An Introduction to the Science of Single Cell Analysis with ICP-MS Instrumentation

Pete WINSHIP
Teledyne CETAC Technologies, Omaha, NE 68144, USA

Introduction

The latest generation of ICP-MS instrumentation, both quadrupole and time-of-flight based, boasts the analytical sensitivity, analyte dwell times and operating software that allows the measurement of analyte elements within, or associated with the exterior of, single biological cells across the gamut of cell types (differing, notably, in size, shape and structural integrity). The data generated by this analytical capability is valuable to biological and clinical studies, particularly when examined in conjunction with data from other analytical techniques such as flow cytometry, microscopy and mass spectrometry. The single cell measurements involve the capture of 'single event' data for cells in a sample as they are introduced to, and pass through, a plasma. There are a number of key variables that define successful single cell analysis and such variables are described in this presentation as well as discussion of new automation and interface technology for this work.

Successful single cell analysis makes use of flexible ICP-MS instrumentation and front-end hardware that meets the demands of differing biological cell types (particularly mammalian cells) and their preparation conditions, reagents and apparatus. Such instrumentation and hardware must maximise the efficiency of the introduction process (the transport efficiency) whilst maintaining the integrity of the cells under investigation.

Typical Sample Introduction and Analytical Workflow

For batch analysis, there are numerous stages involved in the introduction and analytical workflow between the sample and data generation in single cell analysis with a number of associated variables across the whole process. These stages and some of the key analytical variables are shown in the diagram below (Figure 1).

Sample

Samples may be delivered in vials/tubes or well plates for analysis.

Sample matrix will be a buffer solution of some form.

May be held under constant temperature.

Automation

Automation is required to introduce samples at accurate flow rate.

Sample homogenisation is required to address cell settling.

Effective washout procedure

Temperature control

Interface Glassware

Efficient nebulisation and spray chamber transport (near total consumption).

Effective washout

Minimal or no nebuliser blockages

ICP-MS

Quadrupole ICP-MS with fast analyte dwell time.

Or

ICP-TOF-MS.

Data

Fit for purpose operating software for data processing and reporting.

Different data outputs/measurements (cell number, size etc…).

Sample Delivery to Data Generation

Figure 1. The typical workflow for single cell analysis from sample vial or well plate to data.

New Developments

The analytical workflow described in Figure 1. can be delivered by the combination of new automation and interface glassware from Teledyne CETAC Technologies and Glass Expansion as described below.

Teledyne CETAC Technologies MVX-7100 µL Workstation

- Syringe driven automation
- Introduction of sample volumes from 5 µL to 1.5 mL
- Full control of introduction flow rate (nL min^{-1} to mL min^{-1}.)
- Sample homogenisation
- Temperature control from 4°C to 40°C.
- Sampling from vials/tubes
- Sampling from 96 and 384 well plates.

Figure 2. The MVX-7100 µL Workstation.

Glass Expansion Interface Glassware

- New high sensitivity single cell sample introduction system for ICP-MS (see Figure 3.)
  - High efficiency nebuliser
  - On-axis, high transmission efficiency spray chamber
- Specifically designed for cell introduction to ICP-MS
  - For sample introduction flow rates < 50 µL min
  - Wide bore nebuliser capillary minimises blockage
  - Surrounding/focussing spray chamber gas flow to maximise transport efficiency

Figure 3. The Glass Expansion Single Cell Interface.

Other Analytical Considerations

In addition to the analytical variables described in this presentation for successful analysis, the analytical community should also consider the establishment of a coherent approach to measurement standardisation for analyte quantification that is fit for purpose for the breadth of biological cells that may be investigated. Such an approach would better establish this type of analysis and make it more applicable to cell studies. Furthermore, inter-laboratory comparison and collaboration would normalise this analytical approach across all relevant ICP-MS instrumentation and associated automation hardware as well as the interface between the two.

Conclusions

The analysis of single cells by ICP-MS is a new and emerging frontier of elemental analysis. This analysis is widely applicable across a number of areas of scientific study and research. As with all new analytical approaches, the key variables must be fully explored and understood to arrive at the best analytical setup. Collaborative study and ongoing development will be enormously beneficial to the efficacy of single cell analysis and its implementation in research as well as its use with complementary analytical techniques.

TELEDYNE
CETAC TECHNOLOGIES
Everywhereyoulook™