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Inference of Functional Redundancy in Cancer Genes via a Co-Mutation Frequency Network

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Keywords

Cancer, genetics, networks, pathway analysis

Abstract

I have developed a co-mutation frequency network to infer functional redundancy between pairs of cancer genes. In order for a population of cells to progress through tumorigenesis, a series of phenotypic changes must occur. Each of these changes is typically driven by mutations in various cancer-related genes. Often, there are several possible genetic or genomic changes a population of cells can undergo to achieve a given phenotypic modification. This approach rests on the biological assumption that the likelihood that a tumor with a relatively low mutation burden will independently develop two functionally redundant genomic alterations is low. Adjusting for mutation burden, two genes that are each frequently mutated in sequenced tumor samples but mutated in the same sample much less than expected (defined by the joint probability) may be functionally redundant, and will be assigned a high edge weight. By overlaying known biological pathway information, gene pairs inferred to be functionally redundant due to low co-mutation within a given tumor sample can be nominated with higher confidence. This analysis builds on previous work that leverages mutual exclusivity, or low co-mutation frequency, as a way to investigate the genetic mechanisms of tumorigenesis.