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Deafness and espin-actin self-organization in stereocilia

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Espins are F-actin-bundling proteins associated with large parallel actin bundles found in hair cell stereocilia in the ear, as well as brush border microvilli and Sertoli cell junctions. We examine actin bundle structures formed by different wild-type espin isoforms, fragments, and naturally-occurring human espin mutants linked to deafness and/or vestibular dysfunction. The espin-actin bundle structure consisted of a hexagonal arrangement of parallel actin filaments in a non-native twist state. We delineate the structural consequences caused by mutations in espin's actin-bundling module. For espin mutation with a severely damaged actin-bundling module, which are implicated in deafness in mice and humans, oriented nematic-like actin filament structures, which strongly impinges on bundle mechanical stiffness. Finally, we examine what makes espin different, via a comparative study of bundles formed by espin and those formed by fascin, a prototypical bundling protein found in functionally different regions of the cell, such as filopodia.

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