

6th World Congress on

DERMATOLOGY

May 29-30, 2023 | Paris, France

Effects of CTCE-9908 and MAZ-51 on the metastasis of melanoma

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Melanoma is a relentless form of cancer, which predominantly spreads via the lymphatic system and accounts for 1-2% of all cancer-related mortality globally. The metastatic behaviour of these malignancies has accentuated the need for specific therapeutic targets to inhibit metastasis. Tumour cells overexpress lymphatic growth factors namely vascular endothelial growth factor C (VEGFC) and vascular endothelial growth factor-D (VEGF-D). VEGF-C and VEGF-D enhance tumour cell metastasis. VEGF-C/D binding to vascular endothelial growth factor receptor-3 (VEGFR-3) on the tumour cell. Overexpression of VEGF-C/D regulates the expression of a chemokine receptor CXCR-4 on the tumour cell. The phosphorylation of CXCR-4 to CXCL12 and VEGFR-3 to VEGF-C/D activates signalling pathways such as PI3K/AKT and MAPK that promote tumour cell proliferation and adhesion. 3-(4-Dimethylamino-naphthalen-1-methylene)-1,3-dihydroindol-2-one (MAZ-51) inhibits phosphorylation of VEGFR-3. MAZ-51 limits proliferation and activates apoptosis in cancer cells, preventing cancer cell metastasis

through the lymphatic vasculature. CTCE-9908, is a CXCR-4 antagonist which hinders CXCR-4 phosphorylation and is derived from human CXCL12. The research project entails cell culture-related laboratory experimental work on melanoma B-16F10 cell line in vitro. The work will be further translated to mouse in vivo models. Furthermore, mathematical modelling will be used to predict the effects of the compounds. Mathematical models are incorporated in this study due to the current trend in laboratory-based-research moving towards computational design based on mathematics modelling. The use of MAZ-51 and CTCE-9908 and in combination will hopefully hinder tumour metastasis and may prove to be a useful in the therapeutic approach of melanoma metastasis.

Keywords: 3-(4-Dimethylamino-naphthalen-1-methylene)-1,3-dihydroindol-2-one; adhesion; melanoma; endothelioma; vascular endothelial growth factor receptor-3; CXCR-4, CXCL12 and CTCE-9908.

Biography

Yvette Nkondo Hlophe is in the field of cancer therapeutics, with a specific focus on combination treatments used to inhibit melanoma and undifferentiated neuroblastoma adhesion in vitro and in vivo.

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