

## ME1 DEFICIENCY PRIMES FOR FERROPTOSIS

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T-016416

**Background:** Synovial sarcoma is a rare soft tissue sarcoma that most commonly affects young adults. Like many other cancers, there are currently no targeted chemotherapies for synovial sarcoma. Current treatment often consists of a combination of surgery, radiation therapy, and chemotherapy. The method of detecting the absence or presence of malic enzyme 1 (ME1) in cells could lead to a targeted treatment for synovial sarcoma as well as other cancers.

**Technology Description:** Dr. Brian Van Tine and his team at Washington University have developed a method of determining treatment for cancer cells, such as synovial sarcoma, by determining the absence or presence of ME1. Synovial sarcoma cells deficient in ME1 are dependent on glucose-6-phosphate dehydrogenase (G6PD), and are also primed to undergo ferroptosis. As a result, the ME1 deficient synovial sarcoma cell lines died within two hours of glucose withdrawal as opposed to the 24-72 hours in other ME1 proficient sarcoma and carcinoma cell lines. This allows small molecule G6PD inhibitors and ferroptosis-inducers to be developed for the targeted treatment of ME1 deficient tumors. Screening for ME1 deficient tumors could also lead to the development of successful treatments for other rare malignancies that currently have limited treatment options. Using a readily available and inexpensive G6PD inhibitor, DHEA, is the only identified application of synthetic lethality involving deficiency of ME1 in the treatment of cancer.