University of Utah
UNDERGRADUATE RESEARCH JOURNAL

IS ALTERED AUTOPHAGY THE CAUSE OF CELL DEATH IN AML CELLS FOLLOWING SIRT5 KNOCKDOWN?

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Acute myeloid leukemia (AML) is a blood cancer with an overall 5-year survival rate of less than 30%. Chemotherapy remains the main treatment approach, and major advances in AML treatment and patient survival are yet to be seen. Preliminary work by our team identified sirtuin 5 (SIRT5) as vital for the survival of leukemia cells from most AML patients and AML cell lines. SIRT5 is the only enzyme known with desuccinylase, demalonylase, and/or deglutarylase activity, making it an intriguing target for inhibitor development. Autophagy was identified as a pathway of interest since these cells were recently shown to continue proliferating despite greatly reduced RNA and protein synthesis. To begin to understand the function of SIRT5 in the context of AML biology, we measured autophagy in the presence and absence of SIRT5 in various AML cell lines to determine its relevance to the life and death of these cells.

Autophagy is the process by which cells recycle macromolecules, and this includes the formation of an autophagosome that eventually fuses with the lysosome, an organelle of very low pH and destructive capabilities. The impact of SIRT5 knockdown on autophagy was measured using various methods including: flow cytometry, fluorescence microscopy, western blot analysis, and MTS assays.