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Transcriptome variation in human keratinocytes and melanocytes regarding the genomic status of *CDKN2A* and *MC1R* genes

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To analyze the effect of germinal *CDKN2A* mutations or *MC1R* red hair colour variants in the transcriptome of human skin cell types. Keratinocytes and melanocytes were obtained from four familial melanoma patients: two were *CDKN2A* mutation carriers and two were *MC1R* variants carriers. RNA from keratinocyte cultures (containing also melanocytes) derived from each patient was extracted and analyzed with the Whole Human Genome Microarray 4x44K (Agilent). Differential gene expression analysis was carried out using the *limma* package from Bioconductor. Gene set analysis was carried out for the Gene Ontology terms and for the KEGG Pathways using FatiScan. Multiple testing adjustments of p-values were done according to False Discovery Rate method. Overall, 1535 transcripts were differentially expressed in *CDKN2A* mutated cells versus wild-type. Most of them were overexpressed (60.8%) in mutant cells. No pathway or molecular function was overrepresented in this subset of transcripts. In contrast, the downregulated genes group (39.2%) an overrepresentation of transcripts implicated in five molecular functions and Notch signanling pathway was observed. Comparison of *MC1R* variants carriers and non carriers found differences in 3570 transcripts. Upregulated group of transcripts (1954/3570; 54%) showed overrepresentation of 12 molecular functions and 16 pathways. Analysis of downregulated group of transcripts (1616/3570; 46%) identified three associated pathways. No molecular function was statistically significant in this group. In conclusion, both *MC1R* and *CDKN2A* genes modify the transcriptome of human skin cell types. The effect of MC1R variants in transcriptome variation is higher than a *CDKN2A* mutation.