A LINK BETWEEN MYOSIN VII AND TALIN, CONSERVED PROTEINS WITH CRITICAL ROLES IN ADHESION.

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The class VII myosins (M7) are among the most highly conserved members of the myosin superfamily and are found in organisms ranging from *Dictyostelium* to humans. Loss of M7a function in humans results in Usher syndrome type IB, a leading cause of combined deafness and blindness. Careful analysis of M7 function in model systems (mice, flies and *Dictyostelium*) reveals that this myosin plays a conserved role in adhesion and most likely acts as a dynamic link between adhesion receptors and the underlying actin cytoskeleton. The molecular basis of M7 function remains poorly understood and one of the goals of our work is to define how the C-terminal tail (i.e. non-motor) region of M7 contributes to its localization and interaction with binding partners using *Dictyostelium* as a model system. Recent work has shown that talin, another highly conserved adhesion protein, is the major M7 binding protein in *Dictyostelium*. The two proteins are exclusively associated with each other in the cytosol and also interact with each other on the membrane. These data indicate that M7 and talin form an adhesion adaptor complex in *Dictyostelium* that can be recruited from the cytosol to the membrane. Talin has been found to modulate M7-membrane dynamics. *Dictyostelium* GFP-M7 expressed in wild type (WT) or M7 null cells is localized to the leading edge of migrating cells and rapidly disappears as the pseudopod is retracted. The turnover of GFP-M7 on the membrane in both cell lines was measured by FRAP (fluorescence recovery after photobleaching). The half-time of recovery of GFP-M7 fluorescence in M7 null cells is significantly faster than that observed in WT cells. This difference in recovery rates correlates with talin levels – WT cells expressing GFP-M7 have 5X more talin than the M7 nulls expressing GFP-M7. The FRAP analysis suggests that talin plays a role in the association of M7 with membranes, serving to integrate it into an adhesion complex. Together, these findings reveal an intimate relationship between two ancient and highly conserved adhesion proteins and suggest that this link may be preserved in complex systems including, perhaps, the mammalian ear.

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