Effects of Therapeutics on Cell Migration

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Myelodysplastic syndrome (MDS) is a group of cancers in which stem cells in the bone marrow have a clonal advantage and cause irregular maturation of blood cells. Dysplastic cells cannot migrate from the bone marrow to the blood. HL-60 cells, a cell line of immature neutrophils, were transduced with a lentivirus, causing miRNA-378 knockdown. This miRNA was chosen since it was found to be under-expressed in MDS. These cells, called “Zip” cells, are found to be an accurate model for MDS in the lab due to their defects in migration. HL-60 cells were additionally transduced with a random vector, “Scr” cells, to act as a control to the lentivirus. The cell model was used to test for therapeutics that could alleviate the MDS phenotype. LB-100, a PP2A inhibitor, was chosen to asses this problem since PP2A inhibits the AKT pathway which is under-expressed in MDS. Therefore, by inhibiting the inhibitor of the AKT pathway, we hoped to activate it. HL-60, Scr, and Zip cells were incubated overnight with and without LB-100. Then, a migration experiment was performed with a trans-well plate. A significant increase was found in HL-60 and Scr migration due to LB-100 ($p=0.009$ and $p=0.012$, respectively). However, there was no significant increase in Zip migration ($p=0.729$). Since LB-100 did not significantly reverse the MDS phenotype, it would not be an effective drug for treatment. One possibility for this result was that the AKT pathway was activated; however, a different pathway downstream was also affected. The experiment must be repeated in order to confirm these results.

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