

**Title: Tacrolimus improves therapeutic efficacy of umbilical cord blood-derived mesenchymal stem cells in diabetic retinopathy by suppressing DRP1-mediated mitochondrial fission**

**Hang Hyo Jo<sup>1,2,a</sup>, Yeong Seok Goh<sup>3,a</sup>, Hye Jih Kim<sup>1,2</sup>, Dae Hyun Kim<sup>1,2</sup>, Hyemin Kim<sup>3</sup>, Jiye Hwang<sup>3</sup>, Ji Seung Jung<sup>3</sup>, Nanyoung Kang<sup>3</sup>, Sang Eun Park<sup>3</sup>, Kyung Mee Park<sup>3,\*</sup>, and Hyun Jik Lee<sup>1,2,\*</sup>**

**Affiliation**

<sup>1</sup>Laboratory of Veterinary Physiology, College of Veterinary Medicine and Veterinary Medicine Center, Chungbuk National University, Cheongju 28644, Korea

<sup>2</sup>Institute for Stem Cell & Regenerative Medicine (ISCRM), Chungbuk National University, Cheongju 28644, Korea

<sup>3</sup>Laboratory of Veterinary Surgery and Ophthalmology, College of Veterinary Medicine, Chungbuk National University, Cheongju 28644, Korea

<sup>a</sup> These authors contributed equally to this work

**\*Corresponding authors are Kyung-Mee Park and Hyun Jik Lee.**

**\*Kyung-Mee Park, D.V.M., Ph.D.**

Laboratory of Veterinary Surgery and Ophthalmology, College of Veterinary Medicine, Chungbuk National University, Cheongju 28644, Korea

Tel: +82-43-261-2985 / E-mail: parkkm@cbnu.ac.kr

**\*Hyun Jik Lee, D.V.M., Ph.D.**

Laboratory of Veterinary Physiology, College of Veterinary Medicine and Veterinary Medicine Center, Chungbuk National University, Cheongju 28644, Korea

Institute for Stem Cell & Regenerative Medicine (ISCRM), Chungbuk National University, Cheongju 28644, Korea

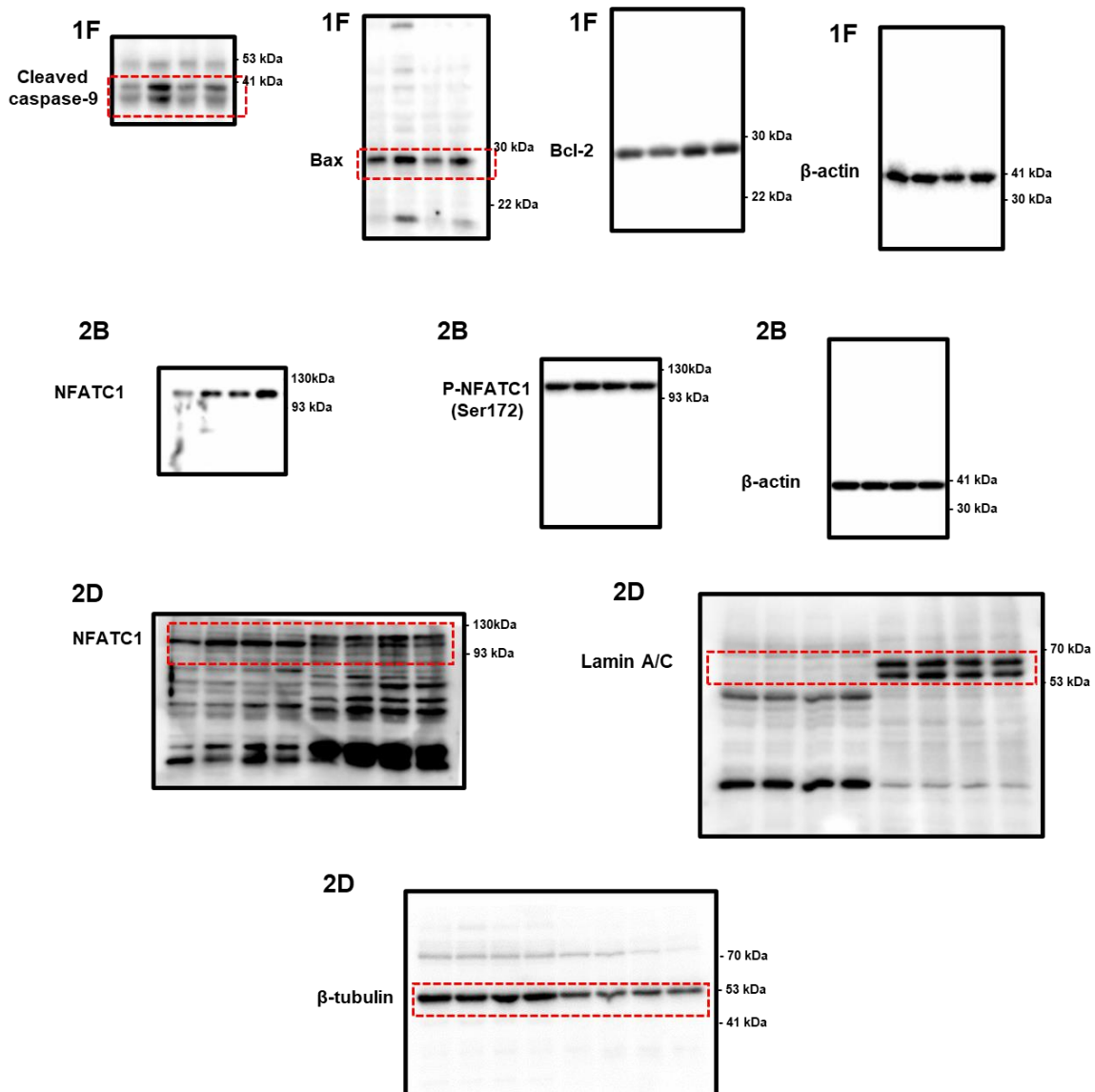
Tel: +82-43-261-2597 / E-mail: leehyunjik@chungbuk.ac.kr

Running Title: Therapeutic effect of tacrolimus-pretreated MSCs on diabetic retinopathy

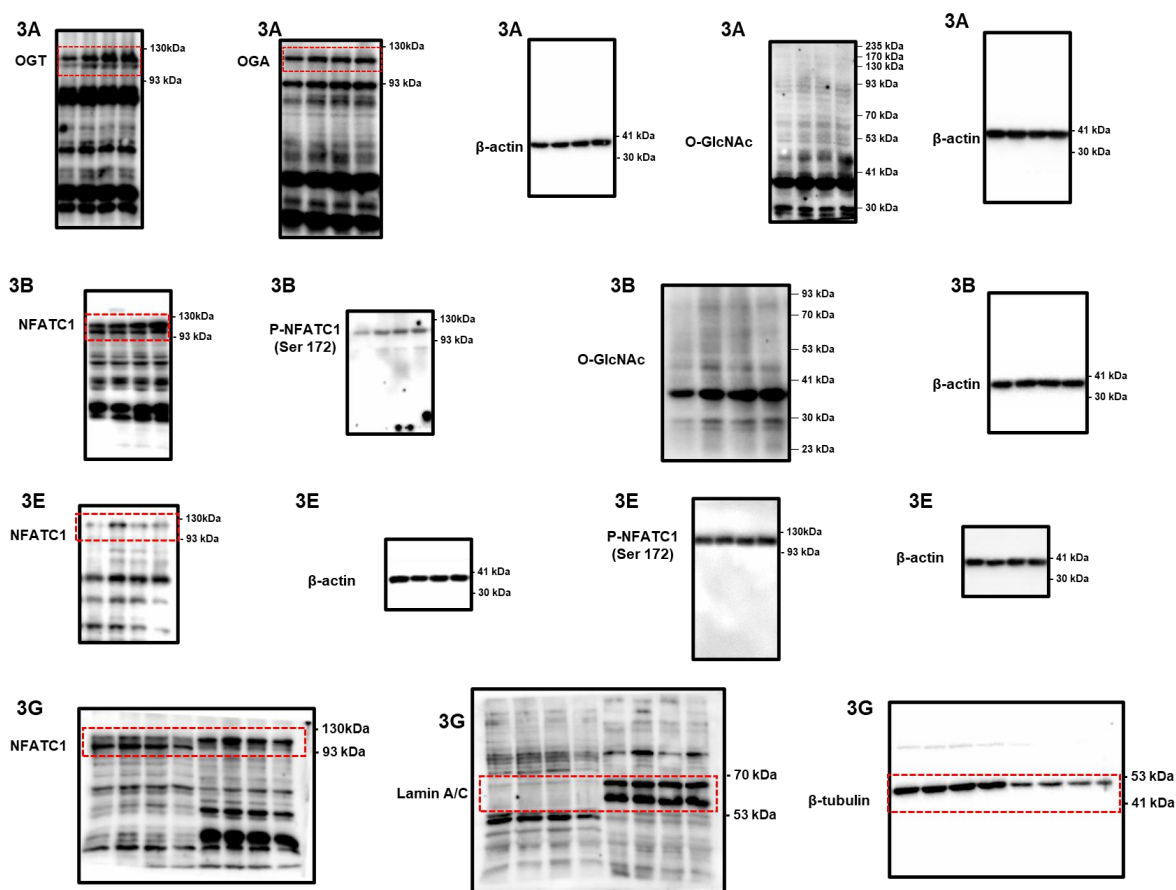
**Key words:** Diabetic retinopathy, Mesenchymal stem cells, Tacrolimus, Mitochondrial dynamics, O-GlcNAc transferase, Apoptosis

-700 GTAATCCCAACACTTTGGGAGGCCGAGGCGGGTGGATCACTAGGTCCGGAGATCGAGACC  
-640 ATCCTGGAAACACAGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCGGGCGT  
-580 AGTGGTGGGTGCCTGTAGTCCCAGCTACTCCGAAGGCTGAGGCAGGAGAATGGCGTGAAC  
-520 CCGGGAGGCGGAATTTGCAGTGGGCCGAGATCGCGCCACTGCACTCCAGCCTGGGCGACA  
-460 GAGTGAGACTCCGTCTCAAAAAAAAAAAAAAAAAATAAATAAATAAATAAATAAAGGA  
-400 AGTGACACTGGATAATTAAGAGACACACCATTGCGCCTTTAACACATATTCACACCCAGC  
-340 ACTGTCACATCCATCGTGCCTTGAGGACAGGCATAAATTACGGCCTTCCTCCTGCGCTC  
-280 CCGGCCTGCTCCTAGCCTTTGACTAGAGCCTGCGCAGCATCCCAGTCCCAGGCTAGGGCC  
-220 CACCGGTGCCGCGCAGCCTCCTGGAAGCTGTGGGGAGTAGCGTTCTCCGCTCCAGAACT  
-160 ACAACTCCCAGCAGGCCTTGCTCCTCTCCACCTCCCTCGCAGCGCATGGCCTGCCGGGAG  
-100 GGGGCAGGTAGCCGGCGGGCCCGGTCCAATGGGTGCCGGCTCCGAGGAGAGGGCGGAGG  
-040 AGAGGAGGAAGGAGGCGAACTGTGGGCCCCGGCCCCATTC

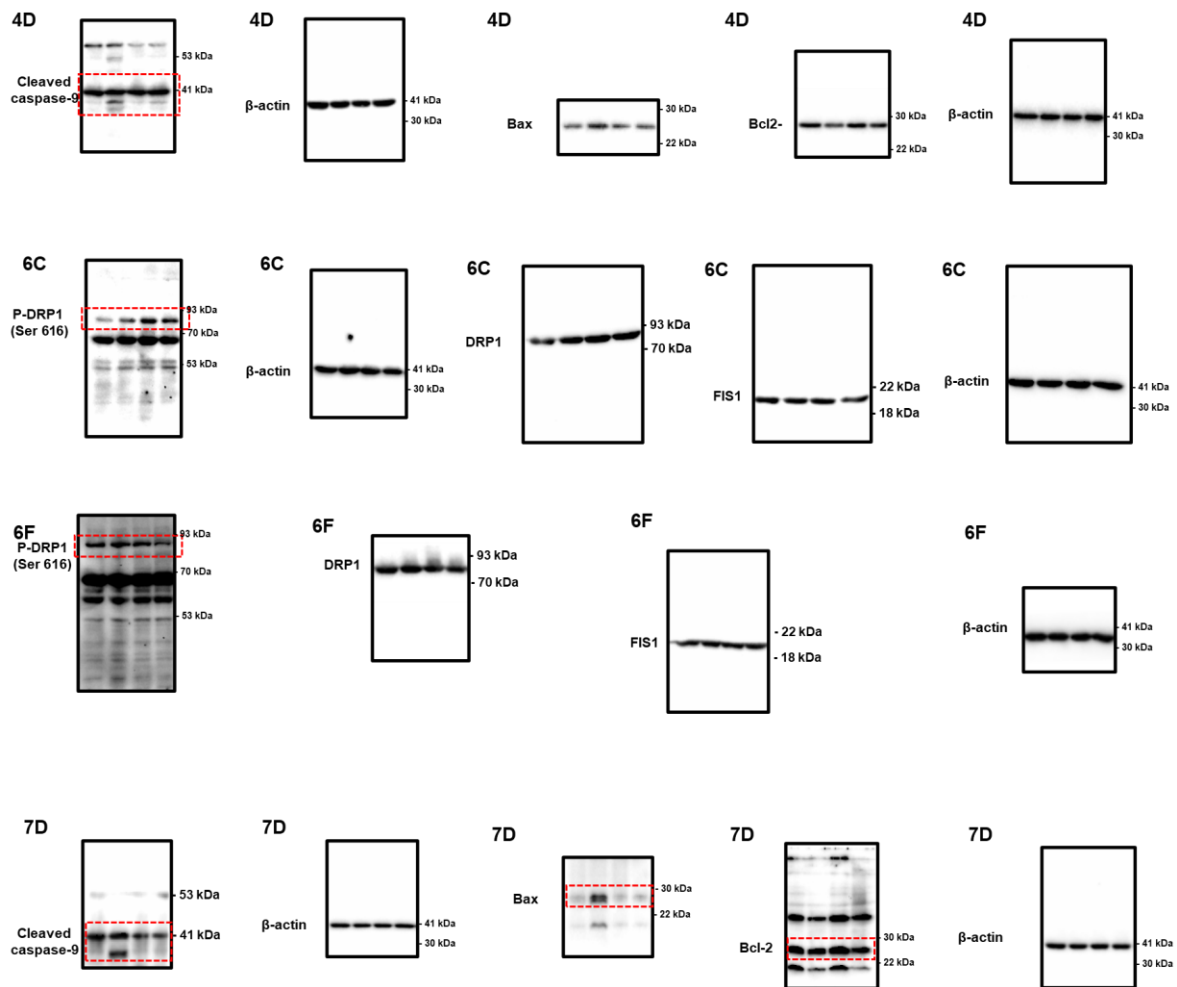
**Fig. S1. The NFAT binding site in the DNML1L\_1 promoter.** The NFAT binding site in the DNML1L\_1 promoter is shown. The yellow shaded box represents the consensus sequences of NFATC1.



**Fig. S2. Full-length gel images for key data in figures 1F-2D.** All western blot images are full-length blot images of key blot data in the figures 1F-2D. Dash line box indicates cropped blot image in the figures 1F-2D.



**Fig. S3. Full-length gel images for key data in figures 3A-3G.** All western blot images are full-length blot images of key blot data in the figures 3A-3G. Dash line box indicates cropped blot image in the figures 3A-3G.



**Fig. S4. Full-length gel images for key data in figures 4D-7D.** All western blot images are full-length blot images of key blot data in the figures 4D-7D. Dash line box indicates cropped blot image in the figures 4D-7D.

**Table. S1. Sequences of primers used for real-time PCR**

Gene	Identification	Sequence (5'-3')	Size (bp)	Accession number
<i>DRP1</i>	Sense	CAGTGTGCCAAAGGCAGTAA	212	XM_054370716.1
	Antisense	GATGAGTCTCCCGGATTCA		
<i>FIS1</i>	Sense	CTTGCTGTGTCCAAGTCCAA	213	XM_054356644.1
	Antisense	CCACAGCCCCGTTTTATTTA		
<i>MFN1</i>	Sense	TTGGAGCGGAGACTTAGCAT	163	NM_033540.3
	Antisense	TTCGATCAAGTTCCGGATTC		
<i>OPA1</i>	Sense	GGCCAGCAAGATTAGCTACG	154	NM_015560.3
	Antisense	ACAATGTCAGGCACAATCCA		
<i>ACTB</i>	Sense	CCACCATGTACCCTGGCATT	189	NM_001101.5
	Antisense	CGGACTCGTCATACTCCTGC		