A07-3 Biological Activity of Xaa-Gly-Yaa Motif Containing Laminin G Domain Peptides

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Laminins are heterotrimeric proteins consist of three distinct alpha, beta, and gamma chains. So far, five laminin alpha chains have been identified and play an important role in the biological activity. The C-terminal globular domain (G domain) of the laminin alpha chains consists of five laminin G domain-like modules (LG1 to LG5) that play a critical role in the biological functions of laminins. The LG module has a sandwich structure consisting of fourteen beta-strands (A-N). Previously, several bioactive sequences have been identified from the E-F loop region. An acidic amino acid (Aaa) -Gly-basic amino acid (Baa) motif containing E-F loop peptides showed integrin binding activity and Baa-Gly-Baa motif containing E-F loop peptides showed syndecan binding activity. In this study, we focused on glycine containing sequences, which are Xaa-Gly-Yaa (both or either of Xaa and Yaa are acidic amino acid or basic amino acid) motifs in the entire laminin alpha chain sequences. Fifty-five peptides contained Xaa-Gly-Yaa motifs in the laminin alpha chain (alpha1-alpha5 chains) G domains were synthesized. First, we examined their cell attachment activity using human dermal fibroblasts (HDFs). Seventeen peptides showed cell attachment activity in a dose-dependent manner. Next, we evaluated the effects of heparin and EDTA on HDF attachment to the active peptides. Eight peptides were inhibited by EDTA, one peptide inhibited by heparin, and five peptides inhibited by heparin and EDTA. Since the HDF attachment to the 13 peptides was divalent cation-dependent, suggesting that integrins are major candidates for the cellular receptors. The cell attachment to eight peptides was significantly inhibited by anti-beta integrin antibody, suggesting the peptides promote beta integrin mediated cell adhesion. The all active peptides locate in loop regions between beta-strands. These results suggest that Xaa-Gly-Yaa motifs in the loop regions of laminin G domain have an important role in the biological activity.

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