Triflavin, an Arg-Gly-Asp-containing peptide, inhibits the adhesion of tumor cells to matrix proteins via binding to multiple integrin receptors expressed on human hepatoma cells.

許準榕
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Abstract

Integrins are a superfamily of cell surface glycoproteins that promote cellular adhesion. The interaction of integrins with extracellular matrices such as fibronectin and vitronectin has been shown to be mediated through an arginine-glycine-aspartic acid (RGD) sequence within adhesive proteins. Triflavin, a 7.5-kDa cysteine-rich polypeptide purified from Trimeresurus flavoviridis snake venom, belongs to a family of RGD-containing peptides, termed disintegrins. Disintegrins have been isolated from the venom of various vipers and have been shown to be potent inhibitors of platelet aggregation. In this study, we found that human hepatoma cell adhesion to immobilized matrix proteins (i.e. fibronectin, collagen, laminin, and vitronectin) was differentially affected by various anti-integrin monoclonal antibodies (mAbs) (i.e., alpha3beta1, alpha5beta1, alpha6beta1, and alpha v beta3) as well as by the peptide GRGDS. Indirect flow cytometric analysis of hepatoma cells with anti-integrin mAbs demonstrated that alpha6beta1 was uniformly expressed at a high density, while alpha3beta1, and alpha5beta1 were moderately expressed and alpha v beta3 was expressed in small amounts on hepatoma cells, consistent with the results obtained from immunofluorescence microscopic analysis. When immobilized on plastic wells, triflavin promoted hepatoma cell attachment; this cell attachment was inhibited by either GRGDS or mAbs against integrins alpha3beta1, alpha5beta1 and alpha v beta3). In addition, the binding of FITC-conjugated triflavin to hepatoma cells was inhibited by GRGDS, anti-alpha3beta1, antialpha5beta1, and anti-alpha v beta3 mAbs. Among these mAbs, anti-alpha5beta1 exerted the most pronounced inhibitory effect (>70%) on the binding of triflavin to hepatoma cells. Taken together, these results suggest that triflavin binds via its RGD sequence to multiple integrin receptors (i.e., alpha5beta1, alpha3beta1, and alpha v beta3) expressed on the surface of hepatoma cells, resulting in inhibition of hepatoma cell adhesion to

extracellular matrices (i.e., fibronectin and vitronectin).