Ovarian cancer cell proliferation and motility is induced by engagement of integrin alpha(v)beta3/Vitronectin interaction.

Abstract:
During tumor metastasis, a fine-tuned balance between the formation and loosening of adhesive cell contacts has to occur, a process based on the regulated expression of integrins. Human ovarian OV-MZ-6 cancer cells express the integrin alpha(v)beta3, which associates with vitronectin (VN) and correlates with ovarian cancer progression. Adhesion and spreading of OV-MZ-6 cells on VN was accompanied by the formation of focal adhesion contacts and the recruitment of activated tyrosine-phosphorylated focal adhesion kinase. Cultivation of OV-MZ-6 cells on VN resulted in a significantly induced cell proliferation. This VN effect could be mimicked by cultivating cells on the immobilized alpha(v)beta3 directed peptide cyclo-Arg-Gly-Asp-D-Phe-Val (cRGDfV). VN-dependent OV-MZ-6 cell adhesion and proliferation was significantly enhanced by overexpression of alpha(v)beta3 and was accompanied by rapid and transient tyrosine-phosphorylation of p44(erk-1)/p42(erk-2) mitogen-activated protein kinase. Moreover, overexpression of alpha(v)beta3 and OV-MZ-6 cell attachment to VN increased cell motility up to 5-fold accompanied by prominent changes in cytoskeletal organization and cell morphology. Upon alpha(v)beta3/VN interaction, by cDNA expression microarray analysis we identified altered mRNA levels of c-myc, epidermal growth factor...
receptor (EGF-R), transcription factor Fra-1, prothymosin-alpha (PTMA), integrin-linked kinase (ILK), and the cell adhesion molecule SQM-1, candidates which are possibly involved in changes of the adhesive, migratory, and proliferative phenotype of human ovarian cancer cells.