Whole Coding Genome Inter-Clade Comparison to Predict Global Cancer-Protecting Variants

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Abstract : In this research, we identified the missense genetic variants that have the potential to enhance resistance against cancer. Such field has not been widely explored, as researchers tend to investigate mutations that cause diseases, in response to the suffering of patients, rather than those mutations that protect from them. In conjunction with the genomic revolution, and the advances in genetic engineering and synthetic biology, identifying the protective variants will increase the power of genotype-phenotype predictions and can have significant implications on improved risk estimation, diagnostics, prognosis and even for personalized therapy and drug discovery. To approach our goal, we systematically investigated the sites of the coding genomes and picked up the alleles that showed a correlation with the species' cancer resistance. We predicted 250 protecting variants (PVs) with a 0.01 false discovery rate and more than 20 thousand PVs with a 0.25 false discovery rate. Cancer resistance in Mammals and reptiles was significantly predicted by the number of PVs a species has. Moreover, Genes enriched with the protecting variants are enriched in pathways relevant to tumor suppression like pathways of Hedgehog signaling and silencing, which its improper activation is associated with the most common form of cancer malignancy. We also showed that the PVs are more abundant in healthy people compared to cancer patients within different human races.

 ${\bf Keywords: comparative \ genomics, \ machine \ learning, \ cancer \ resistance, cancer-protecting \ alleles}$

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