A Novel Design for Investigating Cell Deconvolution Methods for Tumor Microenvironment

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Precision medicine, or personalized medicine, is the most promising direction for treating complex diseases, such as cancer. The deadliest solid cancer, Pancreatic Ductal Adenocarcinoma (PDAC), has a 5-year survival rate of 4%, and hope for finding viable treatment plans to increase this survival rate lies in precision medicine. The execution of such a treatment plan relies on the knowledge of genetic signatures of the pancreatic tumor cells. However, isolation of these tumor cells is not a simple task: they exist in a complex tumor microenvironment along with many other cell types. Learning the composition of cell types in a tumor sample and the genetic signatures of the individual cell types are crucial. This can be done with deep learning methods, which digitally decompose bulk tumor sample data into cell-type-specific information. Yet, a major issue is the lack of "gold standard" benchmarking data sets that can be used to evaluate and compare the accuracy of digital decomposition methods. Existing data have limited sample size and between-patient variability, and thus do not truly represent the patient population. This work proposes a novel design to create synthetic data to investigate deep learning cell deconvolution methods so that their accuracy for predicting cell-specific genetic signatures can be evaluated. The design is applied to PDAC with the hope that accuracy by balaned genetic signatures will enable the initiation of a precision medicine treatment plan for individual patients. This work can also contribute to improved prognosis and treatment of other cancers and complex diseases in general.

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