

Current therapies for metastatic breast cancer (MBC) patients have limited long-term success and cause numerous unwanted toxicities and side effects, illustrating the urgent need for new treatment strategies. An exciting potential therapy being evaluated in clinical trials for a number of aggressive cancers including breast cancer is the use of oncolytic viruses. An “oncolytic” virus is genetically engineered to replicate in and destroy cancer cells while leaving normal cells unharmed. Because oncolytic viruses have the potential to spread throughout and destroy entire tumors, and because their unique mechanism of action avoids the toxicities caused by current treatments, there has been much interest in these agents. The oncolytic herpes simplex virus (oHSV) is of particular interest for the following reasons: it is widely prevalent, it typically does not cause serious disease, specific anti-viral drugs exist if safety intervention is necessary, and the genome is well characterized and can be easily modified in the laboratory. Thus far, clinical trials have demonstrated that oHSV is safe in patients, but is not effective enough to completely eliminate tumors. Dr. Hurst’s group have found that HDAC inhibitors improve oHSV replication in metastatic breast cancer cell lines, including in an aggressive “triple negative” line, but not in normal breast cells. Interestingly, a particularly aggressive and oHSV-resistant cell line responded to oHSV after treatment with select HDAC inhibitors. These preliminary studies support their overall hypothesis that oHSV could be an effective new therapy for metastatic breast cancer when combined with HDAC inhibitors.

For the METAvivor proposal, Dr. Hurst will evaluate oHSV therapy combined with select HDAC inhibitors in multiple pre-clinical animal models of breast cancer metastasis and conduct more detailed experiments to determine how inhibition of HDACs improves viral replication in order to develop more effective and targeted treatments for individualized therapy. These studies have the potential for rapid translation to the clinic because both oHSV and HDAC inhibitors are being evaluated in clinical trials. There is a dire need for innovative new therapeutic strategies for metastatic breast cancer patients and utilizing HDAC inhibitors to improve the effectiveness of the clinically safe oHSV is an exciting avenue to give hope to those breast cancer patients who currently have few treatment options.