

Lay Summary

Our proposal examined characteristics of a type of stromal cell called the mesenchymal stem cell which lends support to the survival and proliferation of acute leukemia cells in the marrow. We found that such cells isolated from acute myelogenous leukemia (AML) patients had a different pattern of expression of lipid (fat) . This was confirmed also by genetic approaches. When expression of these genes was modulated, there was evidence that the fat forming tendency of these cells could be reversed, and their ability to support cells that grow into leukemia blasts could be suppressed. Based on this, we will continue to examine how inhibition of these lipid stimulating pathways can be used to curtail leukemia cell growth. We also examined whether stromal cells express two pathways thought to be important for leukemia cell growth; the mTOR pathway and the NF-kappa B pathway. While both of these pathways are expressed and can be effectively inhibited in endothelial cells and stromal cells from AML patients, we also found that inhibiting these pathways concurrently could reduce their individual effectiveness in suppressing AML growth. We are therefore continuing to examine how suppression of these pathways