Synopsis of Original Research Paper

Cell Adhesion to Transglutaminases

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Transglutaminases (TGases) are enzymes which catalyze cross-link formation between specific glutamine residues and lysine residues in substrate proteins. We report here that two of the TGases, blood coagulation factor XIIIa (FXIIIa) and tissue-type TGase (TGc), are capable of mediating adhesion of various cells through different mechanisms. When coated on plastic surfaces, they promoted adhesion and spreading of various cells of both normal and tumor origin, in a concentration-dependent manner. The adhesion was not inhibited by antibodies against possible contaminants in the enzyme preparation such as fibronectin and vitronectin, but was completely inhibited by a polyclonal antibody against the enzymes. It is obvious, therefore, that contaminants, if there were any, cannot account for the observed cell adhesion to the enzymes. Furthermore, phosphorylations of tyrosine residues in 120 kDa- and 70 kDa-proteins were very clearly shown in human fibroblasts adhered to the enzyme. Formation of actin stress fibers was also quite unambiguously observed in the adhered cells. These biochemical reactions, which are also observed when cells adhered to a typical cell adhesion protein fibronectin, are believed to be of importance in the process of cell adhesion. Although the adhesion to FXIIIa is dependent on its TGase activity, the TGc-mediated cell adhesion is independent of its TGase activity: 1) The modification of the active center cysteine with iodoacetamide blocked the enzyme activity without any effect on the cell adhesion. 2) The addition of Mg^{2+} did not induce the enzyme activity, but it was as effective as Ca^{2+} for the cell adhesion. 3) The addition of NH^{4+} inhibited the enzyme activity, yet it did not affect the adhesion significantly. The integrins involved in these cell adhesions are quite different. In the case of F XIIIa, αvβ3 and α5β1 integrins are involved and consequently the RGD peptide substantially inhibited the adhesion. On the other hand, the cell adhesion to TGc is mediated by α4β1 integrin, and the RGD peptide was without effects. It is possible that these two molecules may mediate cell adhesions under different physiological or pathological situations.