SMARTer single cell total RNA sequencing

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Single cell RNA sequencing methods have been increasingly used to understand cellular heterogeneity. Nevertheless, most of these methods suffer from one or more limitations, such as focusing only on polyadenylated RNA, sequencing of only the 3' end of the transcript, an exuberant fraction of reads mapping to ribosomal RNA, and the unstranded nature of the sequencing data. Here, we developed a novel single cell strand-specific total RNA library preparation method addressing all the aforementioned shortcomings. Our method was validated on a microfluidics system using three different cancer cell lines undergoing a chemical or genetic perturbation. We demonstrate that our total RNA-seq method detects an equal or higher number of genes compared to classic polyA[+] RNA-seq, including novel and non-polyadenylated genes. The obtained RNA expression patterns also recapitulate the expected biological signal. Inherent to total RNA-seq, our method is also able to detect circular RNAs. Taken together, SMARTer single cell total RNA sequencing is very well suited for any single cell sequencing experiment in which transcript level information is needed beyond polyadenylated genes.