The role of DANCE/fibulin-5 in elastic fiber assembly

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Elastic fiber is required for the elasticity of tissues such as skin, lung and arteries, and deterioration of elastic fiber causes many aging-associated diseases. We previously showed that Developing Arteries and Neural Crest EGF-like (DANCE) (also designated fibulin-5), an integrin ligand for αvβ5, αvβ3 and α3β1, is essential for elastic fiber development. DANCE deficient mice recapitulate human aging phenotypes such as loose skin, emphysema and stiff arteries, due to disorganized elastic fibers. However, the specific role of DANCE in elastogenesis and correlation of aging-associated alteration of DANCE with aging phenotypes remains elusive. In this seminar we show that recombinant DANCE protein potently induces elastic fiber assembly even in serum-free cell culture without changing the expression of elastic fiber components, suggesting that DANCE serves as an organizer molecule for elastogenesis. DANCE dimerizes or oligomerizes, deposits on microfibrils, promotes aggregation of tropoelastin molecules through coacervation, and also interacts with lysyl oxidase-like (LOXL) 1, 2 and 4, the enzymes that cross-link elastin. We propose a model that DANCE tethers LOXL enzymes to microfibrils, thus facilitating aggregation and cross-linking of elastin on microfibrils. Intriguingly, much less full-length DANCE and more truncated form of DANCE was detected in aged mouse loose skin than in young mouse skin, due to proteolytic cleavage of the NH2-terminal domain. The cleavage of DANCE abrogates DANCE-DANCE interaction and DANCE-microfibrils interaction, leading to loss of elastic fiber organizing activity of DANCE. These data suggest that decrease in full-length DANCE by proteolytic cleavage may contribute to loss of elastogenic potential in aged elastic tissues.