

題名:Progesterone inhibits human endothelial cell proliferation through a p53-dependent pathway.

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摘要:Abstract. Previous studies have shown that progesterone inhibits endothelial cell proliferation through a nuclear receptor-mediated mechanism. Here, we further demonstrate that progesterone at physiologic levels (5 - 500 nM) dose- and time-dependently inhibited

DNA synthesis of cultured human umbilical vein endothelial cells (HUVEC). The mRNA and protein levels of p21, p27, and p53 in HUVEC were increased by progesterone. The formation of CDK2-p21 and CDK2-p27 were increased and the CDK2 activity was decreased in the progesterone-treated HUVEC. The progesterone-inhibited [3H]thymidine incorporation was completely blocked when the expressions of p21 and p27 were knocked-down together. Transfection of HUVEC with dominant negative p53 cDNA prevented the progesterone-induced increases in p21 and p27 promoter activity and protein level, decreases in thymidine incorporation, and capillary-like tube formation. Matrigel angiogenesis assay in mice demonstrated the antiangiogenic effect of progesterone in vivo. These findings demonstrate for the first time that progesterone inhibited endothelial cell proliferation through a p53-dependent pathway.