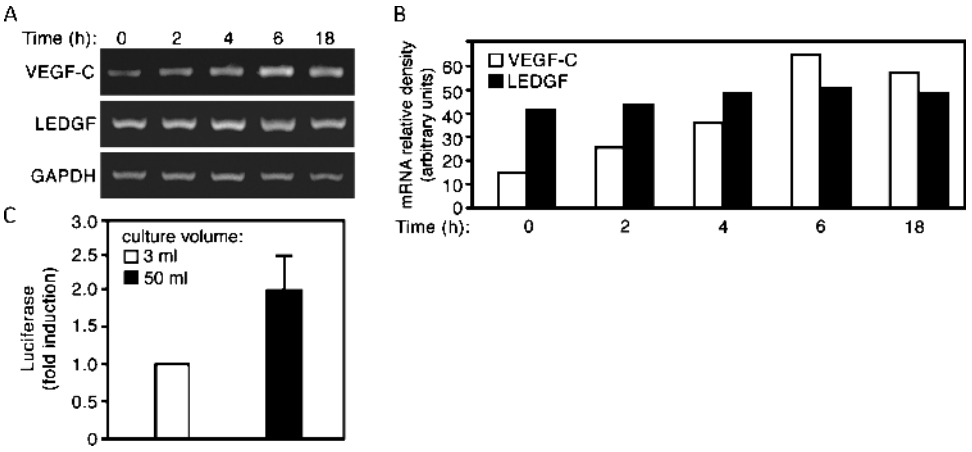

Figure W1. VEGF-C expression is induced by elevated culture medium pressure. (A) VEGF-C and LEDGF/p75 mRNA expression was analyzed by RT-PCR analysis in H1299 human lung cancer cells maintained in elevated column of culture medium (50 ml/1.1 cm) for the indicated time. (B) Relative intensity of the bands normalized against GAPDH. (C) Luciferase assay carried out with H1299 cells transiently transfected with pVEGF-Cwt-Luc reporter and cultured either in 3-ml (0.2 cm) or in high 50-ml culture medium (mean ± SD, $n = 3$).

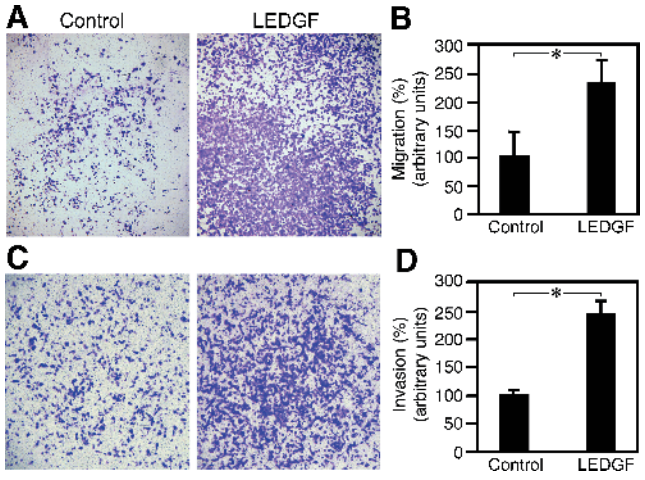

Figure W2. Overexpression of LEDGF/p75 augments migration and invasion rate of H1299 lung cancer cell *in vitro*. (A) Cell migration assay carried out *in vitro* with H1299 encoding the p75 variant of LEDGF (LEDGF) and control cells expressing an empty vector (Control). (B) Density of cells that had migrated through the filter. (C) Invasion of H1299 encoding LEDGF (LEDGF) and control cells (Control) through Matrigel. Cells were plated in transwell invasion chambers coated with Matrigel, and 12 hours later, cells that had migrated through the filter were stained. (D) Density of cells that invaded through the Matrigel. Three independent experiments were each carried out with at least triplicates, *$P < .01$.

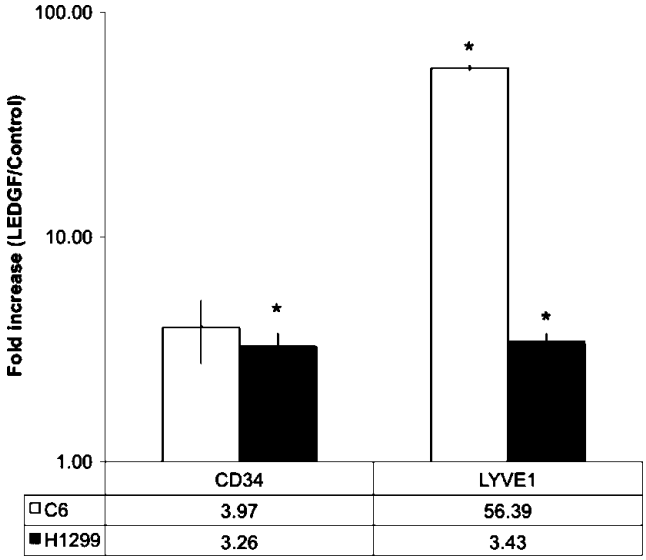

Figure W3. Ectopic expression of LEDGF/p75 augments blood and lymphatic vessels' quantity in H1299 and C6 tumors. The impact of LEDGF/p75 overexpression on blood and lymphatic vessels density was evaluated in the tumors described in Figures 5 and 6. Angiogenesis and lymphangiogenesis rates were deduced by counting the number of blood and lymphatic vessels after immunohistochemical staining using either antibodies against CD34 or LYVE-1, respectively. Data are presented as mean ± SD for fold induction of LEDGF/p75 over control tumors from at least three different tumors from each group normalized to the tumor section area (note the log scale of vessel density fold induction; *$P < .05$).

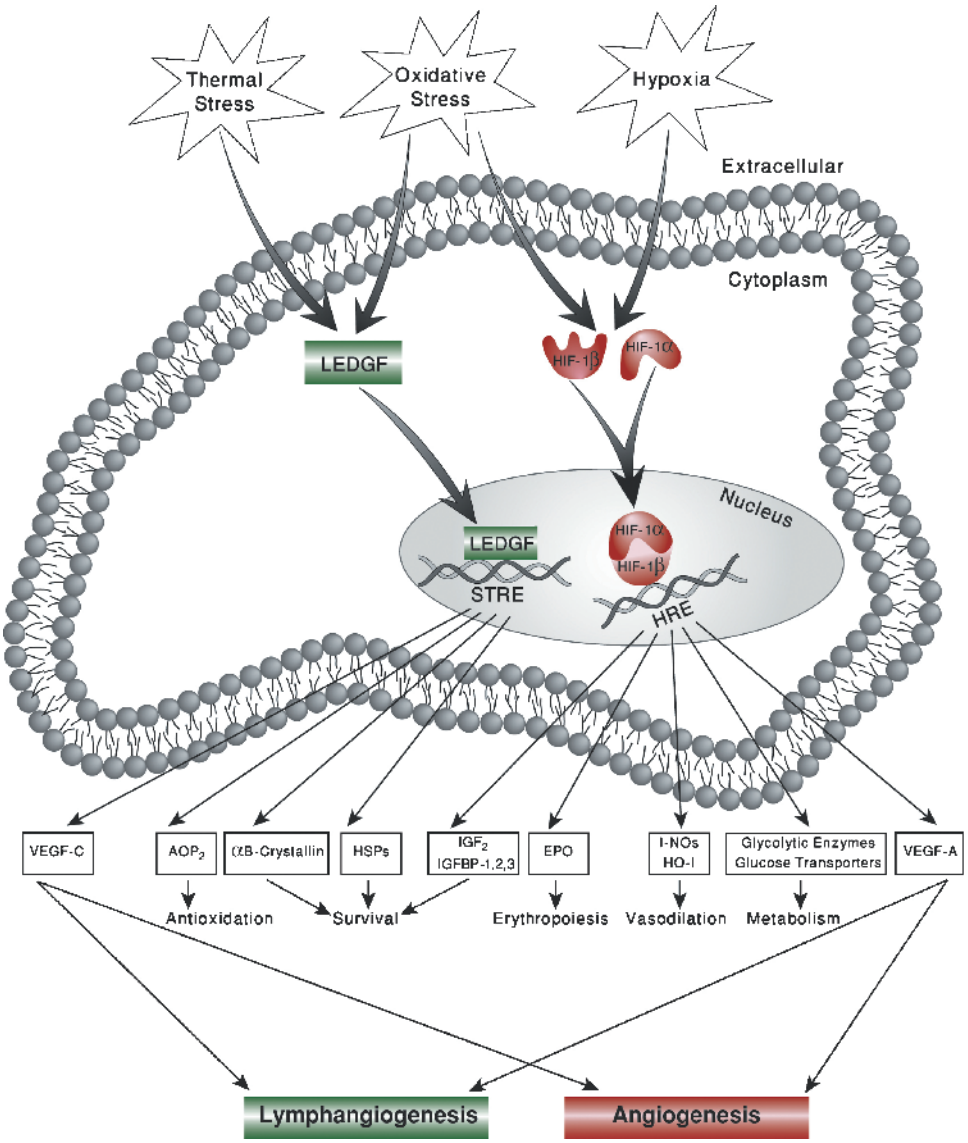

Figure W4. Microenvironmental control of tumor angiogenesis and lymphangiogenesis by LEDGF/p75. Angiogenesis and lymphangiogenesis are two complementary processes that play a vital role in physiological and pathologic circumstances. A key regulator of angiogenesis is the HIF-1 that is activated by hypoxia and oxidative stress. HIF-1 activates the transcription of hypoxia response element–containing genes involved in diverse aspects of cellular and integrative physiology, including energy metabolism (glycolytic enzymes and glucose transporters), survival (insulin-like growth factor 2 [IGF-2] and IGF-binding protein [IGFBP] 1,2,3), erythropoiesis (EPO), vasodilation (inducible nitric oxide synthase [I-NOS] and heme oxygenase 1 [HO-1]), and angiogenesis (VEGF, VEGF receptor fms-related kinase 1 [FLT-1]). In analogy, we show here that LEDGF is elevated by various stress signals including oxidative stress and hyperthermia. LEDGF confers its activity through binding to specific promoter elements (STRE and/or HSE) of many stress-related genes known to be involved in survival (heat shock proteins [HSPs], αB-crystallin) and in antioxidation (antioxidant protein 2 [AOP2]) and activates them. We propose here that LEDGF regulates lymphangiogenesis by mediating stress-induced expression of VEGF-C.