A Bayesian Causal Inference Method for Identifying Cancer Drivers of Individual Tumors

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Abstract

Identifying causative somatic genome alterations (SGAs) driving the development of an individual tumor could both provide insight into disease mechanisms and enable personalized modeling for cancer precision medicine. Although methods exist for identifying driver SGAs at the cohort level, few focus on the drivers of individual tumors. Here, we present a Tumor-specific Driver Identification (TDI) method that infers causal relationships between SGAs and molecular phenotypes (e.g., transcriptomic, proteomic, or metabolomics changes) within a specific tumor. We applied the TDI algorithm to 4,468 tumors across 16 cancer types from The Cancer Genome Atlas (TCGA) and identified those SGAs that causally regulate the differentially expressed genes (DEGs) within each tumor. TDI identified 490 SGAs that had a significant functional impact. The TDI list includes most (86%) of the known drivers published by the TCGA network as well as novel candidate drivers. Our computational evaluation of these SGAs and DEGs support that the causal relationships inferred by TDI are statistically robust, and preliminary experimental results support the predictions by TDI.

Session to which submitted: Research highlights