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Parstatin: a Novel Endogenous Anti-angiogenic Peptide with Potential Therapeutic Applications

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SUMMARY

The proteolytic activation of proteinase-activated receptor 1 (PAR1) unveils the tethered peptide ligand and cleaves a 41-amino acid peptide. We have recently shown that this peptide, which we have designated as *parstatin* is a potent inhibitor of angiogenesis. Synthesized parstatin suppressed both basic angiogenesis and that stimulated by bFGF and VEGF in chick chorioallantoic membrane and in the rat aortic ring model of angiogenesis. Parstatin also abrogated endothelial cell proliferation, migration and capillary-like network formation in vitro, by promoting cell cycle arrest and apoptosis. We have also evaluated parstatin in three animal models of ocular neovascularization. Intravitreous injections of parstatin significantly suppressed retinal neovascularization in mice with oxygen-induced ischemic retinopathy. In mice with laser-induced rupture sites in Bruch's membrane, intraocular injection of parstatin strongly reduced the area of choroidal neovascularization. Similarly, rats with chemical burn-induced corneal neovascularization, that received subconjunctival injections of parstatin had areas of corneal neovascularization that were significantly smaller than those seen in control subjects treated with vehicle. These results support the notion that parstatin represents an important negative regulator of angiogenesis and indicate that it may provide a new agent for consideration for treatment of patients with corneal, retinal, or choriodal neovascularization.