Instituto de Biología Funcional y Genómica

Programa de Seminarios Externos
"Dionisio Martín Zanca"
2023 - 2024

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Building a yeast transcriptome atlas through single cell genetic x environmental screens

Viernes 10 Noviembre 2023

Hora: 12:30 pm
Lugar: Salón de actos del IBFG
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Abstract

Transcriptional response to environmental stress is a critical mechanism of cell survival. Activation of stress-activated protein kinases, such as Hog1/p38, is key to allowing cells to respond to osmotic stress. However, even genetically identical cells to stress are highly variable and potentially affect the overall response of a population. By applying single-cell RNA-seq (scRNA-seq) we characterized the transcriptional landscapes underlying osmoadaptation. Our findings reveal that, within a clonal population, distinct transcriptional states exist. However, the expression of the osmoadaptive gene network is heterogeneous. Transcriptional heterogeneity is a characteristic inherent to virtually all systems, but the molecular mechanisms regulating this remain elusive. Single-cell genetic perturbation experiments provide a means to functionally understand the interplay between genotype and transcriptome. We have integrated scRNA-seq with a functional, genome-wide genetic screen to elucidate the principles governing transcriptional heterogeneity. We repurposed the yeast knockout collection to generate RNA-barcoded deletions, which we then profiled using high-throughput scRNA-seq. We analyzed 1 million cells from 3,400 distinct genotypes under both basal and stress conditions. This allowed us to construct a high-resolution genotype-transcriptome map and evaluate the functional impact of genetic perturbations on the resulting transcriptome.

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