INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	**Rahul Kumar Thaosen**
Roll Number	:	**186106012**
Programme of Study	:	**Ph.D.**

Thesis Title: **Understanding the role of heat shock protein 80 in thermotolerance and cell survival in *Neurospora crassa***

Name of Thesis Supervisor(s)	:	**Prof. Ranjan Tamuli**
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SHORT ABSTRACT

Heat shock proteins (Hsps) are critical molecular chaperones that help maintain cellular protein homeostasis under stress conditions. Among these, Heat Shock Protein 80 (Hsp80), a homolog of Hsp90 in *Neurospora crassa*, plays a significant role in diverse cellular stress responses, including thermotolerance, DNA repair and osmotic stress adaptation. In this study, the molecular mechanisms underlying HSP80 function were explored through both experimental and computational approaches. Using repeat-induced point mutation (RIP), four hsp80 mutant strains (R4 A, R6 A, R9 a, and R14 a) were generated and phenotypically characterized. The mutants exhibited significantly reduced survival under elevated temperatures and various abiotic stress conditions, including oxidative, osmotic, pH and endoplasmic reticulum stress. Additional defects such as impaired aerial hyphae formation, defective cellulose utilization, reduced carotenoid biosynthesis and compromised DNA repair under UV and MMS exposure further underscored the functional importance of Hsp80 in cellular stress adaptation. Transcriptional profiling revealed downregulation of key stress responsive genes and DNA repair genes in the RIP mutants correlating with their phenotypic deficiencies. Complementary in silico analyses, including structure prediction and molecular dynamics simulations across thermal conditions (298K, 333K, 362K) showed that wild type HSP80 maintained superior conformational stability and hydrogen bond retention, while mutants especially R9 a and R14 a exhibited increased flexibility, higher RMSD/RMSF and unfavourable interaction energies under thermal stress.