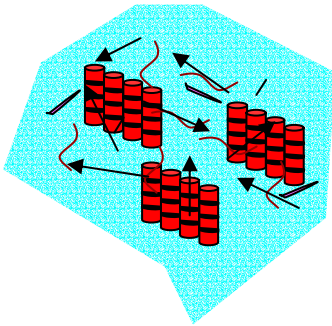


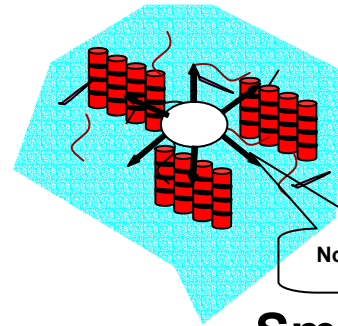
Proposed Phases of healing and mechanisms / processes

Post-wounding

a) Basal

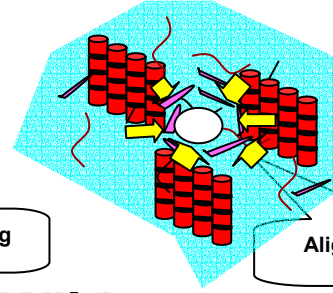


b) Early
(0-1 Day)



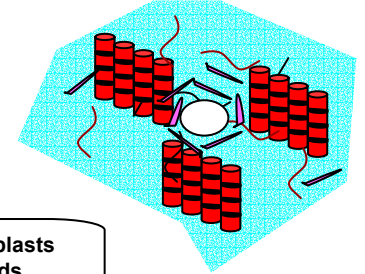
c)

Intermediate Contractile Phase
(5-7 Days)



d)

Late Remodeling Phase
(21-36 Days)

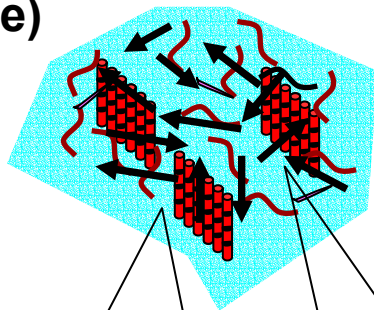


Normal Gapping wounds

Aligned Myofibroblasts contract wounds

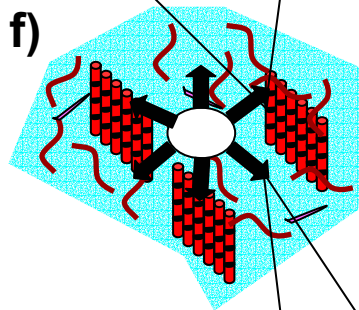
Smad 3 Wild type

e)



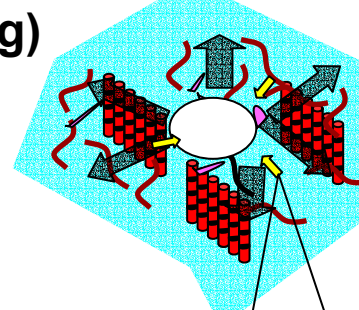
Increased
• Elastin
• GAGs
• Compactly organized Collagen

f)



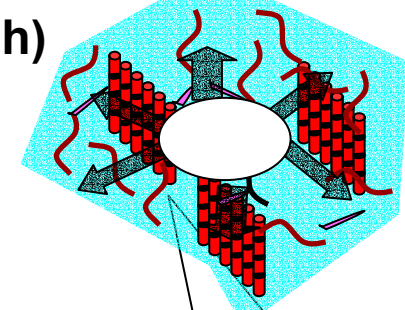
Increased Modulus
(Toe and Linear)

g)



Decreased Wound Contraction

h)




Increased matrix remodeling by MMPs

Smad 3 Knockout

Altered Integrin Expression and Mechanotransduction

i) Time line of post-wounding changes

	Ear Punch Wound		<u>Post-Wounding</u>	
			→	
	<u>Basal</u>	<u>Early</u> <u>(12-24hours)</u>	<u>Intermediate</u> <u>(3-7 days)</u>	<u>Late</u> <u>(21-36 days)</u>
<u>Smad3 Wild Type</u>	Normal ECM composition and Mechanical Properties	Normal Gaping forces	Normal wound contraction (Myofibroblast transformation)	Normal Matrix Remodeling and tissue forces
<u>Smad3 Knockout</u>	Perturbed ECM composition and Increased modulus of Elasticity	Increased Apoptosis Decreased TGFβ1 Decreased MMP 9 Increased tissue forces Increased pSrc (Tyr416), Increased pFAK(Tyr397) Increased pPaxillin(Tyr118), Increased F-Actin assembly Altered mechanotransduction Increased αVβ3Integrin Decreased αVβ5 Integrin	Decreased wound contraction Decreased αSMA Altered mechanotransduction Decreased αVβ3Integrin Increased αVβ5 Integrin pFAK (Tyr397) not detectable	Increased remodeling Increase MMP9 Increase MMP12 Increased Retractive forces Increased pFAK (Tyr397)