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A Signaling Role for the Uncleaved Form of α6 Integrin in Differentiating Lens Fiber Cells

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Abstract

Many α integrin subunits are cleaved during their processing to yield heavy and light chains, which remain associated by disulfide bonds. While uncleaved α integrin subunits can form functional receptors that sometimes have distinct signaling roles from their better-characterized endoproteolytically cleaved counterparts, their expression at the cell surface and their association with signaling complexes have yet to be determined *in vivo*. In this study, we demonstrate that, in differentiating lens fiber cells, the uncleaved form of α6 integrin was expressed at the cell surface. This form of α6 integrin coimmunoprecipitated with both the signaling adaptor molecule Shc and its downstream effector Grb2, suggesting that, in lens fiber cells, uncleaved α6 integrin was associated with a Shc-mediated signaling complex. We show that expression of the cleaved form of α6 integrin progressively decreased relative to uncleaved α6 integrin as the state of lens cell differentiation increased, resulting in the predominance of uncleaved α6 integrin in the lens fiber cell zones. Interestingly, we previously have shown that α6 integrin is localized principally along the extensive cell–cell interfaces of these lens fiber cells, in the absence of its extracellular matrix ligand laminin. While we found that the cleaved form of α6 integrin contained both high mannose and complex sugars, the uncleaved form of α6 integrin contained only high mannose sugars. These properties suggest that the uncleaved form of α6 integrin may have a unique role in the embryonic lens. Its high association with Shc and Grb2 in the differentiating cortical fiber cell zone indicates that α6 integrin may provide a cell survival signal in the presence of the apoptotic-like processes that are initiated in this region of the embryonic lens to clear the lens cells of their organelles.

Keywords

integrin; glycosylation; endoproteolytic cleavage; Shc; Grb2; lens

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