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EFFECT of POLYDEOXYRIBONUCLEOTIDE and POLYNUCLEOTIDE COMBINED with PLATELET RICH PLASMA on HEALING and FATTY DEGENERATION of ROTATOR CUFF in RAT MODEL

Jung-Taek Hwang, MD, PhD

Department Orthopedic Surgery, Chuncheon Sacred Heart Hospital, Hallym University Medical College, KOREA

Faculty Disclosure Information

- Nothing to disclosure

INTRODUCTION

For chronic rotator cuff tear, the rate of healing failure after surgical repair and fatty degeneration is considerably high (Park et al. Arthroscopy. 2013., Goutallier et al. JSES. 2003.).

Polydeoxyribonucleotide (PDRN) has been used as a tissue regeneration activator (Altavilla et al. Surgery. 2011., Galeano et al. Wound Repair Regen. 2008.).

Platelet rich plasma promoted proliferation of myoblast cells, and suppressing fatty degeneration change in rat torn rotator cuff muscles. (Takase et al. J Orthop Res. 2017)

polydeoxyribonucleotide?

What is PDRN

Low molecular weight deoxyribonucleic acid

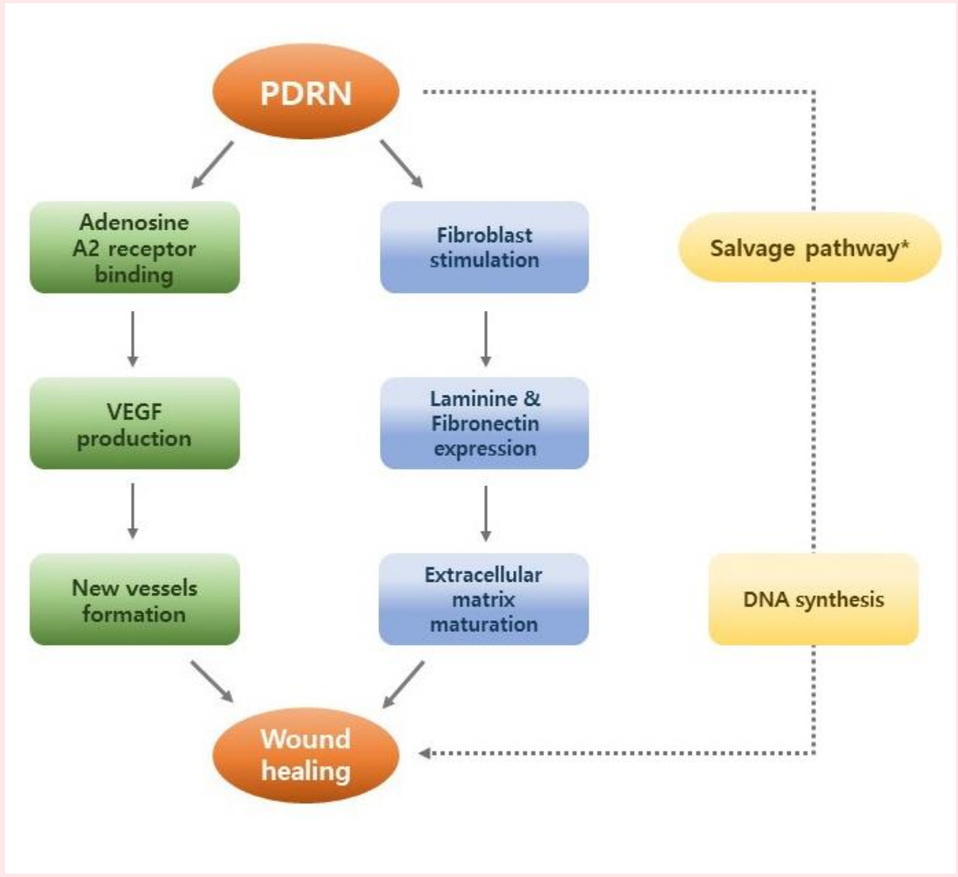
(DNA) fragment (mean molecular weight 350KD)

- thermoduric
- bio-revitalizing agent
- act as tissue regeneration activator

polynucleotide?

What is PN

- a little higher molecular weight nucleotide fragment compared with PDRN
- gel-type
- later onset, longer duration



Mechanism of Polydeoxyribonucleotide (PDRN)

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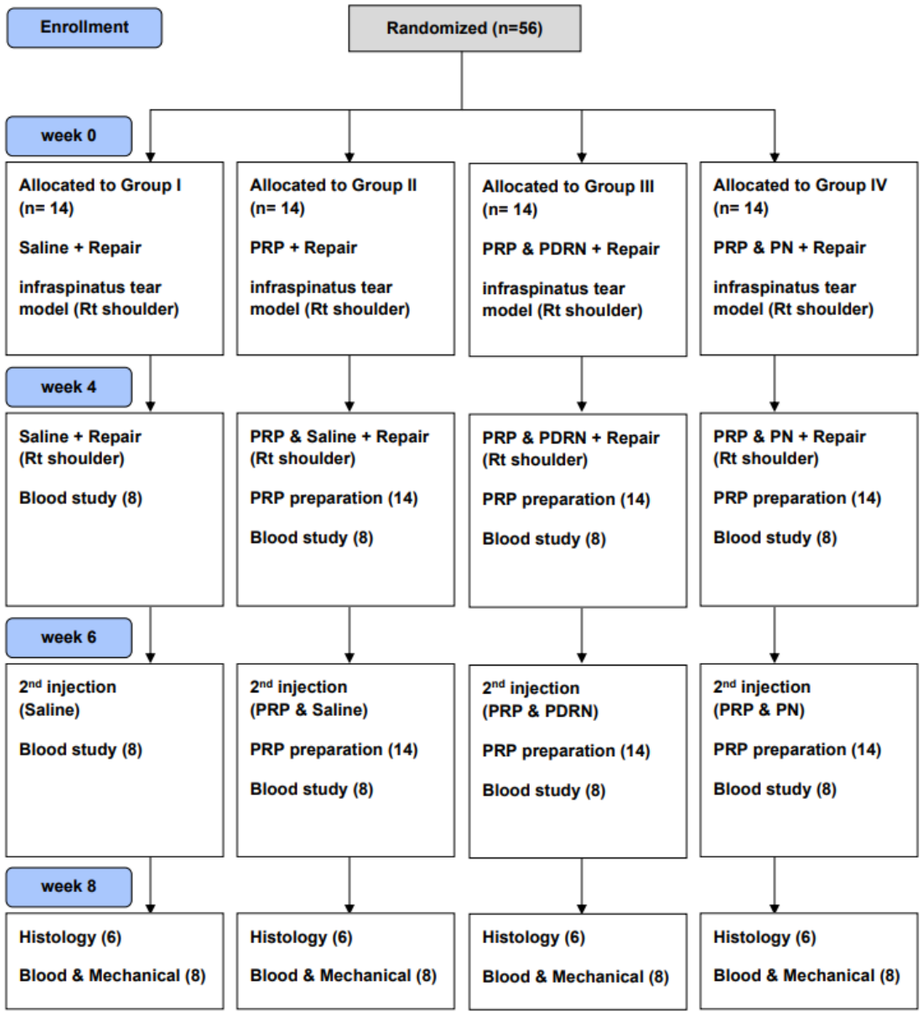
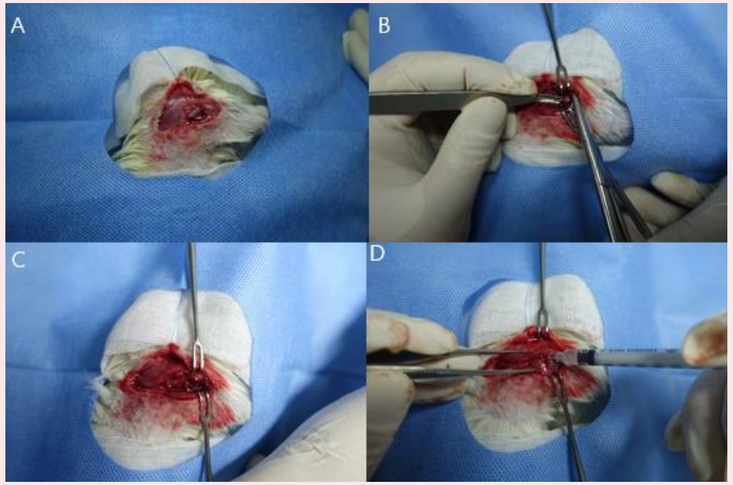
PURPOSE

To verify the effects of polydeoxyribonucleotide (PDRN) and polynucleotide (PN) combined with platelet rich plasma (PRP) on tendon healing and reversal of fatty degeneration in a chronic rotator cuff tear model using the infraspinatus of rat.

METHODS





Week 4 surgery. A. Torn cuff wrapped by penrose hose , B. Hole making using Retractor of Rat Humeral Head (KR Patent 10-2195860) and 22-gauge needle, C. Repaired cuff, D. Injection

PRP : platelet rich plasma

PDRN : polydeoxyribonucleotide

PN : polynucleotide

Blood test : vascular endothelial growth factor, fibroblast growth factor,

insulin like growth factor

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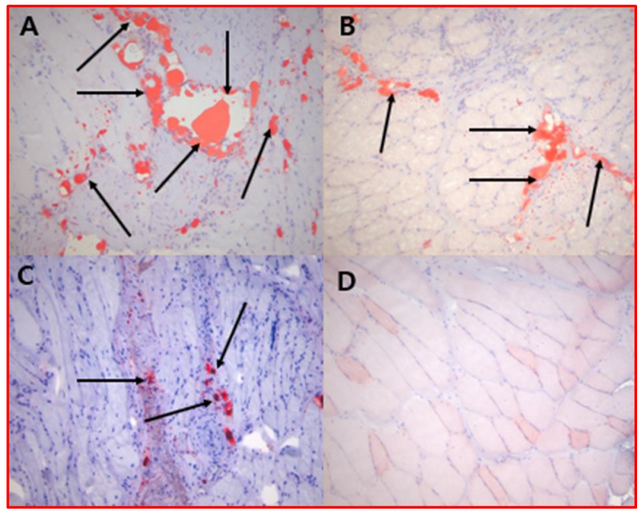
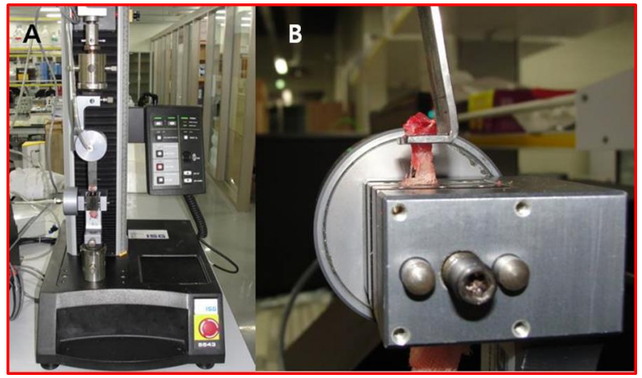


Oil red O stain at musculotendious region: A. Group 1, B. Group 2, C. Group 3, D. Group 4, Arrow indicates adipose cell. x 200.



A. The materials testing machine. Instron 5543, pneumatic grip, and Rat Humeral Head Grip (KR Design Registration 30-0854878). B. Tensile load is being applied to infraspinatus of rat.

Histologic evaluation

Fatty degeneration - musculotendinous (M-T)

H&E stain

Oil Red O stain

Immunohistochemisty

CD68 : macrophage marker indicating tissue degeneration

CD168 :macrophage marker indicating tissue regeneration

CD68/CD168 ratio

Tendon healing - tendon to bone (T-B)

H&E stain

Masson's Trichrome stain

Mechanical evaluation

Instron material testing machine

parameters -peak load to failure (N)

tear pattern (insertional Vs midsubstance)

Blood evaluation

VEGF(vascular endothelial growth factor)

FGF (fibroblast growth factor)

IGF (insulin like growth factor)

RESULTS

	G1 (n=7)	G2 (n=7)	G3(n=7)	G4(n=7)
Load to failure-operated side (N)	18.48 ±4.78	21.64 ±12.17	22.68 ±9.12	24.72 ±6.58
Load to failure-control side (N)	28.89 ± 3.67	33.67 ± 5.49	27.69 ±1.85	31.94 ± 6.88
P value	.001	.043	.200	.068
Tear pattern Insertional : Midsubstance – operated side (n)	6 : 1	5 : 2	5 : 2	4 : 3
Tear pattern Insertional : Midsubstance – control side (n)	0 : 7	0 : 7	0 : 7	0 : 7
P value	.002	.007	.007	.023
Elastic modulus-operated side (MPa)	8.26 ±3.2	10.03 ±3.14	13.1 ±9.42	12.18 ±10.01
Elastic modulus-control side (MPa)	61.98 ± 26.78	61.21 ± 24.19	67.04 ±29	45.4 ± 7.4
P value	.002	.002	.003	.002

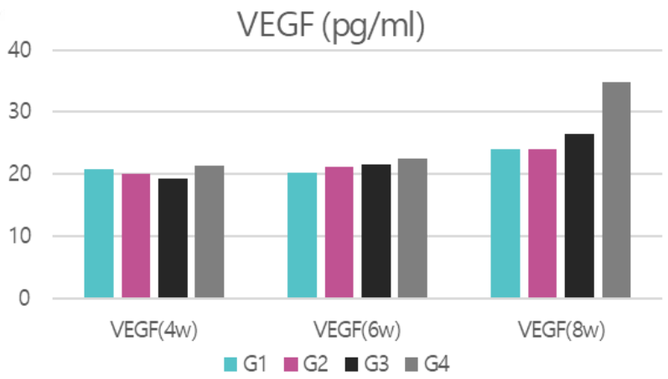
Mechanical testing. G: group, G1: saline+repair, G2: PRP+repair, G3: PRP+PDRN+ repair, G4: PRP+PN+repair, p<.05

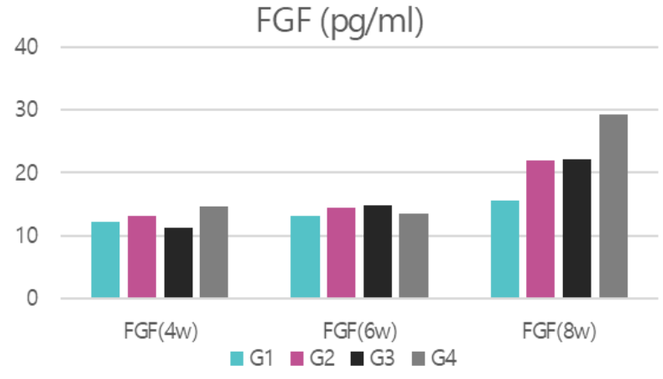
P value		Load to failure (N)		Tear pattern		Elastic modulus (MPa)	
Group	G1 Vs G2	1.000	.598	.530	.717	.277	.773
	G1 Vs G3	1.000		.530		.482	
	G1 Vs G4	1.000		.254		.848	
	G2 Vs G3	1.000		1.000		.949	
	G2 Vs G4	1.000		.591		.655	
	G3 Vs G4	1.000		.591		.565	

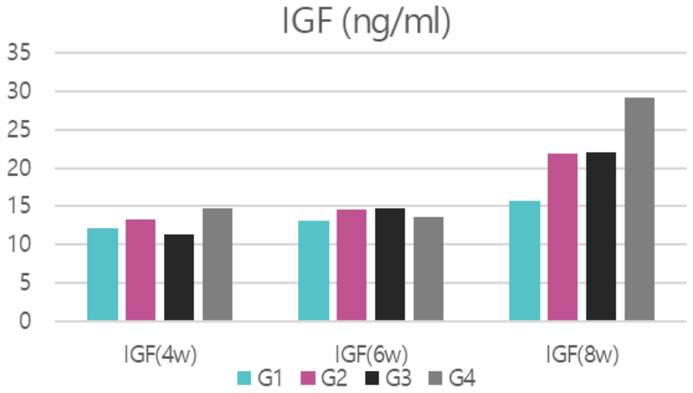
Comparison of outcome in mechanical testing between treated right sides. G: group, G1: saline+repair, G2: PRP+repair, G3: PRP+PDRN+ repair, G4: PRP+PN+repair, p<.05

	MT-H&E	MT-ORO	MT-CD68	MT-CD168	MT-CD68/CD168	TB-V	TB-C	TB-Co	TB-Pa	CSA
Sham Vs G1	.011	.011	.014	.013		.013	.008	.013	.013	.101
Sham Vs G2	.040	.011	.014	.014		.011	.013	.013	.011	.382
Sham Vs G3	.040	.011	.014	.011		.011	.013	.040	.040	.424
Sham Vs G4	.317	.011	.013	.013		.008	.011	.040	.127	.526
One-Way ANOVA or Kruskall Wallis	.032	.032	.009	.161	.021	.475	.210	.114	.100	.454
G1 Vs G2	.040	.040	1.000	1.000	.043	.495	.127	1.000	.495	1.000
G1 Vs G3	.040	.040	.271	.575	.059	.495	.127	.096	.096	1.000
G1 Vs G4	.022	.022	.023	.231	.021	.127	.040	.096	.061	.844
G2 Vs G3	1.000	1.000	.302	1.000	.386	1.000	1.000	.096	.186	1.000
G2 Vs G4	.186	.186	.026	1.000	.021	.317	.495	.096	.096	1.000
G3 Vs G4	.186	.186	1.000	1.000	.386	.317	.495	1.000	.495	1.000

Comparison of outcome in histologic results. Sham: non-operated Lt shoulder of G1, G: group, G1: saline+repair, G2: PRP+repair, G3: PRP+PDRN+ repair, G4: PRP+PN+repair, MT: musculotendinous, TB: tendon to bone, Co: continuity of collagen fiber, Pa: parallelism of collagen fiber, P<.05





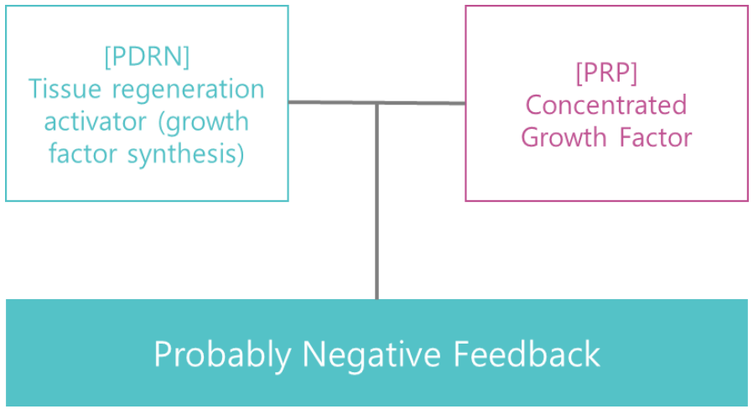


Blood testing. G: group, G1: saline+repair, G2: PRP+repair, G3: PRP+PDRN+ repair, G4: PRP+PN+repair, VEGF: vascular endothelial growth factor, FGF: fibroblast growth factor, IGF: insulin like growth factor. 4w: 2nd operation (repair with 1st injection), 6w: 2nd injection, 8w: sacrifice.

Comparison of outcome in blood tests among the groups. G: group, G1: saline+repair, G2: PRP+repair, G3: PRP+PDRN+ repair, G4: PRP+PN+repair, VEGF: vascular endothelial growth factor, FGF: fibroblast growth factor, IGF: insulin like growth factor. 4w: 2nd operation (repair with 1st injection), 6w: 2nd injection, 8w: sacrifice. P<.05.

One-way ANOVA or Kruskal-Wallis Test	Group Vs Group	P-value (Bonferroni Post Hoc tests or Mann-Whitney test)
VEGF(8w) (P=.007)	I Vs II	0.749
	I Vs III	0.110
	I Vs IV	0.006
	II Vs III	0.142
	III Vs IV	0.025
FGF(8w) (P=.003)	I Vs II	0.030
	I Vs III	0.035
	I Vs IV	0.003
	II Vs III	0.949
	III Vs IV	0.025

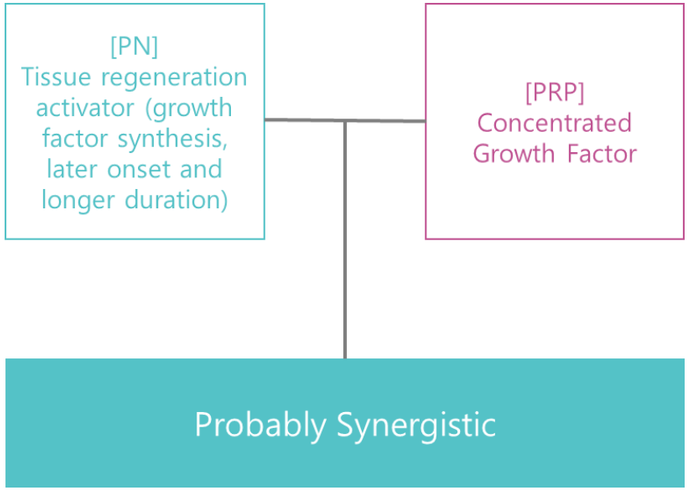
DISCUSSION



In the present study, PDRN and PN combined with PRP showed a property of tendon healing and reversal of fatty degeneration of chronic rotator cuff tear in rat model associated with growth factors.

However, there could be a negative feedback between PRP and PDRN which might not show a synergistic effect because of their mechanism associated with growth factors.

On the other hand, there could be a synergistic effect between PRP and PN because of different timing of growth factors' surges.



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CONCLUSION

PDRN and PN combined with PRP might enhance rotator cuff healing and decrease fatty degeneration.

However, PN could be more suitable for combined therapy with PRP than PDRN to escape a negative feedback due to simultaneous surges of growth factors.

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