Single cell analysis technologies in biomedical research

In recent years, we have seen an explosion of interest in the applications of single cell analysis technologies while seeking answers to biological and medical questions. In every field, from immunology, infectious disease, cancer to developmental biology, single cell analysis is providing answers that have eluded us in bulk analysis. The meteoric growth in adoption of single cell research is not possible without the technologies offered by lab automation. While in the past, single cell analysis was performed manually in laboratories with specialized expertise in mouth pipetting and cell micromanipulation, single cell analysis today is performed at scale for thousands or even millions of cells using fully automated equipment that are commonly available at core facilities. The development of new technologies not only for single cell isolation, but also for downstream processes such as imaging, functional assays and library preparation, promises to put single cell analysis capability in the hands of every laboratory. This special issue, Single-Cell Analysis Technologies, is a timely review of the landscape of technologies that have advanced considerably in the past few years. It also introduces new technology platforms and applications that would push the boundaries of single cell research.

This special issue of SLAS Technology contains two review articles, three full length research papers and one short communication. The first review article by Yu and Scolnick [1] provides a comprehensive coverage of single cell analysis centered around sequencing analysis, which are among the most rapidly adopted recent methods. Single-cell sequencing provides unbiased, high-dimensional information that enables unprecedented resolution in measuring heterogeneity in cell states, as well as deciphering gene regulatory networks that underlie the transition between cell states. Furthermore, combination of single cell analysis with perturbation studies such as CRISPR screening showed great potential for drug discovery efforts. Finally, the authors discuss the recent technologies in spatial transcriptomics, to give a perspective on future promises of single cell sequencing for understanding biology and disease in the native tissue context. Following this, the second review article by Otterstrom et al. [2] presents another facet of single cell analysis, focusing on image analysis at the single cell resolution in whole organisms as a method for high content screening. Various automation approaches are presented to increase the throughput, reproducibility and data quality of zebrafish high-content screening. Image analysis methodologies that capitalize on machine learning to extract features relevant to screening are also explored. The two reviews on single cell analysis technologies in this special issue highlight the progression in the use of single cell technologies in increasingly complex but also more physiological applications, from dissociated single cells to cells in tissue context and finally of cells in whole organisms. The maturation of single cell technologies heralds a new era, where single cell precision medicine could be a reality.

Four original research papers in this special issue highlight how advances in laboratory automation can push the boundaries of single cell research. The work by Rutte et al. [3] describes a method to sort single cells by their functional profile, a challenging feat where few have succeeded. This strategy utilizes “nanovial”, which is a 3D structured microparticle that can be immobilized with various agents to capture secretion products from a cell loaded within it. The authors report that commercial flow cytometers can be configured to sort cell-loaded nanovials according to the combinations of proteins secreted. This unique approach could enable rapid isolation of rare cells secreting specific protein products, and could be an important tool for screening efforts such as antibody discovery. Meanwhile, two works in this special issue describe the use of a traceable impedance-based single cell pipetting for single cell isolation. Hannart et al. [4] describes the transition of this technology from of an academic lab prototype to a fully-automated DispenCell-S1 instrument ready for commercial launch. In Ben Khelil et al. [5], the application of DispenCell-S1 is demonstrated. By combining magnetic cell separation with automated impedance-based single cell pipetting, reliable cloning of specific T-cells, a necessary step in reverse immunology, is achieved. This work demonstrates the utility of an automated single cell isolation technology for routine cloning experiment in the field of immunology and beyond. Finally, the complexity of single cell sequencing library preparation is often a challenge for users with different degrees of experience, or experiments involving very large numbers of single cells. Kind et al. [6] showed that fully automated, reproducible and unbiased single cell sequencing library preparation can be achieved in an automated liquid handler. Removal of the final barriers of getting good quality single cell measurement is key to democratizing single cell analysis in biomedical research.

We thank the contributing authors, the SLAS staff, and editors who helped assemble this special collection, as well as the scientific reviewers for their valuable and thoughtful evaluations of the science. It is an exciting time right now for single cell research, both for basic science and translation applications. Developers of technology platforms play an ever important role in expanding the fields where single cell technologies can make a societal impact. To this end, we hope that this SLAS Technology special issue will help the readers be aware of the tremendous advances that are currently emerging in single cell analysis technologies, as well the opportunities for technology developers to contribute meaningfully in this revolution.

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