

PROTECTIVE EFFECT OF N-ACETYLCYSTEINE ON CHRONIC TENOFOVIR NEPHROTOXICITY

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INTRODUCTION

- Tenofovir is an effective drug for HIV infection and chronic hepatitis B.
- This antiretroviral drug is associated to chronic kidney disease and increased oxidative stress.
- N-acetylcysteine (NAC) has been described as potent antioxidant by increasing glutathione levels.
- Previous study from our Laboratory demonstrated that NAC attenuates the progression of chronic renal failure in rats submitted to 5/6 nephrectomy (Kidney Int 2005;68:2208-17).

OBJECTIVE

The aim of this study was to evaluate the effect of chronic use of tenofovir on renal function and oxidative stress in rats, and a possible protective effect of the N-acetylcysteine (NAC) against Tenofovir nephrotoxicity.

METHODS

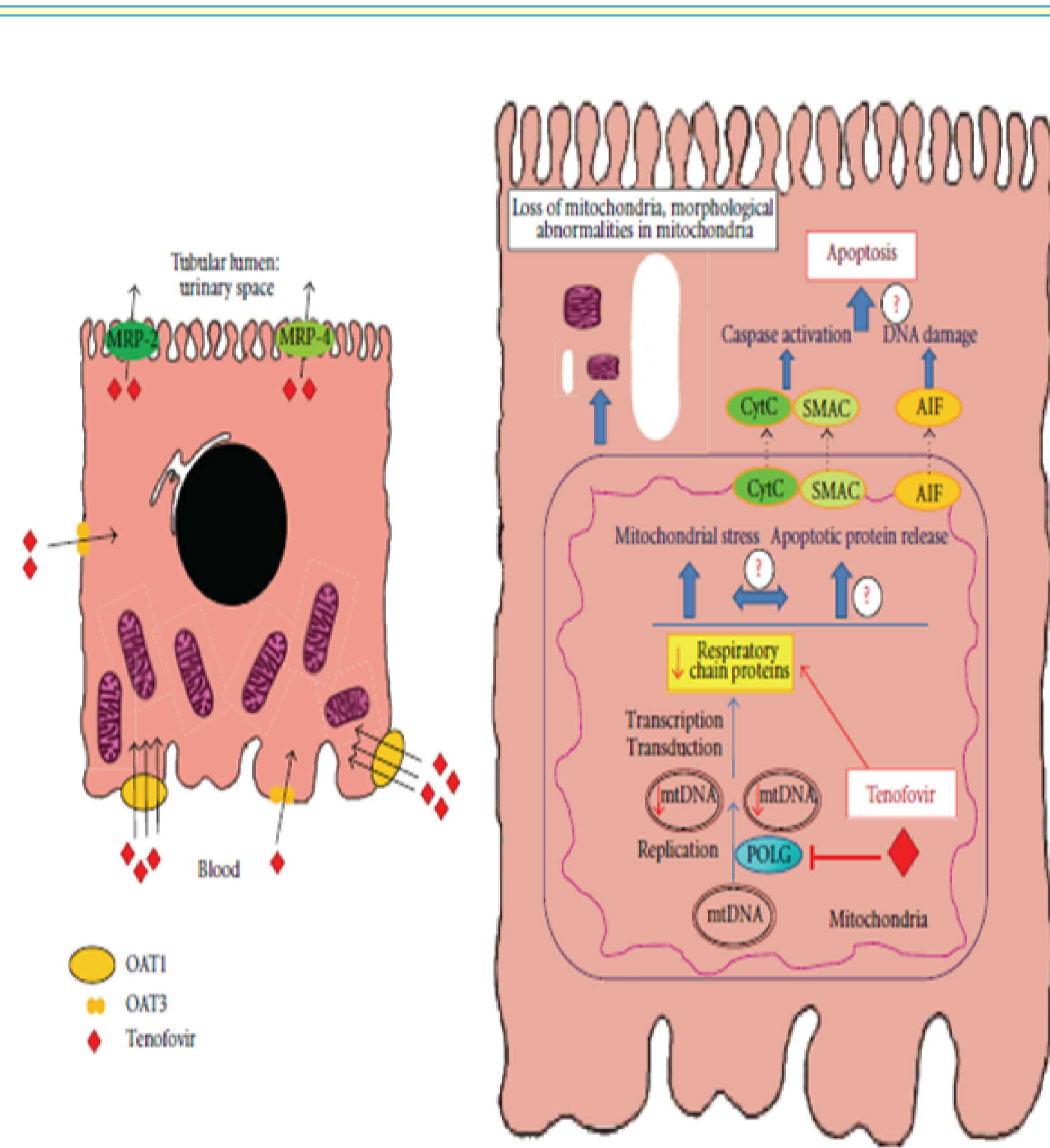
- Three groups of 2-mo-old male Wistar rats were studied:
- Control (n=7)
 - Tenofovir (50 mg/Kg diet, n=10)
 - Tenofovir (50 mg/Kg diet) + NAC (600 mg/L drinking water, n=10)

The rats were monitored during 4 months, after which clearance studies were performed.

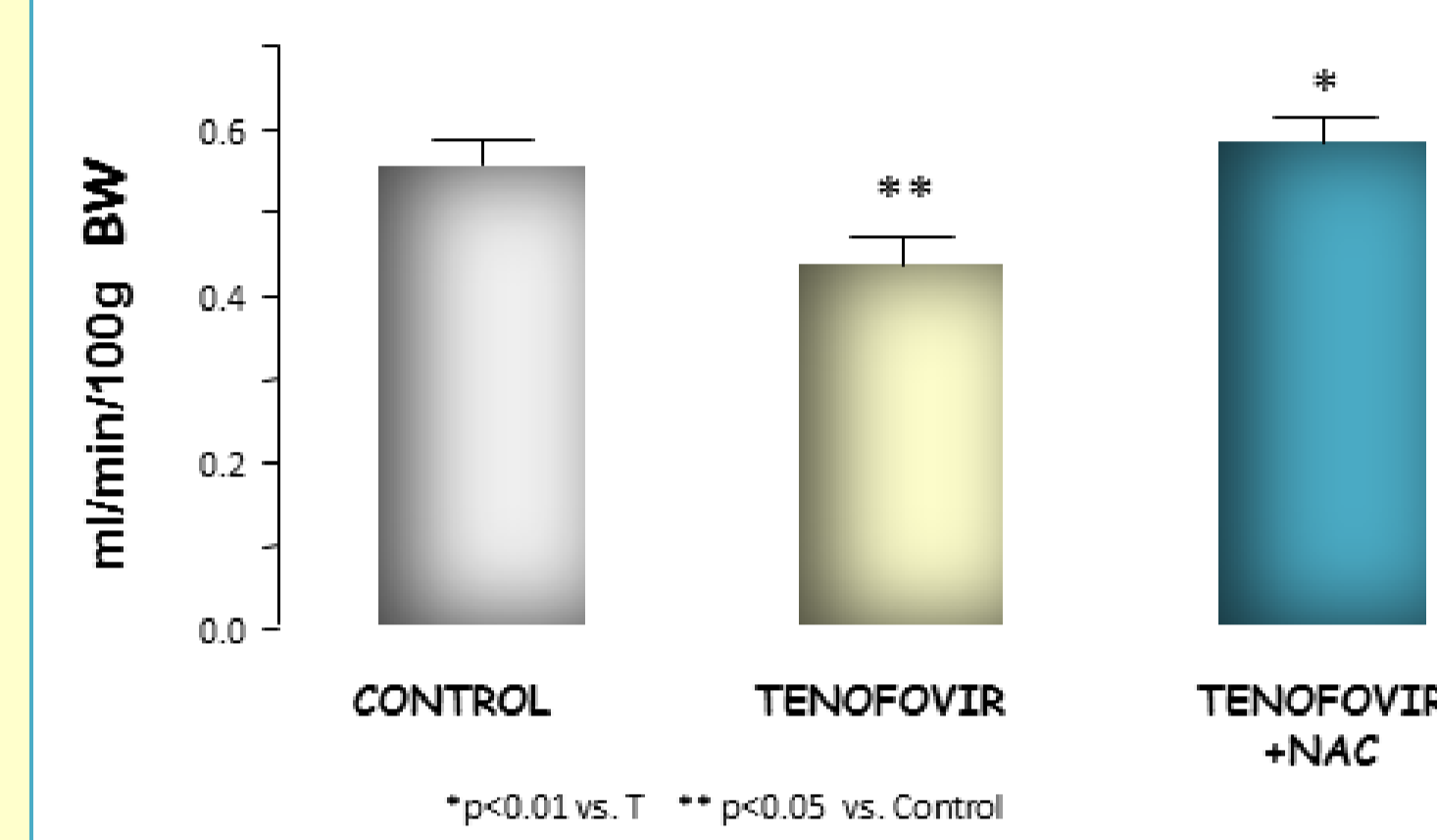
The rats were anesthetized to measure inulin clearance (GFR, ml/min/100g BW), blood pressure (BP, mmHg), renal blood flow (RBF, ml/min flowmeter) and calculated renal vascular resistance (RVR, mmHg/ml/min).

Oxidative stress was evaluated by serum thiobarbituric acid reactive substances, a marker of lipid peroxidation (TBARS, nM/ml), urinary TBARS excretion (nM/24h) and by the endogenous antioxidant, serum glutathione (μ M/ml). Renal tissue was immunoblotted for angiotensin II.

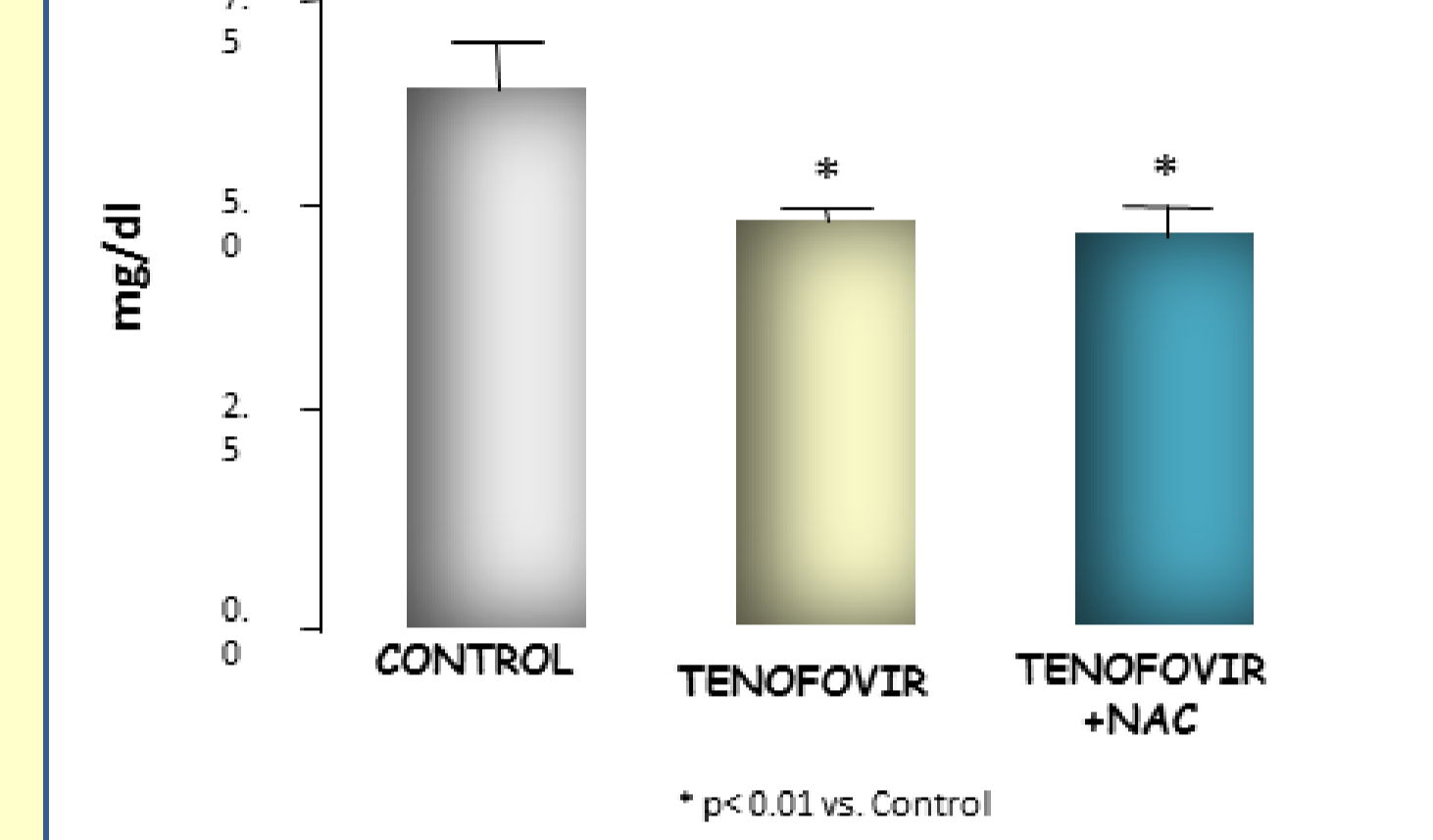
TENOFOVIR HANDLING BY PROXIMAL TUBULAR CELLS



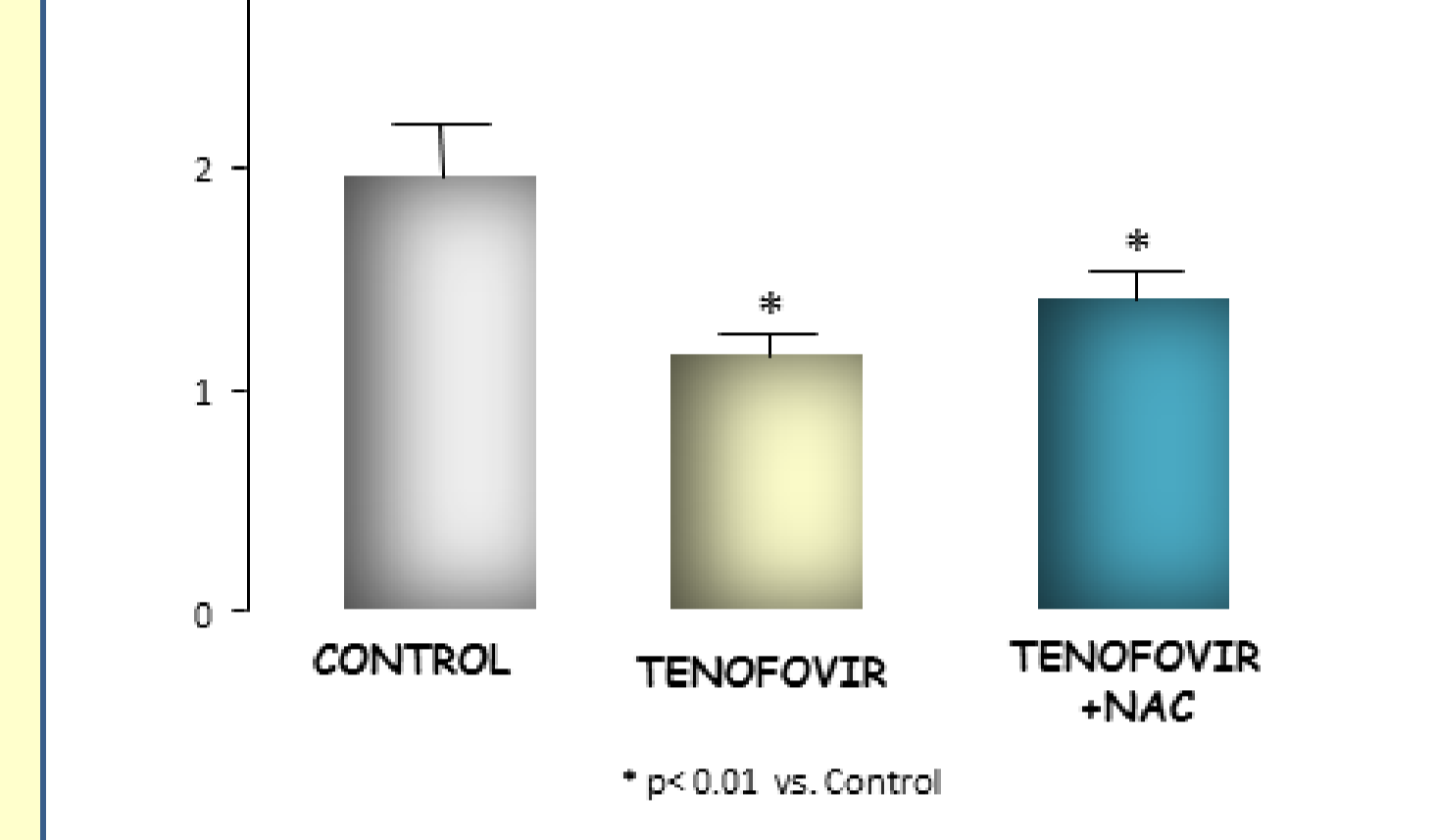
INULIN CLEARANCE



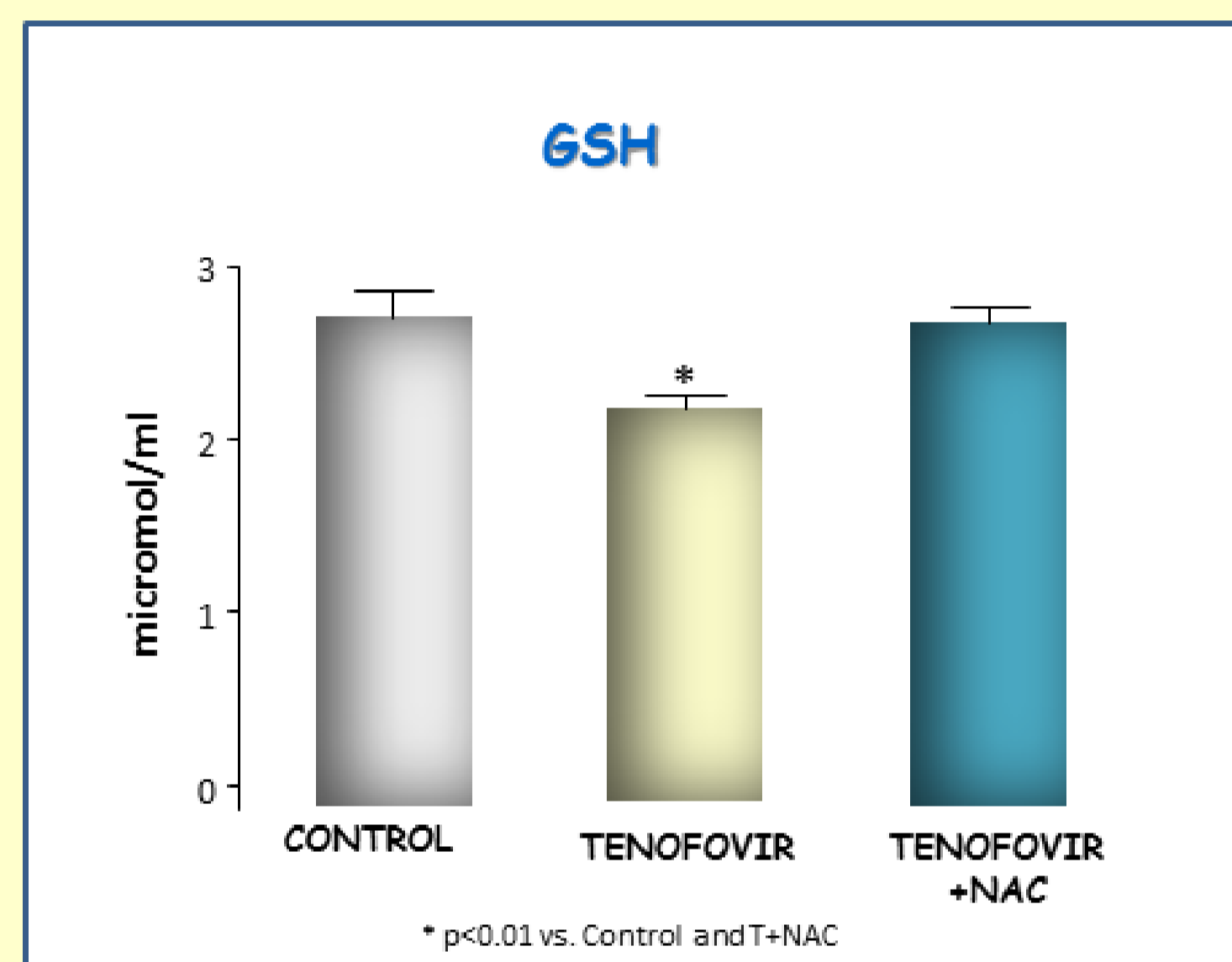
SERUM PHOSPHATE



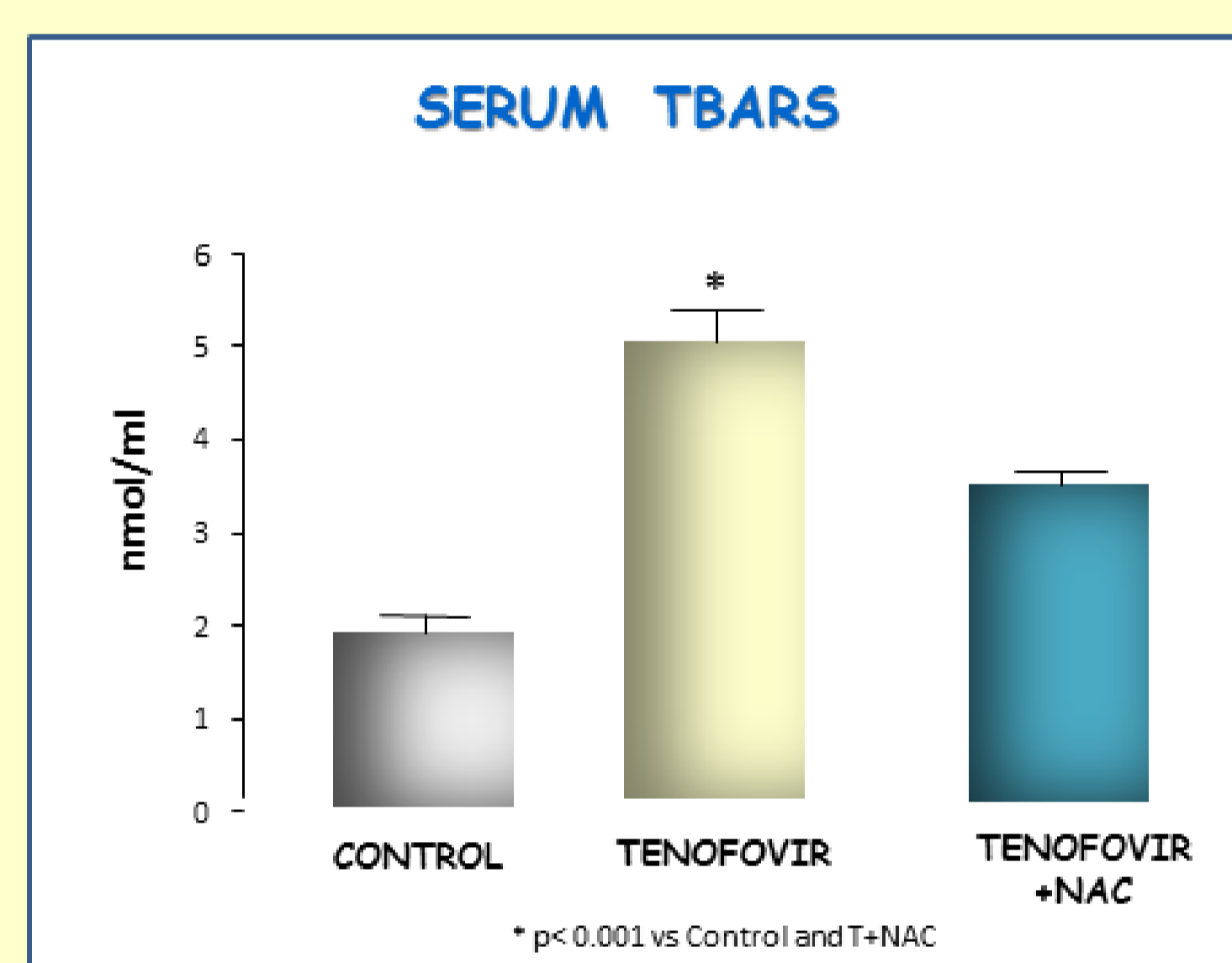
Tm PO₄/GFR



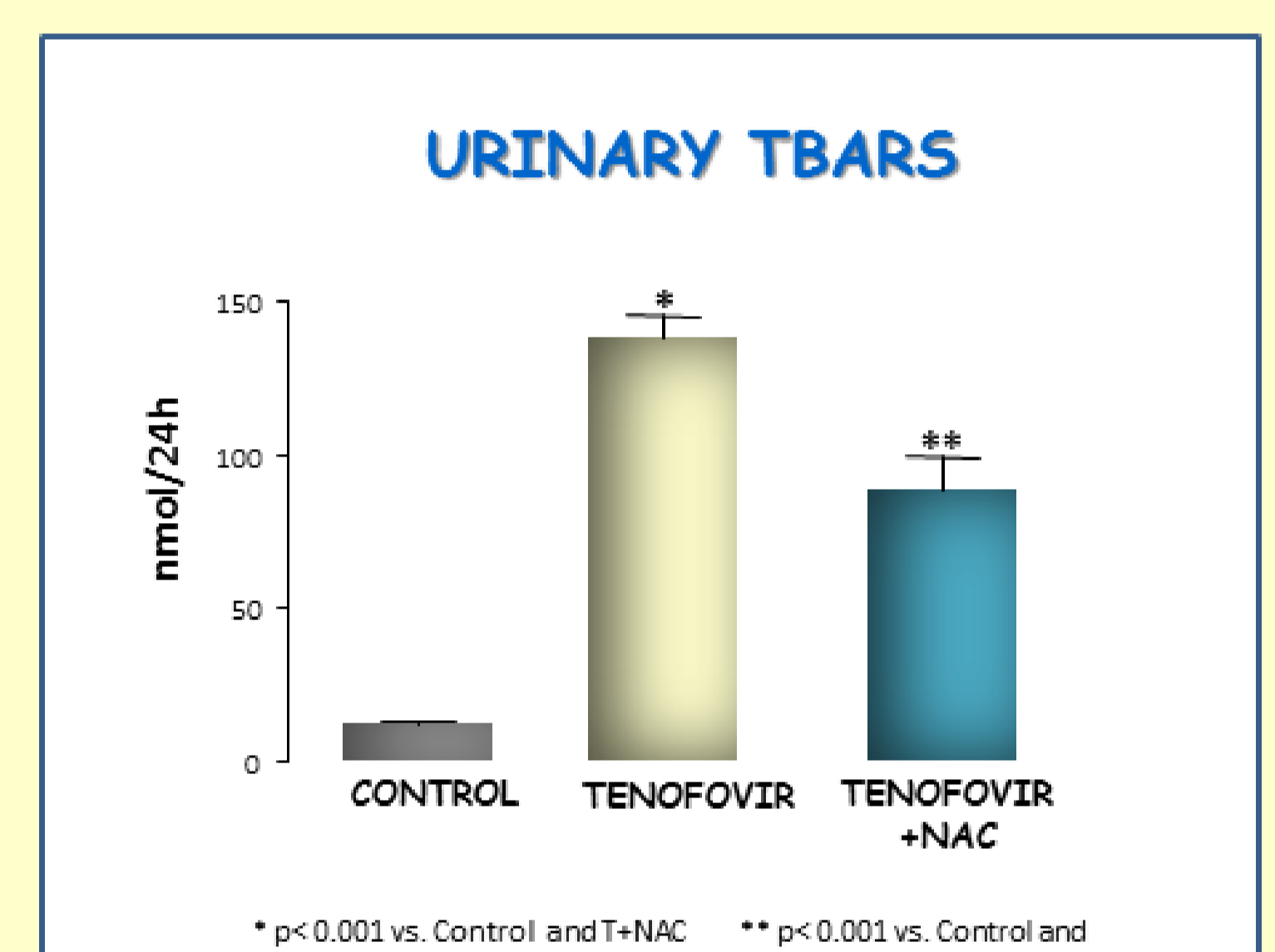
GSH



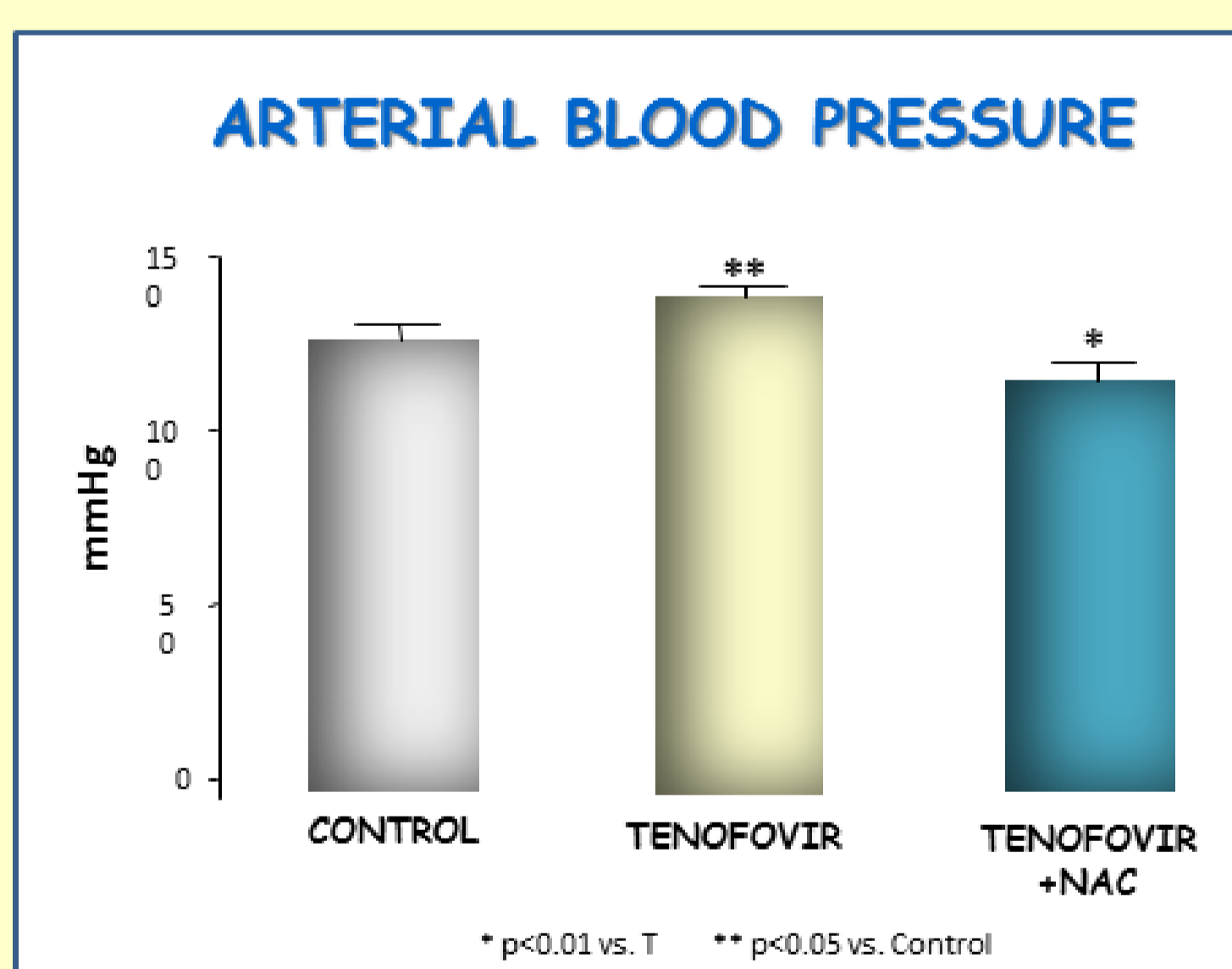
SERUM TBARS



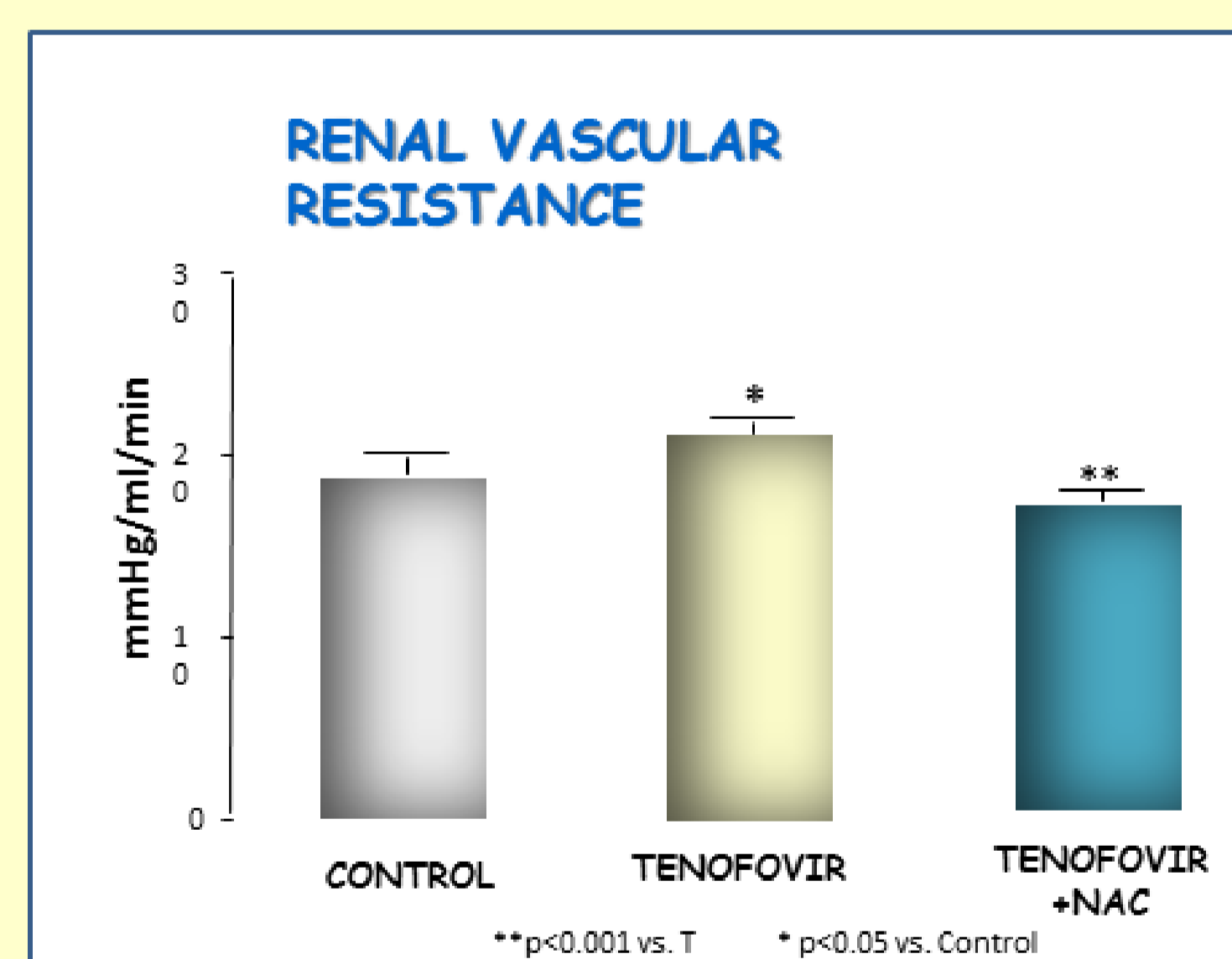
URINARY TBARS



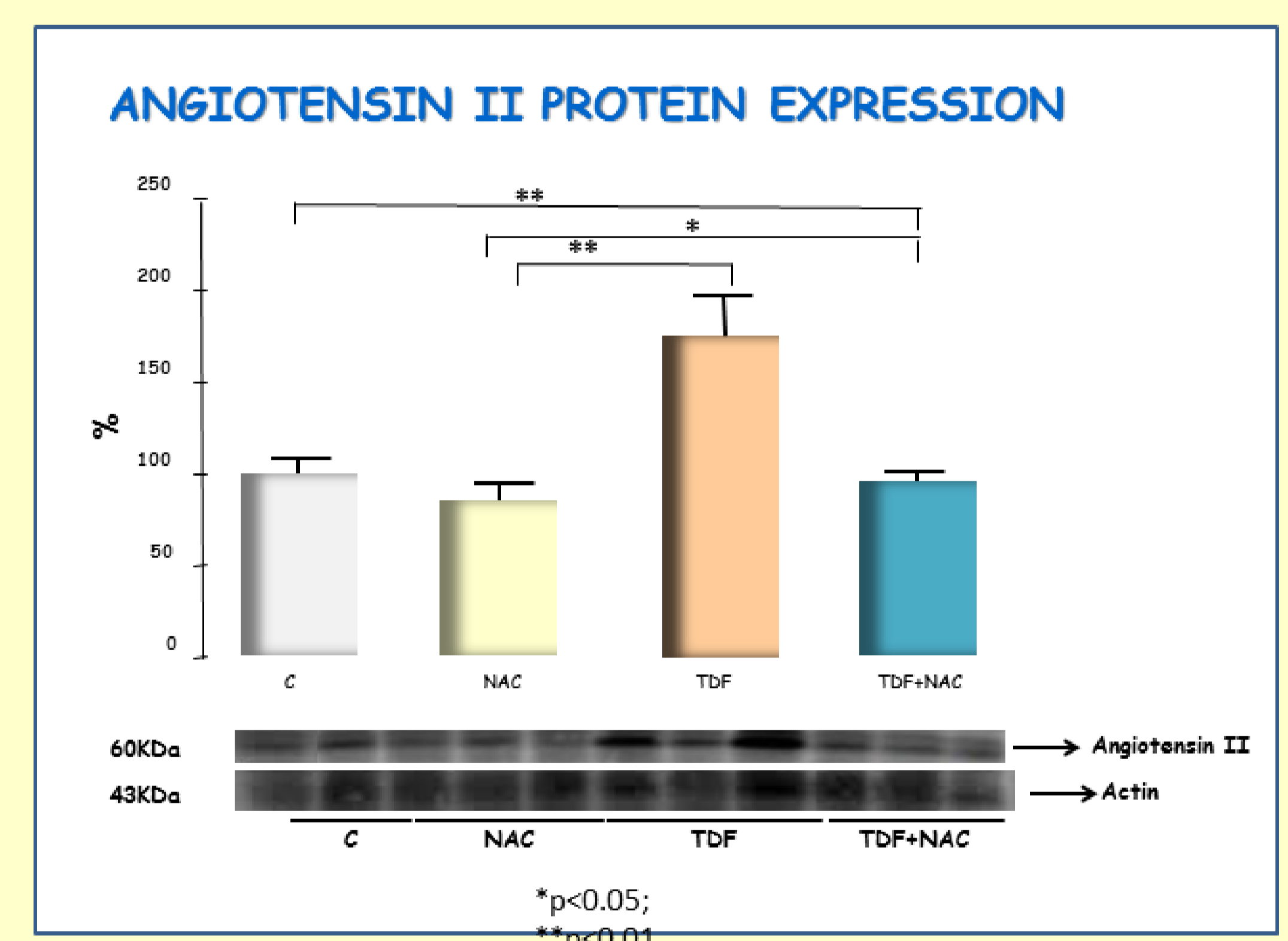
ARTERIAL BLOOD PRESSURE



RENAL VASCULAR RESISTANCE



ANGIOTENSIN II PROTEIN EXPRESSION



CONCLUSIONS

Chronic administration of Tenofovir leads to a decrease in glomerular filtration rate, increase in blood pressure, renal tissue angiotensin II and oxidative stress. NAC treatment has a protective effect attributable to lower levels of lipid peroxidation and higher levels of glutathione. These findings have significant clinical implications for renal protection against Tenofovir nephrotoxicity.

SUPPORTED BY FAPESP

