Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

From internal transcription start site selection to altered protein products:
A systematic survey and a case study in budding yeast sporulation

By

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High-throughput studies unveiled unexpected complexity of the transcriptome in eukaryotes. One particular type of change in transcriptome architecture, transcription initiated within an open reading frame, shortens 5'-UTR and has the potential to generate altered protein products. Budding yeast gametogenesis, or sporulation, is a developmental process where diploid cells undergo meiosis to produce gametes in response to nutrient deprivation. Accompanied by massive changes in gene expression, sporulation is a great system to study transcriptional and post-transcriptional regulation. Among the meiotic transcriptome of budding yeast, internally initiated transcripts have been observed previously. Nonetheless, no analyses on next-generation sequencing datasets have been carried out to determine internal transcriptional initiations along sporulation. To systematically identify novel internal transcription start sites unique to a certain period in sporulation, I have developed a customized bioinformatical pipeline that performs unbiased transcription architecture comparison. By applying this approach to an RNA-Seq dataset of a highly synchronized meiotic time-course, dramatically different sets of genes with novel internal initiations are detected in early and mid-sporulation, suggesting that internal initiations are highly dynamic during sporulation. One key regulator in the transcription cascade of sporulation, Ndt80, is a master inducer of ~300 mid-sporulation genes that are required for meiotic divisions and spore formation. Motif analysis on the upstream sequences of internally initiated transcripts reveals enrichment for Ndt80 binding motifs in the 43 genes that display mid-sporulation specific internal initiation. To further study the detailed regulation, my research focused on the candidate *MRK1*, one of the budding yeast homologs of GSK-3 kinases. Mutation study reveals direct regulation of *MRK1* internal initiation by Ndt80, which results in the expression of an N-terminally truncated protein isoform. Additionally, functional analyses show that *MRK1* promotes sporulation in redundancy to its paralog, *RIM11*. Taken together, my findings using budding yeast sporulation as a model system suggest internal transcriptional initiation to be a dynamic, regulated process with potential functional impacts on development.

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