CDB SEMINAR

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16:00~17:00 A7F Seminar Room

Basement membrane movement breaks tissue boundaries during uterine-vulval attachment in *C. elegans*

Summary

Basement membranes (BMs) are the thin, dense and highly cross-linked formations of extracellular matrix that provide underlying structural support to tissues. They function as strong barriers, separating distinct tissue compartments and disturbing traffic across tissue boundaries. Large breaches in BM are commonly observed at sites of cell invasion in development and carcinoma. Although never followed directly, it has been postulated that BM degradation or alternation in synthesis cause large breach in BM. Anchor cell invasion into the vulval epithelium in *C. elegans* is a recently established in vivo model of cell invasion that is both visually and genetically tractable. The anchor cell is a specialized gonadal cell that penetrates BM and contacts the vulval cell to mediate the initial stage of uterine-vulval connection. The fate of the BM during this later phase of uterine-vulval connection is unknown.

Here we have utilized cell and BM-specific marker to determine the location of the BM during later stage of uterine-vulval connection. We find that the breach in the BM enlarges dramatically beyond the anchor cell in this time. We further notice that this enlargement is totally dependent on vulval cells. Optical markings of laminin and type IV collagen indicate that the BM is not lost, instead, it moves as sheet over the uterine and vulval cells to bring about large BM opening. We identify the laminin binding integrin INA-1/PAT-3 and VAB-19, *C.elegans* ortholog of tumor suppressor protein KANK, as regulators of BM opening. VAB-19 is a member of a conserved family of ankyrin repeat containing proteins thought to function in the actin cytoskeleton. Both proteins show polarized localization within vulval cells at the BM-breach boundary and limit expansion. Genetic analysis and laser directed removal demonstrate that uterine cells use a distinct mechanism to adhere to BM, reinforcing boundary position of breach. BM movement followed by regulated adhesion shows an unexpected mechanism for creating stable large BM breach that can be used by cells to escape compartment boundaries.

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