Characterization of the role of the endocannabinoid system in human melanoma cells

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Cannabinoid signaling regulates cell proliferation, differentiation and survival, with different outcomes depending on the molecular targets and cellular context involved (Galve-Roperh et al., 2013). In the current study, we investigated the role of the endocannabinoid system in human cutaneous melanoma, a skin cancer with high metastatic potential, enhanced heterogeneity, and resistance to chemotherapy (Santini et al., 2014). Model systems used in this study included normal human epidermal melanocytes, different melanoma cell lines, patient-derived primary melanoma cells and melanoma stem cells. Quantitative real-time PCR analyses demonstrated that cannabinoid receptor type 1 (CB_1) was expressed in melanoma cells, primary melanoma cultures and their correspondent melanoma stem cells (melanomaspheres) harboring $BRAF^{V600E}$ mutation, while BRAF-wild type parental cells, their correspondent melanoma stem cells, and normal melanocytes did not express or expressed CB1 at low levels. Noteworthy, CB_2 expression was not found in the tested cell lines. We also demonstrated significant expression levels of genes that code for enzymes involved in endocannabinoid biosynthesis and degradation in the BRAF mutant A375 cells. To clarify CB_1 function, we knocked-down CB_1 in A375 cells using two independent CB1 short hairpin RNA (shRNAs) (LV-shCB1-1 and LV-shCB1-2). In the CB_1-depleted cells we observed a significant reduction in cell growth and in the clonogenic ability of the cells. In conclusion, our findings suggest a possible role of the endocannabinoid system in the phenotype of metastatic melanoma cells.

REFERENCES

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