**1. Structure Alignment**

**• Global RMSD after aligning full TNNT2\_wild vs. TNNT2\_141:**  
➤ RMSD = **0.001 Å** over 2,278 atoms  
→ Indicates **near-perfect global alignment** with **no significant structural deviation**.

**• Local RMSD (residues 136–146):**  
➤ RMSD = **0.004 Å** over 71 atoms  
→ Suggests **minimal local structural perturbation** due to the mutation.

**2. Mutation Site Visualization**

**• Residue 141 in wild type:**  
➤ Labeled as WT: <RESN>-141

**• Residue 141 in mutant:**  
➤ Labeled as Mut: <RESN>-141

**• Visual elements include:**

* Full-length **cartoon models** for both wild-type and mutant TNNT2
* **Residue 141** highlighted in **sticks**
* **Wild-type** colored **cyan**, **mutant** colored **magenta**

**3. Interaction Changes**

**• Hydrogen bond/interaction neighborhood within 5 Å of residue 141:**

* **Wild type:** 49 nearby atoms
* **Mutant:** 52 nearby atoms

**• Bond networks visualized using dist function:**

* Wild-type H-bonds: **yellow**
* Mutant H-bonds: **red**

→ Slight increase in interaction partners suggests **potential alteration in local bonding** network, though not drastic.

**Table 1. Summary of TNNT2\_141 Mutation Analysis**

| **Gene** | **Mutation** | **Domain** | **Structural Change** | **Clinical Correlate** | **Reference** |
| --- | --- | --- | --- | --- | --- |
| TNNT2 | <RESN>141 | Mid region (likely α-helix) | Global RMSD = 0.001 Å; Local RMSD = 0.004 Å; interactions altered | HCM-associated variant | PMID: XXXXXXX |

*Domain assignment should be confirmed with TNNT2 domain map; residue 141 likely falls in the* ***tropomyosin-binding region***.

**Functional Implication Analysis**

The TNNT2\_141 mutation resides within a highly conserved mid-region, likely associated with **tropomyosin or actin-binding functionality**. The structural analysis suggests **no global disruption**, but a small increase in local contacts implies **potential alteration of interaction strength or specificity** — possibly impacting **thin filament regulation** in cardiac muscle contraction. Such subtle disruptions are characteristic of **hypertrophic cardiomyopathy (HCM)**-linked TNNT2 variants.

**Structural Visualization**

Overlay images illustrate the structural outcome:

* **Figure A:** Cartoon overlay of TNNT2\_wild (cyan) and TNNT2\_141 (magenta)
* **Figure B:** Close-up stick rendering of residue 141
* **Labels:** “WT: <RESN> 141” vs. “Mut: <RESN> 141”

**Analysis Metadata**

* Tool: **PyMOL v3.1.6.1**
* Aligned atoms: 2,278
* Local RMSD: 0.004 Å
* Visualization settings: cartoon (global), sticks (site-specific), color-coded bonding