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# Isolating Glioblastoma Stem Cells Based on Their Dielectric Properties

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**Background:** Despite recent advancements, Glioblastoma multiform remains the most fatal type of brain cancer with median survival rate of 14.6 months. Glioblastoma stem cells (GSCs) are a malignant subpopulation with self-renewal properties that resist therapies and cause recurrence. Isolating GSCs from tumor bulk has been challenging, due to lack of appropriate markers. In this study we evaluate the feasibility of using dielectrophoresis (DEP) to isolate glioblastoma cells with increased stemness. DEP is a technique that uses a non-uniform electric field to polarize non-charged particles. Polarized particles experience the DEP force, which is a function of applied electric field as well as physical properties of the particles (i.e. their permittivity and conductivity).

**Cell Culture:** Reynold and Weiss [1] neurosphere assay has become a common method for developing an in vitro model for cells with increased stemness. Following a similar protocol [2], we cultured a glioblastoma cell line (U251) as neurospheres. Spheroid forming cells (SF-U251) and U251 cells cultured under normal conditions, were characterized with immunostaining and western blot assays. Both subpopulations showed expression of three stem cell markers, CD133, CD44 and Nestin, as well as a glial marker, GFAP. However, our western blot assays showed increased Nestin expression as well as decreased GFAP expression for SF-U251, suggesting that SF-U251 cells have increased stem-like properties.

**Microfluidic device:** We evaluated the dielectric properties of U251 and SF-U251 in a microfluidic device, described previously [3]. In our microfluidic platform, cells flow through a channel with an array of 20-micron posts. Maximum DEP force is applied on cells near the posts. The DEP force can be positive (attracting) or negative (repelling) based on the applied frequency. In the positive domain, cells get trapped to the posts when the DEP force is equal to or larger than the drag force, exerted by the flow. Altering the applied electric field, we characterized the trapping range for both U251 and SF-U251 subpopulations. Next we compared the applied voltages needed for the cells to reach their maximum trapping capacity. Interestingly, we showed that SF-U251 cells needed higher voltages to reach the maximum trapping. Our results suggest that the two subpopulations are separable using our microfluidic device.

**Conclusion:** We developed a malignant subpopulation with increased stemness, following a spheroid culture assay. Both U251 and SF-U251 cells showed expression of stem cell markers. However, western blotting showed increased stemness in SF-U251 cells. Since all four markers were expressed in both phenotypes, separating these two subpopulations using marker-based sorting methods such as FACS would be challenging.

**Keywords:** Glioblastoma, Cancer stem cells, Dielectric properties, Stemness, Microfluidic device.

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## REFERENCES

[1] Reynolds BA, Weiss S. Generation of neurons and astrocytes from isolated cells of the adult mammalian central nervous system. Science 1992;255:1707–10.

[2] Yu SC, Ping YF, Yi L, Zhou ZH, Chen JH, Yao XH, et al.Isolation and characterization of cancer stem cells from a human glioblastoma cell line U87. Cancer Lett 2008;265:124–34.

[3] Čemažar J, Douglas TA, Schmelz EM, Davalos RV. Enhanced contactless dielectrophoresis enrichment and isolation platform via cell-scale microstructures. Biomicrofluidics 2016;10: 014109.

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