Calcium Impairment and Altered Dynamics of a Cardiomyopathy-causing Mutation in Troponin C Explains Disease Phenotype

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INTRODUÇÃO.Hypertrophic cardiomyopathy (HCM) is one of the most common cardiomyopathies being the major cause of sudden death in young athletes affecting 1 per 500 persons . Cardiac troponin C (cTnC) is the Ca^{2+} sensor of sarcomere and plays an important role in regulating muscle contraction. **OBJETIVO:** Although several cardiomyopathy-causing mutations were identified in cTnC, no information about their structural effects have been attempted to explain HCM phenotype **MATERIAL E METODOS:** Carr-Purcell-Meiboom-Gill relaxation dispersion has captured a low-populated protein folding intermediate as the result of a disease-related mutation that disrupts ion coordination. **DISCUSSÃO E RESULTADOS**: information about their structural effects have been attempted to explain HCM phenotype . Here we showed the mutant D145E inactivates both Ca^{2+} binding sites at cTnC C-domain and abolishes the binding to $cTnI_{128-147}$ peptide because of an altered dynamics occurring in the µs-ms timescale. **CONCLUSAO:** Our results may help to explain how altered dynamics may affect protein functionality and adaptation to the development of pathological phenotypes in complex systems.

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