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Metal Induced Alpha to Beta Transitions in Collagen Binding Domain. Philominathan Sagaya Theresa Leena, Osamu Matsushita, Joshua Sakon, Dept. of Chemistry and Biochemistry, Univ. of Arkansas, USA.

Clostridium histolyticum ColG collagenase activated by Ca^{2+} is responsible for extensive tissue destruction, and the CBD is a segment of the multi-domain enzyme. Binding of two Ca^{2+} on CBD is co-operative and is both enthalpically and entropically driven ($K_{d1}= 2.13\mu\text{M}$; $K_{d2}= 4.63\mu\text{M}$). Structures in the presence and absence of Ca^{2+} have been solved at ultrahigh resolution ($<1.2\text{\AA}$). N-terminus 14 residues of CBD adopt a α -helical conformation however, addition of Ca^{2+} unwinds the linker into a new β -strand. To rule out the crystal-packing artifact, NMR titration studies were done and it confirms the conformational structure change upon addition of Ca^{2+} . The changes in Stokes and hydrodynamic radii as measured by size exclusion chromatography and dynamic light scattering experiments showed drastic transition upon Ca^{2+} addition; however far UV-CD was not as sensitive. With Ca^{2+} CBD becomes thermally stable ($T_m>90^\circ\text{C}$), less susceptible to proteolysis and stable against chemical denaturants. Different metals trigger different degree of transition and as mutation of metal chelating amino acids. Not only this study provide insights into the drastic structure change thought to accompany upon secretion of the enzyme but also to provide insights into amyloidosis.