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Annual Congress on

Mycology and Fungal Infections

November 16-17, 2017 Atlanta, Georgia, USA

The hnRNP-like yeast termination factor Nab3 can employ heterologous low complexity domains in place of its essential low complexity domain

Travis Loya
Emory University, USA

Many RNA-binding proteins possess domains with biased amino acid content. A common property of these low complexity domains (LCDs) is that they assemble into an ordered amyloid form, juxtaposing RNA recognition motifs in a subcellular compartment in which RNA metabolism is focused. Yeast Nab3 is one such protein that contains RNA-binding domains and a low complexity, glutamine/proline-rich, prion-like domain that can self-assemble. Nab3 also contains a region of structural homology to human hnRNP-C that resembles a leucine zipper which can oligomerize. We determined that the LCD and the human hnRNP-C homology domain of Nab3 are experimentally separable, as cells are viable with either segment, but not when both are missing. In exploiting the lethality of deleting these regions of Nab3, we tested if heterologous prion-like domains known to assemble into amyloid can substitute for the native sequence. These results suggest there are different cross-functional classes of amyloid-forming LCDs and that appending merely any assembly-competent LCD to Nab3 does not restore function or rescue viability. As LCD's are known to be mediators of RNA granule formation *in vivo*, we are also exploring the subcellular localization of wild-type and mutant Nab3's in response to sugar deprivation. Wild-type Nab3 localizes to granules during sugar deprivation, while LCD mutants show a loss of localization, showing this to be an LCD-mediated process. Analysis of Nab3 has provided insights into the diversity of LCD mediated interactions as well as a means of dissecting their function in the cell.

Biography

Travis Loya is a third year graduate student in the Biochemistry, Cell, and Developmental Biology program in the Laney graduate school at Emory University. He has participated in multiple short reviews for F1000 as well as published five manuscripts and one review article during his time in the lab of Dr. Danny Reines. He plans to graduate in 2018 and move on to an academic post-doctoral position continuing to explore the emerging field of low complexity domain containing proteins and their roles in biology.

tloya2@emory.edu

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