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PO-108 - (23745) - INHIBITION OF AP-1 EFFECTIVELY SUPPRESSES CD46-MEDIATED MMP9 ACTIVATION IN BLADDER AND COLON CANCER CELLS

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There are no conflict of interest.
CD46, a transmembrane protein known for protecting cells from complement-mediated damage, is frequently dysregulated in various cancers. Its overexpression in bladder and colon cancers protects cells against both complement and antibody-mediated cytotoxicity. Previous studies explored a new role of CD46 in facilitating cancer cell invasion and metastasis by activating MMP9 expression, but not MMP2 in several bladder cancer cell lines. CD46 triggered phosphorylation of p38 MAPK and AKT, leading to enhanced AP-1 activity via c-Jun upregulation, ultimately upregulating the expression of MMP9. In this study, we tested whether blockade of AP-1 results in suppression of MMP9 and MMP9-mediated cell migration and invasion in bladder and colon cancer cells.
Both bladder and colon cancer cells were used for Western blot analysis and reporter transcription assays. AP-1 inhibitors used are AP-1 decoy oligonucleotide (AP1-ODN) and AP-1 specific inhibitor (SR11032). To test AP-1-mediated inhibition of cell migration and invasion, both wound healing scratch assay and transwell chamber assays with or without gelatin coating were utilized.
Both AP1-ODN and SR11032 significantly inhibited CD46-mediated MMP9 expression in bladder and colon cancer cells. Consequently, SR11032 significantly inhibited MMP9 promoter activity in both wild type and CD46-overexpressed cancer cells. Treatment of SR11032 dramatically reduced CD46-mediated cell migration by wound closure scratching assay and transwell assays.
Taken together, this study suggests that proper blocking of AP-1 effectively protect cells from CD46-mediated migration and invasion through suppression of MMP9 in bladder and colon cancers.

Palavras-chave : CD46, MMP9, invasion