Real-time Monitoring Biomarker Expression of Carcinoma Cells

Vascular endothelial growth factor (VEGF) is an angiogenic signal protein biomarker produced by oxygen-hungry cells to stimulate the growth of blood vessels.[1] It binds to specialized receptors on the surfaces of endothelial cells and directs them to grow new blood vessels during embryonic development. Certain types of tumor cells produce abnormally large amounts of VEGF or block the action of angiogenesis inhibitors. This action is termed as ''angiogenic switch'', which leads to metastasis to the tumor by providing blood supply for new tumors to grow.[2]

In a recent report by Liu et al.[3], a new SPR biosensing configuration was used for real-time monitoring of VEGF secretion study. This novel design integrated a mini cell culture module into the flow cell of a BI SPR setup. Unlike the traditional configuration of SPR systems for biomarker detection, living cells are cultured on the ceiling of the SPR flow cell chamber, and biomarker secretion from cells is rapidly monitored by SPR (Fig. 1).

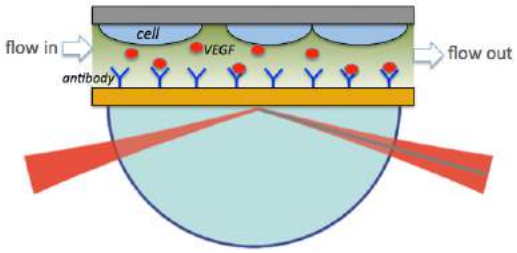

FIG. 1 Experimental setup with cancer cells immobilized onto the ceiling of the BI-SPR flow channel. Cancer cell excretions were detected by capture proteins immobilized on the sensor surface.

In their study, the SKOV-3 ovarian cancer cell line is used as a model system to demonstrate VEGF secretion lifetime measurement. This study was performed with three different population sizes of cultured cancer cells. Injections of 500 mM of Ca^{2+} ionophore were used to stimulate VEGF excretion from the cells. The table below summarizes the amount of VEGF released following exposure to the stimulant, ~ 13.7 fg of VEGF per cell.

Number of Cells	VEGF Response
8 x 10^4	43.4 mDeg
16 x 10^4	100.6 mDeg
32 x 10^4	214.2 mDeg

Using this new strategy, biomarker molecules secreted from living cells were detected and analyzed. The flow setup mimics the natural microenvironment of cells and tissues, which opens the doors to many other potential applications, especially the study of cellular signaling pathways and antineoplastic drug development.

References

[1] Ferrara et al. *Nature Med.* **2003**, *9*, 669.
[2] Hannahan and Weinberg, *Cell* **2000**, *100*, 57.
[3] Liu et al. *Chem. Comm.* **2012**, *48*, 10357.