| **Variant (Human)** | **Mouse residue** | **conserved** | **cDNA variants** | **CADD** | **domain** |
| --- | --- | --- | --- | --- | --- |
| **N-arm** |  | | | | |
| p.Cys118Arg | Trp114 |  | c.352T>C | 2 | N-hand |
| p.Leu133Met | Leu129 | yes | c.397C>A | 13 | N-hand |
| p.Ile209Asn | Lys197 |  | c.626T>A | 0 | N-hand |
| p.Pro395Leu | Pro364 | yes | c.1184C>T | 1 | N-hand |
| p.Gly517Arg | Ser489 |  | c.1549G>[A;C] | 1 | N-arm |
| p.Glu996Lys | Glu969 | yes | c.2986G>A | 10 | N-arm |
| p.Ala1135Val | Asp1112 |  | c.3404C>T | 22 | N-arm |
| **Linker** |  | | | | |
| p.Ser1474Phe | Ser1437 | yes | c.4421C>T | 23 | Linker |
| p.Ala1622Val | Val1586 |  | c.4865C>T | 2 | Linker |
| p.Thr1705Lys | Thr1667 | yes | c.5114C>A | 21 | Linker |
| p.Pro1721Leu | Pro1683 | yes | c.5162C>T | 24 | Linker |
| **AAA** |  | | | | |
| p.Ala1844Thr | Ala1806 | yes | c.5530G>A | 21 | AAA |
| p.Asp2554Glu | Asp2515 | yes | c.7662C>[A;G] | 3 | AAA |
| **E3** |  | | | | |
| p.Arg3846His | Ala3796 |  | c.11537G>A | 2 | E3-back |
| p.Met3891Val | Thr3841 |  | c.11671A>G | 2 | E3-back |
| p.Glu3915Gly | Glu3865 | yes | c.11744A>G | 23 | E3-back |
| p.Arg3922Gln | Arg3872 | yes | c.11765G>A | 10 | E3-back |
| p.Ala3927Thr | Ala3877 | yes | c.11779G>A | 26 | E3-back |
| p.Val3933Met | Val3883 | yes | c.11797G>A | 16 | E3-back |
| p.Glu3950Asp | Thr3900 |  | c.11850G>[C;T] | 9 | E3-back |
| p.Asn3962Asp | Asp3912 |  | c.11884A>G | 24 | E3-back |
| p.Cys3997Tyr | Cys3947 | yes | c.11990G>A | 21 | E3-RING |
| p.Pro4007Arg | Pro3957 | yes | c.12020C>G | 23 | E3-RING |
| p.Asp4013Asn | Asp3963 | yes | c.12037G>A | 24 | E3-RING |
| p.His4014Asn | His3964 | yes | c.12040C>A | 18 | E3-RING |
| p.Arg4019Cys | Arg3969 | yes | c.12055C>T | 26 | E3-RING |
| p.Cys4032Arg | Cys3982 | yes | c.12094T>C | 25 | E3-RING |
| p.Pro4033Leu | Pro3983 | yes | c.12098C>T | 0 | E3-RING |
| p.Glu4042Lys | Lys3992 |  | c.12124G>A | 22 | E3-RING |
| p.His4051Pro | His4001 | yes | c.12152A>C | 17 | E3-back |
| p.His4058Pro | His4008 | yes | c.12173A>C | 14 | E3-back |
| p.Arg4062Gln | Arg4012 | yes | c.12185G>A | 21 | E3-back |
| p.Ile4076Val | Met4026 |  | c.12226A>G | 10 | E3-back |
| p.Ser4118Phe | Ser4068 | yes | c.12353C>T | 21 | E3-shell |
| p.Asp4122Val | Asp4072 | yes | c.12365A>T | 11 | E3-shell |
| p.Arg4131Cys | Arg4081 | yes | c.12391C>T | 9 | E3-shell |
| p.Val4146Ala | Val4096 | yes | c.12437T>C | 24 | E3-shell |
| p.Lys4185Glu | Lys4135 | yes | c.12553A>G | 25 | E3-shell |
| p.Lys4185Thr | Lys4135 | yes | c.12554A>C | 25 | E3-shell |
| p.Ala4188Thr | Ala4138 | yes | c.12562G>A | 32 | E3-shell |
| p.Asp4237Glu | Asp4186 | yes | c.12711C>[A;G] | 27 | E3-shell |
| p.Gln4367Leu | Gln4313 | yes | c.13100A>T | 27 | E3-shell |
| p.Ala4399Thr | Ala4345 | yes | c.13195G>A | 25 | E3-shell |
| p.Val4567Met | Val4513 | yes | c.13699G>A | 15 | E3-shell |
| p.Thr4586Pro | Thr4533 | yes | c.13756A>C | 14 | E3-shell |
| p.Pro4608Ser | Trp4555 |  | c.13822C>T | 23 | E3-shell |
| p.Leu4631Val | Leu4578 | yes | c.13891C>G | 7 | E3-shell |
| p.Gly4640Ser | His4587 |  | c.13918G>A | 14 | E3-shell |
| p.Trp4677Leu | Trp4620 | yes | c.14030G>T | 8 | E3-shell |
| p.Lys4732Thr | Lys4675 | yes | c.14195A>C | 7 | E3-shell |
| p.Val4765Met | Val4708 | yes | c.14293G>A | 26 | E3-core |
| p.Arg4810Gly | Arg4753 | yes | c.14428A>G | 23 | E3-core |
| p.Arg4810Lys | Arg4753 | yes | c.14429G>A | 16 | E3-core |
| p.Asp4863Asn | Asp4806 | yes | c.14587G>A | 5 | E3-core |
| **CTD** |  | | | | |
| p.Ala5021Val | Ala4964 | yes | c.15062C>T | 23 | CTD |
| p.Met5136Ile | Met5079 | yes | c.15408G>[A;C;T] | 10 | CTD |
| p.Asp5160Glu | Asp5101 | yes | c.15480C>[A;G] | 18 | CTD |
| p.Val5163Ile | Val5104 | yes | c.15487G>A | 21 | CTD |
| p.Glu5176Gly | Glu5117 | yes | c.15527A>G | 21 | CTD |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **start** | **end** | **name** | **mutation frequency** | **CADD >20** |
| 1 | 1290 | N-arm | 3 in 1290 | 1 in 1290 |
| 1291 | 1774 | Linker | 4 in 484 | 3 in 484 |
| 1775 | 3405 | AAA | 2 in 1631 | 1 in 1631 |
| 3406 | 3588 | Hinge | 0 in 183 | 0 in 183 |
| **3589** | **4911** | **E3** | **41 in 1333** | **21 in 1333** |
| 3589 | 3939 | E3-back-a | 8 in 351 | 3 in 351 |
| 3940 | 3999 | E3-RING | 8 in 60 | 6 in 60 |
| 4000 | 4027 | E3-back-b | 4 in 28 | 1 in 28 |
| 4028 | 4688 | E3-shell | 17 in 661 | 9 in 661 |
| 4689 | 4911 | E3-core | 4 in 223 | 2 in 223 |
| 4912 | 5148 | CTD | 5 in 238 | 3 in 238 |