DC Impedance-based Label-Free Cell Counter for Circulating Tumor Cell Detection

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INTRODUCTION

◆ Circulating Tumor Cells
  -> Cells that have detached from a primary tumor and circulate in the bloodstream
  -> Powerful tool for medical application
    - cancer prognosis, diagnosis of minimal residual disease
    - assessment of tumor sensitivity to anticancer drugs
    - personalization of anticancer therapy
  -> Characters
    - rare cells (about 1 – 100 cells per mL of whole blood)
    - epithelial type (EpCAM)
    - bigger size than peripheral blood cells

◆ Conventional CTC detection method
  -> PCR-based approaches
    - merit : very sensitive
    - demerit : low specificity (can result in false positives)
  -> Immunoreaction-based techniques
    - merit : multi-parameter (EpCAM, CD45, CK, etc)
    - demerit : miss some CTCs (lack of exact antibody), low purity
  -> Size-based techniques using pores
    - merit : independent with parameters (like antibodies)
    - demerit : physical damages by high pressure

◆ DC Impedance-based CTC counting Method
  -> Size-based cytometry approaches
    - merit : independent with parameters, no physical stresses, potential to sort CTCs
    - no need a sample preparation

METHODOLOGY

◆ Schematic Diagrams of Developed System

- Impedance measurement of the PGE-microchannel-PGE series is done with the Ag/AgCl electrodes under external voltages.
- Double sheath flow for decreasing sample loss
- Flow rate : sheath flow : 2.5ml/h, sample flow : 0.8ml/h (By syringe pumps)
- Test sample
  - Micro-sized beads (8.31um, 10.35um, 15.02um; Bangs Laboratory)
  - CTC model : Ovarian Cancer Cell lines
  - Blood : breast cancer patients (in stage III or IV), obtained from National Cancer Center in Korea

RESULTS

◆ Calibration Curve of the DC Impedance-based cytometer

\[ \Delta R = \frac{4\rho_m d_p^3}{\pi D_t^4} \]

- \[ \Delta R \] : the resistance change of the ionic flow
- \( D_t \) : the cross area of detection region
- \( d_p \) : a diameter of a particle or a cell
- \( \rho_m \) : the resistivity of electrolyte

- Impedance Signal Peak amplitude depends on the third power of the particle diameter.
- The developed system is more suitable for the detection of larger cells.

◆ Ovarian Cancer Cell lines size distribution

- The peripheral blood cell : under 13um (Lara et al.) (13um => 0.46 in peak amplitude)
- Ovarian Cancer Cell lines : 16um to 24um in diameter (by calibration curve)
- threshold over 0.46(peak amplitude)
- # of spiked Cells : 10, 50, 500, 1000
- Blood Volume : 500ul
- Efficiency : about 81.41%
- linear over the entire range

DISCUSSION

- PGEs function as not only separation between main microchannel and Ag/AgCl electrode chambers physically, but also passing ions for connection electrically between two Ag/AgCl electrodes.
- Impedance signal peak amplitude is linear to the volume of the cells, hence the DC-impedance based cell counter is more appropriate for the detection of larger cells such as CTCs.
- Size-based detection method is sufficient enough to count rare CTCs, and sensitive.

* This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (No. 2005-2001287).