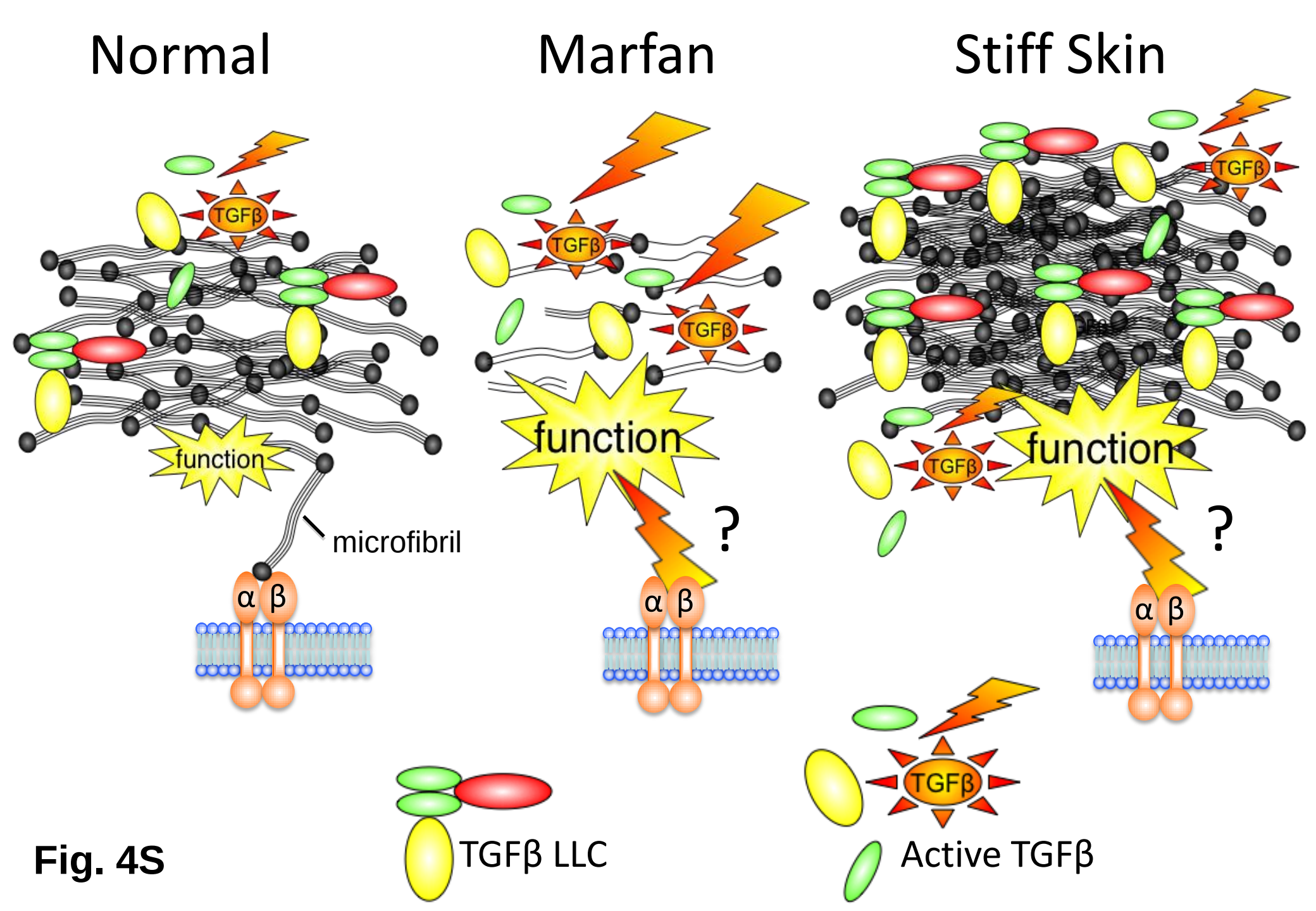
Normal
Marfan
Stiff Skin
TGFβ
function
microfibril
α
β
?
TGFβ LLC
Active TGFβ

Fig. 4S

Fig 4S. Normal: TGFβ activity (proportionate to the size of the starburst labeled “function”) integrates cytokine concentration and activation (proportionate to the size of lightening bolts) and both are regulated by microfibrils (composed of fibrillin-1). The local concentration of the TGFβ large latent complex (LLC) is dependent on the concentration of microfibrils. Binding of integrins (subunits labeled α and β) by the fibrillin-1 component of microfibrils may limit their participation in TGFβ activation. Marfan syndrome: decreased TGFβ concentration (as a consequence of decreased microfibrils) is offset by increased activation. Integrins that are unoccupied by fibrillin-1 may contribute to TGFβ activation. Sustained signaling is dependent on ongoing production of TGFβ. SSS: increased concentration of TGFβ (asa consequence of increased microfibrillar deposition) sustains a chronic increased level of TGFβ signaling whether or not the abnormal character of microfibrils and altered interaction with integrins promotes increased TGFβ activation. Components of the LLC: latent transforming growth factor binding protein (LTBP; yellow oval); latency associated peptide (LAP; green ovals); transforming growth factor beta (TGFβ; red oval).