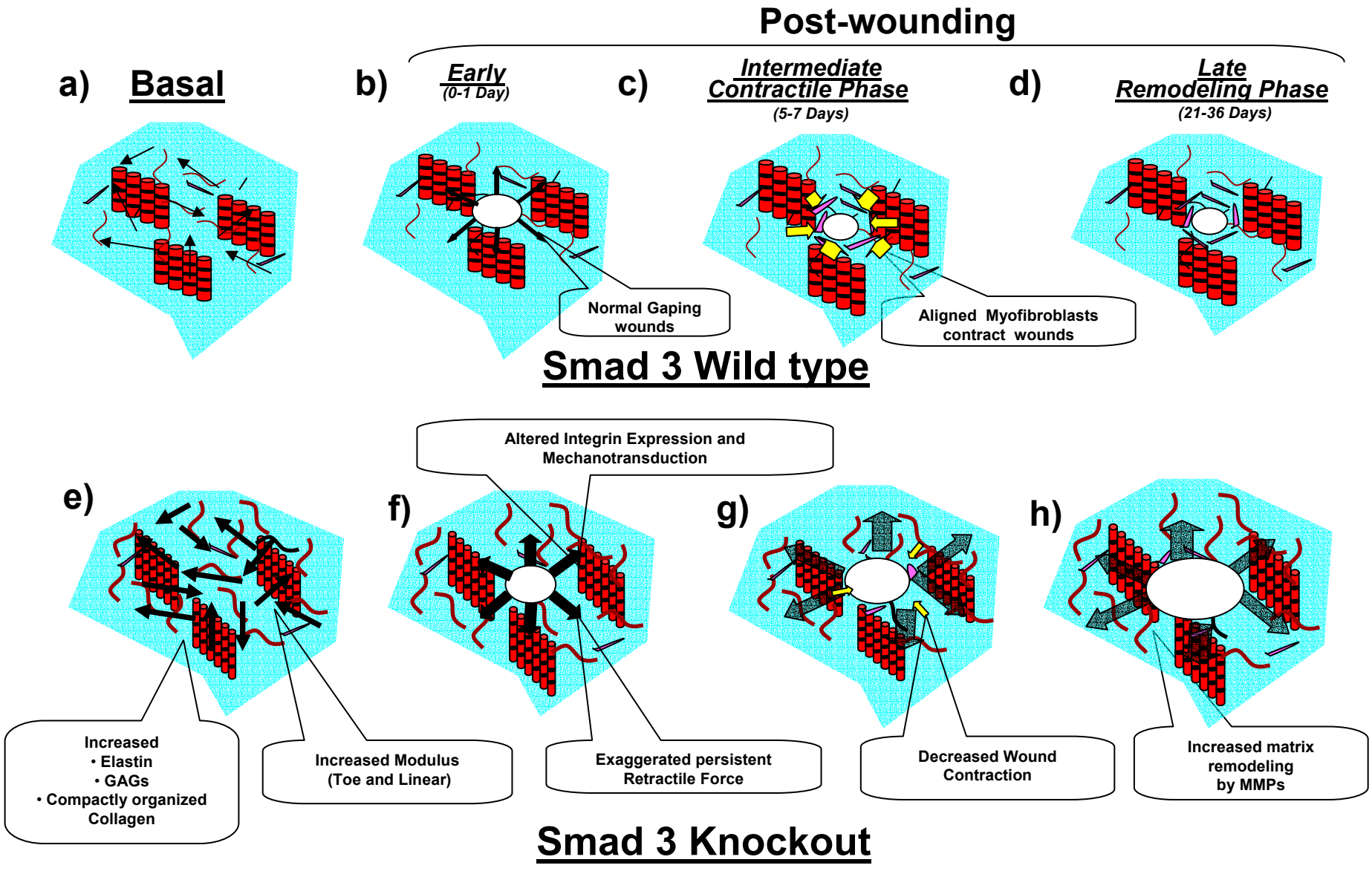
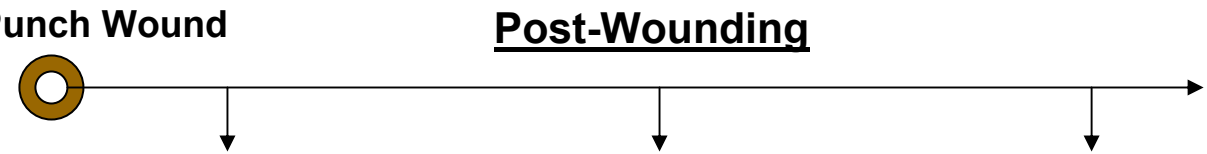
Proposed Phases of healing and mechanisms / processes



i) Time line of post-wounding changes



	Basal	Early (12-24hours)	Intermediate (3-7 days)	Late (21-36 days)
Smad3 Wild Type	Normal ECM composition and Mechanical Properties	Normal Gaping forces	Normal wound contraction (Myofibroblast transformation)	Normal Matrix Remodeling and tissue forces
Smad3 Knockout	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 aVb3Integrin Increased aVb5 Integrin pFAK (Tyr397) not detectable	Increased remodeling Increase MMP9 Increase MMP12 Increased Retractive forces Increased pFAK (Tyr397)