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The human cadherin family protein hFat1 interacts with postsynaptic density PDZ domain-containing proteins

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The giant cadherin family protein hFat1 has been shown to be important during embryonal development, especially of kidney and brain. It localises predominantly at the tips of cellular protrusions and seems to be involved in the organisation of actin cytoskeleton during cell migration. The intracellular domain contains several potential interaction motifs. Among others it possesses a putative PDZ-binding motif on its C-terminus. In an attempt to identify interaction partner of hFat1 various PDZ-domain containing proteins were translated in vitro and the binding to immobilised GST-hFat1 fusion protein was investigated. Binding of the proteins Dlg1, Scribble, PDZ-RhoGEF and MAGI-1 was observed in vitro. Deletion of the C-terminal motif in hFat1 eliminated binding of Dlg1, Scribble and PDZ-RhoGEF, but had no influence on the binding of MAGI-1. The interaction of MAGI-1 appears to be mediated by the WW-domain of MAGI-1 and one of the two putative WW domain binding motifs of hFat1. Among others Dlg1, Scribble and MAGI proteins have been shown to play critical roles in synapse maturation by regulating the assembly of synaptic multiprotein complexes. We have recently shown that hFat1 interacts with Homer proteins, another synaptic scaffolding proteins. In consideration of these facts we believe that hFat1 plays an important role as a scaffolding protein in the organism.