

Publications du Département de Biologie Cellulaire (Université) (2001)

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D'ALESSIO P.

Endothelium as a pharmacological target.

Curr. Opin. Investig. Drugs, 2 (12), 1720-1724, 2001

(Services cités : Département de Biologie Cellulaire)

Over the last few years, the increasing knowledge of the endothelium has highlighted its integral role in a number of pathologies. Endothelial cells are pivotally involved in the recruitment and adhesion of leukocytes and platelets, and they express adhesion molecules and growth factors. This review highlights the recent advances made in the understanding of the endothelium and discusses the endothelium as a potential target in a variety of diseases, including cardiovascular diseases, cancer and inflammatory diseases.

D'ANNA R., LE BUANEC H., BIZZINI B., BURNY A., GIANNOULI C., ZAGURY J.F., GALLO R.C., ZAGURY D., D'ALESSIO P.

Human papillomavirus-16-e7 oncoprotein enhances the expression of adhesion molecules in cervical endothelial cells but not in human umbilical vein endothelial cells.

J. Hum. Virol., 4 (2), 85-95, 2001

(Services cités : Département de Biologie Cellulaire)

Objectives: E7 is one of the oncoproteins encoded by human papillomavirus-16 (HPV-16), the major etiologic factor responsible for cervical cancer. Human papillomavirus-16-E7 expressed by human uterine cervical carcinoma cells is also released in the extracellular compartment where it induces immune suppression. We investigated whether E7 was also responsible for the enhanced endothelial adhesiveness required in cancer progression. Study Design/Methods: We treated cervical microvascular endothelial cells (CrMVE) and human umbilical vein endothelial cells (HUVEC) with E7, tumor necrosis factor-alpha (TNF-alpha), and hydrogen peroxide (H₂O₂) and measured the expression of E-selectin, intercellular adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-1 (VCAM-1) by fluorescent-activated cell sorter analysis. Results: E7 strongly induced the expression of E-selectin, ICAM-1, and VCAM-1 in CrMVE, but not in HUVEC. Tumor necrosis factor-alpha further increased the endothelial expression of adhesion molecules in CrMVE. Hydrogen peroxide pre treatment resulted in an enhanced ICAM-1 and a decreased E-selectin and VCAM-1 expression. We also show indirect effects when endothelial cells were stimulated with the supernatant of E7-pretreated macrophages. Conclusions: These results show that HPV-16-E7 oncoprotein strongly induces adhesion molecules expression in organ-specific endothelial cells. [References: 56]

D'ANNA R., LE BUANEC H., ALESSANDRI G., CARUSO A., BURNY A., GALLO R., ZAGURY J.F., ZAGURY D., D'ALESSIO P.

Selective activation of cervical microvascular endothelial cells by human papillomavirus 16-e7 oncoprotein.

J. Nat. Cancer Inst., 93 (24), 1843-1851, 2001

(Services cités : Département de Biologie Cellulaire)

Background: Human papillomavirus type 16 (HPV16) is strongly implicated in the etiology of

cervical cancer, with the expression of HPV 16-encoded E7 oncoprotein in infected epithelial cells contributing to their malignant transformation. Although nuclear E7 interacts with several nuclear targets, we have previously shown that extracellular E7 can cause suppression of immune cell function. Moreover, cervical microvascular endothelial (CrMVE_n) cells treated with E7 increase their expression of adhesion molecules. High levels of some cytokines in serum and in cervicovaginal secretions are associated with the progression of cervical cancer. In this study, we investigated the effects of extracellular E7 on cytokine production and on cytoskeleton structure of CrMVE_n cells and vascular endothelial cells from different organs. Methods: Immunocytochemical staining and flow cytometry techniques were used to detect E7 in endothelial cells incubated with purified E7 protein. Laser scanning confocal microscopy was used to study the E7-induced modification of the endothelial cytoskeleton. An enzyme-linked immunosorbent assay was performed to measure the production of two cytokines, interleukin 6 (IL-6) and interleukin 8 (IL-8), by E7-treated endothelial cells. All statistical tests were two-sided. Results: Extracellular E7 was taken up by CrMVE_n cells and localized to the cytoplasm. CrMVE_n cells showed a statistically significant ($P < .02$) increase in the production of IL-6 and IL-8 after treatment with E7 compared with the controls. CrMVE_n cells also produced higher levels of these cytokines than did the other endothelial cells ($P < .01$). E7 also induced marked alterations in the endothelial cytoskeleton of CrMVE_n cells as a result of actin fiber polymerization. Conclusion: These findings suggest a novel mechanism by which E7, as an extracellular factor, can play a role in the progression and dissemination of cervical cancer via its selective effects on endothelial cells. [References: 51]