

INFLUENCE OF ANGIOSTATIN AND THALIDOMIDE ON LYMPHANGIOGENESIS

X.J. Shao, X.Y. Chi

Department of Anatomy, Medical College, Qingdao University, Qingdao, PR China

ABSTRACT

Malignant cancers commonly invade locally followed by spread through venous or lymphatic channels or both to distant sites. Hemangiogenesis and its relation to tumor growth and metastasis have been extensively studied. However, the role played by lymphangiogenesis in growth and metastasis of cancer has been largely neglected until just recently. Inhibition of lymphangiogenesis, as compared to inhibition of hemangiogenesis, may provide new insights into the mechanisms of cancer metastasis. The current study was designed to examine the in vitro effect of two commonly used inhibitors of hemangiogenesis, angiostatin and thalidomide, on the growth and proliferation of lymphatic endothelial cells isolated from pig thoracic ducts. We first isolated and characterized the lymphatic endothelial (LE) cells using specific markers for VEGFR3 and LYVE-1. The experimental results showed that treatment of the LE cells with these two drugs resulted in a decrease in the rate of cell proliferation in a dose-dependent manner as assessed by MTT assays. Cell migration rate was assessed by the speed of cell migration from the scrape-wound margin, and the results showed that migration of LE cells was also significantly inhibited in a dose-dependent fashion compared to controls. Treatment with angiostatin and thalidomide both resulted in an increase in apoptosis of LE cells as assessed by Hoechst staining and flow cytometry. We conclude that both angiostatin and thalidomide are able to inhibit LE cell growth in a dose-dependent manner and that the inhibition may be through induction of apoptosis.