

***Global Gene Expression Changes During Retinoic Acid-Induced Growth Arrest and Differentiation of Melanoma: Comparison to Differentially Expressed Genes in Melanocytes vs. Melanoma***

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**Background and Objective:** The incidence of malignant melanoma has significantly increased over the last decade. Some of these malignancies are susceptible to the growth inhibitory and pro-differentiating effects of all-*trans*-retinoic acid (RA). We sought to determine the molecular changes responsible for the biological activity of RA in melanoma.

**Methods:** Control and RA-treated B16 cells were harvested at 4, 10, 24, and 48 h of treatment. Melan-a melanocytes and B16 melanoma cells were harvested 72 h after seeding. Microarrays were used to identify differentially regulated genes.

**Results:** We discovered a set of 203 genes in which RA treatment altered the B16 expression toward the melan-a expression level. Functional analysis of these genes indicated that RA decreased expression of genes that encode proteins involved in carbohydrate and energy metabolism, DNA, RNA and protein synthesis, and cell cycle, and increased expression of genes involved in lipid metabolism, cell-cell signaling and cell differentiation.

**Discussion and Conclusions:** Our analysis of gene expression in B16 and melan-a cells showed that RA “normalized” the expression of genes involved in energy metabolism, DNA replication, DNA repair and differentiation. These results are compatible with the known growth inhibitory and pro-differentiating effects of RA.

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