

The possible anti-proliferative effect of Liraglutide mediated through Rac1/MAPK/KLF5 signaling pathway in experimental model of diabetic nephropathy

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INTRODUCTION

Diabetic nephropathy (DN) is a common complication of diabetes characterized by renal cells proliferation.⁽¹⁾ Although the Glucagon-Like Peptide-1 Receptor (GLP-1R) agonist, Liraglutide, has a reno-protective effects, the impact of this drug on renal cells proliferation in DN remains unknown.⁽²⁾ Therefore, this study was aimed to investigate whether Liraglutide has anti-proliferation effect by inhibiting Rac1/MAPK/KLF5 pathway in experimental model of DN.

OBJECTIVES

- Evaluate the renal protective effect of Liraglutide in DN.
- Investigate the mechanism underlying alleviation of renal cell proliferation mediated by Liraglutide.

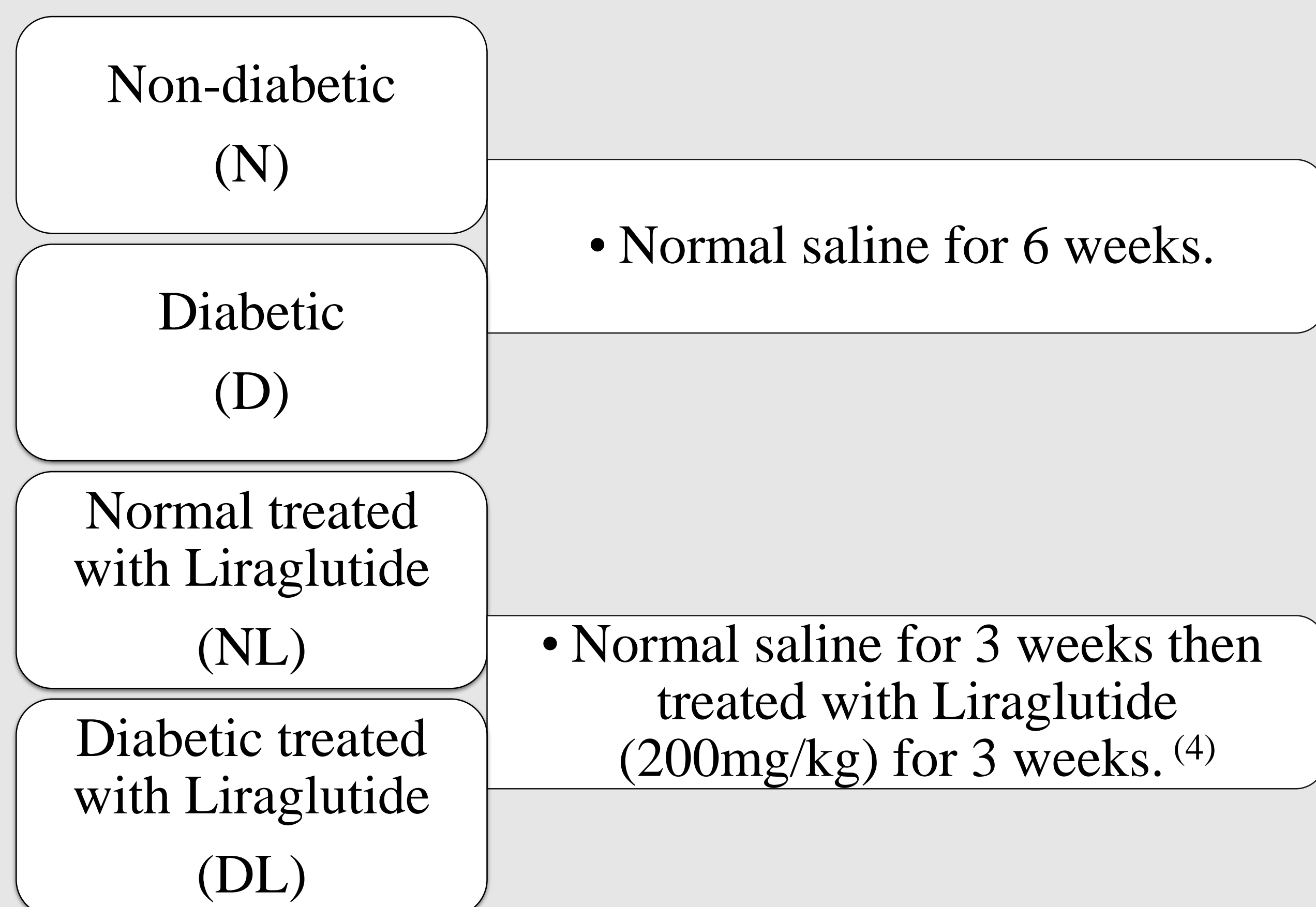
METHODS

Establishment of diabetic model in rats

Diabetes was induced by using a single intraperitoneal injection of Streptozotocin (STZ) (30 mg/kg).⁽³⁾

Experimental design

Twenty-four male Wister rats were divided into four groups.



Evaluation experimental model of DN

- 6 weeks post induction, the kidney weight/body weight (KW/BW) was calculated.
- A biochemical assay measuring the albumin, creatinine and urea levels was conducted.
- Kidney tissues were stained with hematoxylin and eosin.
- Protein expression of proliferating cell nuclear antigen (PCNA) was detected using western blot.

Investigation of KLF5 protein expression

Kidney tissues were subjected to western blotting using a specific antibody against KLF5.

RESULTS

Liraglutide Reduces Diabetic Nephropathy Biomarkers

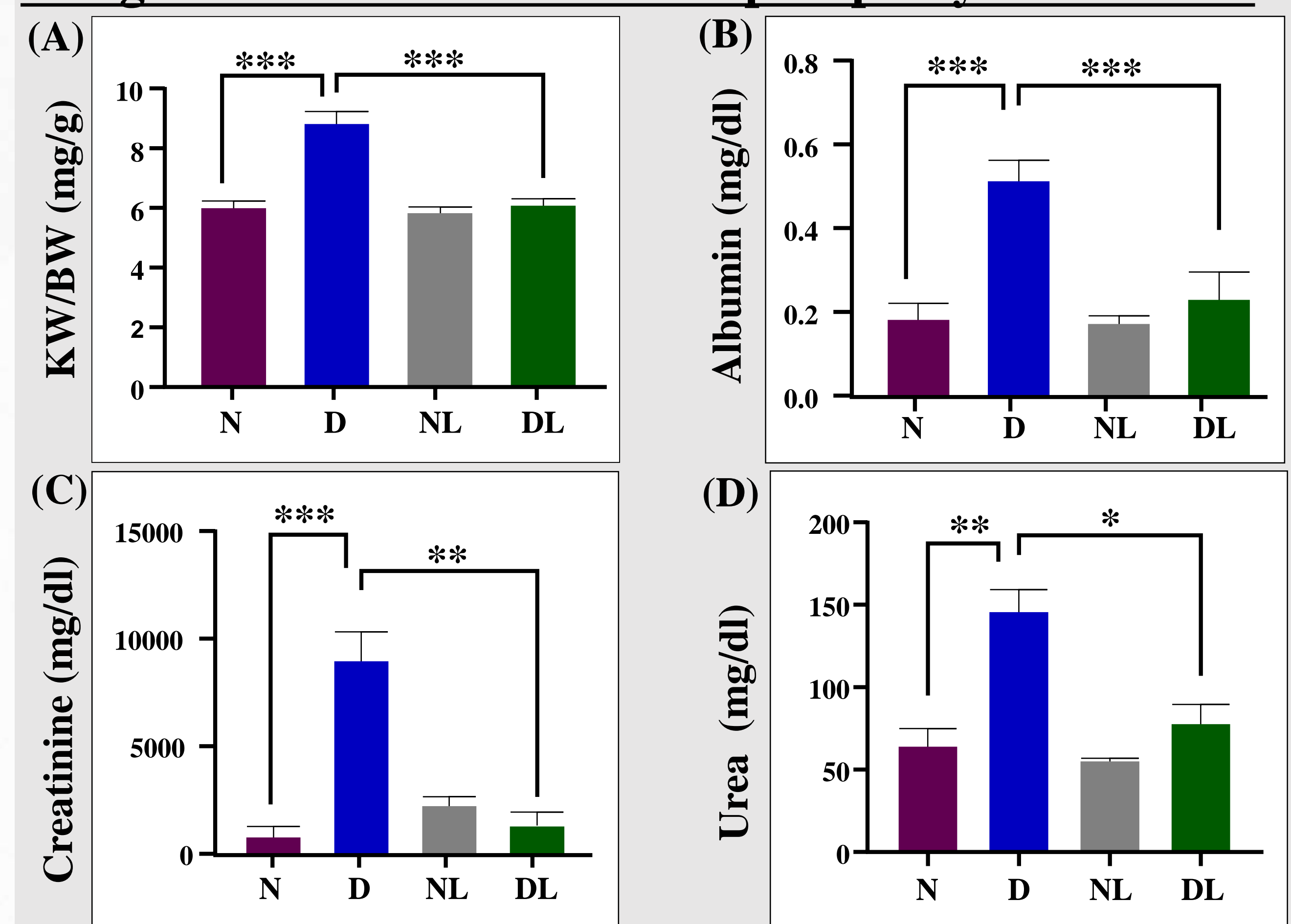


Figure 1: Effect of Liraglutide on the diabetic nephropathy Biomarkers. (A) Kidney weight to body weight ratio. (B) Albumin (C) Creatinine (D) Urea levels. Data are presented as mean \pm SEM. *, $p \leq 0.05$; **, $p \leq 0.01$; ***, $p \leq 0.001$, compared to diabetic group.

Liraglutide Protects from STZ Induced Kidney Injury

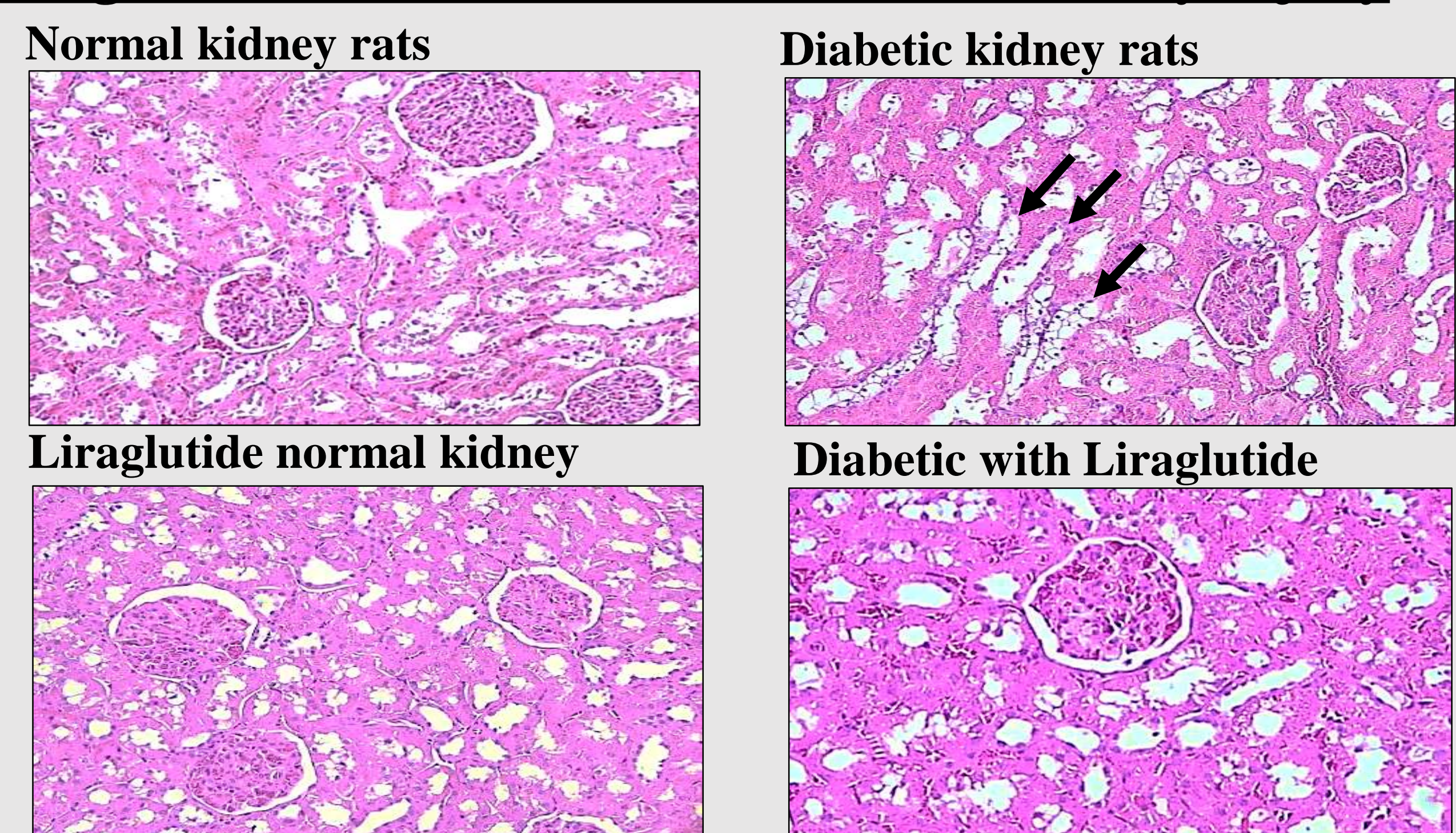


Figure 2: Effect of liraglutide on STZ induced diabetic nephropathy in rats.

Liraglutide Attenuates Renal Cells Proliferation

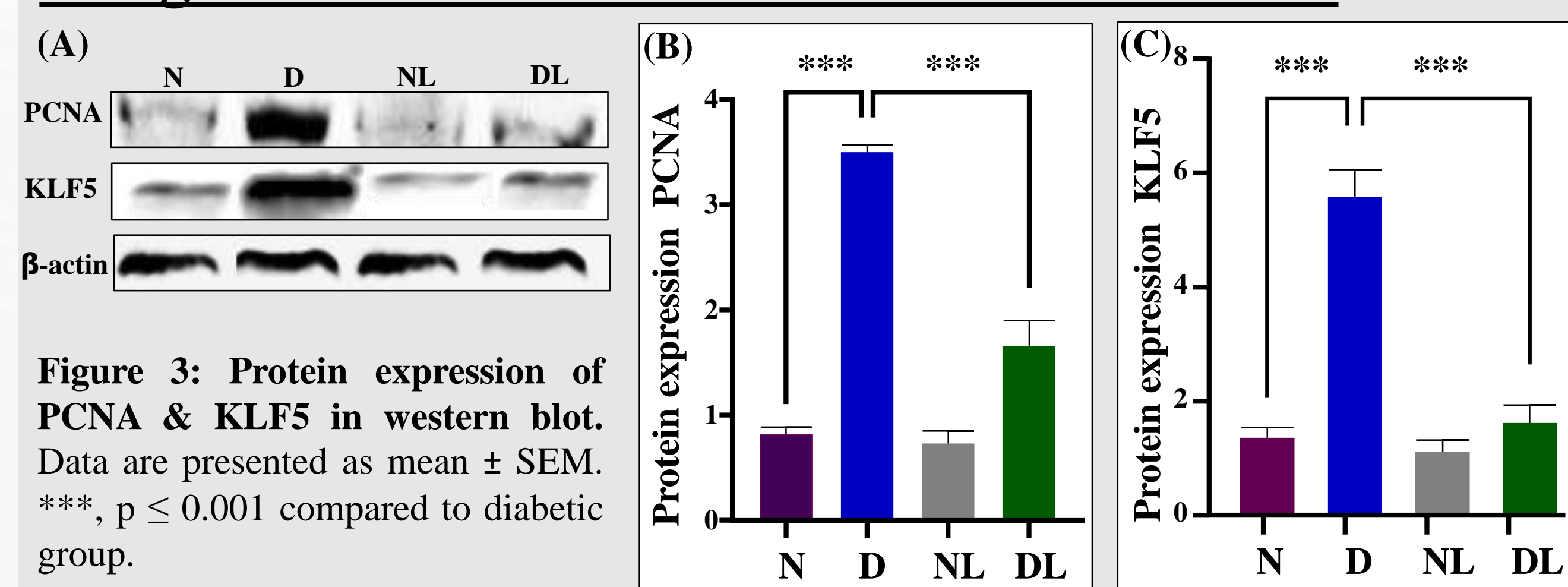


Figure 3: Protein expression of PCNA & KLF5 in western blot. Data are presented as mean \pm SEM. ***, $p \leq 0.001$ compared to diabetic group.

CONCLUSIONS

Liraglutide attenuates renal cells proliferation and reduces risk of DN via modulation of Rac1/MAPK/KLF5 pathway.

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