DIFFERENT EFFECTS OF ANGIOGENESIS INHIBITORS IFN-α AND TIMP-1 ON LYMPHANGIOGENESIS

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ABSTRACT

This study was designed to examine the effects of angiogenesis inhibitors IFN-α and TIMP-1 on lymphangiogenesis. We cultured lymphatic endothelial (LE) cells from pig thoracic ducts and performed morphological observations using light microscopy, TEM, and confocal microscopy to confirm their lymphatic origin. We tested these cells for growth inhibition by angiogenesis inhibitors IFN-α and TIMP-1 using both the scraping line and MTT methods. In addition, we analyzed apoptosis using the Hoechst and Caspase staining methods. Finally, we tested IFN-α and TIMP-1 using in vivo inhibitory assays. By morphological observations, all LE cells in vivo and in vitro were found to be of very similar morphology. Both in vitro inhibitory assays of scraping line and MTT showed significant differences for the IFN-α treatment (p<0.01) and no significant difference for TIMP-1. Hoechst and Caspase apoptosis assays demonstrated that IFN-α could induce apoptosis of LE cells, and TIMP-1 had little effect. IFN-α and TIMP-1 inhibitory in vivo assays showed a lack of healing following IFN-α treatment compared to control and TIMP-1 treatment. In summary, these different angiogenesis inhibitors have different effects on lymphangiogenesis. IFN-α inhibits proliferation and migration of LE cells in a dose-dependent fashion and induces apoptosis of LE cells while TIMP-1 has no significant inhibitory effects on proliferation, migration, or inducing apoptosis.