

P022 Direct association of transglutaminase-2 with syndecan-4 in the formation of RGD-independent focal adhesions on fibronectin

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Externalization of transglutaminase-2 (TG2) and its immobilisation on fibronectin (FN) leads to a cell adhesion process which is independent from the interaction between the ArgGlyAsp (RGD) cell binding domain of FN and integrin receptors and does not involve TG2 cross-linking function. Here we show that the contribution of TG2 to focal adhesions depends on cell surface-heparan sulfate (HS) chains, since its function is impaired following cleavage of HS, finding which is consistent with the hypothesis of TG2 binding to HS proteoglycan receptors. Moreover, dermal fibroblast isolated from syndecan-4-null mice are defective in TG2-mediated RGD-independent FAK-P₃₉₇ and cell spreading compared to wild-type fibroblasts. The direct association of TG2 with syndecan-4 at the cell surface, has been investigated in membrane preparations of human osteoblasts, cells known to be rich in RGD-independent adhesive pathways. TG2 was present in syndecan-4 immunoprecipitates and pre-treatment of cells with heparitinase, lowered the amount of TG2 immunoprecipitated with an anti-syndecan-4 antibody against the core protein, indication that the association involves the HS chains. The TG2-syndecan-4 co-immunoprecipitation was not decreased by competitive concentrations of a peptide which mimics the FN binding site within TG2, suggesting that the TG2-syndecan-4 association is not mediated by heparin-binding FN. Both TG2-null and syndecan-4-null mice have defective wound repair. Our data provide novel insights into the co-operative action of TG2 and syndecan-4 in cell adhesion, which may be relevant to wound repair.