Title: Immature cancer cell discrimination using combined high frequency Electromagnetic Fields and dielectrophoresis forces.

Authors

C. Dalmay¹, R. Manczak¹, S. Saada², T. Provent¹, B. Bessette², A. Casciati³, M. Tanori³, E Porcù⁴, E Rampazzo⁴, L Persano⁴, C. Baristiran Kaynak⁵, M. Kaynak⁵, C. Palego⁶, G. Viola⁴, C. Merla³, M. Mancuso³, F. Lalloue², A. Pothier¹

¹ XLIM-UMR 7252, University of Limoges/CNRS, 87060 Limoges, France,

² CAPTuR-EA 3842, University of Limoges, 87025 Limoges, France,

³ ENEA-Italian National Agency for New Technologies, Energy and Sustainable Economic Development, Rome, Italy

⁴ University of Padova, Department of Women and Children Health and Pediatric Research Institute Foundation, Padova, Italy

⁵ IHP, Innovations for High Performance Microelectronics, 15236 Frankfurt (Oder), Germany

⁶ Bangor University, Bangor, LL57 1UT, United Kingdom

Summary

The SUMCASTEC project aims to isolate and neutralize brain cancer stem-like cells (CSC) using electromagnetic stimulation¹. We present the main results on identifying and isolating CSCs from others differentiated cells using a combined dielectrophoresis approaches with high frequency (MHz range) cell sensing thanks especially developed lab-on-chip (LOC) cell sensors.

Abstract

Glioblastoma (GBM) is one of the most frequent and the most aggressive tumor of the central nervous system. About 240,000 brain tumor new cases were diagnosed over the worldwide; the majority are GBMs with an incidence of 3–4 per 100 000 persons per year [2]. Medulloblastoma (MB) is the most common malignant pediatric brain tumor [3]. Despite the progress of new treatments, the risk of recurrence, morbidity, and death remains significant. Hence, the dark prognosis of these diseases, especially for GBM, is primarily due to the recurrence of tumor, which can be resistant to conventional treatments closely linked to the existence of very immature and undifferentiated cells, as cancer stem-like cells (CSC) [3].

Conventional markers for normal stem cells as CD133, CD44, OCT-4, SOX2, pSTAT3 and NANOG are currently used and combined to have clues of CSC occurrence. However, CSCs subpopulation are very rare in tumors and their isolation often requires enriching them in specific culture medium followed with functional test to established with certainty the diagnosis. Such strategy is really time consuming and makes the results longer. Consequently, alternatives cell analysis methods are required to get around this issue in order to efficiently discriminate and identify undifferentiated cancer cell populations from the whole heterogeneity that occurs in the tumor biopsies.

High frequency dielectrophoresis might be one of them. Hence, this study discusses about the significant correlation between dielectrophoresis signatures in the UHF frequency domain we have established related to own CSC biological specificities [4-5]. Especially, we will discuss about how relevant the UHF signatures vs the conventionally measured ones in the kHz range are. Such new physical marker can be used to isolate CSC from others cells and applied to characterize various patient tumors. Original lab on chip concepts to exploit such physical properties will be also introduced.

References

- 1. www.sumcastec.eu
- J. Chen, R. M. McKay, L. F. Parada, "Malignant glioma: lessons from genomics, mouse models, and stem cells", Cell. 2012 Mar 30; 149(1): 36-47. doi: 10.1016/j.cell.2012.03.009.
- Ostrom, Q.T.; Gittleman, H.; Fulop, J.; Liu, M.; Blanda, R.; Kromer, C.; Wolinsky, Y.; Kruchko, C.; Barnholtz-Sloan, J.S. CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2008–2012. Neuro Oncol. 2015, 17 (Suppl. 4), iv1–iv62. doi:10.1093/neuonc/nov189.
- Casciati, A.; Tanori, M.; Manczak, R.; Saada, S.; Tanno, B.; Giardullo, P.; Porcù, E.; Rampazzo, E.; Persano, L.; Viola, G.; Dalmay, C.; Lalloué, F.; Pothier, A.; Merla, C.; Mancuso, M. Human Medulloblastoma Cell Lines: Investigating on Cancer Stem Cell-Like Phenotype. Cancers 2020, 12, 226.
- R. Manczak, S. Saada, T. Provent, C. Dalmay, B. Bessette, G. Begaud, S. Battu, P. Blondy, M.O. Jauberteau, C. Baristiran Kaynak, M. Kaynak, C. Palego, F. Lalloue, A. Pothier, HF-Dielectrophoresis Crossover Frequency as a New Marker for Discrimination of Glioblastoma Undifferentiated Cells, IEEE Journal of Electromagnetics, RF and Microwaves in Medicine and Biology, On page(s): 1-8, feb 2019, Doi: 10.1109/JERM.2019.2895539

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 737164 SUMCASTEC.