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Switching septins spurs sporulation

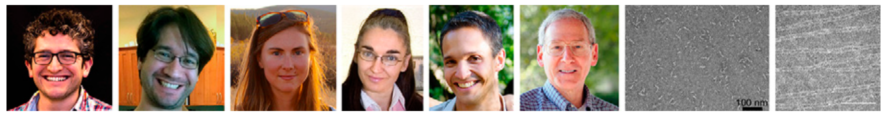
Researchers investigate how developmental changes in subunit composition allow septins to perform different functions.

Septins are a family of GTP-binding proteins that, in most fungi and animals, form hetero-octameric rods containing two copies each of four different family members. These rods can then assemble into higher-order structures that perform a variety of cellular functions, depending on their subunit composition. The human genome, for example, encodes 13 different septins expressed by specific cell types at specific times. How distinct family members affect the overall structure and function of septin complexes remains unclear, however. Garcia et al. examine how two meiosis-specific septins alter the properties of septin complexes in order to support budding yeast sporulation (1).

Mitotic budding yeast express five different septins that can assemble into two types of hetero-octamer containing a Cdc12–Cdc3–Cdc10–Cdc10–Cdc3–Cdc12 core capped at both ends by either Cdc11 or Shs1. In vitro, Cdc11-capped rods assemble into tightly paired filaments that are long and straight, whereas Shs1-capped octamers polymerize into spirals and rings (2, 3). In vivo, the two types of octamer combine to form a collar at the bud neck that regulates cytokinesis.

Under starvation conditions, however, diploid budding yeast undergo meiosis to produce four haploid spores. Meiotic cells express two additional septins—Spr3 and Spr28—that, together with Cdc3 and Cdc10, localize to horseshoe-shaped septin structures associated with the prospore membranes that form around each haploid nucleus (4). One possibility, says Jeremy Thorner, from the University of California, Berkeley, is that Spr3 and Spr28 replace the mitotic septins they most resemble—Cdc12 and Cdc11/Shs1, respectively—to form a meiosis-specific hetero-octamer with distinct structural and functional properties.

FOCAL POINT



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A team of researchers including (left to right) Galo Garcia, Gregory Finnigan, Lydia Heasley, Eva Nogales, Michael McMurray, and Jeremy Thorner investigate how two budding yeast septins that are specifically expressed during meiosis affect the structure and function of septin complexes. The researchers find that the meiotic septins Spr3 and Spr28 replace the mitotic septins Cdc12 and Cdc11/Shs1 at the ends of hetero-octameric rods (second from right) that also contain Cdc3 and Cdc10. In the presence of lipid monolayers containing PtdIns4,5P_2 (far right), the rods assemble into long paired filaments, potentially mimicking the assembly of septin complexes on the prospore membrane in sporulating yeast cells. Yeast lacking *SPR3* and *SPR28* fail to sporulate properly. This phenotype can't be rescued by the expression of Cdc12 and Cdc11, indicating that Spr3 and Spr28 endow septin complexes with unique functional properties.

To test this idea, Thorner and colleagues expressed and purified different combinations of septins and found that, indeed, Spr28 and Spr3 can replace Cdc11 and Cdc12 to form stable Spr28–Spr3–Cdc3–Cdc10–Cdc10–Cdc3–Spr3–Spr28 hetero-octamers in vitro (1). Unlike mitotic septin octamers, these meiosis-specific complexes didn't assemble into higher order structures in solution. In the presence of PtdIns4,5P_2-containing membranes, however, the meiotic octamers polymerized end-on-end to form ladder-like structures consisting of two long filaments connected together by regularly spaced "rungs." "PtdIns4,5P_2 can electrostatically attract the septins out of solution and help organize them on the surface of the membrane," Thorner explains. Similar events may occur in vivo, since PtdIns4,5P_2 is enriched in the prospore membrane.

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The incorporation of Spr3 and Spr28 therefore affects the higher-order assembly of septin octamers. But do they alter septin function? Despite their meiosis-specific expression, previous studies failed to identify any sporulation defects in Spr3- or Spr28-deficient cells. But coauthors Lydia Heasley and Michael McMurray found that cells lacking either of the meiotic septins sporulated poorly (5), and didn't form any spores at all when both proteins were missing. Crucially, these sporulation defects weren't rescued by expressing Cdc11 and Cdc12 during meiosis, indicating that Spr3 and Spr28 confer a unique function on meiotic spetin complexes.

"Conversely, if you express Spr28 and Spr3 in mitotic cells, they don't support cell division in the absence of Cdc11 and Cdc12," Thorner says. "So it's clear that these two pairs of septins do distinct things, one that supports mitosis and one that supports meiosis."

Exactly what the meiosis-specific complex does to promote sporulation remains unclear. In addition to altering the septins' higher-order architecture, Spr28 and Spr3 likely interact with a unique set of proteins that need to be recruited to the prospore membrane. "We want to identify what those proteins are," Thorner says. The researchers hope that their findings will help elucidate how distinct septin complexes perform specific roles in mammalian development, particularly during gametogenesis, which is essentially analogous to yeast sporulation. A number of septins are specifically expressed in the male germline, and mutations in the corresponding genes are known to cause infertility.

1. Garcia, G. III, et al. 2016. *J. Cell Biol.* http://dx.doi.org/10.1083/jcb.201511029
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4. Fares, H., et al. 1996. *J. Cell Biol.* 132:399–411.
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