Structural Modelling and In Silico Analysis of Human Superoxide Dismutase 2 (SOD2) Polymorphisms

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Introduction Aging in the world population has increased every year. Superoxide dismutase 2 (Mn-SOD or SOD2) protects against oxidative stress, a main factor influencing cellular longevity. Polymorphisms in SOD2 have been associated with the development of neurodegenerative diseases, such as Alzheimer's and Parkinson’s disease, as well as psychiatric disorders, such as schizophrenia, depression and bipolar disorder. Material and Methods In this study, all of the described natural variants (S10I, A16V, E66V, G76R, I82T and R156W) of SOD2 were subjected to in silico analysis using eight different algorithms: SNPeff, PolyPhen-2, PhD-SNP, PMUT, SIFT, SNAP, SNPs&GO and nsSNPAnalyzer. Structural theoretical models were created for variants through comparative modelling performed using the MHOLine server (which includes MODELLER and PROCHECK) and ab initio modelling, using the I-Tasser server. The predicted models were evaluated using TM-align. Results and Discussion This analysis revealed disparate results for a few of the algorithms. The results showed that, from at least one algorithm, each single-nucleotide mutation appears to harmfully affect the protein. The models were constructed with high accuracy, according to TM-align. The RMSD values of the modelled mutants indicated likely pathogenicity for all missense mutations. Structural phylogenetic analysis using ConSurf revealed that human SOD2 is highly conserved. Conclusion A human-curated database was generated that enables biologists and clinicians to explore SOD2 nsSNPs, including predictions of their effects and visualisation of the alignment of both the wild-type and mutant structures. The database is freely available at http://bioinfogroup.com/database/ and will be regularly updated.

Keywords: Single Nucleotide Polymorphism, SOD2, Database

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