CDB SEMINAR

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16:00~17:00 A7F Seminar Room

Stoichiometry of the integrin adhesion complex in *Drosophila* tissues

Summary

Cell adhesion to the extracellular matrix (ECM) occurs via integrin-mediated adhesion, generated a link from the ECM to the actin cytoskeleton. More than 100 integrin-associated proteins have been implicated in the connection between the cytoplasmic domains of integrins and the actin cytoskeleton, indicating the complexity of the integrin adhesion complex. We wish to understand how the integrin adhesion complex is assembled and what mechanisms control the amount of each component in the complex. As the first step in achieving this, we have established a method to measure the stoichiometry of components of the integrin adhesion complex within the intact living animal. We have started with a subset of components, consisting of the main integrin subunit and 7 associated proteins. For each of these we have null mutations in the genes encoding them, and transgenic constructs encoding green fluorescent protein(GFP)-tagged versions of the protein, expressed from their own promoter. Each of the GFP-tagged versions is able to rescue the mutations in the endogenous gene, demonstrating that the GFP-tagging does not impair function. Using quantitative confocal microscopy, I have measured the relative amount of each protein in different integrin adhesive structures in the developing animal. This has revealed a consistent stoichiometry of some components while other vary. Unexpectedly, even though mutations in the integrin-associated proteins are recessive, in heterozygous animals protein levels are reduced at the integrin adhesive sites, demonstrating that half the gene dosage is unable to provide sufficient protein for normal levels. This demonstrates that several of the proteins are not made in substantial excess. I am currently examining how the reduction of each component impacts on the amount of the others that are recruited, thus building up a network of interactions that control protein levels in the integrin adhesive complex.

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