

# A New Front in Evolution: A Structural Landscape of Frameshift Mutations

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Currently, evolution is known to be caused by natural selection, gene flow, environmental factors, and mutations such as missense, nonsense, and duplications. Frameshift mutations are very rarely associated with evolution, and no comprehensive process to identify all evolutionarily significant frameshift mutations exists. These mutations are currently identified and studied in the context of disease by analyzing tissue samples collected from patients affected by pathogenic frameshift mutations. Therefore, many frameshift mutations, along with the evolutionary information they may contain, remain unidentified. An algorithm was developed to simulate all possible frameshift mutations that can occur in a human. This algorithm retrieved human mRNA sequences from the NCBI Nucleotide database, simulated frameshift mutations, and aligned the sequences to human proteins using BLAST. InterPro and SMART were used to create protein domain architectures for mutated, functional protein products. A total of three frameshift mutations were shown to conserve the original protein of the gene in which the mutation occurred. Additionally, a frameshift mutation in each of the RIPK2, STK25, ZNF410, PMPCA variant 2, and PMPCA variant 3 genes was shown to contribute to an evolutionary pathway. This work serves as an innovative and comprehensive approach to studying frameshift mutations at the protein domain level, and establishes a new frontier into evolutionary biology research.