|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Modified Residue | Nearby Variant | Location | Association by Literature | Cardiomyopathy Designation | Literature Review | ClinVar (Classification) |
| K34/ K58 | R17C | SH3 | LP | HCM | Alamo et al. 2017 | --------- |
| A26V | SH3 | P | HCM | Van Driest et al. 2004 | Benign |
| V39M | SH3 | P | HCM | Van Driest et al. 2004 | Conflicting interpretations of pathogenicity |
| R54X | SH3 | P | HCM | Van Driest et al. 2004 | --------- |
| V59I | SH3 | P | HCM | Alamo et al. 2017 | --------- |
| G181R | P-Loop | P/LP | DCM | Alamo et al. 2017 | --------- |
| R190T | Near P-Loop | P | HCM | Van Driest et al. 2004 | --------- |
| Q193R | Near P-Loop | LP | HCM | Alamo et al. 2017 | --------- |
| A196T | Near Loop 1 | P | HCM | Woo et al. 2003 | --------- |
| A199V | Near Loop 1 | LP | HCM | Alamo et al. 2017 | --------- |
| I201T | Near 25/50 junction (Loop1) | P | DCM | Uniprot | Pathogenic/ Likely pathogenic |
| R204C | Loop 1 | P | HCM | Alamo et al. 2017 | --------- |
| R204H | Loop 1 | P | HCM | Uniprot | Conflicting interpretations of Pathogenicity |
| K207Q | Loop 1 | P | HCM | Uniprot | Conflicting interpretations of pathogenicity |
| P211L | Loop 1 | LP | HCM | Woo et al. 2003 | Uncertain significance |
| G214D | Loop 1 | P | HCM | Alamo et al. 2017 | --------- |
| Q222K | Near Loop 1 | P | HCM | Van Driest et al. 2004 | --------- |
| A223T | Near Loop 1 | P | DCM | Uniprot | Uncertain significance |
| L227V | Near Switch 1 | P | HCM | Uniprot | --------- |
| N232S | Near Switch 1 | Benign | ---- | Marin-Garcia et al. 2014 | --------- |
| N232H | Near Switch 1 | P | HCM | Alamo et al. 2017 | --------- |
| D239N | Switch 1 | LP | HCM | Alamo et al. 2017 | --------- |
| R243H | Switch 1 | P | DCM | Alamo et al. 2017 | Conflicting interpretations of Pathogenicity |
| G245E | Switch 1 | P | DCM | Alamo et al. 2017 | --------- |
| I248F | Near Switch 1 | p | DCM | Alamo et al. 2017 |  |
| K429 | R403W/G/L/Q | CM-Loop | P | HCM | Alamo et al. 2017 | Uncertain significance/ Pathogenic |
| V406M | CM-Loop | LP | HCM | Alamo et al. 2017 | --------- |
| G407V | CM-Loop | LP | HCM | Uniprot | Likely Pathogenic |
| Y410D | CM-Loop | LP | HCM | Alamo et al. 2017 | --------- |
| V411I | CM-Loop | P | HCM | Woo et al. 2003 | Conflicting interpretations of pathogenicity |
| T412N | CM-Loop | P | DCM | Villard et al. 2005 | --------- |
| G425R | Near CM-Loop | P | HCM | Uniprot | Conflicting interpretations of pathogenicity |
| L427M | Near CM-Loop | LP | HCM | Alamo et al. 2017 | --------- |
| A428V | Near CM-Loop | P | HCM | Van Driest et al. 2004 | Likely pathogenic |
| A430E | Near CM-Loop | P | HCM | Uniprot | Likely pathogenic; Uncertain significance. |
| M435T | Near Switch 2 | P | HCM | Uniprot | --------- |
| V440M | Upper 50 KDa Domain | P | HCM | Van Driest et al. 2004 | Conflicting interpretations of pathogenicity |
| T441M | Upper 50 KDa Domain | Benign | Myopathy | Uniprot | Conflicting interpretations of pathogenicity |
| R442C | Upper 50 KDa Domain | P | HCM | Alamo et al. 2017 | --------- |
| I443T | Near Switch 2 | P | HCM | Van Driest et al. 2004 | --------- |
| T449S | Near Switch 2 | LP | HCM | Alamo et al. 2017 | --------- |
| R453C | Sequentially Near Switch 2 | P | HCM | Alamo et al. 2017 | Uncertain significance/ Pathogenic |
| R453S/H | Sequentially Near Switch 2 | LP | HCM | Alamo et al. 2017 | Uncertain significance/ Pathogenic |
| K951 | E930K | Ring 2 | P | HCM | Alamo et al. 2017 | Pathogenic/Likely Pathogenic |
| E931K | Ring 2 | P | HCM | Van Driest et al. 2004 | --------- |
| E935K | Ring 2 | P | HCM | Van Driest et al. 2004 | Pathogenic |
| E949K | Ring 3 | P | HCM | Anan et al. 1994 | Uncertain significance |
| D953H | Ring 3 | P | HCM | Van Driest et al. 2004 | --------- |
| L961R | Near Ring 3 | P | HCM | Van Driest et al. 2004 | --------- |
| E967K | Near Ring 3 | LP | HCM | Alamo et al. 2017 | --------- |
| K1195 | R1193S | Near Skip 1 | P | DCM | Villard et al 2005 | Uncertain significance |
| R1193H | Near Skip 1  | P | DCM | Alamo et al. 2017 | --------- |

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**Supplemental Table 2**