UHN Microarray Centre

Publications using UHNMAC arrays for Gene Expression Profiling

A number of researchers have used UHNMAC arrays for genomic research including gene expression profiling using human, mouse, and yeast DNA microarrays, as well as the Immunarray and custom-printed arrays. This collection includes articles published since 2007; most recent articles are listed first (alphabetically)

Human cDNA arrays

References	Summary
Bane AL, *et al*. Expression profiling of familial breast cancers demonstrates higher expression of FGFR2 in *BRCA2*-associated tumors. Breast Cancer Res Treat 2009, 117(1):183	Using Human 19k arrays, Bane *et al*. profiled breast tumour RNA from *BRCA1* and *BRCA2* mutation carriers. The results of this study found that *BRCA1*-associated tumours had increased expression of component genes of the Notch and TGFbeta pathways and *BRCA2*-associated tumours had higher expression of FGFR2 and FGF1.
Behera RK, Nayak R. Expression Profiling of Nucleotide Metabolism-Related Genes in Human Breast Cancer Cells After Treatement wih 5-Fluorouracil. Cancer Investigation 2009, 27(5):561	The goal of this study was to determine the number of nucleotide metabolism genes regulated by 5-fluorouracil (5-FU), a widely used cancer drug, in the MCF-7 breast cancer cell line. This study identified novel genes, such as thioredoxin reductase, ectonucleotide triphosphate dephosphorylase, and CTP synthase, that are regulated by 5-FU, and revealed differentially expressed genes not involved directly in the known mechanism of action of 5-FU.
Hussein S, *et al*. Charaterization of human septic sera induced gene expression modulation in human myocytes. Int J Clin Exp Med 2009, 2:131-148	The Human 1.7k array was used to profile the gene expression of cultured human fetal cardiac myocytes with either 10% sera from septic patients or 10% sera from healthy volunteers. The septic sera resulted in the down-regulation of 178 genes and led to cell cycle, metabolic, transcription factor and apoptotic gene expression changes.
Peterkova M, *et al*. Microarray Analysis Using a Limited Amount of Cells. Folia Biologica (Praha) 2009, 55:53-60	This study evaluated various RNA isolation and amplification methods in order to obtain enough input RNA for microarray experiments from small samples. The study found that the combination of RNAqueous™ Kit (Ambion) and SenseAmp Plus Kit (Genisphere) produced the best results following microarray experiments using the Hum19k array.
Purbey PK, *et al*. Acetylation-Dependent Interaction of SATB1 and CtBP1 Mediates Transcriptional Repression by SATB1. Mol Cell Biol 2009, 29(5):1321	Special AT-rich binding protein 1 (SATB1) is a global regulator of gene expression that acts predominantly as a repressor via the recruitment of histone deacetylase 1 (HDAC1) complexes. This study has found that SATB1 and C-terminal binding protein 1 (CtBP1) form a repressor complex *in vivo*. Gene expression studies using cells in which both SATB1 and CtBP1 were silenced have indicated commonly targeted genes that could be coordinately repressed by the SATB1-CtBP1 complex.

Human cDNA arrays (continued)

References	Summary
Veitch ZW, *et al*. Induction of 1C aldoketoreductases and other drug dose-dependent genes upon acquisition of anthracycline resistance. Pharmacogenet Genomics 2009, 19(6):477	This study used microarrays and qPCR to identify genes whose expression can be correlated with the onset and/or magnitude of anthracycline resistance in breast tumour cells. The genes identified included the redox genes AKR1C2 and AKR1C3, in addition to genes associated with drug transport, cell signalling, cell proliferation or apoptosis, and protection from reactive oxygen species.
Anraku M, *et al*. Impact of Human Donor Lung Gene Expression Profiles on Survival after Lung Transplantation: A Case-Control Study. Am J of Transplantation 2008, 8(10):2140	This study identified the distinctive donor lung gene expression signature associated with primary graft dysfunction, a major cause of death after lung transplantation.
Borland MK, *et al*. Chronic, low-dose rotenone reproduces Lewy neurites found in early stages of Parkinson's disease, reduces mitochondrial movement and slowly kills differentiated SH-SY5Y neural cells. Mol Neurodegeneration 2008, 3:21	In this study, a differentiation protocol for human SH-SY5Y neuroblastoma that yielded non-dividing dopaminergic neural cells was developed. Following exposure to rotenone, a complex I inhibitor used in Parkinson's disease models, transcript expression was profiled using Human 19K cDNA arrays.
Camats M, *et al*. P68 RNA Helicase (DDX5) Alters Activity of *Cis*- and *Trans*-Acting Factors of the Alternative Splicing of H-Ras. PloS ONE 2008, 3(8):e2926	Using Human 19K cDNA arrays, researchers profile the gene expression of several knockdown models (including the knockdown of *hnRNP A1*, *FUS/TLS* and *hnRNP H*) to further investigate the role of p68 RNA helicase in the regulation of *H-Ras* expression and a vital transduction signal pathway linked to cell proliferation.
Chen L, *et al*. Gene expression profiling of early primary biliary cirrhosis: possible insights into the mechanism of action of ursodeoxycholic acid. Liver International, 2008, 28(7):997	Gene expression profiling using Human 19K cDNA arrays was performed to compare liver tissue from patients with primary biliary cirrhosis (treatment-naïve and ursodeoxycholic acid (UDCA)-treated patients). This study found that the effects of UDCA are mediated, at least in part, via a modulation of protein biosynthetic pathways.
Flatscher-Bader T, *et al*. Smoking and alcoholism target genes associated with plasticity and glutamate transmission in the human ventral tegmental area. Hum Mol Genet 2008, 17(1):38-51	This study utilised Human 19K cDNA arrays to identify genes sensitive to chronic alcohol abuse and smoking. This study, which found smoking induced the expression levels of vesicular glutamate transporters SLC17A6 and SLC17A7, concluded that plasticity within the VTA may be a molecular mechanism for the maintenance of smoking addiction and that alcohol, nicotine and co-abuse have distinct impacts on glutamatergic transmission.
Hauck TS, *et al*. Assessing the Effect of Surface Chemistry on Gold Nanorod Uptake, Toxicity, and Gene Expression in Mammalian Cells. Small 2008, 4(1):153	Human 10K cDNA arrays were used to examine the molecular changes of cells exposed to gold nanorods coated with polydiallyldimethylammonium chloride (PDADMAC). The finding that these nanorods have negligible impact on cell function suggests the nanorods are well suited for therapeutic applications, such as thermal cancer therapy, due to their tunable cell uptake and low toxicity.
Prasher B, *et al*. Whole genome expression and biochemical correlates of extreme constitutional types defined in Ayurveda. J Translational Medicine 2008, 6(48)	This article discusses Ayurveda, an ancient system of personalised medicine practiced in India since 1500 B.C., and whether the different constitution types described in Ayurveda have molecular correlates. This is a first attempt at integrating the clinical phenotyping principle of a traditional system of medicine with modern biology.

Human cDNA arrays (continued)

References	Summary
Wong V, *et al*. The effects of timing of fine needle aspiration biopsies on gene expression profiles in breast cancers. BMC Cancer 2008, 8:277	In order to examine a critical variable in DNA microarray experimentation, the timing of tissue acquisition, Wong *et al*. compared the expression data from biospecimens taken *in vivo* and *ex vivo*. The data shows that FOS-related genes, which have been associated with hypoxia and breast cancer development, were differentially expressed before and after surgery.
Bianchini M, *et al*. cDNA microarray study to identify expression changes relevant for apoptosis in K562 cells co-treated with amifostine and imatinib. Cancer Chemotherapy and Pharmacology, 2007,59(3): 349-360	Using Human 19K arrays for transcriptional profiling of cells treated with amifostine and imatinib (treatment for leukemia), researchers were able to identify a transcriptional repressor of survival genes that could potentially be helpful to overcome imatinib resistance. This study demonstrates the importance of *in vitro* testing of a novel drug combination most likely to predict its potential usefulness for *in vivo* application.
Cameron MJ, *et al*. Interferon-Mediated Immunopathological Events Are Associated with Atypical Innate and Adaptive Immune Responses in Patients with Severe Acute Respiratory Syndrome. J Virol, 2007, 81(16):8692	Researchers use gene expression signatures of patients with severe acute respiratory syndrome (SARS) to analyse host innate and adaptive immune responses during discrete phases of illness. A novel signature of high interferon (IFN)-α, IFN-γ, and IFN-stimulated chemokine levels, plus robust antiviral IFN-stimulated gene (ISG) expression, accompanied early SARS sequelae.
Haque T, *et al*. Gene Expression Profiling from Formalin-Fixed Paraffin-Embedded Tumors of Pediatric Glioblastoma. Clin Cancer Res 2007, 13(21):6284	This study found that gene expression profiling using archived formalin-fixed, paraffin-embedded tissue sample was possible in most (16 of 19) test samples and that the expression pattern was similar to that of fresh frozen samples.
Chattopadhyay I, *et al*. Gene expression profile of esophageal cancer in North East India by cDNA microarray analysis. World J Gastroenterol 2007, 13(9):1438	This study has identified differential gene expression in tumors isolated from patients with esophageal cancer. Most significantly upregulated genes were involved with the MAPK pathway, G-protein coupled receptor family, ion transport, and serine or threonine kinase activity, and most downregulated genes were involved with ribosome structure, endopeptidase inhibitor activity, cytoskeleton structure, antioxidant activity, acyl group transferase activity, and translation elongation factor activity. Several altered genes were also reported from a high incidence area of esophageal cancer in China.
Gilbert I, *et al*. A molecular analysis of the population of mRNA in bovine spermatozoa. Reproduction 2007, 133:1073	Researchers address the possible functional role for RNA transcripts present in spermatozoa, which are generally considered to be remnants of spermiogenesis. This study indicates that the sperm transcriptome harbors a complex mixture of messengers implicated in a wide array of cell functions and suggest that sperm RNA profiling could allow the molecular diagnosis of male gamete quality.
Panigrahi P, *et al*. Prebiotic bacteria change *Escherichia coli*-induced gene expression in cultured colonocytes: Implications in intestinal pathophysiology. World J Gastroenterol, 2007, 13(47):6370	This study used Human 19K cDNA microarrays to examine the expression profile of Caco-2 cells infected with strains of normal *E. coli* and *Lactobacillus plantarum*. The study concludes that commensal bacterial strains induced the expression of genes involved in important cellular processes, including regulation of transcription, protein biosynthesis, metabolism, cell adhesion, and apoptosis, and that such changes may influence physiologic and pathologic responses in the host.

Human cDNA arrays (continued)

References	Summary
Siriwardhana N, Wang H-CR. Precancerous carcinogenesis of human breast epithelial cells by chronic exposure to benzo[a]pyrene. Mol Carcinogenesis, 2007, 47(5):338	The molecular changes involved in the carcinogenesis of human breast epithelial cells induced by exposure to benzo[a]pyrene was studied to understand the effects of chronic exposure to environmental pollutants. Using Human 19K cDNA microarrays, researchers detected seven genes related to human cancers in B[a]P-transformed breast epithelial cells. In addition, this study verified that green tea catechin significantly suppressed B[a]P-induced carcinogensis.
Wong WW-L, *et al*. Determinants of sensitivity to lovastatin-induced apoptosis in multiple myeloma. Mol Cancer Therapeutics, 2007, 6:1886	Statins, commonly used to treat hypercholesterolemia, have the ability to trigger tumour-specific apoptosis in certain cancers including multiple myeloma (MM). This study shows that of a panel of 17 genetically distinct MM cell lines, half were sensitive to statin-induced apoptosis and, despite pharmacodynamic evidence of drug uptake and activity, the remainder was insensitive. This suggests that statins trigger apoptosis by blocking many signaling cascades, directly or indirectly deregulated by the oncogenic lesions of the tumour cell.

Yeast ORF arrays

References	Summary
Marin MJ, *et al*. Different modulation of the outputs of yeast MAPK-mediated pathways by distinct stimuli and isoforms of the dual-specificity phosphatase Msg5. Mol Genet Genomics 2009, 281(3):345	The Yeast 6.4k arrays were used to compare the expression profile of an msg5Δ mutant to that of the isogenic wild type strain during vegetative growth. When analysing the impact of Msg5, this study found that both Msg5 isoforms interact similarly with Slt2, whereas the long form binds Fus3 with higher affinity.
Molin C, *et al*. mRNA stability changes precede changes in steady-state mRNA amounts during hyperosmotic stress. RNA 2009, 15:600	This study investigates mRNA turnover rates and mRNA steady-state levels following hyperosmotic shock in *S. cerevisiae* cells. The MAP kinase Hog1 affects both steady-state levels and stability of stress-responsive transcripts, whereas the Hog1-activated kinase Rck2 influences steady-state levels without a major effect on stability. The study concludes that mRNA turnover is coordinated with transcriptional induction.
Cui Y, *et al*. Genome wide expression analysis of the CCR4-NOT complex indicates that it consists of three modules with the NOT module controlling SAGA-responsive genes. Mol Genetics and Genomics 2008, 279(4):323-337	Using deletions in seven of the *CCR4-NOT* genes, researchers used whole genome microarray analysis to determine the overall mRNA expression patterns that are affected by members of the yeast CCR4-NOT complex. The results of the study indicate that distinct portions of the CCR4-NOT complex control a number of cellular processes. Microarray analysis indicated that BTT1 and CAF130 correlate very highly in their control of gene expression and preferentially repress genes involved in ribosome biogenesis.
Hausmann A, *et al*. Cellular and Mitochondrial Remodeling upon Defects in Iron-Sulfur Protein Biogenesis. J Biol Chem, 2008, 283(13):8318	This study compared the global transcriptional responses to defects in three biogenesis systems in *S. cerevisiae* to define the integration of iron-sulfur biogenesis into cellular homeostasis. The results of the differential gene expression analysis indicated that mitochondria and their ISC systems serve as global regulators in iron-dependent processes.
Ilina Y, *et al*. Characterization of the DNA binding motif of the arsenic-responsive transcription factor Yap8p. Biochem J, 2008, Jun 26 [Epub ahead of print]	Using the Yeast 6.4K array, researchers determined the principal function of Yap8p, an AP-1-like transcription factor, is to control expression of *ACR2* (arsenate reductase) and *ACR3* (arsenite efflux protein) expression in response to arsenic. This study also characterised the DNA sequence targeted by Yap8p, a pseudo-palindromic sequence that is related to but distinct from the sequence recognised by other fungal AP-1 proteins.

Yeast ORF arrays (continued)

References	Summary
Schäfer G, *et al*. The *Saccharomyces cerevisiae* linker histone Hh01p is essential for chromatin compaction in stationary phase and is displaced by transcription. PNAS 2008, 105(39):14838	This investigation found a genome-wide anticorrelation between the level of bound linker histone Hho1p and gene expression in *S. cerevisiae*. Despite the importance of core histones in transcriptional regulation, this study suggests that Hho1p has only a limited role in transcriptional regulation.
Abruzzi K, *et al*. A Novel Plasmid-Based Microarray Screen Identifies Suppressors of rrp6Δ in *Saccaromyces cerevisiae*. Mol Cell Biol, 2007,27(3):1044-1055	To find suppressor genes in yeast, this study compares a traditional plate screen and a novel microarray enhancer/suppressor screening (MES) strategy. Both screening methods identified overlapping, but also different, suppressor genes. Only MES identified the novel mRNP protein Nab6p and the tRNA transporter Los1p, which could not have been identified in a traditional plate screen; both genes are toxic when overexpressed in rrp6Δ strains at 37°C.
Hickman MJ & Winston F. Heme Levels Switch the Function of Hap1 of *Saccharomyces cerevisiae* between Transcriptional Activator and Transcriptional Repressor. Mol Cell Biol 2007, 27(21):7414	This study found that Hap1, originally identified as a heme-dependent transcriptional activator, can also act as a repressor of three ERG genes under hypoxic conditions. The data found that Hap1 binds to ERG gene promotors while other experiments indicated that a corepressor (Tup1/Ssn6) is also required for repression.
Joseph-Strauss D, *et al*. Spore germination in *Saccharomyces cerevisiae*: global gene expression patterns and cell cycle landmarks. Genome Biology 2007, 8:R241	Using Yeast 6.4K arrays, researchers used expression profiling to follow the progression of spore germination and divide this process into two major stages; one in which spores respond only to glucose and the second in which cells respond to other nutritional components in the environment. Components of the mitotic cell cycle machinery are involved in spore germination but in a distinct pattern.
Koren A, *et al*. Autocorrelation analysis reveals widespread spatial biases in microarray experiments. BMC Genomics 2007, 8:164	Researchers conclude that spatial biases comprise a major source of noise in microarray studies and demonstrate the utility of autocorrelation analysis for the efficient identification and filtering of spurious chromosomal-position-dependent correlations. This study suggests that such biases may generate more than 15% false data per experiment. Computer simulations have shown that large spatial biases caused in the microarray hybridisation step can account for the observed spurious correlations, in contrast to previous suggestions.

Mouse cDNA arrays

References	Summary
Hill JJ, *et al*. Glycoproteomic analysis of two mouse mammary cell lines during transforming growth factor (TGF)-β induced epithelial to mesenchymal transition. Proteome Science 2009, 7:2	This study used proteomic approaches to find proteins that change in abundance upon the induction of epithelial-to-mesenchymal transition (EMT) by TGF-β in two mouse mammary epithelial cell lines. Cell adhesion molecules and regulators of cell signalling were among the proteins that were modulated during the EMT process. Mouse 15K cDNA arrays were used to validate the proteomic data.
Penaloza C, *et al*. Sex of the cell dictates its response: differential gene expression and sensitivity to cell death inducing stress in male and female cells. FASEB J 2009, 23:1869	By profiling the gene expression of mice at three points in their development (embryos before sexual differentiation, embryos after the first assertion of sex hormones, and pubescent mice), this study concluded that cells differ innately according to sex irrespective of their history to sex hormones. These differences may have consequences in the course of sexually dimorphic diseases and their therapy.

Mouse cDNA arrays (continued)

References	**Summary**
Pru JK, *et al*. Induction of proapoptotic gene expression and recruitment of p53 herald ovarian follicle loss caused by polycyclic aromatic hydrocarbons. Reprod Sci 2009, 16(4):347	Using Mouse 15k arrays, this study shows that exposure to polycyclic aromatic hydrocarbons (PAH) not only upregulates the ovarian expression of Bax, but of many other proapoptotic genes that function at multiple steps fo the cell death signalling pathway. The study also provides mechanistic insights into how PAH accelerate oocyte depletion.
Gerbe F, *et al*. Dynamic expression of Lrp2 pathway members reveals progressive epithelial differentiation of primitive endoderm in mouse blastocyst. Dev Biol 2008, 313:594	This study used a microarray strategy (involving Mouse 15K cDNA arrays) that combines transcriptome analysis of three stem cell lines and early embryos to isolate Lrp2 as a novel primitive endoderm precursor marker.
Marquis J-F, *et al*. Fibrotic Response as a Distinguishing Feature of Resistance and Susceptibility to Pulmonary Infection with Mycobacterium tuberculosis in Mice. Infect Immun 2008, 76(1):78	This study, which investigated the differential susceptibilty of DBA/2J (susceptible) and C57BL/6J (resistant) mouse strains to pulmonary tuberculosis, found that significant differentially expressed genes were associated with tissue remodeling and the fibrotic response.
Mamane Y, *et al*. Epigenetic Activation of a Subset of mRNAs by eIF4E Explains Its Effects on Cell Proliferation. PLoS ONE, 2007, 2(2):e242	The induction of eIF4E, an mRNA 5’ cap-binding protein, resulted in increased translation of specific mRNAs, including those that encode anti-apoptotic proteins and cell growth-related factors. By studying mRNA targets that are translationally responsive eIF4E, researchers were able to shed new light on the mechanisms by which eIF4E prevents apoptosis and transforms cells.
Yu Y, *et al*. Influence of murine maternal diabetes on placental morphology, gene expression, and function. Archives of Physiology and Biochemistry 2008, 114(2):99	Using Mouse 15K cDNA arrays, Yu *et al*. investigate the mRNA expression of diabetic mouse placentas and control placentas. Most of the differentially expressed genes identified are involved in metabolism, immunity and defence, and signal transduction.
Karar J, *et al*. Expression and functional activity of pro-oxidants and antioxidants in murine heart exposed to acute hypobaric hypoxia. FEBS Letters 2007, 581(24):4577	Using Mouse 15k cDNA arrays, this study provides insight on the cellular antioxidant defence mechanisms in murine heart under acute hypobaric hypoxia. Interestingly, a decrease in the protein level of Cyba, a subunit of NADPH oxidase (a major ROS generator in the heart) was found in AHH exposed heart.
Prasanna SJ, *et al*. Involvement of oxidative and nitrosative stress in modulation of gene expression and functional responses by IFN-γ. International Immunology, 2007, 19(7):867	Mouse 15K cDNA arrays were used to screen a mouse hepatoma cell line for IFNγ-modulated genes. This study revealed modulation of genes involved in oxidative and nitrosative stress (*iNos*, *gp91phox* and *Catalase*) and increased generation of reactive oxygen species (ROS) and reactive nitrogen intermediates (RNIs) upon IFNγ treatment. IFNγ-modulated genes can be categorised into two distinct sets: oxidative and nitrosative stress independent (transporter associated with *antigen processing 2*, *Cd80*, *Lmp10* and *Icosl*) and oxidative and nitrosative stress dependent (*iNos*, *gp91phox*, *Catalase* and *Id2*).

Immunarray

References	Summary
Baron C, *et al*. Prediction of Graft-Versus-Host Disease in Humans by Donor Gene-Expression Profiling. PLoS Med, 2007, 4(1):e23	By measuring the expression profiles of CD4+ and CD8+T cells from allogeneic hematopoietic cell transplantation (AHCT) donors, researchers tested the hypothesis that some donors may be "stronger alloresponders" than others, and consequently more likely to elicit graft-versus-host disease (GVHD). This study finds that pre-AHCT profiling segregates donors whose recipient suffered from GVHD or not and concludes that the ability to discriminate strong and weak alloresponders could pave the way to personalised transplantation medicine.

Custom arrays

References	Summary
Golkari S, *et al*. Microarray analysis of *Fusarium graminearum*-induced wheat genes: identification of organ-specific and differentially expressed genes. Plant Biotechnol J, 2007,5(1):38-49	This study investigated the transcriptome patterns of six organs (glume, lemma, palea, anther, ovary and rachis) dissected from infected wheat spikes after inoculation with the fungus *Fusarium graminearum*, the causal agent of fusarium head blight disease. Using custom-printed wheat cDNA arrays, researchers learned that each organ had a defined and distinctive profile in response to the fungal infection and they were able to uncover new up-regulated genes expressed in specific organs.