BMP4 Prevents Thrombin Induced Inflammation and Vascular Damage in Endothelial Cells

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Cardiovascular Disease (CVD) is the leading cause of death globally. Thrombosis is the most common underlying pathology of CVD. Thrombin, an enzyme responsible for converting fibrinogen to fibrin, plays a key role in thrombosis by regulating coagulation through processes such as cell proliferation, angiogenesis, and inflammation. In CVD, the prothrombic state causes aberrant cellular responses and further damage of the endothelium. Bone Morphogenic Protein 4 (BMP4) plays an important role in angiogenesis and literature suggests that dysfunctional BMP4 may play a role in CVD. Therefore, this research aims to study whether BMP4 prevents and reverses the damaging effects of Thrombin and endothelial vasculature, as observed in CVD. To study this, the effect of Thrombin on endothelium was first determined using rtPCR for IL-6, IL8, and MMP1 to determine extent of inflammation and matrix degradation. Then, the effect of thrombin on BMP4 expression was measured using PCR. Then, varying BMP4 dosages were used in combination with thrombin to determine the preventative effect of BMP4. Data showed that thrombin induced inflammatory markers IL-6, IL-8 and matrix degradation protein MMP1. However, pretreatment with BMP4 prevented this affect. Furthermore, Thrombin significantly reduced cell survival, however, adding BMP4 treatment to thrombin treated cells reversed this affect. Additionally, 10ng/mL of BMP4 induces angiogenesis, suggesting it can induce vessel formation in damaged endothelium of CVD patients. These results indicated that BMP4 has a protective effect against thrombin-induced endothelial inflammation and vascular damage. Thus, BMP4 can potentially be used as a therapeutic in pathological conditions to inhibit the damaging effects of excess thrombin generation.