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The role of SAM domain in $\Delta Np63\alpha$

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The p53 family member p63 exhibits multiple isoforms and functional domains, with $\Delta Np63\alpha$ serving as a critical transcriptional regulator implicated in epithelial-mesenchymal transition. While the various domains of $\Delta Np63\alpha$ have been extensively characterized, the precise function of its Sterile Alpha Motif (SAM) domain stays elusive. Mutations within the SAM domain are associated with Ankyloblepharon-Ectodermal Defects-Cleft Lip/Palate (AEC) syndrome and Rapp-Hodgkin syndrome (RHS), primarily due to SAM domain destabilization. These conditions are characterized by severe skin erosions, underscoring the domain's significance in maintaining epithelial integrity. SAM domains are ubiquitous in eukaryotic proteins and are renowned for their propensity to oligomerize through diverse mechanisms. However, the p63 SAM domain has not previously demonstrated such oligomerization tendencies. Intriguingly, the presence of a putative zinc-binding motif within the SAM domain prompted our investigation into zinc-mediated effects using Nuclear Magnetic Resonance (NMR) spectroscopy. In this study, we present evidence of zinc-induced dimerization of the p63 SAM domain and elucidate its dimeric structure. Additionally, we explore the potential implications this dimerization might have on the full protein.

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