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Involvement of cytosolic phospholipase A2 alpha in pathological and experimental cardiovascular mineralization

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Cytosolic phospholipase A_2 alpha ($cPLA_2a$) is a calcium-dependent enzyme constitutively expressed by most human cells catalyzing the hydrolysis of membrane glycerophospholipids bearing arachidonic acid at the *sn*-2 position with production of downstream pro-inflammatory lipid mediators (Murakami and Kudo, 2002). Although $cPLA_2a$ seems to facilitate the release of pro-calcific matrix vesicles by hypertrophic chondrocytes during ossification (Wuthier et al., 1977), its involvement in pathological biomineralization has not yet been elucidated. Here, $cPLA_2a$ expression was assessed in the context of both pathological and experimentally induced mineralization affecting cardiovascular tissues and cultured aortic valve interstitial cells (AVICs). $cPLA_2a$ resulted to be expressed by fibroblasts, smooth muscle cells, macrophages, and activated endothelium populating both calcified aortic valves and atherosclerotic aorta walls. $cPLA_2a$ was also expressed by cultured AVICs, with enzyme expression rate correlating with mineralization rate, being enhanced by inflammation and high phosphate concentrations. For all calcific contexts, ultrastructural examination revealed mineralization to depend on progressive accumulation and release of acidic lipids, acting as major hydroxyapatite nucleators, followed by cell disgregation into a multitude of particles having calcium nucleation capability, according to peculiar degenerative patterns as those previously described (Ortolani et al., 2010).

In conclusion, enzyme expression and ultrastructural patterns being shared by both pathological and experimental calcific conditions suggests that $cPLA_2a$ might be actually involved in the etiopathogenesis of cardiovascular mineralization, besides representing a potential target for novel therapeutic strategies aimed to counteract the progression of cardiovascular calcific diseases.

References

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Keywords
cPLA2 alpha, dystrophic calcification, AVIC, ultrastructure.