scONE-seq: A Versatile Single-cell Multi-omics Method for Simultaneous Dissection of Phenotype and Genotype Heterogeneity from Frozen Tumors

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The invention of genomic technologies in the 1900's dramatically changed how we understand biology, health, and disease. It has enabled breakthrough applications including the rapid sequencing of pathogens like SARS-CoV-2; personalized diagnosis of cancer; and accelerated development of drugs and other therapies. Now, new genomic technologies like single-cell sequencing offer opportunities to understand cell-to-cell variations and the identification of different cell subtypes at high resolution, and in multiple dimensions. Single-cell multi-omics can provide a unique perspective on tumor cellular heterogeneity. Most previous single-cell-whole-genome-RNA-sequencing (scWGS-RNA-seq) methods demonstrate utility with intact cells from fresh samples. Among them, most are not applicable to frozen samples that cannot generate intact single-cell suspensions. We have developed scONE-seq, a versatile scWGS-RNA-seq method that amplifies single-cell DNA and RNA without separating them from each other [1]. Compared with existing methods, scONE-seq is a one-tube reaction that eliminates loss due to DNA and RNA separation and thus is compatible with frozen biobanked tissue. We applied it to analyze a 2-year-frozen astrocytoma sample and identified a unique transcriptionally normal-like tumor clone. scONE-seq makes it possible to perform single-cell multi-omics interrogation on the vast quantities of biobanked tissue, to this end we have also developed a droplet array platform for implementing multi-step single-cell reactions at scale. The commercialization of this platform technology will greatly enhance academic research, drug discovery, and multiplex drug screening.

References:

[1] L. Yu, X. Wang, Q. Mu, S. S. T. Tam, D. S. C. Loi, A. K. Y. Chan, W. S. Poon, H.-K. Ng, D. T. M. Chan, J. Wang, A. R. Wu, scONE-seq: A single-cell multi-omics method enables simultaneous dissection of phenotype and genotype heterogeneity from frozen tumors. *Sci Adv*. **9**, eabp8901 (2023).