The role of ADAMTS-9 in interdigital web regression

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Background: ADAMTS9 is the most conserved member of a large family of secreted metalloproteases having diverse functions. Combinatorial Adamts9 haploinsufficiency with either Adamts20 or Adamts5 nullizygosity previously disclosed a cooperative role in interdigital web regression (McCulloch DR et al. Dev Cell 2009).

Purpose: Adamts9 null mice die without gastrulating, precluding investigations of its roles later in embryogenesis, in adult mice and disease models. We therefore generated a floxed Adamts9 allele to bypass embryonic lethality.

Methods: To make the mutant, unidirectional loxP sites flank exons 5-8, which encode much of the catalytic domain, including the protease active site. Adamts9 was conditionally deleted in limb mesoderm using Prx1-Cre mice.

Results: Mice with limb-specific Adamts9 deletion developed soft-tissue syndactyly (STS) with 100% penetrance. The severity had not changed during the growth. Tunel staining and Acridine orange staining at the web of E14.5 revealed that the number of apoptotic cells in limb-specific Adamts9 deletion is less than those in control mice.

Conclusions: We conclude that Adamts9 has both non-redundant and cooperative roles in regulating interdigital apoptosis. This new allele will be useful for identifying other biological functions of ADAMTS9.