

While cell functional annotation is a crucial step, it often presents challenges when dealing with single-cell transcriptional data. Several existing methods attempt to address this task, but many rely on techniques initially designed for bulk RNA sequencing or simply utilize marker genes identified through cell clustering followed by supervised annotation. To address these limitations and streamline the process, we introduce two novel methods: single-cell gene set enrichment analysis (scGSEA) and single-cell mapper (scMAP). The scGSEA method leverages latent data representations and gene set enrichment scores to identify coordinated gene activity at the resolution of individual cells. On the other hand, scMAP employs transfer learning techniques to repurpose and contextualize new cells within a reference cell atlas. Through the use of both simulated and real datasets, we demonstrate that scGSEA effectively captures recurrent patterns of pathway activity shared by cells from different experimental conditions. Additionally, scMAP reliably maps and contextualizes new single-cell profiles using a breast cancer atlas recently released by our team. Both tools are integrated into an efficient and straightforward workflow, providing a comprehensive framework for determining cell function. The introduction of scGSEA and scMAP significantly enhances the annotation and interpretation of single-cell RNA sequencing (scRNA-seq) data, offering valuable insights into cell functionality.