The Role of Basement Membrane Proteins for Proper Q Neuroblast Migration in *C. elegans*

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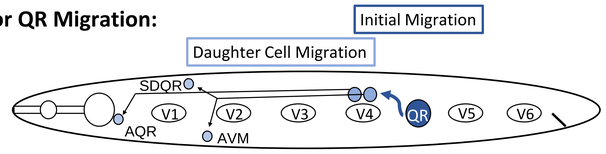
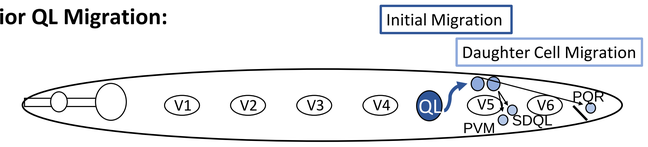
Background on the Q Neuroblasts

Neuronal migration is crucial for proper nervous system development. If this process gets disrupted, it can result in a number of serious neurological disorders such as lissencephaly, epilepsy, and even schizophrenia. In *C. elegans*, migration can be modeled by studying the migration of the two Q neuroblasts (QR and QL). (Middelkoop & Korswagen 2014)

Anterior QR Migration:

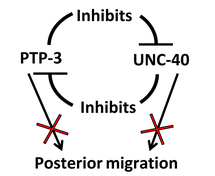


Posterior QL Migration:

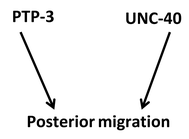


Two genetic pathways are known to control the initial migration of the Q neuroblasts - one involving the protein UNC-40, an immunoglobin receptor, and the other involving the protein PTP-3, a receptor tyrosine phosphatase. (Sundararajan et al., 2012)

Anterior QR Migration:

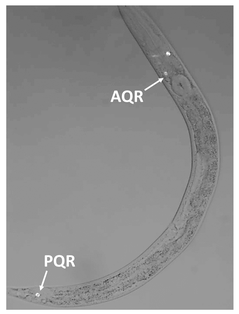


Posterior QL Migration:

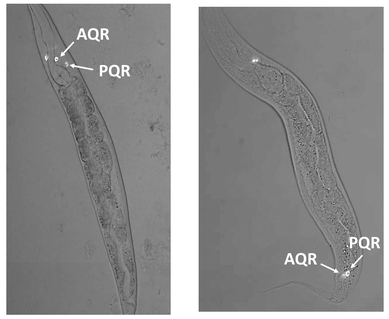


The Role of Basement Membrane Proteins

DPY-17, a collagen protein present in the basement membrane, influences Q cell migration.

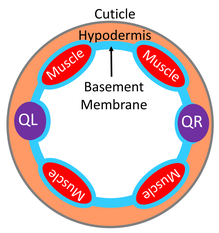


Wild Type



dpy-17 (e164)

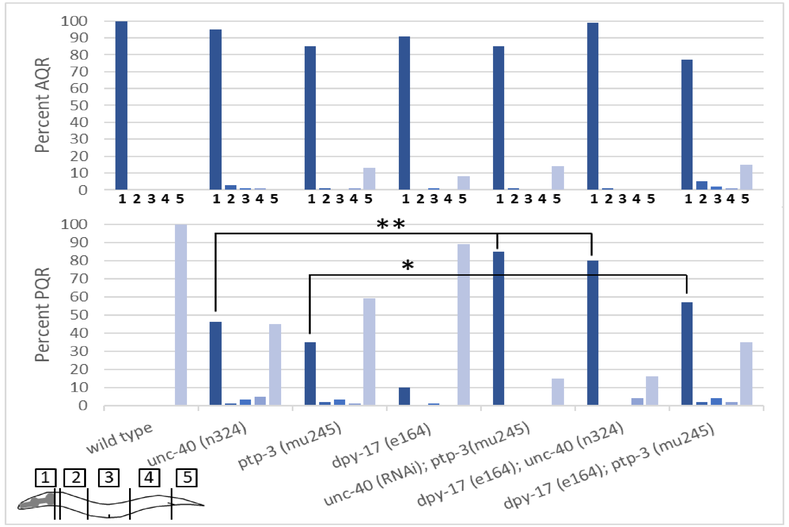
The involvement of DPY-17 suggests a larger role for the basement membrane in Q cell migration



Basement membranes often serve as substrates for migration, but it surprising that a structural protein like collagen could provide directional information to migrating neurons

DPY-17 and the PTP-3 Pathway

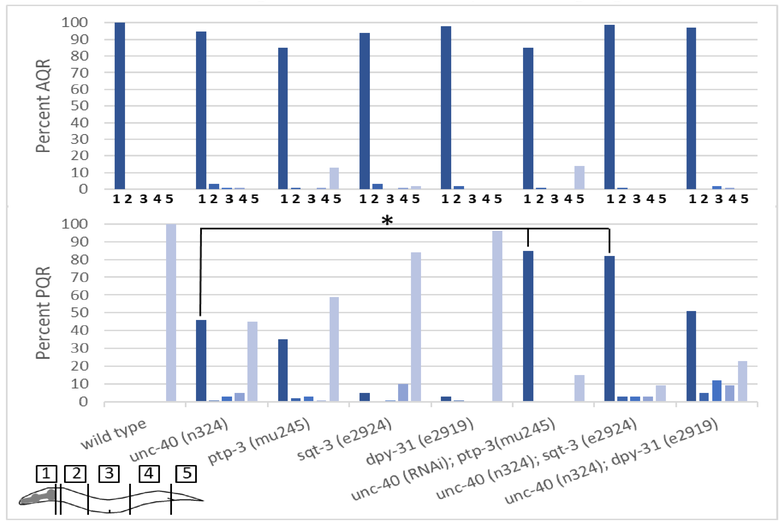
Analysis of the migration defects in double mutants suggests that DPY-17 is likely operating primarily in the same pathway as PTP-3 as the double mutant does not show as significant an increase in migration defects compared to UNC-40.



*p < .02, **p < .0001 Fisher's Exact Test

DPY-17 Mechanism of Directional Regulation

Analysis of other proteins known to interact with DPY-17 further revealed the mechanism through which DPY-17 is likely influencing migration.

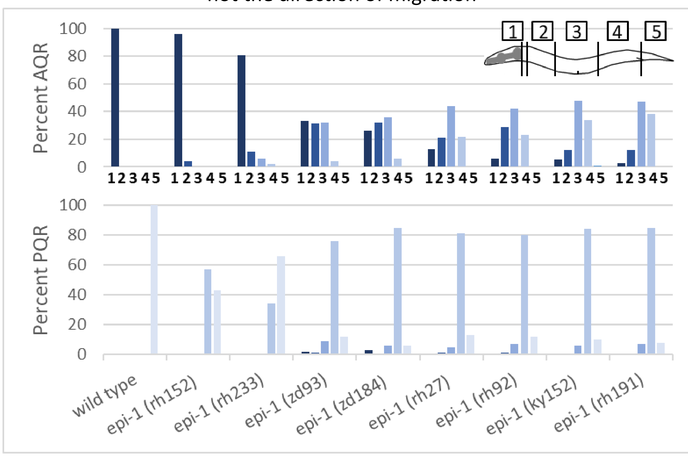


*p < .0001 Fisher's Exact Test

SQT-3, a collagen protein that forms heterotrimers with DPY-17 (Novelli et al., 2006), shows similar genetic interactions with UNC-40. DPY-31, a metalloprotease which interacts with DPY-17 and also regulates the hormone TGFβ (Novelli et al., 2006), does not. This suggests that it is likely the structural orientation of the DPY-17 and SQT-3 collagen fibers that controls the direction of the migrating Q neuroblasts

The Role of Other Structural Proteins

Analyzing the AQR and PQR migration defects in EPI-1, a laminin protein present in the basement membrane of the worm, shows defects in the ability of cells to migrate, but not the direction of migration



This finding indicates that simply disrupting the basement membrane is not enough to alter the direction of migration. Therefore, DPY-17 must be providing some sort of directional information.

Conclusions and Future Directions

My work sets up a revised model for neuronal migration in which migrating cells receive directional information from structural proteins in the basement membrane. In *C. elegans*, the proteins DPY-17 and SQT-3 form collagen heterotrimers that may align themselves along the anterior-posterior axis of the worm. Receptors such as PTP-3 may then read this alignment to control the direction of Q cell migration. Other structural basement membrane proteins, such as the laminin protein EPI-1, appear to be important for permitting cells migrate but do not influence migration direction.

From here it will be important to explore the roles of other basement membrane proteins in Q cell migration. It will also be important to look the migration of the Q cells in larval stage worms to support the findings with AQR and PQR.

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