**EXTRACELLULAR MATRIX TURNOVER IN VASCULAR CALCIFICATION**

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Cumulative studies have demonstrated that extracellular matrix (ECM) turnover play a critical role during cardiovascular remodeling. Intima calcification is highly correlated with atherosclerotic plaque burden, but the underlying mechanism is poorly understood. We recently reported that cartilage oligomeric matrix protein (COMP), a component of vascular extracellular matrix, is an endogenous inhibitor of vascular smooth muscle cell calcification. Hererin We further investigate whether COMP affects atherosclerotic calcification. ApoE−/−COMP−/− mice fed with chow diet for 12 months manifested more extensive atherosclerotic calcification in the innominate arteries than did ApoE−/− mice. To investigate which origins of COMP contributed to atherosclerotic calcification, bone marrow (BM) transplantation was performed between ApoE−/− and ApoE−/−COMP−/− mice. Enhanced calcification was observed in mice transplanted with COMP−/−ApoE−/− BM compared to mice transplanted with ApoE−/− BM, indicating that BM-derived COMP may play a critical role in atherosclerotic calcification. Furthermore, microarray profiling of wild type and COMP-/- macrophages revealed that COMP-deficient macrophages exerted atherogenic and osteogenic characters. Integrin β3 protein was attenuated in COMP-/- macrophages, and overexpression of integrin β3 inhibited the shift of macrophage phenotypes by COMP deficiency. Furthermore, AAV2-integrin β3 infection attenuated atherosclerotic calcification in COMP−/−ApoE−/− mice. Mechanistically, COMP bound directly to β-tail domain of integrin β3 via its C-terminus, and blocking of the COMP-integrin β3 association by β-tail domain mimicked the COMP deficiency-induced shift in macrophage phenotypes. Similar as COMP deficiency in mice, transduction of AAV2-β-tail domain enhanced atherosclerotic calcification in ApoE-/- mice. In summary, these results reveal that COMP deficiency acted via integrin β3 to drive macrophages towards the atherogenic and osteogenic phenotype and thereby aggravate atherosclerotic calcification.