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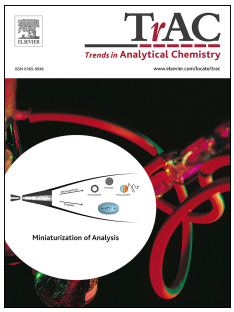

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PII: S0165-9936(18)30177-8

DOI: 10.1016/j.trac.2018.06.019

Reference: TRAC 15196

To appear in: *Trends in Analytical Chemistry*

Received Date: 29 April 2018

Revised Date: 13 June 2018

Accepted Date: 19 June 2018

Please cite this article as: S. Mao, W. Li, Q. Zhang, W. Zhang, Q. Huang, J.-M. Lin, Cell analysis on chip-mass spectrometry, *Trends in Analytical Chemistry* (2018), doi: 10.1016/j.trac.2018.06.019.

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ARTICLE INFO

Keywords:
Microfluidic chip
Cell analysis
Mass spectrometry
Metabolism
Cell signaling
Chip-MS platform
Microenvironment
Migration
Subcellular analysis

ABSTRACT

Benefit from the development of microfluidic chip and mass spectrometry, chip-mass spectrometry (Chip-MS) has become an ambient platform for cell analysis. Microfluidic chip has been demonstrated as a powerful tool for cell studies, where identical cells or multiple types of cells were co-cultured and constructed to be an organ or tissue. Improvements of interfaces between microchip and mass spectrometry allow rapid detection and analysis of cell metabolites. Moreover, the chip-MS platform makes monitoring of cell secretion possible. As the environments on microchip are easy to control, various types of cell researches could be carried out, such as cell metabolism, cell migration, cell signaling, proteomics and single-cell analysis. Here, we review the recent fundamental developments of chip-MS platform for cell analysis. In particular, we discuss the improved integration of chip-MS platform, as well as its application towards single cell analysis.

Contents

1. Introduction

Cell, as the fundamental unit of human life, has been widely studied for biological processes, such as metabolism, signaling and cytotoxicity.[1-4] Cell as the origin of living, one research direction is to study bigger targets, such as organ, tissue, and organism[5-7]; the other research direction is to explore smaller targets, such as single-cell analysis and subcellular studies.[8-11] Originally, cell studies were carried out *in vivo*, which including animal experiments and clinical medicine. With the developments of analytical technologies, more and more cell researches were carried out *in vitro*.[12, 13] Cell and tissue were well cultured in petridish, transwells, microdevices and so on. Cell cultures extended from identical cell culture[14, 15] to cell co-culture,[16, 17] cell-cell interaction and tissue construction.[18, 19] Those efforts are benefit for cell biology, drug screening and disease diagnosis. There are two key points for in vitro cell researches: one is the precise control of microenvironments, the other is accurate characterization of cell state and its metabolites.

Microfluidic chip provides an excellent approach for cell culture and lateral analysis.[20, 21] They offer many advantages, including precise control of environments, reduced sample and reagent consumption, integration, and high throughput analysis.[22-25] Many methods have been developed from microfluidic chips for cell culture, cell co-culture, cell signaling, and single cell analysis.[15, 26-28] In contrast to traditional cell-culture methods in Petri dishes, microfluidics was potential for a series of cell researches that were unable in former one. We could easily realize coculture of different types of cells on a microchip with special design. Although many cell researches such as cell