epistem

Plucked Hair Biomarker Analysis

Reproducible Gene Expression Profiles from Plucked Hair

summary

Plucked hair is an attractive non-invasive surrogate tissue to aid drug development programs, particularly with respect to phamacodynamic biomarker discovery and clinical applications. With low intra- and inter-donor variation key to successful utility, Epistem can consistently demonstrate through robust methodologies, that variability is inherently low for a large majority of the expressed transcriptome.

Plucked Hair as Surrogate Tissue

Plucked scalp hair is an ideal surrogate tissue for measuring direct response to drug treatment. Highly vascularised, the hair follicle can respond to treatment within hours of exposure. The bulb region of plucked scalp hair predominantly consists of epithelial cells with rapid rates of proliferation. In addition, the genes and signalling pathways expressed in plucked hair indicate it is a highly relevant surrogate tissue to monitor drug response for solid tumours and inflammatory diseases.

Plucked Hair Reproducibility

As plucked hair mainly consists of epithelial cells, there is less variability in gene expression compared to blood which contains many different cell populations. However, some genes still remain highly variable in plucked hair. To reduce the effects of this innate variability and to yield accurate gene expression profiles, Epistem have developed robust sampling and gene expression analysis workflows. Underpinned by our proprietary amplification technology, RNA-Amp™, validated in BioMed Central Genomics (Rothwell *et al*. (2014) 15:1129), we can generate powerful gene expression information from single cell inputs of RNA. As a result we have successfully derived the number and quality of hair samples required to obtain reproducible results.

Our expert scientists have concluded that:

- Collection and analysis of plucked hairs in the anagen (growing) phase is required

- 3 to 5 plucked hairs per time point gives almost complete coverage of the transcriptome (demonstrated in figure 1)
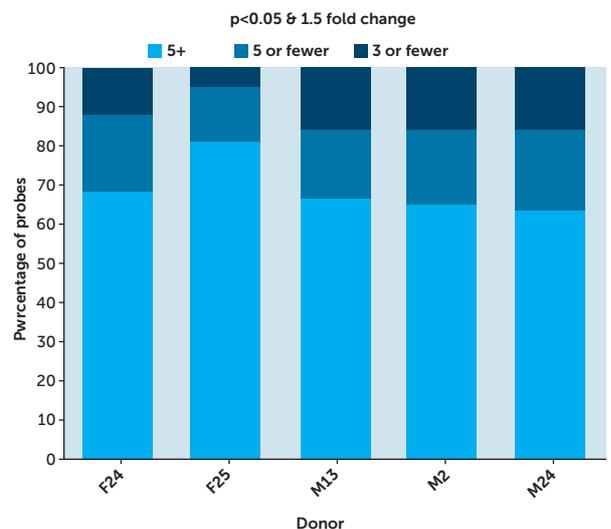

Figure 1: Percentage (Stdev) of U133 Microarray probes required to detect significant differential expression ($p<0.05$ & 1.5 fold change). Plucked hairs are grouped as 3 or fewer, 5 or fewer or 5+. Plucked anagen hairs (n=6) taken from 5 donors (3 males and 2 females). Donor hairs taken at 9am on two occasions (12 hairs per donor), 60 anagen hairs in total analysed via Affymetrix microarray.

Plucked Hair Biomarker Analysis

Male Hairs

A

RMA Expression Correlation

M3 Day1 1 (y-axis)
M1 Day1 2 (x-axis)
R2 is 0.9805

Female Hairs

B

RMA Expression Correlation

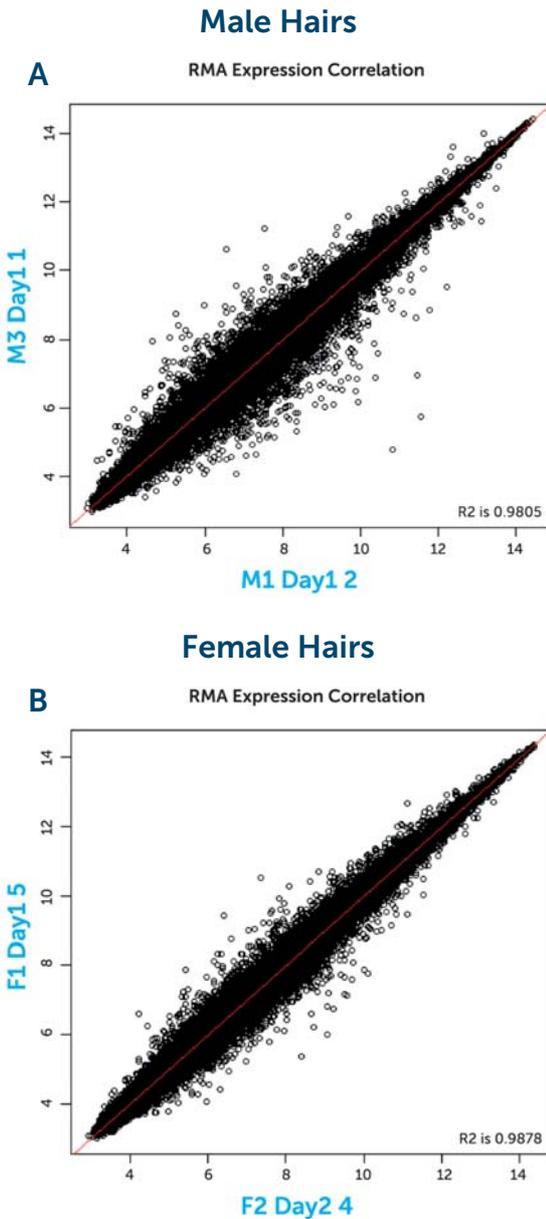*F1 Day1 5* (y-axis)
F2 Day2 4 (x-axis)
R2 is 0.9878

Figure 2: RMA expression correlations between two male donors on two different days (A) and between two different female donors on two different days (B).
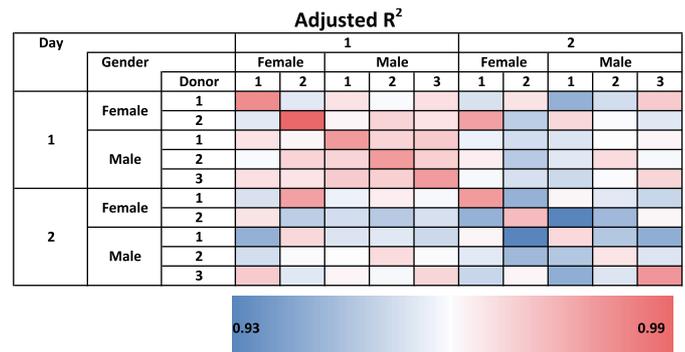
Contact us now to discuss how our expertise can aid your clinical biomarker strategies:

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Adjusted R^2

Day			1					2				
	Gender		Female		Male			Female		Male		
		Donor	1	2	1	2	3	1	2	1	2	3
1	Female	1										
		2										
	Male	1										
		2										
		3										
2	Female	1										
		2										
	Male	1										
		2										
		3										

0.93   0.99

Figure 3: Table showing average adjusted R^2 values across all hairs and days (n=5). Within a donor, hairs correlate between 0.97-0.99.

We have also demonstrated very strong correlations between genes expressed in hair both between donors and across days of samples taken (figure 2) and also within single donors (figure 3). This emphasises Epistem's expertise in reducing variability and achieving reproducible expression profiles in pharmacodynamic biomarker studies involving plucked hair.

Why Choose Epistem?

Our Expertise: Epistem Pharmacogenomics (PGx) provides high quality biomarker information to pharmaceutical and biotechnology companies from very limited quantities of RNA. We specialise in advancing drug development programs for oncology, inflammatory and fibrotic disease indications through our innovative plucked hair analysis and laser capture microdissection techniques as well as offering GCLP accredited gene expression and DNA genotyping services.

Outstanding Service: Our high level of expertise and customer focus has led to an enviable track record of providing biomarker solutions bespoke to our client's specific R&D requirements. We have worked with over 200 pharmaceutical and biotechnology companies worldwide and have developed long term collaborative relationships with several market leaders.

Quality Management: Our PGx laboratories are GCLP accredited.