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Essential Role for Platelet-Activating Factor-Induced Activation of NF- κ B in Tumor Angiogenesis

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Based on our previous reports showing that platelet-activating factor (PAF) has an ability to enhance tumor metastasis and PAF is a potent NF- κ B inducer in vivo and in vitro, we investigated the role for PAF-induced activation of NF- κ B in tumor angiogenesis. Antisense oligonucleotides to p65 subunit of NF- κ B and antioxidants inhibited PAF-induced NF- κ B activation in vitro. Subcutaneous injection of Matrigel containing PAF caused neovascularization. PAF-induced angiogenesis was significantly reduced in mice receiving Matrigel containing PAF plus BN 50739, p65 antisense, or antioxidants. Matrigel containing mouse peritoneal macrophages caused rapid angiogenesis. This was also prevented by BN 50739, p65 antisense, or antioxidants. PAF was found to induce the expression of the most potent angiogenic factor, vascular endothelial growth factor, which was prevented by p65 antisense. Collectively, these data indicate that PAF enhances tumor angiogenesis through inducing NF- κ B activity, which in turn promote the expression of NF- κ B-dependent angiogenic factor(s).