# Terbinafine inhibits endothelial cell migration through suppression of the Rho-mediated pathway

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摘要

## Abstract

We showed previously that terbinafine, an allylamine with fungicidal activity, could inhibit angiogenesis by suppressing the endothelial cell proliferation. In the present study, we further showed that terbinafine (0 – 120 μmol/L) dose dependently inhibited the adhesion and migration of human umbilical vascular endothelial cells (HUVEC). Western blot analysis showed that terbinafine decreased the levels of Ras protein and membrane-bound RhoA protein. Moreover, the terbinafine-induced migration inhibition in HUVEC was prevented by pretreatment with farnesol or geranylgeraniol. Pretreatment of HUVEC with Ras inhibitor peptide or a ROCK (a kinase associated with RhoA for transducing RhoA signaling) inhibitor, Y27632, abolished the farnesol- or geranylgeraniol-induced prevention effect on the terbinafine-induced migration inhibition, respectively. These data suggest that the consuming or depletion of geranylgeranyl pyrophosphate and consequent suppression of protein geranylgeranylation and farnesylation, which is essential for activation of Rho GTPases and Ras, respectively, might account for the terbinafine-induced inhibition of HUVEC migration. The levels of phosphorylated focal adhesion kinase and paxillin protein and the mRNA levels of matrix metalloproteinase-2 and matrix metalloproteinase-9 were also decreased by terbinafine treatment. Taken together, these results indicate that suppression of Rho-mediated pathway might be involved in the signal transduction leading to the inhibition of cell migration caused by terbinafine in HUVEC. [Mol Cancer Ther 2006;5(12):3130 – 8]