Supplemental Table: Detailed information of each study (N = 26) included in the review.

Study	Growth Factor	Animal Model	Surgical Approach	Fusion Level(s)	Study Groups	Spinal Fusion Findings	p-value	Spinal Fusion Assessment Technique	Other Methods of Assessment	Excluded/ peri-operative death	Post-operative analgesia/ antibiotic	Post-operative follow-up
Zheng et al., 2017	AB204	Beagle dog	Posterolateral	L1-2, L4-5	A. Osteon II (biphasic calcium phosphate), 2 mL	6.3% (1 of 16)	-	Manual palpation (no motion)	Radiography (AP and Lateral), CT, Histology (H&E) Volume of newly formed bone was significantly higher in Group C compared to Group A and B ($p<0.01$)	3/17 (perioperative death; bleeding)	Anti-biotics, IM injection of Biotril, 0.1 mL/kg daily for 3 days after surgery	8 weeks
					B. Osteon II, 2 mL, + rhBMP-2, 50 µg	15% (3 of 20)	-					
					C. Osteon II, 2 mL, + AB204, 50 µg	90% (18 of 20)	<0.01, compared to A or B					
Park et al., 2011	COMP-Ang-1	Sprague-Dawley rat	Posterolateral	L3-5	A. ICBG, 1 mL	38.9% (7 of 18)	-	Manual palpation (*at least one side* lacked motion)	Radiography (PA), micro-CT, biomechanical testing, histology (H&E), histomorphometry, immuno-histochemistry (factor VIII-related antigen), RT-PCR (Runx2, BSP, Osteopontin, Type I collagen, Osterix, Osteocalcin, Tie-1, VEGF, Flt-1, Factor VIII, Egr-1) Optical density of fusion masses was significantly higher in Group C compared to Group A and B ($p<0.001$). Total bone volume was significantly higher in Group C compared to Group A and B	2/20 (perioperative death)	Analgesics, butorphanol, 0.1 mg/kg body weight	6 weeks
					B. ICBG, 1 mL, + Bovine serum albumin-impregnated absorbable collagen sponge, 100 µg	42.1% (8 of 19)	-			1/20 (perioperative death)		
					C. ICBG, 1 mL, + COMP-Ang-1-impregnated absorbable collagen sponge, 100 µg	89.5% (17 of 19)	<0.01 compared to A or B			1/20 (perioperative death)		

									(p<0.001). The mechanical strength was significantly greater in Group C compared to Groups A and B (p<0.01). Immunostaining of endothelial cells for factor VIII revealed higher levels of vascularity in the fusion site in Group C compared to Groups A and B (p<0.01). Runt-related transcription factor 2 and its target genes were significantly up-regulated in Group C compared to Group B (p<0.05).			
Babat et al., 2005	Calcitonin	New Zealand White rabbit	Posterolateral	L5-L6	A. ICBG, 3 mL	56% (10 of 18)	No significant differences	Manual palpation (no motion)	Biomechanical testing Group B had significantly less peak load compared to Groups A and C (p<0.01) and were less stiff than Group A (p<0.01) and Group C (p<0.05).	4/60 (1 perioperative death; 1 euthanasia for hind-limb palsy; 1 infection; 1 incorrect fusion level)	Buprenorphine 0.08 mg subcutaneously immediately after surgery. Each animal then received additional buprenorphine 0.08 mg in 12-h intervals,	5 weeks
					B. ICBG, 3 mL + pamidronate, 1.2 mg subcutaneously three times/week for 4 weeks preoperatively, then 0.6 mg/day via mini-osmotic pump for 4 weeks postoperatively	37% (7 of 19)						
					C. ICBG, 3 mL + calcitonin, 14 IU/day via mini-osmotic pump for 4 weeks postoperatively only.	68% (13 of 19)						

											as needed	
Liu et al., 2012	Calcitonin	New Zealand White rabbit	Posterolateral	L4-5, L6-7 (for L6-L7, steel wire was used to bind the spinous processes; for L4-L5, no wire fixation was performed)	A. L4-L5: ICBG, 2.5 mL	75% (3/4)	No significant differences	Radiography (AP)	Histology (H&E), histomorphometry, RT-PCR (BMP-2, Col I, VEGF, IGF-1) Starting at week 2, mRNA levels of Col I , BMP-2 , IGF-I , and VEGF were higher in the groups of grafts with calcitonin (B and D) compared to the groups without (A and C) ($p < 0.05$ for each)	N/A	Antibiotics, Penicillin-G; 40,000 U	1, 2, 4, 8 weeks (data included for 8 weeks)
					B. L4-L5: ICBG, 2.5 mL, + calcitonin, 1 IU/kg/day postoperatively until sacrifice	100% (4/4)						
					C. L6-L7: ICBG, 2.5 mL + steel wire fixation of the L6-7 spinal processes	75% (3/4)						
					D. L6-L7: ICBG, 2.5 mL + steel wire fixation of the L6-7 spinal processes + calcitonin, 1 IU/kg/day postoperatively until sacrifice	100% (4/4)						
Liu et al., 2015	Calcitonin	Sprague-Dawley rat (normal and ovariectomized four weeks before intervention)	Posterolateral	L4-5 (including wire fixation of spinous processes)	A. Sham surgery (not ovariectomized); after four weeks, NO L4-L5 fusion, followed by subcutaneous injection of saline vehicle every 2 days until sacrifice (12 weeks)	Fusion rates not directly given. Fusion outcomes via Radiography: Given scale of 0, no bone; 1, poor new bone formation; 2, moderate new bone formation and definite pseudarthrosis; 3, moderate new bone formation and possible pseudarthrosis; 4, good new bone formation and probable fusion; 5, definite fusion Group C average (n=10): 3.00 ± 0.92 Group D average (n=10): 2.15 ± 0.88		Radiography	Manual palpation, dual energy X-ray absorptiometry (bone mineral density), micro-CT, histology (van Gieson), histomorphometry, and immuno-histochemistry (Col I, Col II, aggrecan, MMP-13, ADAMTS-4) Significantly higher Bone Mineral Density observed in Group B v. Group A Bone Mineral Density: • Groups B and	NA	NA	12 weeks
					B. Ovariectomized; after four weeks, NO L4-L5 fusion, followed by subcutaneous injection of saline vehicle every 2 days until sacrifice (12 weeks)							
					C. Sham surgery (not ovariectomized); after four weeks, L4-L5 fusion (ICBG),							

					followed by subcutaneous injection of saline vehicle every 2 days until sacrifice (12 weeks) D. Ovariectomized; after four weeks, L4-L5 fusion (ICBG), followed by subcutaneous injection of saline vehicle every 2 days until sacrifice (12 weeks) E. Ovariectomized; after four weeks, L4-L5 fusion (ICBG), followed by subcutaneous injection of salmon calcitonin (16 IU/kg) every 2 days until sacrifice (12 weeks)	Group E average (n=10): 3.20 ± 0.9 Group C v. D, p = 0.043 Group D v. E, p = 0.013			D (ovariectomized) significantly lower than all others (p<0.05) • Group E (treated with salmon calcitonin) significantly greater than group D (not treated with salmon calcitonin) (p<0.05)			
Rolfing et al., 2012	EPO	New Zealand White rabbit	Posterolateral	L5-6	A. ICBG, 2 g + 0.3 mL saline daily via subcutaneous injection beginning two days preoperatively and continuing for 17 days postoperatively	71% (10 of 14)	-	Manual palpation (no motion)	Micro-CT, Radiographs (AP), histomorphometry, immunohistochemistry (alpha-actin) Bone volume of the fusion mass was significantly greater in Group B compared to Group A (p<0.01). Group B increased vasculature and increased hemoglobin levels (p<0.01)	3/20 (2 perioperative deaths; 1 deep infection)	Prophylactic antibiotics given intravenously (25 mg/kg cerufoxime) For pain relief, 5 ml of lidocaine was injected at the iliac crests. In addition, a fentanyl plaster releasing	2, 4, and 6 weeks (6-week data provided)
					B. ICBG, 2 g + EPO, 250 IU/kg in 0.3 mL saline daily via subcutaneous injection beginning two days preoperatively and continuing for 17 days postoperatively	86% (12 of 14)	0.65, compared to A			3/20 (perioperative deaths)		

											7.5 mg/h for 72 h was attached after surgery.	
Inoue et al., 2017	bFGF	Sprague-Dawley rat	Posterolateral	L4-5	A. Femoral freeze-dried bone allograft (FDBA), 150 mg incubated with phosphate buffered saline B. FDBA, 150 mg incubated with bFGF, 0.58 nmol	Fusion rates not directly given. Radiography and micro-CT: Mean grafted bone volume was significantly higher in B than in A P<0.05		Radiography, micro-CT,	Histology (hematoxylin-eosin and von Kossa staining). increase in the number of chondrocytes and fibroblasts around the newly formed bone in B compared to A.	N/A	NA	2 weeks
Spiro et al., 2000	GDF-5	Baboon	Posterolateral	L4-5	A. ICBG, 5 cm3 B. Healos® (collagen matrix strips), two strips per side, 5 cm^3 per strip C. Healos®, two strips per side, 5 cm^3 per strip + rh-GDF-5, 500 micrograms/cm^3 of Healos® D. Healos®, two strips per side, 5 cm3 per strip + rh-GDF-5, 1500 micrograms/cm^3 of Healos®	22% (2 of 9) 0% (0 of 9) 44% (4 of 9) 11% (1 of 9)	Not reported	Radiography/ CT	Histology Group C showed the most robust bone formation histologically, with well-organized fusion masses consisting of inner zones with a high volume of trabecular bone and a provisional cortex with well-formed osteons. Overall cellularity and osteoblast numbers were increased in Group C compared to autograft (Group A).	Not reported	NA	20 weeks
Spiro et al., 2001	GDF-5	New Zealand White	Posterolateral	L5-6	ICBG, 1 cm^3 per side	33% (1 of 3)	Not reported	Histology analysis (bilateral	Radiography (AP), biomechanical	1/11 (premature death)	NA	12 weeks

		rabbit			Hydroxyapatite-mineralized collagen matrix (Matrix)	0% (0/3)		fusion)	testing In the most efficacious group (80% fusion), most samples demonstrated normal trabecular bone structure with thin outer cortical plates and modest amounts of hematopoietic bone marrow.	1/11 (premature death)		
					Matrix + bone marrow, 4.0 +/- 1.6 mL per animal	0% (0 of 4)				0		
					Healos strips, 1.0x3.0x0.5 cm^3, + rhGDF-5, 0.1 mg/cm^3 of matrix	0% (0/2)				1/11 (premature death)		
					Healos strips, 1.0x3.0x0.5 cm^3, + rhGDF-5, 1.0 mg/cm^3 of matrix	67% (2/3)				2/11 (premature death)		
					Non-crosslinked 1.0x3.0x0.5 cm^3 mineralized collagen strips + rhGDF-5, 0.1 mg/cm^3 of collagen	75% (3 of 4)				0		
					Non-crosslinked 1.0x3.0x0.5 cm^3 mineralized collagen strips + rhGDF-5, 1.0 mg/cm^3 of collagen	80% (4 of 5)				1/11 (premature death)		
					Collagen fiber slurry + rhGDF-5, 0.1 mg/cm^3 of collagen; then molded into1.0x3.0x0.5 cm^3 strips	25% (1/4)				0		
					Collagen fiber slurry + rhGDF-5, 1.0 mg/cm^3 of collagen; then molded into1.0x3.0x0.5 cm^3 strips	0% (0/3)				1/11 (premature death)		
Jahng et al., 2004	GDF-5	Sheep	Posterolateral (endoscopic) (screws and plate)	L4-5	In each animal, ICBG was placed on one side of spine and Healos + rh-GDF-5 was placed on the	ICBG, 5 cm^3	0% (0 of 4) at 2 months; 100% (4 of 4) at 4 months; 100% (4 of 4) at 6 months)	Not reported	Manual palpation (no unilateral motion)	Radiography (PA), CT, and Histology (osteochrome bone stain), histomorphometry At 6 months, the	0/12 sheep	NA	2, 4, 6 months

					other	GDF-5, 0.5 mg/cm3 Healos®, using two strips of 5cm x 2cm x 0.5 cm Healos®	25% (1/4) at 2 months; 100% (4/4) at 4 months; 100% (4/4) at 6 months			autograft and Healos/rh-GDF-5 groups were virtually indistinguishable in histological appearance.			
Magit et al., 2006	GDF-5	New Zealand White rabbit	Posterolateral	L5-6	A. ICBG		38% (5 of 13)	0.013 compared to B	Manual palpation	Radiography, histology (toluidine blue) Groups B-E showed a dose-dependent progression of bone maturation histologically. Unique to Group E, trabecular bone matrix formation was not found within the fusion mass; rather, the region was filled primarily with hematopoietic adipose cells.	2/67 (perioperative death, anesthetic related)	Preoperative antibiotics (enrofloxacin 10 mg/kg) Once recovered, the rabbits received Buprenex (0.04 mg/kg) for perioperative analgesia. In addition, Enrofloxacin (10 mg/kg every day) was given for 5 days and Buprenex (0.04 mg/kg twice a day) for 2 days.	8 weeks
					B. Healos®, 1.0x3.0x0.5 cm		0% (0 of 13)	-					
					C. rhGDF-5, 0.5 mg/cc Healos®		100% (13 of 13)	<0.01 compared to A or B					
					D. rhGDF-5, 1 mg/cc Healos®		100% (13 of 13)						
					E. rhGDF-5, 1.5 mg/cc Healos®		100% (13 of 13)						

Kandziora et al., 2002	IGF-1/TGF-beta	Sheep	Anterior, interbody	C3-4	A. Titanium cage (Cage)	0% (0/8)	N/A	CT analysis (complete bony fusion)	Radiography (lateral, PA, flexion-extension); biomechanical testing; histology, histomorphometry, and fluorochrome analysis (safranin-O/Lightgreen, Safranin-O/v. Kossa, Astrablue, and Masson-Goldner) Bone mineral content (BMC) and bony callus volume (BCV) were similar between Groups B, C and D; Group A had lower BMC and BCV than Groups B-D. Bone mineral density of Group 4 was significantly higher than in any other group ($p<0.05$). No significant differences found in range of motion, neutral zone, or elastic zone between Groups C and D. Groups C and D showed extensive callus formation and bony islands between	0	The sheep received two doses of 0.5 g metamizol-natrium per day for 5 days intramuscularly	12 weeks
					B. Cage + ICBG	13% (1/8)						
					C. Cage + poly-(D,L-lactide) (PDLLA) carrier including rh-BMP-2, 5% w/w (~150 microgram)	13% (1/8)						
					D. Cage + PDLLA carrier including rh-IGF-1, 5% w/w, and rh-TGF-beta-1, 1% w/w (~150 microgram IGF-1 and 30 microgram TGF-beta-1).	13% (1/8)						

									endplates, accompanied by capillary ingrowth and resorptive lacunae, without major differences between the two groups. No differences were found in the bone volume/total volume ratio between Groups B-D.			
Kandziora et al., 2002	IGF-1/TGF-beta	Sheep	Anterior, interbody (left anterolateral)	C3-4	A. ICBG (average of 8 mm x 14 mm x 11 mm) B. Titanium cage C. Cage + PDLLA carrier D. Cage + PDLLA carrier including rh-IGF-1, 5% w/w, and rh-TGF-beta-1, 1% w/w (~150 microgram IGF-1 and 30 microgram TGF-beta-1)	0% (0 of 8) 0% (0 of 8) 0% (0 of 8) 12.5% (1 of 8)	N/A	Histology (complete bony fusion)	Radiography (lateral, PA, and flexion-extension), CT, Biomechanical testing, histomorphometry and fluorochrome analysis No significant differences between Groups A-C were found regarding bone mineral content or bony callus volume. Bone mineral density (BMD) was significantly greater in Groups C and D compared to Groups A and B ($p<0.05$). There was no significant	2/34 (1 died perioperatively due to anesthesiologic complications; another was euthanized during week 6 because of a sore mouth); both animals were replaced in the study.	2 g of amoxicillin intravenously (intravenous Augmentan) before surgery. Postoperatively, the sheep received two doses of metamizol-natrium 0.5 g per day intramuscularly for 5 days.	12 weeks

									difference in BMD between Groups C and D. Bony callus volume of Group 4 was significantly higher than in any other group ($p<0.05$).			
Kandziora et al., 2003	IGF-1/TGF-beta	Sheep	Anterolateral, interbody (left anterolateral approach)	C3-4	A. Titanium cage coated with PDLLA carrier (Cage) B. Cage + IGF-1 (2.5% w/w = 75 micrograms) + TGF-beta-1 (0.5% w/w = 15 micrograms) C. Cage + IGF-1 (5.0% w/w = 150 micrograms) + TGF-beta-1 (1% w/w = 30 micrograms) D. Cage + IGF-1 (10% w/w = 300 micrograms), TGF-beta-1 (2.0% w/w = 60 micrograms)	Fusion rates not directly given. CT & Histomorphometry: Groups C & D demonstrated significantly higher bony callus volumes via CT and an advanced interbody bone matrix formation (bone volume/total volume ratio) via histomorphometrical analysis compared to Groups A and B ($p<0.05$).		CT and Histomorphometry	Radiography (PA and lateral); biomechanical testing; histomorphological and fluorochrome analysis (safranin-O/lightgreen, safranin-O/van Kossa, Astrablue, and Masson-Goldner) Groups C and D showed extensive callus formation, accompanied by capillary ingrowth and small resorptive lacunae, without major differences between the groups.	0/32	Postoperatively, the sheep received two doses of 0.5 g metamizol-natrium per day for 5 days intramuscularly	12 weeks
Gu et al., 2016	IGF-1/TGF-beta	Goat	Anterior, interbody (right anterolateral approach)	C3-4	A. ICBG B. Hat-shaped titanium cage (Cage), 14 mm width, 12 mm depth, 8 mm anterior height C. Cage coated with hydroxyapatite D. Cage coated with hydroxyapatite + IGF-1 (5% w/w) and TGF-beta-1 (1% w/w)	0% (0/8) 25% (2/8) 38% (3/8) 63% (5/8)	N/A	Histology (complete bony fusion)	Radiography (lateral and AP), biomechanical testing, histology (Masson-Goldner), histomorphology The stiffness of Group D in flexion, extension, and lateral	2/34 (due to anesthesia-related complications during surgery)	All goats received penicillin of 3.2 million-units intramuscularly before surgery Post-	12 weeks

									bending was significantly greater than that of any other group ($p<0.05$) In Group D, a slightly more advanced bone matrix formation was shown histomor-phologically compared to groups 2 and 3.		operativel y, all goats received two 800 thousand-unit doses of penicillin intramusc ular injections per day for 5 days.	
Koerner et al., 2013	Insulin	Sprague-Dawley rat	Posterolateral	L4-5	A. Sham implant (100% microrecrystalized palmitic acid; 0.3 g) + ICBG (0.3 g) B. Linplant (95% micro-recrystallized palmitic acid and 5% bovine insulin; 4U/kg/day insulin release for a minimum of 40 days; 0.3 g) + ICBG, 0.3 g	11% (1 of 9) 60% (6 of 10)	<0.05	Manual palpation (no motion)	Growth factor analysis (ELISA), Radiography (PA) and CT At Day 4, there was a significant increase in IGF-I in Group B compared with Group A ($p=.001$). There was no significant increase in TGF beta-1, PDGF-AB or VEGF. Group B had a greater bone volume by micro-CT compared to Group A ($p<0.001$).	1/20 (periopera tive death) 0/20	Postoperat ively, the surgical site was treated with an antibiotic ointment, and the rats were given a dose of enrofloxac in antibiotic (10 mg/kg).	8 weeks
Lee et al., 2009	NELL-1	Athymic rat	Posterolateral	L4-5	A. PBS lyophilized onto apatite-coated alginate/chitosan particles, 10 mg; resuspended in PBS and mixed with 100 mg of demineralized bone powder and	0% (0 of 5)	NA	Manual palpation (no motion)	Micro-CT, histology (H&E) | Micro-CT-based morphometric analysis demonstrated significantly	NA	Postoperat ively, the rats were given analgesics (0.05 mg/kg buprenorp	4 weeks

					220 mg hyaluronan to form a moldable putty.				higher bone volume (bone volume/total volume) between the transverse processes in Group B compared to Group A ($p = 0.007$). Histologically, cortical -like bone bridges connecting the transverse processes were observed in Group B; the appearance was suggestive of endochondral bone formation, without a significant inflammatory reaction in the graft area.		hine) for two days and antibiotics (trimethoprim/sulfamethoxazole) for seven days.	
					B. rh-NELL-1 (10 micrograms) lyophilized onto apatite-coated alginate/chitosan particles, 10 mg; resuspended in PBS and mixed with 100 mg of demineralized bone powder and 220 mg	60% (3 of 5)						
Li et al., 2010	NELL-1	Athymic rat	Posterolateral	L4-5	A. PBS lyophilized onto β-tricalcium phosphate (β-TCP) microparticles, 50 mg + DBX (demineralized bone matrix mixed with sodium hyaluronate to form a moldable putty), 0.3 mL	25% (2 of 8)	NA	Manual palpation (no motion)	Radiography (PA), micro-CT, Histology (H&E and Masson tri-chrome), immuno-histochemistry (osteocalcin) Bone volume in each Nell-1-treated group was significantly greater than that in the Nell-free control group ($p<0.001$). No significant	NA	Postoperatively, about 0.05 mg/kg buprenorphine was given twice daily for 2 days, and 48mg/mL trimethoprim/sulfamethoxazole antibiotic was given for 10	4 weeks
					B. NELL-1, 2.5 micrograms, lyophilized onto β-TCP microparticles, 50 mg + DBX, 0.3 mL	75% (6 of 8)						
					C. NELL-1, 5 micrograms, lyophilized onto β-	88% (7 of 8)						

					TCP microparticles, 50 mg + DBX, 0.3 mL				difference in bone volume was observed between the two Nell-1-treated groups. Histologically, Nell-1-treated groups (Groups B and C) contained more bone matrix and bone remodeling compared to Group A; Groups B and C also had greater staining for osteocalcin compared to Group A.		days.	
Siu et al., 2011	NELL-1	Ramboui llet×Colu mbian sheep	Ventrolateral retroperitonea l, through the oblique abdominal muscles to the plane ventral to the transverse processes; interbody	L3-4, L5-6	A. Cage (9-mm parallel radiolucent, Vertebral Spacer-CR 889.915; Synthes, Monument, CO) + DBM, 0.4 mL	50% (4/8)		micro-CT	Radiography, micro-CT, histology (H&E, Masson's Trichrome, von Kossa) Bone volume/total volume **and** bone mineral density were greater in Group D compared to Group A ($p<0.01$) (no differences were observed between Group C and Group A). Similarly, bone volume/total volume **and** bone mineral density were greater in	NA	Sheep were perioperat ively premedica ted with midazola m and ketamine for pain managem ent and cefazolin as an antibiotic	3 months
					B. Cage + heat-inactivated DBM (inDBM), 0.4 mL	50% (2/4)						4 months
					C. Cage + DBM, 0.4mL + NELL-1, 0.3 mg/mL	87.5% (7/8)	0.002, DBM/Ne ll-1-treated groups compare d to DBM/Ne ll-1-free groups (chi-square)					3 months
					D. Cage + DBM, 0.4mL + NELL-1, 0.6 mg/mL	100% (8/8)						3 months
					E. Cage + inDBM, 0.4mL + NELL-1, 0.3 mg/mL	100% (4/4)	0.01, inDBM/ Nell-1-treated					4 months
					F. Cage + inDBM,	100%						4 months

					0.4mL + NELL-1, 0.6 mg/mL	(4/4)	groups compared to inDBM/ Nell-1-free groups (chi-square)		Group E and F compared to Group B ($p<0.03$). No differences between Groups A and B were observed regarding bone volume/total volume or bone mineral density. Histologically, the fusion masses of Group D-F, with complete bone fusion, resembled adjacent native bone.			
Yuan et al., 2013	NELL-1	Athymic rat	Posterolateral	L4-5	A. DBX (type of DBM), 0.3 mL + PBS	20% (1/5)	NA	Manual palpation (no motion)	Radiography, micro-CT, histology (H&E and Masson trichrome), immuno-histochemistry (osteocalcin), alkaline phosphatase (ALP) expression assay *in vitro*, Runx2 expression assay *in vitro* Group C showed greater fractional bone volume (BV/TV) compared to any other group ($p<0.01$). Group C showed	NA	NA	4 weeks
					B. DBX, 0.3 mL + NELL-1, 10 micrograms	100% (4/4)						
					C. DBX, 0.3 mL + NELL-1, 50 micrograms	100% (5/5)						
					D. ACS (acellular	0% (0/2)						

					collagen sponge, 1.25 x 1.25 cm strip per fusion bed) + PBS				greater fractional bone volume to all other groups besides Group F ($p<0.01$). Histologically, Nell-1-treated groups (Groups B and C) showed increased vascularization and endochondral ossification, whereas Group E showed lipid rich bone formation. Separately, alkaline phosphatase staining and Runx2 expression were significantly increased with Nell-1 (800 ng/mL) and BMP-2 (150 ng/mL) in *in vitro* assays.			
					E. ACS + BMP-2 (90 microgram)	100% (5/5)						
					F. ICBG (300 microliter)	0% (0/5)						
James et al., 2017	NELL-1	Rhesus macaque	Ventrolateral retroperitoneal approach to L3/ L4 and L5/L6 was made through the oblique abdominal muscles to the plane ventral to the L3–L6 transverse processes; 3-hole titanium	L3-4, L5-6	A. Cage (Vertebral Spacer-CR; Synthes) + DBX (morselized Rhesus macaque cortical-cancellous demineralized bone chips with sodium hyaluronate), 0.4 mL + saline-loaded apatite-coated β-tricalcium phosphate (aTCP) microparticles, 25 mg	25% (1 of 4)	NA	CT (50% or greater area of contiguous bridging bone within implant)	Radiography, micro-CT, finite element analysis, histology, histomorphometry, immuno-histochemistry (CD31, CD45, Sca-1) Significant increase in bone mineral density **and** increase in fractional bone	NA	NA	12 weeks
					B. Cage + DBX, 0.4 mL	25% (1 of						

			plate with 2 screws.		+ rhNELL-1-loaded aTCP microparticles, 1.0 mg/ml	4)			volume (bone volume/total volume) **and** reduction in trabecular spacing in Group C compared to Groups A and B ($p<0.01$). Significant increase in trabecular number in Group C compared to Groups A and B ($p<0.05$). Via finite element analysis, Group C showed reduced predicted stress among cubic volumes of interest compared to Groups A and B ($p<0.05$). Via von Kossa histomorphometry quantification, significantly increased percentage of bone area per field in Group C compared to Groups A and B ($p<0.01$); significant increase in Group B compared to Group A. Immunofluorescence staining			
					C. Cage + DBX, 0.4 mL + rhNELL-1-loaded aTCP microparticles, 1.7 mg/ml	100% (4 of 4)						

									analysis showed significant increase in Sca-1+CD31–CD45– stromal cells in Group C compared to Groups A and B ($p<0.01$); also increase in Group B compared to Group A ($p<0.01$).			
Klineberg et al., 2014	Noggin	New Zealand White rabbit	Posterolateral	L5-6	A. ICBG, 2mL + scrambled noggin siRNA injected into bilateral paraspinal muscles between L5-L6, 2 nMol/100mL	-	NA (fusion not significantly enhanced compared to established ICBG controls from earlier work from same group [which is a "reliable 67%"])	Manual palpation (no motion)	Radiography (PA), CT, histology (H&E), PCR (BMP-2, -7, noggin), Western blot (BMP-2, BMP-7, Noggin) Noggin protein successfully knocked down *in vivo* for the initial 7 days and returned to detectable levels by 4 weeks and to normal levels by 6 weeks	1/26 (perioperative death, anesthesia-related)	NA	6 weeks
					B. ICBG, 2mL + scrambled noggin siRNA injected into paraspinal muscles on one side and functional noggin siRNA injected on the other side, 2 nMol/100microliter	-						
					C. ICBG, 2mL + functional noggin siRNA injected into bilateral paraspinal muscles, 2 nMol/100mL	50% (6/12)						
Sherman et al., 2010	P-15	Sheep	Anterior-lateral (Retroperitoneal lateral); interbody	L3-L4, L4-L5 (two-level)	A. Polyetheretherketone (PEEK) interbody ring (interbody), 8 mm thick with a total internal volume of 0.4 cm^3 + ICBG, 0.4 mL	83% (5/6) inside PEEK cage; 83% (5/6) outside PEEK cage	0.30 comparing inside PEEK cage; 0.37 comparing outside PEEK cage | no statistically significant	Micro-CT	Histology, histomorphometry The histomorphometric data demonstrated no statistically significant group differences between the two graft	0/12	NA	6 months
					B. Interbody + ABM/P-15 (P-15 = 15-amino-acid residue with a sequence identical to cell-binding domain of Type I collagen	100% (6/6) inside PEEK cage; 5/6 outside						

					alpha-1; ABM = anorganic bovine-derived hydroxyapatite matrix).	PEEK cage	difference found between Groups A and B		materials "ABM/P-15 was as successful as autogenous bone graft"			
Smucker et al., 2008	Peptide B2A	New Zealand White rabbit	Posterolateral	L4-5	A. ICBG, 3 mL	25% (2 of 8)		Manual palpation (bilateral no motion)	Radiography, micro-CT, histology (H&E) Histologically, there was no detection of adverse inflammatory reaction to the B2A/CG regardless of coating concentration (Groups C-E). The newly formed bone in Groups C-E appeared morphologically normally without hyperplasia. Additionally, Group C tended to have more histologic evidence of new bone development across the intertransverse process space compared to Groups A and B.	2/10 animals ("complications arising from surgery")	NA	6 weeks
					B. 1:1 ICBG:Ceramic Granules (20% hydroxyapatite and 80% tricalcium phosphate; CG), 3 mL	22% (2 of 9)						
					C. 1:1 ICBG:CG (coated with 50 µg B2A/mL), 3 mL total	56% (5 of 9)				1/10 animals ("complications arising from surgery")		
					D. 1:1 ICBG:CG (coated with 100 µg B2A/mL), 3 mL total	78% (7 of 9)	0.029 compared to A; 0.017 compared to B			1/10 animals ("complications arising from surgery")		
					E. 1:1 ICBG:CG (coated with 300 µg B2A/mL), 3 mL total	40% (4 of 10)						
Cunningham et al., 2009	Peptide B2A	Crossbred Suffolk sheep	Anterolateral (retroperitoneal) (screw and rod; PEEK cage)	L2-3, L4-5	A. PEEK cage (interbody), 11 mm x 11 mm x 24 mm with 1:1 ICBG:Ceramic Granules (20% hydroxyapatite, 80%	63% (5 of 8)	No significant difference between	CT ("contiguous bone from endplate to endplate")	CT, Histology, histomorphometry, biomechanical testing Histologically, all	2/20 animals died perioperatively (secondar	Pre-operatively, 0.1 mg/kg butorphanol and 1 g	4 months

					tricalcium phosphate; CG), ~4 mL total		any of the groups		concentrations of B2A (Groups B-E) were characterized as undergoing a normal healing process, without evidence of an inflammatory response or any other significant histopathological change. Group A similarly had good to excellent osseointegration. In biomechanical testing, no differences were observed between any of the groups.	y to pulmonary complications caused by the surgical procedure)	cefazolin sodium Post-operatively, Buprenorphine (0.01–0.1 mg/kg twice a day, intramuscularly) and Ketofen (2.2 mg/kg once a day, subcutaneously) for at least 3 days. All sheep received Cefazolin (1 g twice a day, intramuscularly for 3 days) and then a long-acting penicillin (1 ml = 150,000 U penicillin G-benzathine and 150,000 U penicillin G-procaine)	
					B. Interbody with 1:1 ICBG:CG coated with 50 µg B2A/mL; ~4 mL total	88% (7 of 8)						
					C. Interbody with 1:1 ICBG:CG coated with 100 µg B2A/mL; ~4 mL total	88% (7 of 8)						
					D. Interbody with 1:1 ICBG:CG coated with 300 µg B2A/mL; ~4 mL total	88% (7 of 8)						
					E. Interbody with 1:1 ICBG:CG coated with 600 µg B2A/mL; ~4 mL total	75% (6 of 8)						

											for a period of 7 days (4 ml every other day).	
Sintuu et al., 2011	SPP24	Male Lewis rat	Posterolateral	L3-4	A. Collagen sponge, 10 mm x 5 mm x 5 mm	0%	Truncated spp18 (all concentrations grouped together) and full-length spp24 (all concentrations grouped together) were shown to significantly inhibit rh-BMP-2-induced bone formation ($p<0.001$), as assessed via manual palpation. Full-length spp24 showed a greater inhibitory impact compared to the truncated	Manual palpation	Radiography (AP and lateral), micro-CT, histology (H&E) "when rhBMP-2 was implanted in combination with TR-spp18 or FL-spp24, only single-level fusion or no fusion was observed." Samples that received either absorbable collagen sponge alone or 1 microgram of rhBMP-2 showed little new bone growth between the transverse processes. The surface of the transverse processes of L4 and L5 receiving 1 microgram of rhBMP-2 was irregular and exhibited features of immature, woven bone. All animals implanted with 10 micrograms of rhBMP-2		NA	8 weeks
					B. Collagen sponge, 10 mm x 5 mm x 5 mm + rhBMP-2, 10 micrograms	100%						
					C. Collagen sponge, 10 mm x 5 mm x 5 mm + rhBMP-2, 1 microgram + SPP24, 0.1 mg	0%						
					D. Collagen sponge + rhBMP-2, 1 microgram + SPP24, 0.5 mg	0%						
					E. Collagen sponge + rhBMP-2, 1 microgram + SPP24, 1 mg	0%						
					F. Collagen sponge + rhBMP-2, 1 microgram + SPP24, 2.5 mg	0%						
					G. Collagen sponge + rhBMP-2, 1 microgram + SPP18 (truncated form), 0.1 mg	0%						
					H. Collagen sponge + rhBMP-2, 1 microgram + SPP18, 0.5 mg	0%				1 (of unknown) (perioperative death); supplemental table online cannot be accessed		
					I. Collagen sponge + rhBMP-2, 1 microgram + SPP18,	0%						

					1 mg		spp18 form		contained bone masses so large that the interface between the transverse processes was indistinguishable. The new bone has features characteristic of endochondral ossification. Specimens receiving 1 microgram of rhBMP-2 and TR-spp18 did not exhibit any new bone formation. Specimens receiving 10 micrograms of rhBMP-2 and TR-spp18 showed some areas of normal remodeling and a smaller area of new bone formation compared to rhBMP-2 implantation alone. Specimens receiving either 1 or 10 micrograms of rhBMP-2 and FL-spp24 exhibited healthy, viable bone, suggesting that FL-spp24 is not toxic to existing bone and only inhibits new bone			
					J. Collagen sponge + rhBMP-2, 1 microgram + SPP18, 2.5 mg	0%						
					K. Collagen sponge + rhBMP-2, 10 micrograms + SPP24, 0.1 mg	0%						
					L. Collagen sponge + rhBMP-2, 10 micrograms + SPP24, 0.5 mg	0%						
					M. Collagen sponge + rhBMP-2, 10 micrograms + SPP24, 1 mg	0%						
					N. Collagen sponge + rhBMP-2, 10 micrograms + SPP24, 2.5 mg	0%						
					O. Collagen sponge + rhBMP-2, 10 micrograms + SPP18, 0.1 mg	0%						
					P. Collagen sponge + rhBMP-2, 10 micrograms + SPP18, 0.5 mg	0%						
					Q. Collagen sponge + rhBMP-2, 10 micrograms + SPP18, 1 mg	0%						
					R. Collagen sponge + rhBMP-2, 10 micrograms + SPP18, 2.5 mg	0%						

									formation mediated by rhBMP-2.			