ISAKOS CONGRESS 2023

Boston
Massachusetts
June 18 – June 21

Welcome

isakos.com/2023 • #ISAKOS2023

ISAKOS CONGRESS 2023

Boston
Massachusetts
June 18–June 21

Title: **Effect of polydeoxyribonucleotide and polynucleotide on healing and fatty degeneration of rotator cuff in hypercholesterolemic rat model**

Author/s: Jung-Taek Hwang, MD, PhD

Department of Orthopedic Surgery,

Chuncheon Sacred Heart Hospital,

Hallym University Medical College, Chuncheon, Gangwon, SOUTH KOREA

ISAKOS CONGRESS 2023

Boston
Massachusetts
June 18–June 21

Disclosures:

I (and my co-authors) have nothing to disclose.

BACKGROUND

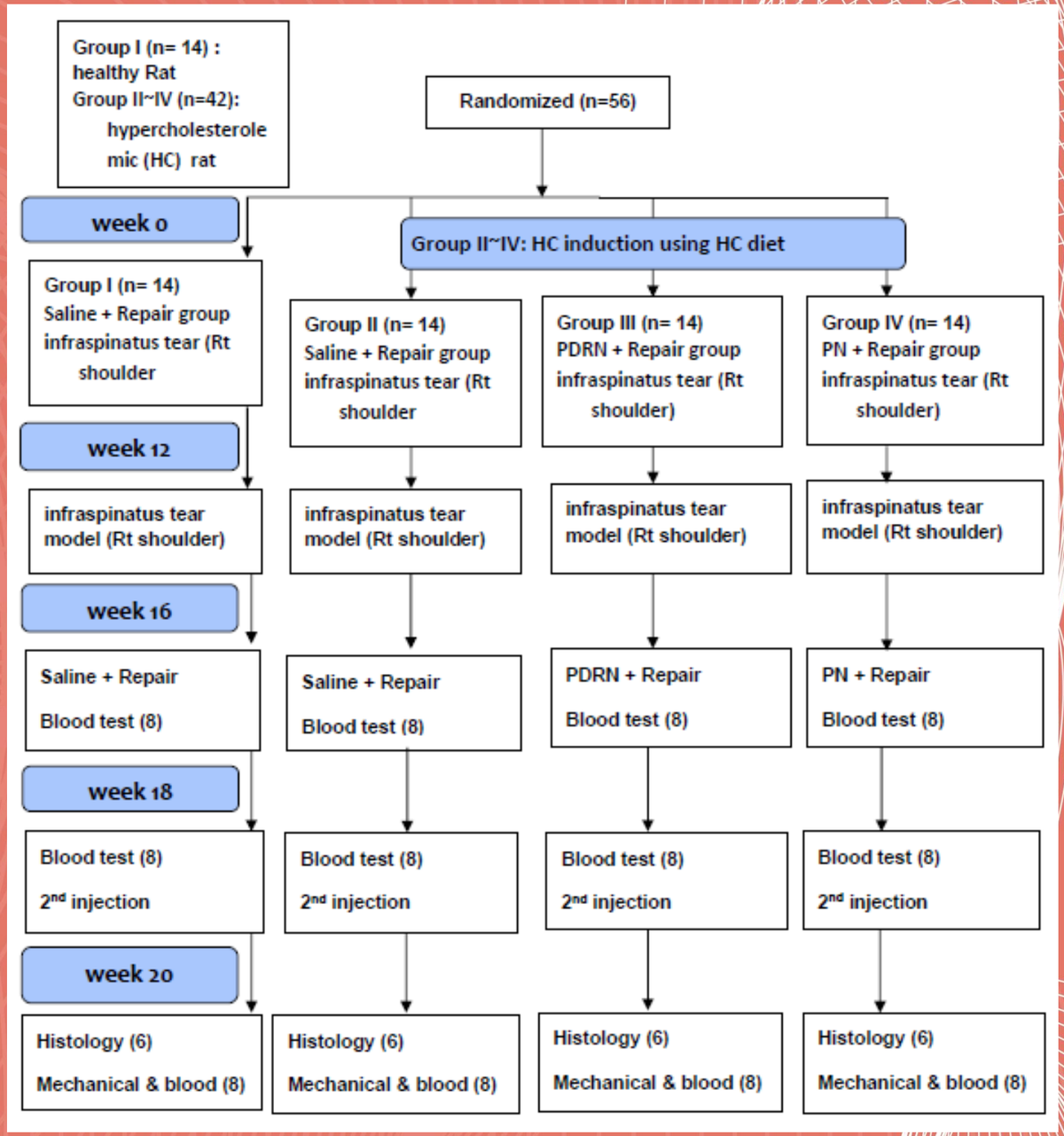
- For chronic rotator cuff tear, the rate of healing failure after surgical repair and fatty degeneration is considerably high (Park et al. Arthroscopy. 2013., Goutallier et al. JSES. 2003.).
- Polydeoxyribonucleotide (PDRN) has been used as a tissue regeneration activator (Altavilla et al. Surgery. 2011., Galeano et al. Wound Repair Regen. 2008.).
- Hypercholesterolemia may have an adverse effect on biomechanics of rotator cuff healing (Bearson et al. JSES. 2013.) and on fatty infiltration on repaired rotator cuffs. (Chung et al. AJSM. 2016)

THE AIM OF THIS STUDY

- To verify the effects of polydeoxyribonucleotide (PDRN) and polynucleotide (PN) on tendon healing and reversal of fatty degeneration in a chronic rotator cuff tear model using the infraspinatus of hypercholesterolemic rat.

METHODS

- One normal rat group (saline+repair: NSR, G1), three hypercholesterolemic (HC) diet-induced HC rat groups (saline+repair: HSR, G2, PDRN+repair: HPR, G3, and PN+repair: HPNR, G4).
- The right shoulder was used for experimental interventions, and the left served as a control.



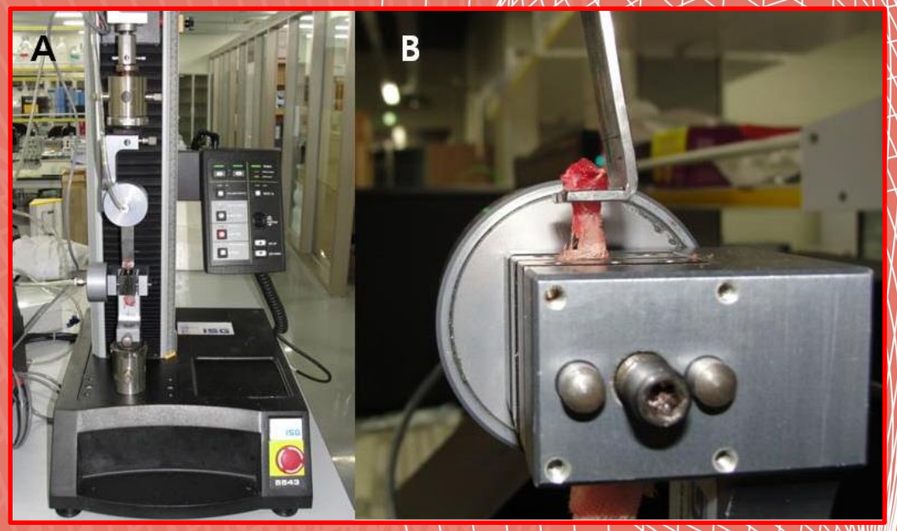
Flow diagram of the present study. HC: hypercholesterolemic, PDRN: polydeoxyribonucleotide, Rejuran: polynucleotide (PN).[6]

- Histologic evaluation

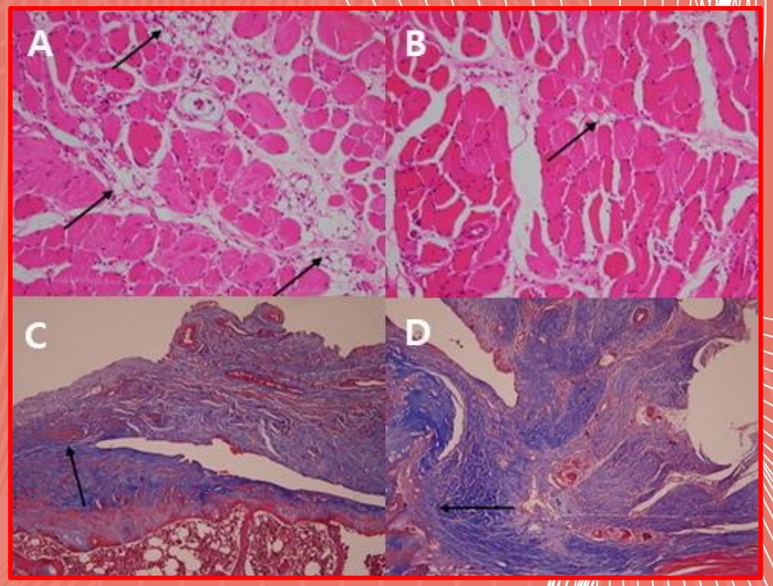
- Fatty degeneration - musculotendinous (M-T)
  - H&E stain
  - Oil Red O stain
  - Immunohistochemisty
  - CD68 : macrophage marker indicating tissue degeneration
  - CD168 :macrophage marker indicating tissue regeneration
  - CD68/CD168 ratio
- Tendon healing - tendon to bone (T-B)
  - H&E stain,
  - Masson's Trichrome stain

- Mechanical evaluation

- Instron material testing machine parameters - peak load to failure (N)
  - tear pattern (insertional Vs midsubstance)



Mechanical testing: A. The materials testing machine. Instron 5543, pneumatic grip, and rat muscle fixation device (KR Design Registration 30-0854878). B. Tensile load is being applied to infraspinatus of rat. Hwang et al. TERM. 2021 Dec;18(6):1009-1020.



A-B: Musculotendinous junction on H&E stain(x200). A. Adipocyte in Saline group. B. Adipocyte in PN group. C-D: Tendon to bone junction on Masson-Trichrome stain(x100) C. Saline group. D. PDRN group. Hwang et al. TERM. 2021 Dec;18(6):1009-1020.

RESULTS

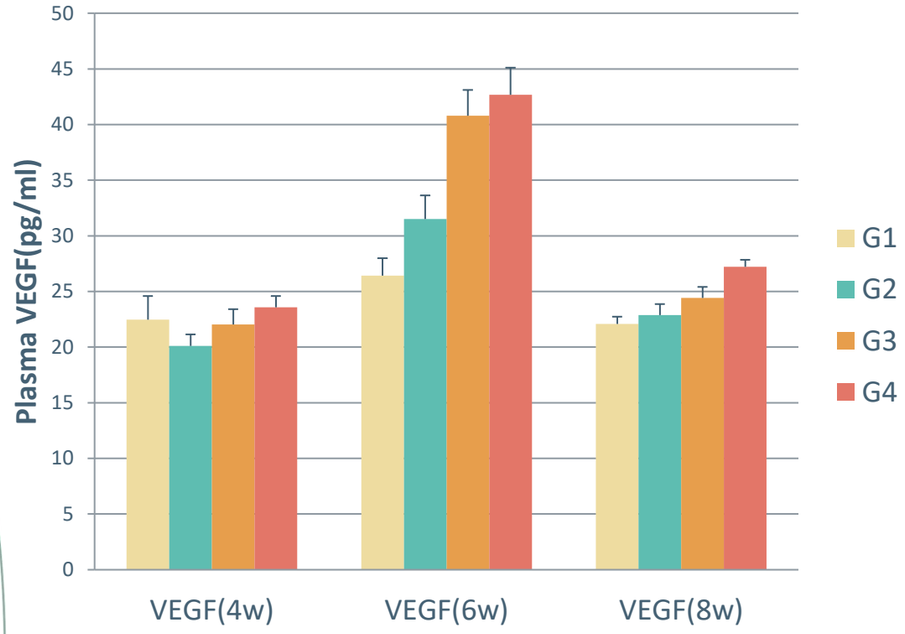
Mechanical testing. G: group, G 1 & 2: saline + repair, G 3: PDRN + repair, G 4: PN + repair, G1: normal rat, G2~4: hypercholesterolemic rat, p<.05

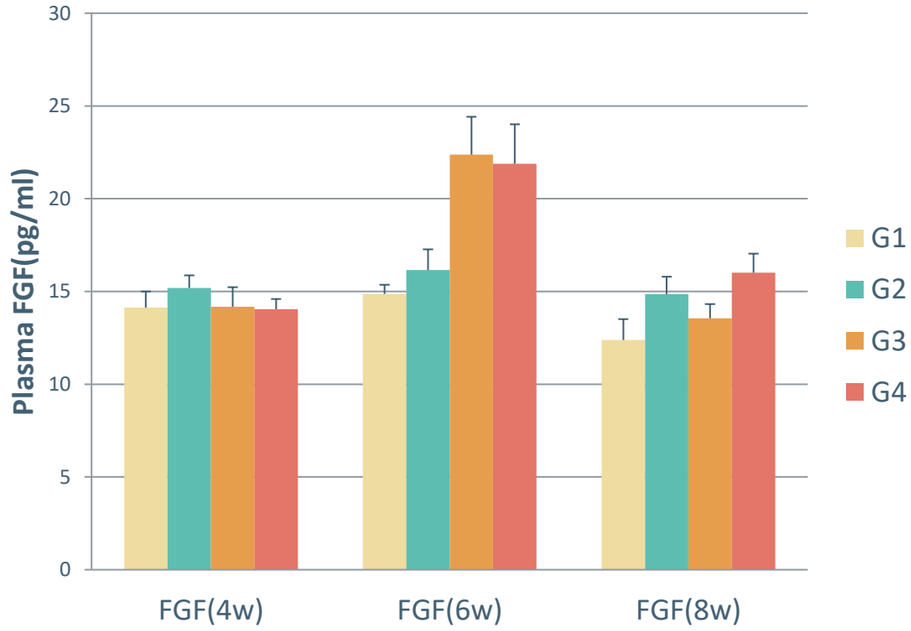
	G1 (n=7)	G2 (n=7)	G3(n=7)	G4(n=7)
Load to failure-operated side (N)	18.60 ± 8.26	14.33 ± 6.52	24.64 ± 10.76	20.42 ± 6.21
Load to failure-control side (N)	28.60 ± 4.74	29.91 ± 5.74	30.14 ± 2.78	28.82 ± 3.12
P value	.017	<.001	.215	.008
Tear pattern Insertional : Midsubstance – operated side (n)	7 : 0	7 : 0	6 : 1	6 : 1
Tear pattern Insertional : Midsubstance – control side (n)	0 : 7	0 : 7	0 : 7	0 : 7
P value	<.001	<.001	.002	.002

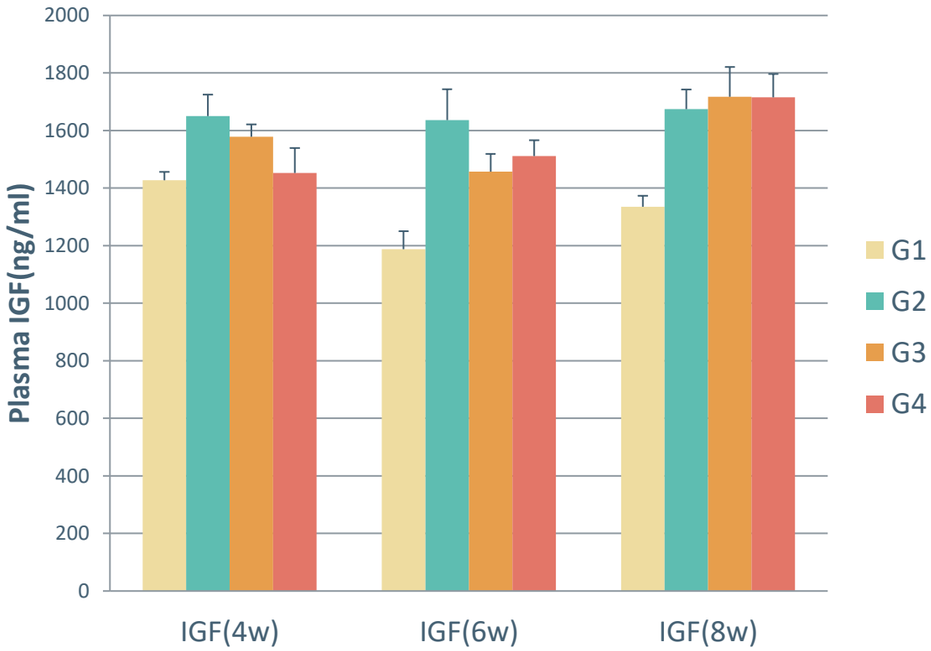
Among Rt shoulders		**Load to failure (N)**		**Tear pattern**	
Normal Vs HC	**G1 Vs G2**	.304		1.000	
Among HC	**G2 Vs G3**	.086	.083	.317	.591
	G2 Vs G4	.528		.317	
	G3 Vs G4	1.000		1.000	

Groups		MT-H&E	MT-ORO	MT-CD68	MT-CD168	MT-CD68/CD168	TB-Co	TB-Pa
4-week	Sham1 Vs G1	.004	.005	.005	,034		.003	.003
	Sham2 Vs G2	.004	.005	.005	.002		.005	.005
	Sham2 Vs G3	.065	.007	.005	.001		.014	.014
	Sham2 Vs G4	.015	.007	.005	.030		.003	.003
	One-Way ANOVA or Kruskall Wallis	.016	.005	.011	.229	.765	.024	.024
	G2 Vs G3	.020	.012	.023	.279	1.000	.028	.028
	G2 Vs G4	.067	.012	.025	1.000	1.000	.116	.116
	G3 Vs G4	1.000	1.000	1.000	.992	1.000	1.000	1.000

Histologic evaluation. Sham1 or 2: non-operated Lt shoulder of G1 or 2, G1 or 2: saline + repair, G3: PDRN + repair, G4: PN + repair, MT: musculotendinous, TB: tendon to bone, Co: continuity of collagen fiber, Pa: parallelism of collagen fiber,P<.05







Blood testing. G 1~4: Group 1~4, Group 1: normal rat (saline), Group 2: HC rat (saline), Group 3: HC rat (PDRN), Group 4: HC rat (PN), VEGF: vascular endothelial growth factor, FGF: fibroblast growth factor, IGF: insulin like growth factor. 4w: 2nd operation, 6w: 2nd injection, 8w: sacrifice. Error bars indicate standard errors.

Comparison of outcome in bold tests among the groups. Group 1: normal rat (saline), Group 2: HC rat (saline), Group 3: HC rat (PDRN), Group 4: HC rat (PN), VEGF: vascular endothelial growth factor, FGF: fibroblast growth factor, IGF: insulin like growth factor. P<.05

	Normal Vs HC (G1 vs G2)	
G1 vs G2	VEGF (2nd OP)	.406
	VEGF (2nd injection)	.077
	VEGF (sacrifice)	.528
	FGF (2nd OP)	.357
	FGF (2nd injection)	.482
	FGF (sacrifice)	.120
	IGF (2nd OP)	.016
	IGF (2nd injection)	.004
	IGF (sacrifice)	.001
One-way ANOVA or Kruskal-Wallis testing P<.05	Among HC (G2~4)	
VEGF (2nd injection) P=.006	G 2 Vs G 3	.031
	G 2 Vs G 4	.009
	G 3 Vs G 4	1.000
VEGF (sacrifice) P=.009	G 2 Vs G 3	.693
	G 2 Vs G 4	.008
	G 3 Vs G 4	.118
FGF (2nd injection) P=.048	G 2 Vs G 3	.079
	G 2 Vs G 4	.117
	G 3 Vs G 4	1.000

DISCUSSION & CONCLUSION

- In the present study, polydeoxyribonucleotide (PDRN) and polynucleotide (PN) showed a property of tendon healing and reversal of fatty degeneration of chronic rotator cuff tear in hypercholesterolemic rat model associated with growth factors.
- PDRN and PN might be effective for hypercholesteolemic human rotator cuff healing similar to PRP or stem cell.
- The use of PDRN and PN might have a possibility to improve tendon healing and decrease fatty degeneration in hypercholesterolemic state after cuff repair.

REFERENCES

1. Hwang JT, Lee SS, Han SH, Sherchan B, Panakkal JJ. Polydeoxyribonucleotide and Polynucleotide Improve Tendon Healing and Decrease Fatty Degeneration in a Rat Cuff Repair Model. Tissue Eng Regen Med. 2021 Dec;18(6):1009-1020.
2. Seo SJ, Park JY, Park HJ, Hwang JT. Protocatechuic acid impacts rotator cuff healing and reduces fatty degeneration in a chronic rotator cuff tear model in rats. Clin Shoulder Elb. 2022 Mar;25(1):5-14.
3. Chung SW, Park H, Kwon J, Choe GY, Kim SH, Oh JH. Effect of Hypercholesterolemia on Fatty Infiltration and Quality of Tendon-to-Bone Healing in a Rabbit Model of a Chronic Rotator Cuff Tear: Electrophysiological, Biomechanical, and Histological Analyses. Am J Sports Med. 2016 May;44(5):1153-64.Sugaya H, Maeda K, Matsuki K, Moriishi J. Repair integrity and functional outcome after arthroscopic double-row rotator cuff repair. A prospective outcome study. J Bone Joint Surg Am. 2007 May;89(5):953-60.
4. Beason DP, Abboud JA, Kuntz AF, Bassora R, Soslowsky LJ. Cumulative effects of hypercholesterolemia on tendon biomechanics in a mouse model. J Orthop Res. 2011 Mar;29(3):380-3.Ticker JB, Beim GM, Warner JJ. Recognition and treatment of refractory posterior capsular contracture of the shoulder. Arthroscopy. 2000 Jan-Feb;16(1):27-34.
5. Beason DP, Tucker JJ, Lee CS, Edelstein L, Abboud JA, Soslowsky LJ. Rat rotator cuff tendon-to-bone healing properties are adversely affected by hypercholesterolemia. J Shoulder Elbow Surg. 2014 Jun;23(6):867-72.Park JY, Lhee SH, Oh KS, Kim NR, Hwang JT. Is arthroscopic coracoplasty necessary in subcoracoid impingement syndrome? Arthroscopy. 2012 Dec;28(12):1766-75.
6. Park JY, Lhee SH, Oh KS, Moon SG, Hwang JT. Clinical and ultrasonographic outcomes of arthroscopic suture bridge repair for massive rotator cuff tear. Arthroscopy. 2013 Feb;29(2):280-9.
7. Kang SH, Choi MS, Kim HK, Kim WS, Bae TH, Kim MK, Chang SH. Polydeoxyribonucleotide improves tendon healing following achilles tendon injury in rats. J Orthop Res. 2018 Jun;36(6):1767-1776.