**Cellular Heterogeneity: Role of Variability and Noise in Biological Decision-Making**

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**Heterogeneity in Glioma – Macrophage Interaction and Its Quantification in terms of Protein Expression**

Glioblastoma multiform (GBM) is the most common and most aggressive malignant type of brain tumor in humans. GMBs are of a high degree of intratumoral heterogeneity with respect to the presence of diverse cell types and the complex cell-cell communication network forming a dynamic and hierarchical cell society. In clinical oncology, one of the great importances of quantifying heterogeneity of the tumor and the immune cells will improve identification of the functional state of tumors and, correspondingly, the anticipated personal response to treatment.

We are implementing our high-density microchip platform to interrogate heterogeneity of tumor cells, immune cells and their co-culture. The microfluidic device was fabricated from PDMS and glass using standard microfabrication techniques. The PDMS slit consists of 5000+ sub-nanoliter microchambers where we can isolate single and multi-cell combinations. The glass slide is patterned form mutli-plex antibody barcode array for quantifying secreted proteins from each microchambers. Individual cells from glioma alone, macrophage alone cultures or from glioma-macrophage co-cultures were seeded randomly in each microchamber and antibody-patterned (flow based micropatterning) glass slide was clamped on top on PDMS block. Prior to the experiment, macrophage and glioma cells were stained with green and red live cell tracker dyes (Invitrogen). The clamped device was imaged and replaced into the incubator overnight for the protein secretion. Upon removal of the PDMS block, the glass slide was developed for protein detection using antibodies and fluorescent probes. We analyzed the intensity of the antibody barcode array in order to quantify the heterogeneity of the cells in terms of protein secretion profile.

Our high-throughput microfluidic protein detection platform will be useful to reveal cellular heterogeneity levels in terms of protein expression not only for tumor or immune cells but also for their complex interactions.