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Combination treatment with ornidazole and dacarbazine inhibits proliferation, cell migration and induces DNA damage in melanoma cells

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Metastatic cancers are responsible for 90% of cancer related deaths and melanoma is known as one of the deadliest cancers. Dacarbazine (DTIC) for metastatic melanoma has become an approved first-line treatment in routine clinical practice. However, response rates to single-drug therapy with dacarbazine are quite low. Therefore, combination drug therapy as a method of treatment that combines two or more therapeutic agents is the cornerstone of cancer therapy. Here, we examined the effects of the combination of ornidazole, a derivative of 5-nitroimidazole which is active against protozoa and anaerobic bacteria, and DTIC on melanoma cells to investigate novel advanced combination therapies for melanoma. Doses in this study are 0, 800 and 1200μg/mL for ornidazole, 0, 5, 25, 50, 100, 200, 300, 600, 1200μM/L for DTIC and 800μg/mL+100μM/L, 800μg/mL+200μM/L, 1200μg/mL+100μM/L, 1200μg/mL+200μM/L for ornidazole+DTIC combination. Treatment effect of ornidazole and DTIC as a single-agents and in combination on cell viability was investigated with crystal violet and MTT assays. As well as the effect of them on migration ability was assessed by wound healing assay, the effect of them on DNA damage induction was evaluated by comet assay in B16F10 melanoma cells *in vitro*. Our data showed that combination treatment with ornidazole and DTIC markedly inhibited cancer cell proliferation and migration. DNA damage was also significantly induced by this combination treatment. Our study showed that ornidazole/DTIC combination drug therapy has more effective therapeutic potential for melanoma compared to DTIC therapy alone. In conclusion, our findings suggest that combination therapy with ornidazole/ DTIC could serve as a new and valuable approach for melanoma treatment.

Keywords: Cancer cells, Combined therapy, Tumour targeting

Melanoma has the highest mortality rate of all skin