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

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Abstract : We identified missense genetic variants with the potential to enhance resistance against cancer. Such a field has not been widely explored as researchers tend to investigate the 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 have significant implications for improved risk estimation, diagnostics, prognosis, and even personalized therapy and drug discovery. To approach our goal, we systematically investigated the sites of the coding genomes and selected the alleles that showed a correlation with the species' cancer resistance. Interestingly, we found several amino acids that are more generally preferred (like the Proline) or avoided (like the Cysteine) by the resistant species. Furthermore, Cancer resistance in mammals and reptiles is significantly predicted by the number of the predicted protecting variants (PVs) a species has. Moreover, PVs-enriched-genes are enriched in pathways relevant to tumor suppression. For example, they are enriched in the Hedgehog signaling and silencing pathways, which its improper activation is associated with the most common form of cancer malignancy. We also showed that the PVs are mostly more abundant in healthy people compared to cancer patients within different human races.

Keywords : cancer resistance, protecting variant, naked mole rat, comparative genomics
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