

EVALUATION OF CCR5 INHIBITION IN BREAST CANCER USING NOVEL, POTENT INHIBITORS

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Background: Targeting the chemokine CCL5 and its receptor CCR5 has emerged as a promising strategy in the treatment of breast cancer. Different approaches are studied today to inhibit or slow down the growth of cancer cells using the CCL5/CCR5 axis. Inhibition of the CCL5/CCR5 has demonstrated the promising results in preclinical studies and early-phase clinical trials for breast cancer treatment. Small molecule inhibitors targeting CCR5, such as maraviroc, have been investigated for its ability to block the interaction between CCL5 and CCR5, thereby inhibiting cancer cell proliferation, migration, and invasion. CCL5 5p12 5m is a highly potent CCL5-based CCR5 antagonist, at least a 1000-fold more potent than MVC in cellular HIV-1 inhibition assays (Vangelista et al., 2006). We expect that CCL5 5p12 5m will potentially exert a superior inhibitory activity, as compared to MVC, therefore furthering the development of a novel lead compound in the fight to anti-cancer drug development.

Materials and methods: Cell culture; FACS analysis; Western Blot; MTT proliferation assay; Cell scratch assay were conducted as previously described (Zhang et al., 2009). MDA-MB-231 and MCF7 cells were used for this project.

Results: The expression of CCR5 have been found in both MDA-MB-231 and MCF7 cell lines through FACS and Western Blot analysis. MCF7 cell proliferation was significantly inhibited with CCL5 5p12 5m treatment at the concentration 100 ng/ml, whereas no significant effect on MDA-MB-231 cell proliferation were found. The effect of CCL5 5p12

5m at 10 ng/ml concentration demonstrated inhibitory effect on cell migration potential in comparison to MVC in both cell lines.

Conclusion: The obtained results demonstrated that CCL5 and CCR5 interaction may support breast cancer progression by stimulating cell growth of MCF-7 cells. Our findings proved that CCR5 antagonist CCL5 5p12 5m has superior effect in inhibition of growth rate in one of the cell lines (MCF-7) in comparison with MVC. The findings also demonstrated an antagonistic effect on cell migration for both cell lines. The additional study may be necessary to shed more light on the inhibitory effect of the CCL5 5p12 5m on breast cancer inhibition.

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