Growth factors tested *in vivo* in animal models with experimentally induced intervertebral disc (IVD) degeneration						
Growth factor	**Mechanism of action**	**Animal model Induction of degeneration**	**Treatment dose; duration Control treatment**	**GAG/PG content of the NP**	**Histo(patho)logy**	**MRI/radiograph**
BMP-2	Differentiation signalling factor; anabolic	17 rabbits [1] AF tearing	0.1 mg (in 0.1 mL); 12 wks Control: saline	ND	Vascularity, fibroblast proliferation, inflammation	Degenerative changes; disc space narrowing/irregularity, subchondral sclerosis, osteophytes, EP hypertrophy
BMP-7/OP-1	Differentiation signalling factor; anabolic	34 rats [2] Compression	0.2 µg (in 1 µL); 4 wks Control: saline	ND	ECM content + (NS) NP size +	ND
		90 rabbits [3] AF puncture	100 µg (in 10 µL); 2, 4, 8, 12, 24 wks Control: lactose	+	Total histological scores (AF fibers, NP cellularity and matrix) +	DH + MRI score + MRI T2W intensity + (NS)
		16 rabbits [4] AF puncture	100 µg (in 10 µL); 8 wks Control: lactose	+	ND	DH + MRI T2W intensity +
		54 rabbits [5] Chondroitinase	100 µg (in 10 µL); 6, 8, 12, 16 wks Control: lactose	+	Some BMP-7-treated IVDs with abundant matrix	DH +
		24 rabbits [6] None	2 µg (in 10 µl); 2, 4, 8 wks Control: saline	+ (only significant at 2 wks)	ND	DH +
BMP-14/GDF-5	Differentiation signalling factor; anabolic	16 mice [7] Compression	8 ng (in 8 µL); 1, 4 wks Control: saline	ND	DH + PC + (NS) Collagen 2, aggrecan expression (NP)	ND
		16 rabbits [8] AF puncture	10 ng, 1 or 100 µg (in 10 µl); 12 wks Control: puncture alone, puncture + PBS	ND	Total histological score (AF fibers, NP cellularity and ECM) at 100 µg + (vs. puncture alone)	DH + (only significant at 1 and 100 µg) MRI scores + (all doses, NS) MRI T2W intensity + (all doses)
FGF	Signalling factor; anabolic	10 mice [7] Compression	8 ng (in 8 µL); 1, 4 wks Control: saline	ND	Cell density in middle/inner AF + (NS)	ND
IGF-1	Insulin-like activity; anabolic	16 mice [7] Compression	8 ng (in 8 µL); 1, 4 wks Control: saline	ND	DHI, inner annular fibrochondrocytes, and PC + (all NS)	ND
Link N	Peptide, stabilizing PG aggregates	28 rabbits [9] AF puncture	100 µg (in 10 µl); 12 wks Control: saline	+ (NS)	Less signs of IVD degeneration (NS)	DH +
P2K	Peptide, possibly regulating TGFβ signalling	14 rabbits [10] AF puncture	10 µg (in 15 µL); 12 wks Control: lactose	+	Less signs of IVD degeneration ECM content +	DH + MRI scores + MRI T2W intensity +
PRP	Plasma fraction with highly concentrated growth factor levels	36 rabbits [11] NP aspiration	20 µL gelatin hydrogel microspheres (GHM) impregnated with PRP (sustained release); 2, 4, 8 wks Control: PBS-GHM	ND	Less signs of IVD degeneration PG expression + (NS)	ND
		128 rabbits [12] NP aspiration	20 µL GHM impregnated with PRP (sustained release); 2, 4, 8 wks Control: PBS-GHM	ND	Less apoptotic NP cells	DH + MRI scores + MRI T2W intensity + (NS)
		12 rabbits [13] AF puncture	20 µL PRP; 12 wks Control: PBS	ND	CLC number + Histological scores not different	DH + MRI T2W intensity + (NS)
Simvastatin	Stimulates BMP-2 pathway *in vitro*	30 rats [14] AF puncture	PEG gel with 10 µg simvastatin; 2 wks Control: PEG gel	+ (NS)	Total histological scores (AF fibers, NP cellularity and ECM) +	MRI scores + MRI T2W intensity +
TGFβ	Signalling factor; anabolic	19 mice [7] Compression	1.6 ng (in 8 µL); 1, 4 wks Control: saline	ND	PC + (NS)	ND

Additional file 1. Growth factors tested *in vivo* in animal models with experimentally induced intervertebral disc (IVD) degeneration.
+: significantly better/higher than in the control group; AF, annulus fibrosus; BMP, bone morphogenetic protein; DH, disc height; ECM, extracellular matrix; EP, end plate; FGF, fibroblast growth factor; GAG, glycosaminoglycan; GDF-5, growth and differentiation factor-5; GHM, gelatin hydrogel microspheres; IGF-1, insulin-like growth factor 1; MRI, magnetic resonance imaging; ND, not done; NP, nucleus pulposus; NS, not significant; OP-1, osteogenic protein-1; P2K, Peniel 2000; PC, percentage proliferating cells; PG, proteoglycan; PRP, platelet rich plasma; TGFβ, transforming growth factor-β; T2W, T2-weighted; wks, weeks.

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