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

At UB, this project will exploit two state-of-the-art complementary approaches for metabolomic measurements: direct infusion Fourier transform ion cyclotron resonance mass spectrometry (FT-ICR MS) and 1H nuclear magnetic resonance (NMR) spectroscopy. These will be used to study the metabolic consequences of air and dust exposures to several engineered eukaryotic and prokaryotic cell lines (in collaboration with ESR10). We will also study samples from a murine asthma model (ESR12) The transcriptomic analyses conducted in this project will focus on human and mouse Agilent microarrays. Raw data will be captured by Axon GenePix 4000B. Experiments will comply with MIAME/MGED. Data will be deposited in ArrayExpress using Maxdload2. Functional significance of gene expression changes will be assessed by hierarchical clustering and Gene Ontology using the Blast2GO. We will use qRT-PCR to quantify gene transcript levels of selected candidate genes. Bioinformatic analyses will identify combinations of molecular markers associated with specific treatments and phenotypic responses. Data analysis will be based primarily on multivariate methods, designed to select “optimal” subsets of features predictive of an outcome variable. Initially data will be analyzed by univariate hypothesis-testing techniques identifying differentially-expressed genes and metabolites across different exposure groups. This initial analysis will - combined with pathway analysis software tools - identify the pathways potentially involved in response to FRs. Modelling will be performed at the gene level as well as on indices of pathway activity in order to facilitate mechanistic interpretation.