

Poster Presentation

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Two crystal forms of peptidylarginine deiminase type III (PAD3)

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Peptidylarginine deiminase (PAD) is a Ca²⁺-dependent enzyme that catalyzes the conversion of protein arginine residues to citrulline. Protein citrullination by PAD confers large structural and mechanical effects on the target proteins by altering intermolecular and intramolecular ionic or hydrophobic interactions. Five paralogous genes (PADI1 - 4 and 6) on human chromosome 1p35-36 encode the human PAD isozymes. Among the PADs, PAD3 shows the highest substrate specificity for synthetic and natural substrate. S100A3 is an EF-hand-type Ca²⁺-binding S100 protein family member that colocalizes with PAD3 in hair cuticular cells. PAD3 converts a symmetric pair of Arg51 residues on an S100A3 dimer surface to citrullines, causing assembly of a homotetramer, but does not convert other arginines. Although this specific citrullination is largely affected by the formation of two intramolecular disulfides in S100A3, it is not clear how the sheltered Arg51 residues is recognized by PAD3. We are aiming structural analysis of the substrate bound forms to elucidate structural factor that PAD3 recognize Arg51 residues only. Although X-ray crystal structures of the PAD4 isozyme and its complexes with substrate peptides have been reported, structural analysis of other PAD isozymes has not yet been conducted. To obtain the crystals of the substrate-complex, we prepared the C646A mutant and the other inactive mutants (D350A, H470A, D472A) of PAD3. We determined the crystal structures of wild-type PAD3, at first. Then, we have tried to determine the structure of the substrate complex with the mutants of PAD3. However, the solved structures did not contain the substrate at present stage. From our structural analysis, only the crystals of C646A were belonged to different crystal system from the others, and its difference didn't relate to their crystallization condition. In this conference, we discuss the origin(s) of the differences in the crystal system of C646 from the others.

[1] Unno, M. et al., *Acta Cryst.*(2012), F68, 668-670, [2] Kizawa, K. et al., *JBC.*(2008), VOL. 283, NO. 8, pp. 5004-5013

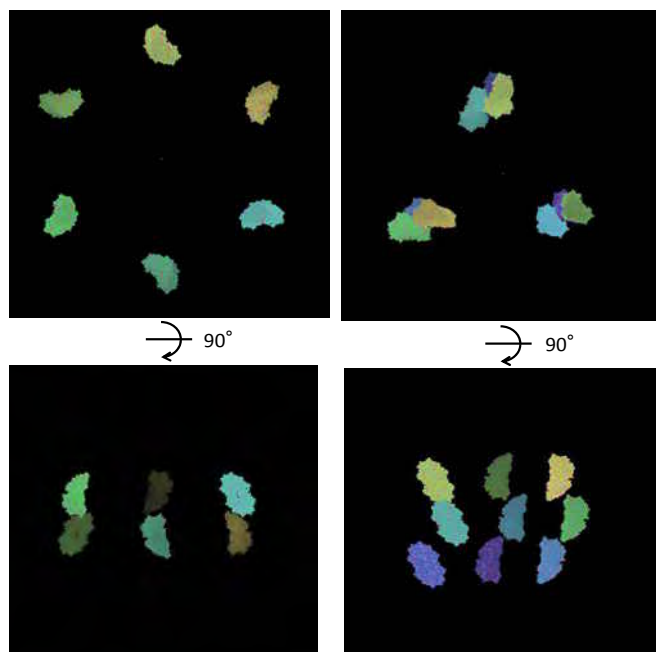


Fig. (left) R₆₃ crystal form of PAD3C646A
(right) R₃ crystal form of the other mutants

Keywords: PAD3, mutant, crystal form