INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	**Serena Ngiimei D**
Roll Number	:	**176106005**
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Name of Thesis Supervisor(s)	:	**Prof. Ranjan Tamuli**
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Thesis Title: Cell functions and molecular mechanisms of zinc transporters in *Neurospora crassa*

In this thesis work, I studied the cellular functions and molecular mechanisms of zinc resistance-conferring 1 (ZRC-1), meiotic sister chromatid 2 (MSC-2), and zinc-regulated gene 17 (ZRG-17) that are members of the cation diffusion facilitator (CDF) family of zinc transporters in *Neurospora crassa*. The Δ*zrc-1* mutant was unable to grow under high zinc conditions (≥ 0.5 mM). However, the expression of *zrc-1* was elevated ~3-fold under low zinc conditions in comparison to normal and high zinc concentrations. The Δ*msc-2* mutant showed colony growth and aerial hyphae similar to wild type and the expression of *msc-2* was independent of zinc. Furthermore, the double mutant Δ*zrc-1*; Δ*msc-2* and Δ*zrc-1*; Δ*zrg-17* showed additive phenotypes of both the parental single mutants. However, the phenotypic defects such as slow growth rate, defective in asexual sporulation, and inability to degrade cellulose of the Δ*zrg-17* single mutant were restored in the Δ*msc-2*; Δ*zrg-17* double mutant, which showed phenotypes similar to the wild type. The double mutant Δ*zrc-1*; Δ*zrg-17* showed severe growth defects, stunted aerial hyphae, short septa, and defects in conidiation. In addition, the Δ*zrc-1*; Δ*msc-2* and Δ*zrc-1*; Δ*zrg-17* double mutants showed sensitivity to DTT-induced ER stress and were unable to grow in the medium containing cellulose. Furthermore, zinc-responsive activator protein 1 (ZAP-1) was also studied to understand the molecular mechanism and the interaction of the CDF zinc transporters with the transcription factor. The *zap-1* of *N. crassa* was found to be crucial for survival under low zinc conditions and ZAP-1 was localized in nucleus under all zinc conditions tested. The double mutants Δ*zap-1*; Δ*zrc-1*, Δ*zap-1*; Δ*msc-2*, and Δ*zap-1*; Δ*zrg-17* showed slow growth under low zinc like Δ*zap-1*, indicating that ZAP-1 might be functioning upstream of *zrc-1*, *msc-2*, and *zrg-17*. Furthermore, expression analysis of the CDF family of zinc transporter, *zrc-1*, *msc-2*, *zrg-17*, and *zrt-3* in Δ*zap-1* mutant showed very low-level expressions compared to expression in wild type, indicating that the ZAP-1 transcription factor regulates the CDF zinc transporters under low zinc conditions.