Computational approach to study human immunogenetic diversity in tumor-immune interactions

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Abstract

Immune molecules such as B and T cell receptors, human leukocyte antigens (HLAs) and killer Ig-like receptors (KIRs) are encoded in the most diverse genetic loci in the human genome. Many of these immune genes are hyperpolymorphic, showing high allelic diversity across human populations. In addition, typical immune molecules are polygenic, which means that multiple functionally similar genes encode the same protein subunit.

Bioinformatic methods commonly used to analyze immune cells in large patient cohorts do not take into account this polygeny and allelic diversity. This leads to erroneous quantification of important immune mediators and impaired inter-donor comparability.

In this work we assess the impact of human immunogenetic diversity on the quantification of immune gene expression in different bulk, single-cell and spatial transcriptomic datasets. Moreover, we propose an improved quantification method that is based on the incorporation of public immunogenetic reference databases into state-of-the-art transcriptomic quantification algorithms. We illustrate how our method can be used to study tumor-immune interactions throughout genomic and proteomic data layers. We demonstrate that bioinformatic approaches that take into account the polygenic and hyperpolymorphic characteristics of immune genes lead to improved inter-donor comparability in large patient cohorts.