Matrix Gla protein negatively regulates calcification of human aortic valve interstitial cells isolated from calcified aortic valves

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Aortic valve stenosis (AS) is a common heart valve disease in elderly people, and is mostly accompanied by ectopic valve calcification. We recently demonstrated that tumor necrosis factor- α (TNF- α) induces calcification of human aortic valve interstitial cells (HAVICs) obtained from AS patients. In this study, we investigated the role of matrix Gla protein (MGP), a known calcification inhibitor that antagonizes bone morphogenetic protein 2 (BMP2) in TNF- α -induced calcification of HAVICs. HAVICs isolated from aortic valves were cultured, and calcification was induced with 30 ng/mL TNF- α . Gene expression of the calcigenic marker, BMP2, was significantly increased in response to TNF- α , while the gene and protein expression of MGP was strongly decreased. To confirm the role of MGP, MGP-knockdown HAVICs and HAVICs overexpressing MGP were generated. In HAVICs, in which MGP expression was inhibited by small interfering RNA, calcification and BMP2 gene expression were induced following long-term culture for 32 days. In contrast, HAVICs overexpressing MGP had significantly decreased TNF- α -induced calcification. These results suggest that MGP acts as a negative regulator of HAVIC calcification.