Whole transcriptomic evaluation of SK-MEL-3 melanoma cells in response to histone deacetylase inhibitor trichostatin A.

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Malignant melanoma has a proclivity for resistance to radiation and chemotherapy drugs such as dacarbazine or kinase inhibitors that target RAS-independent auto-activated serine/threonine kinase, a consequence of somatic missense mutant BRAF V599E. An underlying controlling component of aggressive melanoma is a change to the epigenetic histone landscape to which overexpression of histone deacetylases (HDACs) has been attributed. The full effects of direct inhibition of HDAC on the entire transcriptome are not well understood, yet there is growing number of synthetic drugs classified as HDAC inhibitors (HDACis). In this work, we evaluated the whole transcriptome response in SK-MEL-3 human melanoma to trichostatin A using both Affymetrix 2.1 Human Arrays and 4.1 miRNA chips. TSA was confirmed as a potent HDAC inhibitor in nuclear lysates, and in cells trichostatin A (TSA) [10nM] at sublethal concentrations were used for to evaluate transcriptomic shifts at 24 hours exposure. Of interest, the data show no changes to the expression of 12 HDAC transcripts (HDACs subtypes 1-12) or B-raf protooncogene V599E by TSA. In contrast, TSA evoked differential expressed changes with 833 up-regulated and 810 down-regulated genes. The top 10 up-regulated genes were TSPAN13, SERPINI1, ATP1B2, NMAPT2, PDGFRB, CYP1A1, PARM1, SCG2, SYT1, ROPN1L and top 10 down-regulated genes GALNT3, CA14, BCL2A1, TRPM1, PYCARD, UBAIP1L, GPX8, IL-6, TP53, SERPINH1. Functional pathway analysis shows TSA effects to negatively impact cell survival systems, cell cycle progression, migration and biological pH buffering specifically that of carbonic anhydrase 14. These changes occurred concomitant to an elevation of miRs 185-3p, 4783-3p, 6716-3p and reduction of miR-6795-5P. In conclusion, data from this work provide an overall effect of TSA on the whole transcriptome of coding and non-coding RNA in malignant melanoma.

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