

Analysis of global gene expression profile changes during the differentiation of the EpiDerm™ in vitro human skin equivalent. T.L. Street, PhD ¹, P.J. Hayden, PhD ², L. Hao, MSc ¹, J. Taylor, PhD ³, R. Copley, PhD ¹, J. Hein, PhD ³, M. Moffatt, PhD ¹ and W.OCM. Cookson, MD PhD ¹. ¹ Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, England; ² MatTek Corporation, Ashland, MA, United States and ³ Oxford Centre for Gene Function, University of Oxford, Oxford, England.

The EpiDerm in vitro human skin model is produced by culturing normal human epidermal keratinocytes (NHEK) on microporous membranes at the air-liquid interface (ALI). Beginning from an undifferentiated monolayer, the NHEK are induced to develop into a highly differentiated multi-layered epidermis possessing basal, spinous, granular and stratum corneum components. This study aimed to characterize the development of NHEK from basal cells to fully differentiated human epidermis by observing global gene expression profiles. Total RNA was extracted from triplicate samples of EpiDerm™ after 0, 3, 5, 7 and 10 days of differentiation. Gene expression profiles were analyzed using Affymetrix U133A microarrays, which contain over 22,000 gene-specific probes. Microarray data was preprocessed as per Affymetrix recommendations and filtered so only genes present in all three replicates at any one time point were included for further analysis. Genes showing statistically significant levels of expression between the five time points were selected using the Significance Analysis of Microarrays (SAM) method, and K-means clustering grouped these 1013 genes into 10 unique clusters. The expression data was integrated with known functional gene annotations and chromosomal localization information. It was observed that some of the clusters are highly enriched for genes with certain functions and/or chromosomal locations. For example, Cluster 6 contained the genes of the Epidermal Differentiation Complex (EDC) that are expressed late in epithelial differentiation from chromosome 1q21. These results offer a working knowledge of normal epidermal differentiation that may prove useful for advancing understanding of various epidermal disease states and for comparison to other epithelia such as those of the airways. *Funded by Wellcome Trust & MRC-HAMKA*

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