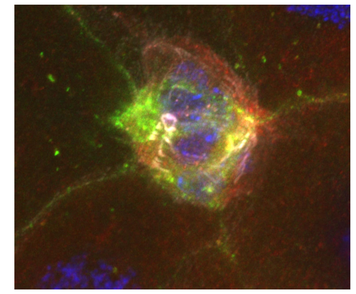
Septins are Required for Collective Cell Migration in the *Drosophila* Ovary

Allison Gabbert, James Mondo, Joseph Campanale, Denise Montell

Department of Molecular, Cellular, and Developmental Biology

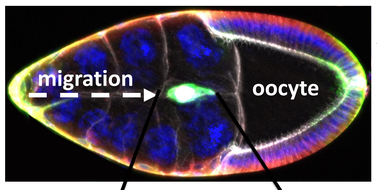
University of California, Santa Barbara

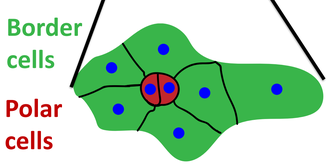


Septins are required in the border cell cluster

Collective cell migration is essential for embryo development, wound healing, and cancer metastasis. Border cells in the *Drosophila* ovary serve as a model for collective cell migration but the molecular mechanisms driving migration remain incompletely understood. Septins are filament-forming proteins that curve membranes and bend and bundle actin. Septin mRNAs are enriched in border cells and/or centripetal cells. I found that multiple septins are required for collective cell migration in the migratory cells of the cluster and septin expression is co-dependent on other septins.

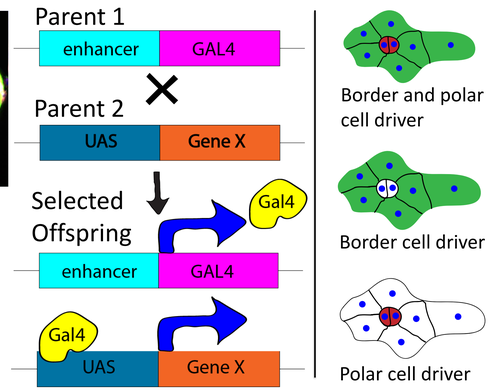
Border Cell Migration





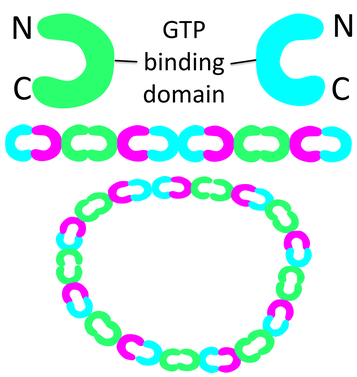
Border cell clusters migrate on nurse cells through the egg chamber.

UAS-Gal4 System

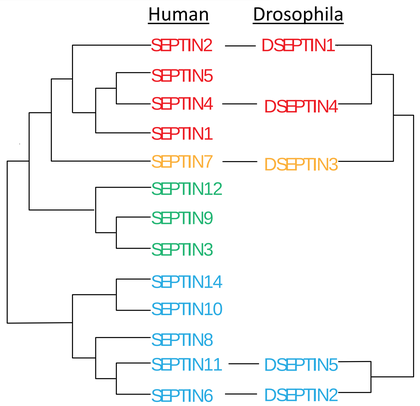


The UAS-Gal4 system provides cell-specific gene expression.

Septins: the 4th Cytoskeletal Element



Septins are cytoskeletal proteins and GTPases that can form bundles and rings.



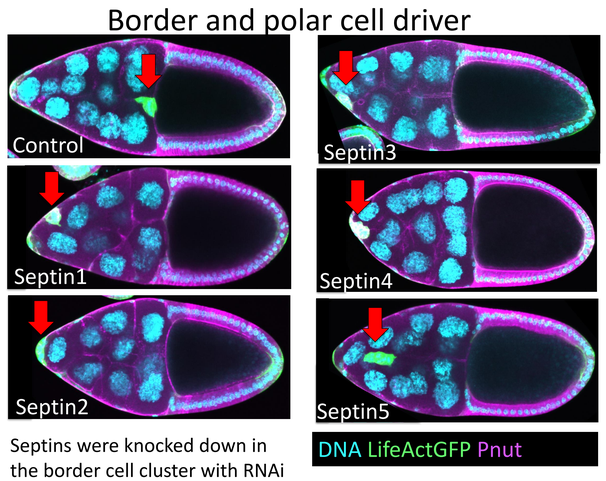
Drosophila septins represent four human septin groups.

Septins are enriched in border cells and/or centripetal cells.

Gene Symbol	Protein Name	Fold Change	Proposed Function	Mammalian Homolog	Conserved Protein Domains
Sep2	Septin 2	1.42	Cleavage furrow	Septin 11	GTPase
Sep1	Septin 1	2.13	Cleavage furrow	Septin 2	GTPase

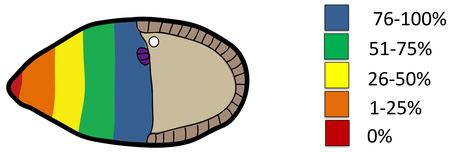
Table adapted from *Analysis of Cell Migration Using Whole-Genome Expression Profiling of Migratory Cells in the Drosophila Ovary* by Wang, et. al 2006.

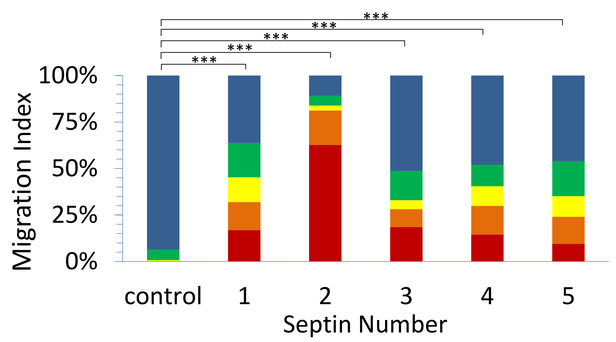
All five septins are required for border cell migration



Septins were knocked down in the border cell cluster with RNAi and *Drosophila* egg chambers were stained for the septin Pnut.

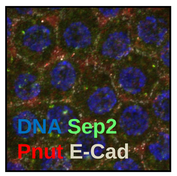
Migration index shows distance border cells travel:



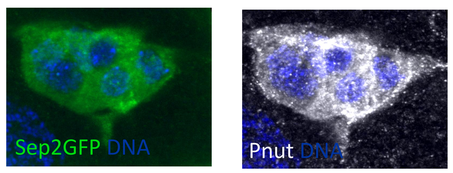


Knockdown of each septin significantly impedes border cell migration.
*** = p-value < 0.001.

Septins localize to cell cortices in follicle cells and share localization patterns in the border cell cluster

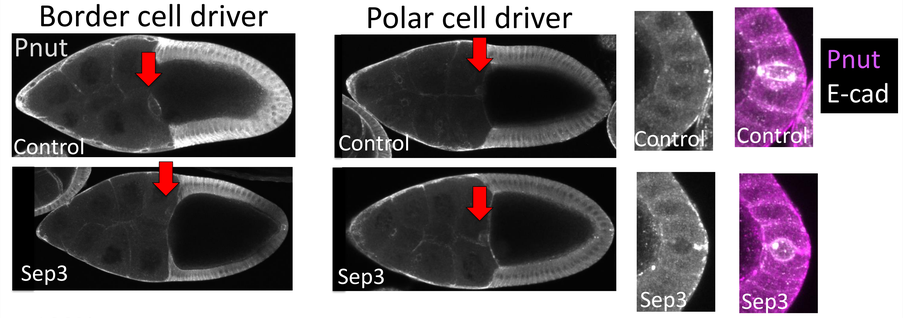


Sep2 and Pnut in follicle cells



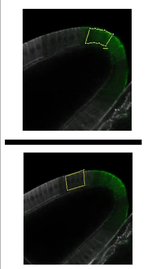
Sep2 compared to Pnut in the border cell cluster

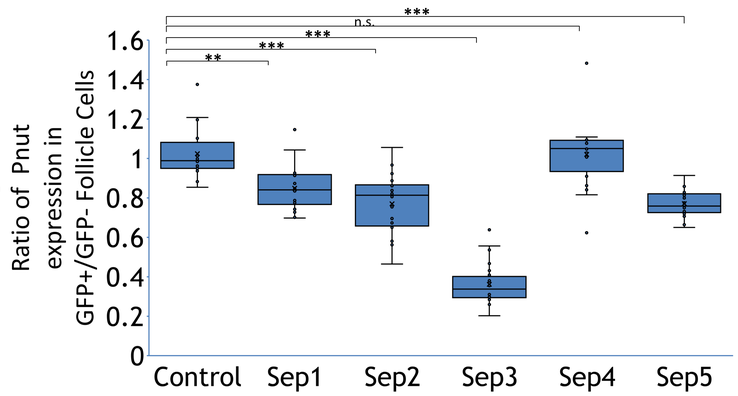
Septins likely required in the migratory border cells



Knocking down septins in the border cells led to less frequent occurrence of complete migration but the differences between the RNAi lines and control were not significant.

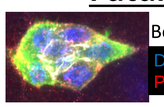
Knockdown of Septin 1, 2, or 5 leads to a decrease in Pnut (Sep3) expression

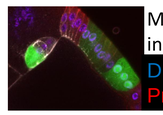




GFP positive cells express RNAi of one septin and GFP negative cells do not. Pnut expression was measured in GFP positive cells and normalized to Pnut expression in adjacent GFP negative cells. A ratio of 1 suggests no change in Pnut expression. Knockdown of Sep1, Sep2, Sep3 (Pnut), and Sep5 resulted in significantly less Pnut expression. ** = p-value < 0.01 and *** = p-value < 0.001.

Future Directions: Septin functions and localization





I plan to quantify co-localization of septins in the border cell cluster and further test if septin expression depends on other septins using mutants and mosaic clones. This will add to our understanding of the role of septins in collective cell migration, which is not understood. I would like to thank Dr. Denise Montell and all members of the Montell lab. A special thank you to Dr. Joseph Campanale and Dr. James Mondo for mentorship and guidance and to Miles Keats for assistance with the project.