STUDY OF THE MAGNETIC PROPERTIES OF GLIOBLASTOMA CANCER STEM-LIKE CELLS AND NON-STEM TUMOR CELLS USING MAGNETOPHORESIS FOR LABEL-LESS SEPARATION

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Over the years, we have conducted various studies focusing on the characterization and exploiting the intrinsic magnetic susceptibility of various biological entities, including the red blood cells at different chemical state, spores, Hela cells, etc. Moreover, the development of various instruments, such as the cell tracking velocimetry (CTV) system, which can measure the magnetic susceptibility of hundreds to thousand individual cells using charge coupled device camera and square glass channel under constant magnetic energy gradient, and the quadratic magnetic sorter (QMS), a novel magnetic separation system that uses centrifugal magnetic force to sort a mixture into magnetic and non-magnetic population, has led us to explore the possibility of separating the mentioned magnetic entities. Using these novel technologies, our proposed study focuses on conducting label-less magnetic separation of the mixture of GBM CSCs and NSTCs.

The xenografted GBM tumor cells were obtained from primary human brain tumor patient and were sorted into CSCs and NSTCs based on the presence of CD133 epitope. After culturing them until >1 MM cells were obtained for experiments, the CSCs and NSTCs were incubated at varied iron concentration for 24 hours. Afterward, each population's magnetic susceptibility was measured and analyzed through the CTV system, which showed a clear difference in magnetic susceptibility between the two populations. Using the same incubation condition, the pre-dyed blue CSCs and red NSTCs were mixed and were introduced into the QMS channel with a running buffer. The two sorted populations, the collection fraction (weakly magnetic) and the deposit fraction (strong magnetic) were observed under the fluorescent microscope and the analyzed result showed a successful separation of the CSCs and NSTCs from a mixture. Moreover, when the unseparated GBM cells were introduced to excess iron, our CTV system and custom density analysis algorithm was able to confirm two population with similar magnetic characteristic of GBM CSCs and NSTCs.

Future works needs to be done in order to understand the separation in more details. First, contrary to our expectation, the NSTCs had higher magnetic susceptibility distribution compared to that of the CSCs. Our speculation of this unexpected result is that when iron is stored in ferritins (in CSCs) to protect themselves from generating ROS, they are stored in a highly ordered, pseudo-crystalline mineral core, and this results in iron being much more stable compared to the free iron present in the NSTCs. Therefore, effect of iron on viability and growth of the GBM cells would have to be explored. Moreover, exploring the effect of lowered iron incubation concentration is necessary, since easier experimental condition will reduce the chance of cells deviating from their normal behavior. Then, finally the label-less magnetic separation of the unsorted mixture of GBM CSCs and NSTCs will be carried out, which we believe will eventually bring benefit to the cancer community for diagnosis and research purposes.

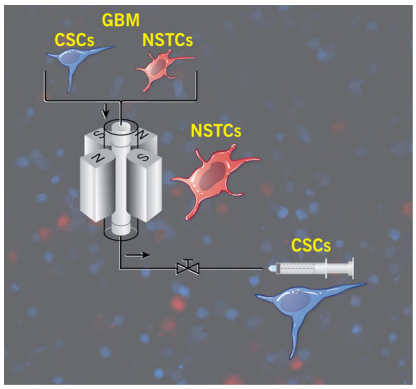

Figure 1 – Overall schematic for the unlabeled magnetic separation of CSCs and NSTCs based on their iron consumption difference.

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