Targeting Brain Tumor Stem Cells through Natural Antioxidants

Glioblastoma Multiforme is the most frequent and devastating malignant brain tumor among adults with an average life expectancy of one year after diagnosis. This is partly due to its multi-drug resistance and recurrence properties, which have been recently linked to a small sub-population of cancer cells known as brain tumor stem cells (BTSCs). These BTSCs exhibit self-renewal, drug resistance, and tumor initiation capabilities. Current therapies, such as the standard chemotherapy treatment, temozolomide (TMZ), target only cancer cells but not BTSCs. Thus, therapeutic approaches that eradicate the BTSC population must be developed. The objective of this study was to determine the use of natural antioxidants, curcumin, quercetin, and melatonin in targeting BTSCs. Through WST-1 cell proliferation assays it was determined that the addition of curcumin, quercetin, and melatonin resulted in a dose-dependent decrease in proliferation of BTSCs. Interestingly, while treatment with temozolomide induced modest effect, addition of temozolomide in combination with these antioxidants further attenuated BTSC proliferation. Similarly, flow cytometry analyses showed that while treatment with TMZ induced minimal apoptosis and necrosis of BTSCs in culture, treatment with TMZ in combination with these antioxidants further increased apoptotic and necrotic deaths. Further analyses using quantitative real time PCR showed that curcumin, quercetin, and melatonin alone or in combination with TMZ decreased the expression of stemness gene Nanog in BTSCs. These findings demonstrate that these natural antioxidants attenuate growth, survival, and self-renewal of BTSCs, and suggest their use in the treatment of Glioblastoma Multiforme.

Awards Won:

Second Award of $2,000