INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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SHORT ABSTRACT

Neuronal calcium sensor-1 (NCS-1) belongs to the neuronal calcium sensor family of proteins consisting of N terminal myristoylation domain and four conserved calcium (Ca^{2+}) binding EF-hand domains. NCS-1 is a highly conserved protein from lower to higher eukaryotes. In mammals NCS-1 is a very important protein as it is associated with synaptic transmission, memory and learning. In *Neurospora crassa*, NCS-1 plays an important role in vegetative growth, Ca^{2+} and ultraviolet stress survival. The molecular pathway of the neuronal calcium sensor-1 (NCS-1) mediated Ca^{2+} stress tolerance in *N. crassa* was studied in this research work. The expression of *ncs-1* inceases with increasing Ca^{2+} stress condition; however, addition of the calcineurin inhibitor FK506 in the medium caused a severe downregulation of *ncs-1* transcription. In addition, chromatin immunoprecipitation (ChIP) assay revealed that the transcription factor calcineurin responsive zinc finger-1 (CRZ-1) binds to the *ncs-1* promoter, and upregulates *ncs-1* expression during the Ca^{2+} stress condition. These results suggest the regulation of NCS-1 function through calcineurin -CRZ-1 signaling pathway. Furthermore, the electrophoretic mobility shift assay (EMSA) revealed that CRZ-1 specifically binds to an 8 bp sequence 5'-CCTTCACA-3' in the *ncs-1* promoter, located 216 bp upstream of the ATG start codon. A physical interaction between NCS-1 and the Ca^{2+} permeable channel MID-1 during Ca^{2+} stress was also shown. Therefore, CRZ-1 binds to a unique sequence in the *ncs-1* promoter for its upregulation, and NCS-1 interacts with MID-1 for Ca^{2+} stress survival. In addition, the rat NCS-1 was expressed in *N. crassa* and the

heterologous expression of rat NCS-1 complemented the slow growth, Ca^{2+} and UV sensitive phenotypes of Δ*ncs-1* mutant of *N. crassa* suggesting an interspecific functional conservation of NCS-1. Moreover, the glutamic acid at position 120 was found to be critical for the functioning of rat NCS-1.