Title: A Structural Approach to Identify Activating and Loss of Function Somatic Mutation

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Affilations: MedGenome, Inc.

Abstract: Large scale sequencing of cancer genomes have revealed several mutations that remain uncharacterized. Only few mutations are tested using functional assays for activating or loss of function. In this study, we have applied in-silico method to characterize 4096 mutations in 190 cancer census genes spread across 33 cancer groups. We mainly studied mutations to identify gain and loss of function mutations. We have used features related to the three dimensional structure of the protein related to stability, protein-protein interactions, post translational modification and binding properties. Our analysis revealed 2,614 destabilizing mutations which would relate to a loss of function in 185 genes and 433 stabilizing mutations in 125 genes which could have a gain of function role. Interestingly, we found that the highly stabilizing mutations are enriched in proteins with nucleic acid binding activity, transcription regulators and kinases. Our analysis revealed that the D769 mutation in ERBB2 kinase domain is infact a stable mutation which makes the kinase constitutively active. It was also observed that majority of the mutations in the cancer census genes that are involved in binding have a destabilizing effect on the protein structure in general. Higher number of stabilizing mutations have been identified in TP53,CDKN2A and PIK3CA and destabilizing mutations are widely distributed across several genes.

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Abstract are below :

Title: SAGVDB â€“ An Integrated resource for South Asian genome variation

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Abstract: South Asian population, predominantly contributed by Indian sub-continent, represents a unique blend of genetically homogeneous, but socially and geographically stratified groups of individuals that can be leveraged to investigate complex diseases and disease phenotypes. However, a thorough understanding of the underlying genetic variation in different groups in South Asia is still not extensively explored. Although there is data out in terms of publication no attempt have been made to systematically analyze the South Asian genome and make it available to general public. In this study we have analyzed 215 whole genomes and 121 whole exomes from individuals from four South Asian countries, such as India, Pakistan, Sri Lanka and Bangladesh. Further, South Asian sample variants from 1000-genome-phase3 and ExAC databases are also integrated into the database. Overall, the integrated database contains ~ 34.2 million variants of which ~ 31 million SNPs and ~ 3.2 million are short InDels. Of the total variants in the database, 56.7% of the variant falls inside known gene. A total of 933,688 variants were found to be of coding non-synonymous type. Copy number analysis of the whole genome revealed 50,829 duplications and 67,984 deletions. Analysis of mitochondrial genome revealed that majority of samples belongs to M (45%), haplogroup followed by U (20%) and H (13%) haplogroup. The database shows allele frequencies statistics for population/sub-population, genome browser with adequate genome tracks, gene/transcript level annotation etc. The database also integrates variants from other studies including 1000-genome, ExAC, UK10K, GoNL, Iceland, EVS, 1000Japanese, Wellderly. SAGVDB will be a great resource for South Asian population based studies including identifying disease causal variants.

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