

CDB SEMINAR

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The first family of eukaryotic cell-cell fusion proteins

Summary

Developmental cell fusion is found in germlines, bones, muscles, placentas and stem cells. To dissect the pathway of cell fusion in C. elegans, we do genetic and kinetic analyses using live-confocal and electron microscopy. We monitor the rates of multiple cell fusions in embryos and find kinetically distinct stages of initiation and completion of membrane fusion, that can be differentially blocked by mutations and low temperatures.

Despite the detailed characterization of cell fusion events in several organisms, little is known about the molecular mechanisms of cell fusion. EFF-1 (Epithelial Fusion Failure-1) is necessary and sufficient to mediate homotypic cell fusion in C. elegans. Epidermal cell fusion requires EFF-1 to initiate and expand membrane merger. Ectopic expression of EFF-1 in *C. elegans* and in heterologous Sf9 insect cells is sufficient to form giant syncytia. AFF-1 (Anchor cell Fusion Failure-1) is a novel *C. elegans* fusogen that mediates anchor cell-utse fusion to form a hymen. Surface expression of AFF-1 is sufficient to fuse nematode and insect Sf9 cells. AFF-1 and EFF-1 type I membrane proteins are members of a family of developmental cell fusogens in nematodes. The expression patterns of eff-1 and aff-1 correlate with their fusogenic activities in different fusing cells. We will discuss how EFF-1 and AFF-1 fuse cells via hemifusion. Thus, we identified and characterized a family of developmental fusogens (the FF family) required for ectodermal and mesodermal fusion in nematodes. The FF proteins are bona fide fusogens because they are: (1) Expressed at the time of fusion on the surface of both fusing cells. (2) Essential for most somatic cell fusion events in *C. elegans*. (3) Sufficient to fuse cells that normally do not fuse in vivo and in vitro. Identifying new fusogens will allow in depth understanding of the cell fusion mechanisms in *C. elegans* and may promote the discovery of additional fusogens in other organisms either by evolutionary conservation or by implementation of similar approaches.

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