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DIVERGENT EFFECTS OF CORTICOTROPIN RELEASING HORMONE (CRH) ON ENDOTHELIAL CELL NITRIC OXIDE SYNTHASE ARE ASSOCIATED WITH DIFFERENT EXPRESSION OF CRH TYPE 1 AND 2 RECEPTORS

D'Alcamo M. 1° anno di corso del Dottorato in Farmacologia Preclinica e Clinica, XVI ciclo. Durata del dottorato in anni: 3. Sede di servizio: Dipartimento di Farmacologia Preclinica e Clinica, Università di Catania.

Endothelium is target for pro- and anti-inflammatory factors. Endothelial cells express receptors for corticotropin releasing hormone (CRH), a neuropeptide produced during inflammation. We report both the concentration-dependent inhibitory effects of CRH upon cytokine-stimulated nitrite release in H5V murine endothelioma cells, which turned stimulatory in HUVEC cells. Western blot analysis showed that CRH inhibits cytokine-stimulated inducible nitric oxide synthase (iNOS) in H5V cells, which, in turn, was increased in HUVEC cells. Both H5V and HUVEC cells expressed iNOS mRNA after 1 h and up to 24 h after addition of cytokines. H5V cells expressed both CRH type 1 and 2 receptor (CRH-R1 and R2) mRNAs, whereas HUVEC cells expressed the CRH-R2 mRNA solely. CRH induced increase of medium nitrites and iNOS protein expression in H5V cells pretreated with the selective CRH-R1 antagonist CP 154,526. However, these effects of CRH were not observed in the presence of the selective CRH-R2 antagonist anti-Svg-30. In contrast, anti-Svg-30 inhibited CRH-induced increase of nitrite release and iNOS expression in HUVEC cells. The effects of CRH on H5V cells nitrite were paralleled by decreased proliferation. Our results confirm the stimulatory role of CRH on endothelial cells, but also suggest its possible inhibitory role in the late phase of the inflammatory response, depending upon different receptor expression. Antiproliferative effects of CRH could be exploited in antiangiogenic therapy or in endothelial tumor treatment.