Alternative splicing of KAI1 abrogates its tumor-suppressive effects on integrin \( \beta^3 \)-mediated ovarian cancer biology.

Loss or downregulation of the tumor-suppressor KAI1 correlates with poor cancer patient prognosis. KAI1 functions by interacting with other proteins, including integrin cell adhesion and signaling receptors. We previously showed that KAI1 physically and functionally crosstalks with the tumor-biologically relevant integrin \( \beta^3 \), thereby suppressing ovarian cancer cell migration and proliferation. Interestingly, in metastases, a KAI1 splice variant had been identified, indicating poor patient prognosis. Thus, we here characterized differential effects of the two KAI1 proteins upon their cellular restoration. Opposite to KAI1, KAI1-splice reduced \( \beta^3 \)-mediated cell adhesion, thereby inducing cell migration. This was accompanied by elevated \( \beta^3 \) levels and drastically elevated focal adhesion kinase activation, however, without any obvious colocalization with \( \beta^3 \), as observed for KAI1. Moreover, codistribution of KAI1 with the cell/cell-adhesion molecule E-cadherin was abrogated in KAI1-splice. Whereas KAI1 diminished cell proliferative activity, KAI1-splice prominently enhanced cell proliferation concomitant with elevated transcription and cell-surface expression of the epidermal growth factor receptor. Thus KAI1-splice does not only counteract the tumor-suppressive actions of KAI1, but - beyond that - promotes
?v?3-mediated biological functions in favor of tumor progression and metastasis.