A compact chip realizing highly precise simultaneous single-cell analysis of 100 cells

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Hitachi announced the development of a compact 1-mm square chip that can efficiently analyze small amounts of various genetic material, specifically mRNA, expressed from DNA with high precision. The chip is able to precisely extract and analyze the various types of mRNA which only exist in minute quantities at any one time - 15 molecules per cell in a maximum sample of 100 cells. In general, a few hundred to thousands of cell analyses are required to accurately characterize biological tissue. A demonstration experiment confirmed that the genetic material of 2000 cells could be simultaneously analyzed with high precision using a prototype device on which these chips are arranged in parallel. The results indicated that the characteristics of entire tissue, such as cancer, as well as those of individual cells, could be understood at the same time. This result will contribute to accelerating the elucidation of disease mechanisms as well as the development of treatment methods.

Progress in medicine has shown that cells that compose biological tissue such as cancer, have individual and differing characteristics. As a result, it is considered necessary to measure the amount of mRNA in each cell to understand the mechanisms of disease. With conventional methods however, measurement results are averaged for cells, thus preventing differences to be discriminated between individual cells within tissue. Single-cell analysis technology which overcomes this by analyzing individual cells, is the focus of attention, but issues such as precision and cost exist in relation to the dependence on skilled technicians in the manual process, as well as the large equipment and the large amount of reagent required.

To realize a single-cell analysis device that is compact, precise and provides parallel processing, Hitachi began research to develop a chip which could efficiently extract and analyze mRNA from individual cells. In March 2016, a 1-mm square chip (Vertical Flow Array Chips) integrated with 100 micro-reaction chambers that extract mRNA from individual cells was developed. Delivering the reagent in one lot from above to the chips arranged on an analytical device, allowed mRNA to be automatically extracted from many cells as well as reduce the amount of reagent required to approximately one-twentieth of that previously required. This reduced the cost of analysis, but issues related to the efficient extraction of mRNA and sufficient precision, remained a challenge due to the small size of the micro-reaction chamber which made it difficult to pack the beads necessary to extract the mRNA.

To address these issues, Hitachi developed technology to efficiently pack more beads in the micro-reaction chamber and by increasing the surface area, improved extraction by about ten-fold. A compact device prototype (cf.figure) was created using these new chips to conduct DNA analysis experiments. The experiments demonstrated a high parallel processing capability of simultaneous analyzing genetic material from 2,000 cells, as well as the ability to extract the minute amount of mRNA existing in each cell with high precision. Hitachi has also developed a prototype device capable of simultaneously genetic analysis of 10,000 cells thus allowing the analysis of several thousand cells considered effective for accurate understanding of tissue characteristics at the same time as cell characteristics.

Hitachi will apply the technology developed to the analysis of representative cells for various diseases such as cells within cancer tissue or early stage cancer, to demonstrate the efficacy of the technology towards elucidating the mechanisms of disease and the development of treatment methods.

This achievement was published in the journal *Scientific Reports*.

More information: Masataka Shirai et al. Vertical flow array chips reliably identify cell types from single-cell mRNA sequencing experiments, *Scientific Reports* (2016). DOI: 10.1038/srep36014

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