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Table 1 In vivo studies in PD utilizing TGF- β 1 stimulation model

Authors	Year	Cell species	Type of TA	Compound investigated	Timing of administration	Outcomes
Target-based approach						
Piao <i>et al.</i>	2010	Human	Both PD and normal TA samples	SKI2162; small-molecule inhibitor of activin receptor-like kinase 5 (ALK5), a type I receptor of TGF- β	Pretreatment with compound	Inhibition of phosphorylation Smad2/3; inhibition ECM production (protein)
Shindel <i>et al./Lin et al.</i>	2010	Human	Both PD and normal TA samples	Pentoxifylline	Pretreatment with compound	Inhibition of collagen fiber deposition and elastogenesis
Jung <i>et al.</i>	2013	Human	PD samples	HS-173; novel inhibitor of phosphoinositide 3-kinase (PI3K)/Akt	Co-stimulation (compound + TGF- β 1)	Reduction of α -SMA, vimentin, plasminogen activator inhibitor-1 (PAI-1), fibronectin, collagen I/IV and Smad2/3; inhibition of PI3K/Akt by impeding Akt, mTOR and P70S6K
Ryu <i>et al.</i>	2013	Human	PD samples	small interfering RNA (siRNA)-mediated silencing of histone deacetylase 2 (HDAC2)	Pretreatment with compound	Inhibition FB>MFB; inhibition of phosphorylation and nuclear translocation of Smad2/3
Jiang <i>et al.</i>	2015	Sprague-Dawley rats	Normal TA samples	estrogen [17 β -estradiol (E2)]	Co-stimulation (compound + TGF- β 1)	Inhibition of α -SMA expression, concentration of hydroxyproline (collagen marker) and cellular contraction
Choi <i>et al.</i>	2015	Human	PD samples	Smad7 gene overexpression	Pretreatment with compound	inhibition of phosphorylation and nuclear translocation of SMAD2/3, MFB transformation, and production of ECM
Mateus <i>et al.</i>	2018	Human	Both PD and normal TA samples	BAY 60-6583 (ADORA2B agonist)	Co-stimulation (compound + TGF- β 1)	Inhibition of FB > MFB
Milenkovic <i>et al.</i>	2019	Human	PD samples	Simvastatin a Y-27632 (ROCK-inhibitor)	Co-stimulation (compound + TGF- β 1)	Inhibition of FB > MFB, inhibition of α -SMA, collagen I/III, elastin, CTGF (mRNA) and impairment of ROCK-signalling through prevention of YAP/TAZ nuclear transformation
Phenotypic-based approach						
Jiang <i>et al.</i>	2017	Sprague-Dawley rats	Normal TA samples	Adipose-derived stem cells (ADSC)	ADSC administration after MFB transformation	Inhibition of expression of α -SMA and collagen I in MFBs; Reduction in phosphorylation and activity of Smad2, RhoA, ROCK1/2 and an upregulation of MMPs and caspases
Ilg <i>et al.</i>	2019	Human	Both PD and normal TA samples	Tamoxifen and Vardenafil (separately and in combination)	Co-stimulation (compound + TGF- β 1)	Inhibition of MFB transformation, cellular contraction, and ECM production

TA, tunica albuginea; PD, Peyronie's disease; ADSC, adipose-derived stem cell; ECM, extracellular matrix; MMP, matrix metalloprotease; FB, fibroblast; MFB, myofibroblast; CTGF, connective tissue growth factor.

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