

Barcode Microchips for Single-Cell Proteomic and Transcriptomic Analyses

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Abstract

With recent progress in high-throughput single-cell analysis, we gradually realize that most multicellular systems are intrinsically heterogeneous. However, how the cellular heterogeneity emerges is not well understood, which is largely limited by the availability of single-cell tools. To answer this question and address the need for clinical diagnosis, I have developed two high-throughput barcode microchips for the analysis of single-cell proteome and transcriptome. Compelling evidences show that cell-cell interactions can significantly induce heterogeneity and redirect cell development. In the first part of my talk, I will describe the principle of the barcode microchip for single-cell or two-cell proteomic analysis and its application to cancer cell interactions. We have found cancer cell communications strongly influence oncogenic signaling in a manner that is dependent upon the mutations carried by the cells, and on the separation distance between the interacting cells. We have developed a theoretic approach that permits the translation of these functional proteomics assays of quantized cell populations into accurate and experimentally verifiable predictions for how those cells will distribute in bulk culture. In the second part of my talk, I will focus on single-cell proteomic and transcriptomic analysis of cell-cell interactions of embryonic stem cells (ESC). ESCs spontaneously form *in vitro* niche to sustain their growth and proliferation under a feeder-free condition. We discovered that the subpopulations that are capable of secreting growth factors are dynamically changed with the expansion of a colony. Using the barcode microchip technology, we profiled the transcriptional networks of functionally distinctive stem cells that act as feeder cells and form *in vitro* niche. In all, the use of single-cell barcode microchips can reveal the spatial and temporal heterogeneity of complex systems, and will be helpful to advance cancer therapy development and tissue engineering in the future.