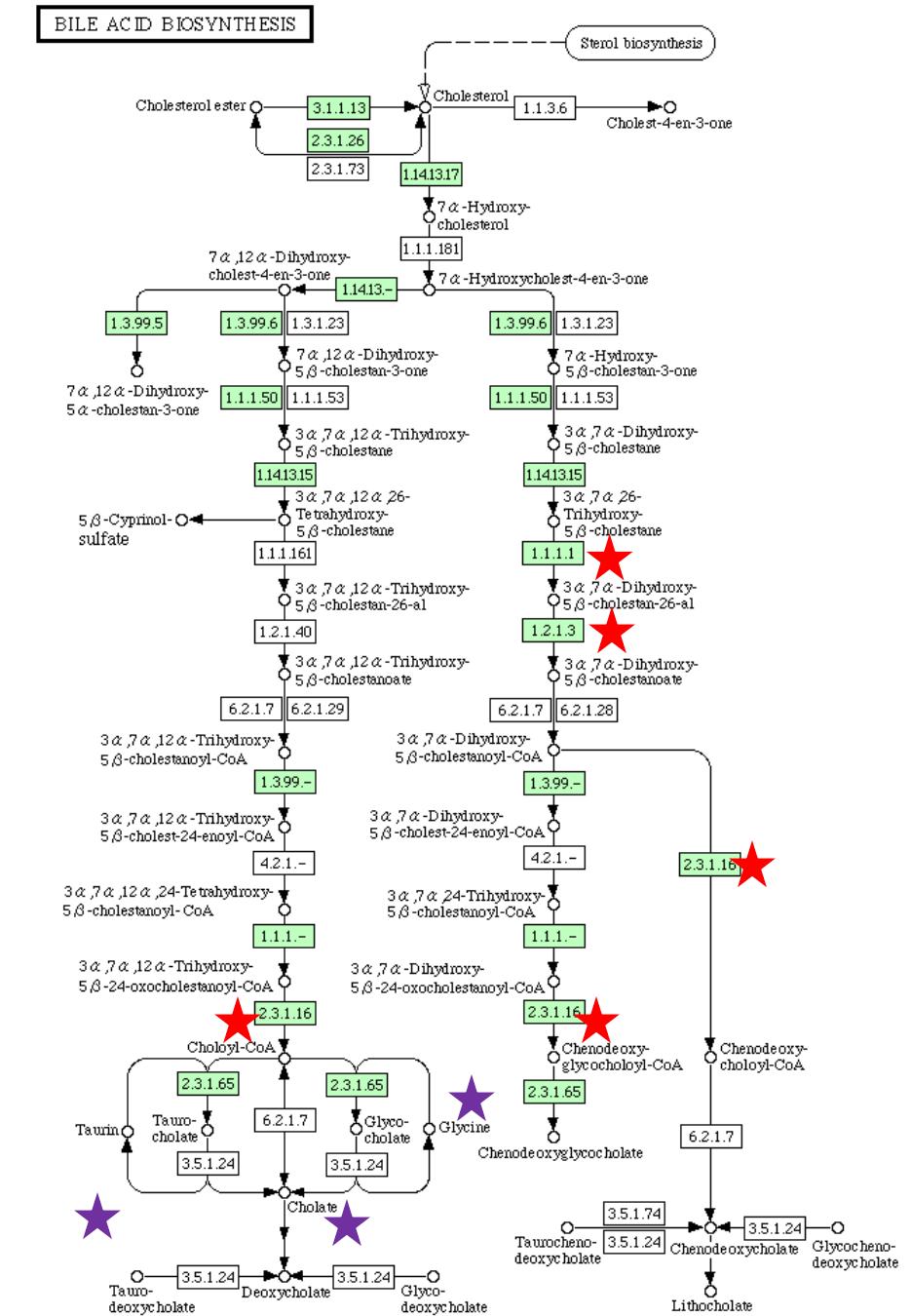


Linking Transcripts and Metabolites



e.g. Bile acid biosynthesis

- ★ Red star = enzyme encoded by 1st neighbour gene
- ★ Purple star = metabolite identified



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