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| **WD DOMAIN** |
| **SUBSTITUTION** | **DDG** | **STABILITY OF VARIENT** |  | **Predict SNP** |
|  C386W | -0.45 | DECREASE | Cavity altered | The substitution leads to the contraction of cavity volume by 111.024 Å^3 | DELETERIOUS |
| S396N  | -1.93 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| G397D | -2.09 | DECREASE | Buried charge introduced Buried Gly replaced  | This substitution replaces a buried uncharged residue (GLY, RSA 0.0%) with a charged residue (ASP) AND This substitution replaces a buried GLY residue (RSA 0.0%) with a buried ASP residue (RSA 0.0%) | DELETERIOUS |
| G411S  | -0.98 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  V418M | -0.53 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
| H420Y  | -0.6 | DECREASE |  Buried charge replaced AND CLASH | Tolerated | Tolerated |
| G422C | -0.49 | DECREASE |  Clash AND Gly in a bend! | This substitution triggers clash alert. The local clash score for wild type is 146.89 and the local clash score for mutant is 167.99. AND This substitution replaces glycine originally located in a bend curvature. | DELETERIOUS |
|  G423R | -0.7 | DECREASE | Buried Gly replaced, CLASH AND Buried / exposed switch | This substitution replaces a buried GLY residue (RSA 4.7%) with an exposed ARG residue (RSA 38.7%),,This substitution results in a change between buried and exposed state of the target variant residue. GLY is buried (RSA 4.7%) and ARG is exposed (RSA 38.7%). | DELETERIOUS |
| S426L  | -0.84 | DECREASE | Buried H-bond breakage | This substitution disrupts all sidechain / side-chain H-bond(s) and/or sidechain / main-chain bond(s) H-bonds formed by a buried SER residue (RSA 5.3%) | DELETERIOUS |
| G437V | -0.26 | DECREASE | Buried Gly replaced | This substitution replaces a buried GLY residue (RSA 0.0%) with a buried VAL residue (RSA 0.0%) | DELETERIOUS |
| G437R | -0.37 | DECREASE | Buried charge introduced,Buried Gly replaced  | This substitution replaces a buried uncharged residue (GLY, RSA 0.0%) with a charged residue (ARG). | DELETERIOUS |
| G437E | -0.39 | DECREASE | Buried charge introduced,Buried Gly replaced  | This substitution replaces a buried uncharged residue (GLY, RSA 0.0%) with a charged residue (GLU). | DELETERIOUS |
| D440N  | -0.96 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| W446C | -1.6 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| H460Y | -0.85 | DECREASE |  Buried charge replaced AND CLASH | This substitution triggers clash alert. The local clash score for wild type is 163.20 and the local clash score for mutant is 190.85 AND This substitution replaces a buried charged residue (HIS, RSA 3.2%) with an uncharged residue (TYR). | DELETERIOUS |
| H460R | -0.94 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | TOLARATED |
| S462Y | -0.64 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| V464E | -1.81 | DECREASE | Buried hydropilic introduced AND Buried charge introduced | This substitution replaces a buried hydrophobic residue (VAL, RSA 0.0%) with a hydrophilic residue (GLU, RSA 0.0%). | DELETERIOUS |
| V464M  | -1.12 | DECREASE | CLASH | This substitution triggers clash alert.The local clash score for wild type is 153.74 and the local clash score for mutant is 175.15. | DELETERIOUS |
| H470P | -0.1 | DECREASE | Secondary structure altered AND Disallowed phi/psi  | This substitution changes 'E' (extended strand in parallel and/or anti-parallel β-sheet conformation) to ' ' (no secondary structure). | Tolerated |
| S476R | 0.07 | DECREASE | Buried charge introduced, Buried H-bond breakage | This substitution replaces a buried uncharged residue (SER, RSA 0.0%) with a charged residue (ARG). | DELETERIOUS |
| G477S | -0.44 | DECREASE | Buried Gly replaced | This substitution replaces a buried GLY residue (RSA 0.0%) with a buried SER residue (RSA 0.0%) | Tolerated |
|  R479S | -1.03 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  R479H | -0.97 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  R479Q | -0.81 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  R479G | -2.13 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
| D480Y  | -0.19 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
|  H500R | -1.59 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
|  H500Y | -0.7 | DECREASE | Buried charge replaced | This substitution replaces a buried charged residue (HIS, RSA 4.8%) with an uncharged residue (TYR) | DELETERIOUS |
|  H500D | -1.06 | DECREASE | Buried charge switch | This substitution replaces a buried positive-charged residue (HIS, RSA 4.8%) with a negative-charged residue (ASP). | DELETERIOUS |
| A503T | -1.36 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  V504I | -1.16 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
| S516R | 0.11 | DECREASE | Buried charge introduced, Buried H-bond breakage  | This substitution replaces a buried uncharged residue (SER, RSA 0.0%) with a charged residue (ARG). AND This substitution disrupts all sidechain / side-chain H-bond(s) and/or sidechain / main-chain bond(s) H-bonds formed by a buried SER residue (RSA 0.0%). | DELETERIOUS |
|  S516N | -0.29 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| G517E | -1.23 | DECREASE | Buried charge introduced, Buried Gly replaced, Buried H-bond breakage | This substitution replaces a buried uncharged residue (SER, RSA 0.0%) with a charged residue (ARG). AND This substitution disrupts all sidechain / side-chain H-bond(s) and/or sidechain / main-chain bond(s) H-bonds formed by a buried SER residue (RSA 0.0%). | DELETERIOUS |
| D520N  | -0.67 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| W526R | -0.4 | DECREASE | Buried hydrophilic introduced, buried charge introduced AND Buried H-bond breakage  | This substitution replaces a buried uncharged residue (GLY, RSA 0.0%) with a charged residue (GLU), This substitution replaces a buried GLY residue (RSA 0.0%) with a buried GLU residue (RSA 0.0%). AND This substitution disrupts all sidechain / side-chain H-bond(s) and/or sidechain / main-chain bond(s) H-bonds formed by a buried GLY residue (RSA 0.0%). | DELETERIOUS |
| W526L | -0.48 | DECREASE | Buried H-bond breakage | This substitution disrupts all sidechain / side-chain H-bond(s) and/or side-chain / main-chain bond(s) H-bonds formed by a buried TRP residue (RSA 0.4%) | DELETERIOUS |
|  S546L | -0.85 | DECREASE | Buried H-bond breakage | This substitution disrupts all sidechain / side-chain H-bond(s) and/or side-chain / main-chain bond(s) H-bonds formed by a buried TRP residue (RSA 0.4%) | DELETERIOUS |
|  S558F | -0.84 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| D560G | -0.14 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
|  S562L | -0.75 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| I563T | -0.18 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| D600H | -1.59 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| S601F  | 0.3 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
| R658Q | -1.95 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| G597E | -1.71 | DECREASE | Buried charge introduced Buried Gly replaced | This substitution replaces a buried uncharged residue (GLY, RSA 0.0%) with a charged residue (GLU) | DELETERIOUS |
| S582L | -0.69 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  H379R  | -0.21 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| H382N | -2.09 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
| K404E | -0.3 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
|  R441W | 0.34 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
|  G579W | -0.22 | INCREASE | Disallowed phi/psi! | This substitution results in a change between buried and exposed state of the target variant residue. SER is buried (RSA 2.3%) and LEU is exposed (RSA 15.8%). | DELETERIOUS |
| D600Y | -0.2 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
|  A481V  | 0.46 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  R479L | -0.14 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
|  R479P | -0.6 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
| S476I | 0.83 | INCREASE | Buried H-bond breakage | This substitution disrupts all sidechain / side-chain H-bond(s) and/or sidechain / main-chain bond(s) H-bonds formed by a buried SER residue (RSA 0.0%) | DELETERIOUS |
| S398F | 0.49 | INCREASE | Buried H-bond breakage! | This substitution disrupts all sidechain / side-chain H-bond(s) and/or sidechain / main-chain bond(s) H-bonds formed by a buried SER residue (RSA 0.0%) | DELETERIOUS |

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| **F BOX DOMAIN** |
| SUBSTITUTION | DDG | STABILITY OF VARIENT | Predict SNP |
| P285H | -0.64 | DECREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| L301P | -1.26 | DECREASE | This substitution introduces a buried proline. | DELETERIOUS |
| E287V | 0.08 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | DELETERIOUS |
| P298L | 0.09 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |
| L320I  | 0.64 | INCREASE | NO STRUCTURAL DAMAGE DETECTED | Tolerated |