Beyond the average: single-cell ICP-MS study of copper distribution within HEK cell populations challenged with external stimuli.

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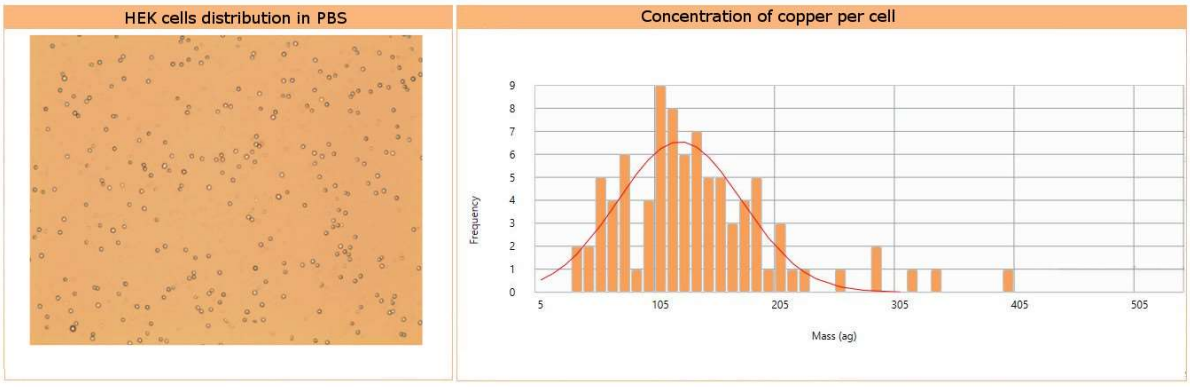
ABSTRACT:

Until recently, quantitative characterization of elemental contents of cells was routinely possible by collecting large numbers of cells and determining average values using analytical techniques, such as ICP-MS. Single cell resolution could be obtained, in principle, by fluorescent probes and confocal microscopy. but the character of chemical reactions underlying the signals provided by such probes makes absolute and global determinations essentially impossible [1]. Combination of analytical studies on cell populations and molecular studies on metal transporters brought O'Halloran and coworkers to raise a concept of zinc quota, stating that most cells contain relatively constant formal concentrations of Zn(II) ions. This concept was later extended on other metal ions, including copper [2].

Single-cell ICP-MS technique provided the research community with the opportunity to reach beyond the limitation of cell population averages of elemental compositions and determine the distributions of individual metal ions within cell populations [3]. Such information, combined with cell size distributions can help decipher the actual requirements of cells in terms of minimal, optimal and toxic metal contents.

We performed a series of studies on copper contents in HEK cell populations challenged with a variety of molecules, known or suspected to affect the performance of hCTR1 copper transporter [4]. An exemplary experiment is presented in Fig. 1. The altered copper contents distributions were analyzed to provide the preliminary view of deeper relations between copper exposure, intake, cell viability and activity of copper=dependent physiological pathways. These data will provide a basis for a better understanding of copper biology, with applications in research into cancer and neurological disorders.



KEY WORDS: HEK cells, copper, single-cell ICP-MS, hCTR1.

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