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Letter to the Editor

Development of Biosensors Enabling Cytoskeleton Characterization of Single Tumor Cells

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Letter to the Editor

Cancer (malignant tumor) is a deadly disease resulting from the imbalance between cellular proliferation and death. Based on the statistics of World Health Organization, in 2012, there were roughly 14 million newly diagnostic tumor patients and there was an estimation of 8.2 million cancer related death [1].

In 2013, in one issue of nature insight, *Tumor Heterogeneity* was highlighted, revealing single-cell differences in proliferation, invasion and drug responses even from the same tumor portions [2]. This nature insight systematically illustrated the recent developments of tumor heterogeneity, emphasizing its role in the failure of tumor treatment. Furthermore, the lack of effective biosensors enabling single-cell analysis was listed as one of the key technical bottlenecks compromising the studies of tumor heterogeneity.

From the perspective of cytoskeletons, variations in biochemical (i.e., numbering, composition and distribution) and biophysical (i.e., deformability, migration and invasion) properties of single tumor cells have been reported. Currently, biosensors including flow cytometry [3] and atomic force microscopy [4] can measure cytoskeleton proteins (i.e., actin and tubulin) and cellular mechanical properties (i.e., instantaneous and equilibrium Young's moduli), respectively. However, flow cytometry cannot provide absolute quantification of cytoskeleton protein expressions of single cells while atomic force microscopy suffers from the key issue of low through and cannot collect statistically significant data of single cells.

Microfluidics is the manipulation and detection of small volumes of liquids [5]. Due to its dimensional comparison with biological cells, microfluidics has been widely used as biosensors for single-cell analysis [6]. As to the characterization of single-cell cytoskeleton, both biophysical (e.g., deformability) and biochemical markers (e.g., expressions of cytoskeleton proteins) have been quantified and evaluated with a few key milestones listed as follows.

As a proof-of-concept demonstration of absolute quantification of single-cell cytosolic proteins, the Heath group from Caltech. Developed a microfluidic biosensor (barcoding microchip) [7] where large-array microfluidic values were integrated to confine individual cells within micro chambers. Following cell lysis, the proteins released by individual cells were trapped by primary antibodies pre-patterned on the surface of the micro chamber, enabling the absolute quantification of interested proteins. Although this approach can be used to measure multiple proteins in one experiment, it suffered from the issue of device complexity and low throughput in comparison to flow cytometry, compromising its applications in tumor heterogeneity.

In 2014, Prof. Herr and her coworkers from UC Berkeley successfully demonstrated a single-cell western blotting [8] where cells under measurement were individually confined within micro wells. Following cell lysis, electrophoresis was used to effectively classify proteins released from single cells. In this study, antibodies for specific protein types were not required and the assay can to an extent function in a semi-quantitative manner. However, this approach cannot provide absolute quantification of cytoskeleton proteins and also cannot measure proteins with low copy numbers within single cells.

As to the development of microfluidic biosensors enabling the quantification of biophysical properties of cytoskeletons of single tumor cells, Di Carlo et al from UCLA proposed a high-throughput microfluidic assay [9] where single cells were flushed rapidly within microfluidic channels and deformed in a cross channel due to fluid stress. This study was featured with ultra-high throughput, which, however, was not capable of quantifying intrinsic size-independent biophysical markers (i.e., Young's modulus) of cellular cytoskeletons. To address this issue, Guck et al. [10] proposed a numerical model to translate the raw deformation data of single cells under fluid stress into instantaneous Young' modulus, enabling the high-throughput quantification of intrinsic mechanical properties of single cells.

In summary, although several types of microfluidic biosensors have been developed to quantify biophysical or biochemical properties of cellular cytoskeletons, there are still huge research rooms left for further technical innovations since high-throughput single-cell biosensors capable of the quantification of 1) absolute cytoskeleton protein copy numbers and 2) instantaneous and equilibrium Young's moduli are still not available. In addition, biosensors enabling the simultaneous characterization of both biochemical and biophysical properties of single-cell cytoskeletons are also under demand, which may provide a more comprehensive evaluation of single-cell cytoskeletons.

Reference

1. W. H. Organization 2013. GLOBOCAN. 2012.
2. Marte B. Tumour heterogeneity. Nature. 2013; 501: 327.
3. Chang Q, Hedley D. Emerging applications of flow cytometry in solid tumor biology. Methods. 2012; 57: 359-367.
4. Benitez R, Toca-Herrera JL. Looking at cell mechanics with atomic force microscopy: experiment and theory. Microscopy Research and Technique. 2014; 77: 947-958.

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5. Whitesides GM. The origins and the future of microfluidics. Nature. 2006; 442: 368-373.

6. Reece A, Xia B, Jiang Z, Noren B, McBride R, Oakey J. Microfluidic techniques for high throughput single cell analysis. Current Opinion in Biotechnology. 2016; 40: 90-96.

7. Shi Q, Qin L, Wei W, Geng F, Fan R, Shin YS, et al. Single-cell proteomic chip for profiling intracellular signaling pathways in single tumor cells. Proceedings of the National Academy of Sciences of the United States of America. 2012; 109: 419-424.

8. Hughes AJ, Spelke DP, Xu Z, Kang CC, Schaffer DV, Herr AE. Single-cell western blotting. Nature Methods. 2014; 11: 749-755.

9. Gossett DR, Tse HT, Lee SA, Ying Y, Lindgren AG, Yang OO, et al. Hydrodynamic stretching of single cells for large population mechanical phenotyping. Proceedings of the National Academy of Sciences of the United States of America. 2012; 109: 7630-7635.

10. Otto O, Rosendahl P, Mietke A, Golfier S, Herold C, Klaue D, et al. Real-time deformability cytometry: on-the-fly cell mechanical phenotyping. Nature Methods. 2015; 12: 199-202.

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