Nutrient Starvation-Induced Cancer Cell Death in Acute Myeloid Leukemia Cells

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Cancer cells metabolize some basic nutrients, such as glucose, differently than normal cells do. Recently, investigation on cancer metabolism has increased due to the discovery of new metabolic targets in many types of cancer cells. Treatment through these targets could be a promising approach for curing cancer patients and should have lower toxicity than conventional methods. In this project, the effect of nutrient deprivation on the growth of two acute myeloid leukemia (AML) cell lines was investigated. The results from cell proliferation assays, cell cycle analyses and apoptosis measurements demonstrated that arginine and glutamine deprivation both inhibit AML cancer cell growth, but that arginine deprivation had a larger effect. A western blot analysis of various signal transduction proteins showed that P-S6, an important protein for regulating cell growth, was down-regulated in glutamine and arginine deprived cells but unchanged in glucose deprived cells. A proteomic analysis was conducted to compare protein expression levels between nutrient deprived and non-deprived cancer cells. This analysis indicated that arginine deprivation produced more abnormally expressed proteins than other nutrient deprivations, which may be linked to the greater apoptotic rates seen in arginine deprivation and shows that targeting arginine metabolism may represent a better path to pursue than glutamine deprivation in the cells studied. In addition, this analysis revealed that many proteins, such as histones that are important in gene regulation, showed different changes in their expression level upon depletion of different nutrients. These results should provide useful information for further investigation on cancer cell metabolism and discovery of drug targets and biomarkers.

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