Poster abstracts

Teichmann, Ulrike

Development of a mouse-specific cDNA set for microarray gene expression analysis: differential gene expression in melanocyte lineage samples of the neural crest

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We are developing sets of mouse cDNAs with low redundancy for use in microarray analysis. The sets are based on sequence information from GenBank and the Washington University/Merck EST sequencing project. Related sequences from the non-redundant GenBank database were compared with mouse EST clones from the IMAGE consortium. A single EST for a given cluster was selected, colony purified and sequence validated. To evaluate this set of cDNAs for its use in differential gene expression studies, we generated cDNA microarrays. Those microarray slides were used in hybridization experiments using samples of the melanocyte-specific lineage of the neural crest as a model system. Gene expression was compared between RNA samples obtained from mouse melanoma tissue samples of a transgenic hepatocyte growth factor/scatter factor melanoma mouse model and a MEF-derived mouse fibroblast cell line (NIH3T3). Applying a confidence level of 99%, 8.5% of the arrayed genes were found to be differentially expressed. The melanocyte lineage marker genes *Dct*, *Pmel17* and *Sox10* are overexpressed in the melanoma samples with a ratio of 7.6, 6.9 and 7.8, respectively. A low expression ratio of 0.6 is seen for the fibroblast marker gene fibronectin. Genes encoding ubiquitin and the heat shock protein Hsc73 display no significant expression changes between the two differential samples.

Teng, Chi-Hse

Experimental designs using Affymetrix GeneChips

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Affymetrix GeneChip has been a popular and power tool for detecting mRNA transcripts to monitor genome-wide gene expression. Several sources of variability could have influence on the results, for example, different genetic background, RNA sample pooling, labeling/hybridisation processes, and different chips. Statistical concepts, randomisation, replication, blocking, and averaging, are introduced. Five experimental designs providing different information are demonstrated. Design 1 provides information on chip-to-chip variability. Design 2 provides information on treatment effects. Design 3 provides information on treatment effects and probe/chip-to-probe/chip variability. Design 4 provides information on treatment effects and individual/probe/chip-to-individual/probe/chip variability. Design 5 provides information on treatment effects, individual-to-individual variability, and probe/chip-to-probe/chip variability. The strength and weakness of each design will be discussed. These design

examples are intended to demonstrate the concepts rather than real scenarios. Different prior knowledge and assumptions will have an effect on the design choice.

Theilhaber, Joachim

Bayesian estimation of fold-changes in gene expression: the PFOLD algorithm and its uses in the analysis of complex expression profiles

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The relatively low signal-to-noise ratio prevalent in expression technology, typically in the range 2-5 when "signal" is defined as the median level of gene expression, makes quality metrics such as confidence intervals and statistical significance essential in interpreting the data. We present models for the several sources of noise which affect expression measurements, including cross-hybridisation and chip-to-chip variation, and discuss how the model parameters may be obtained on-the-fly, either from single-scan data or from replicate experiments. These noise models have been integrated into the PFOLD algorithm: this is a method, grounded in a Bayesian framework, which not only estimates fold-changes, but also assigns a statistical significance to the change through a *P*-value. We have found that the ability to make selections in the two-dimensional space of fold-changes/*P*-values (rather than fold-change alone) can greatly enhance the selectivity of detection. In turn, the PFOLD algorithm has been fully integrated into our suite of analysis tools called GECKO (Gene Expression Computation and Knowledge Organisation). Turning to the analysis of entire expression profiles, as obtained for instance from time-courses, we shall present results on cross-technology comparisons (e.g. Affymetrix vs. MD) and also on the biological reproducibility of expression profiles, including protocols for estimating false-positive rates in the presence of complex queries. We shall finally present some graphical methods for the display of expression profiles with moderate number of samples, including what we have called the "Gene Planet."

Van Belle, Patricia

Gene expression of RNA for b3 integrin and CD9 in malignant melanoma and melanocytic nevi, evaluated by cDNA expression array profiling

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The expression pattern of mRNA was investigated in a pooled set of seven human tumorigenic vertical growth phase (VGP) melanomas and a pooled set of nine compound or dermal nevi (benign melanocytic tumours) using the Atlas Human Cancer cDNA Expression Array system. We hypothesized that expression of mRNA for beta 3 integrin would be increased in melanomas compared with nevi, because this has already been demonstrated at the protein level. We studied 587 genes from 6 functional groups, and the results were compared between the two