

RESVERATROL INHIBITS THE INTRACELLULAR CALCIUM INCREASE AND RAS/ENDOTHELIN SYSTEMS ACTIVATION INDUCED BY SOLUBLE URIC ACID IN MESANGIAL CELLS

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OBJECTIVES

The objective of this study was to evaluate the effect of RESV on the intracellular calcium increase and RAS/Endothelin activation induced by uric acid (UA) in immortalized human mesangial cells (ihMCs).

METHODS

The cells were pre incubated with RESV (12,5 μ M) for 1 h and then treated with UA (10mg/dL) for 6 and 12hr. Angiotensinogen (AGT) and Pre-pro ET (ppET-1) expression was evaluated by the PCR technique. Angiotensin II (All) and endothelin -1 (ET-1) protein synthesis were assessed by ELISA technique. Additionally, the level of $[Ca^{++}]_i$ was quantified by fluorescence with Fluo-4 AM by flow cytometry and expressed as fluorescence intensity (FI).

RESULTS

Figure 1. Effect of RESV in ihMCs treated with UA (10mg/dL) upon the level of $[Ca^{++}]_i$

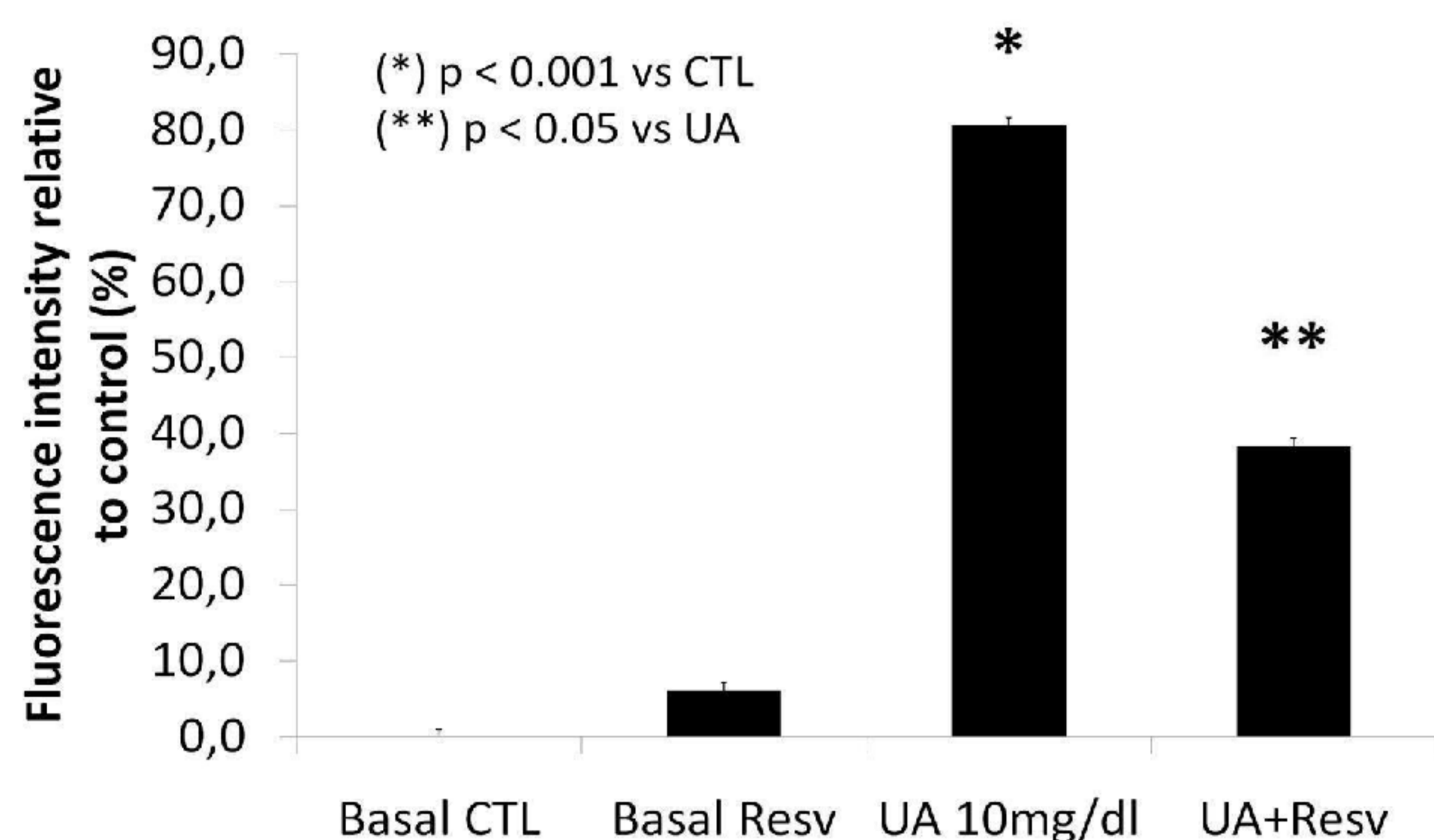


Figure 2. Effect of RESV in ihMCs treated with UA (10mg/dL) upon All production

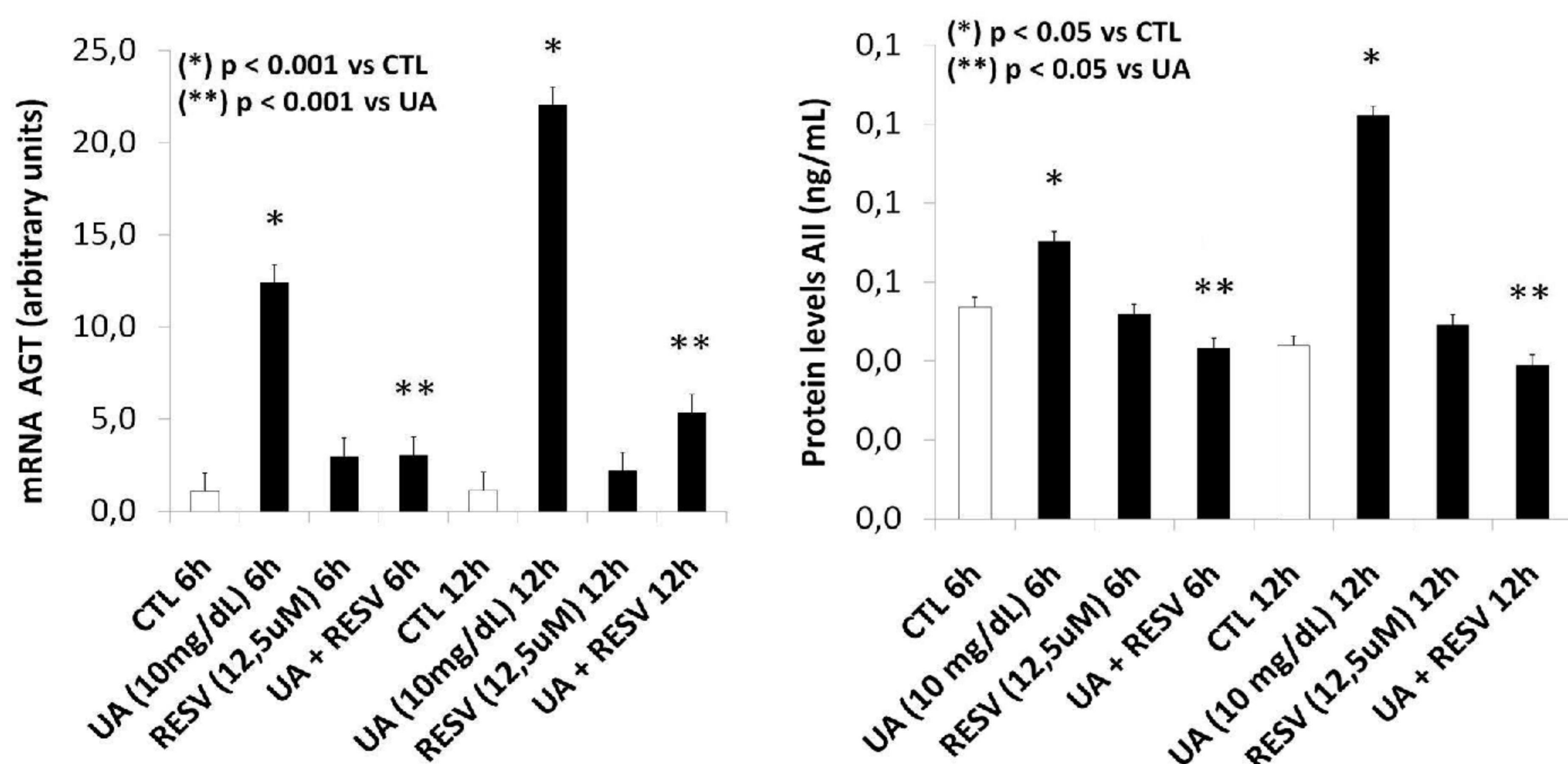
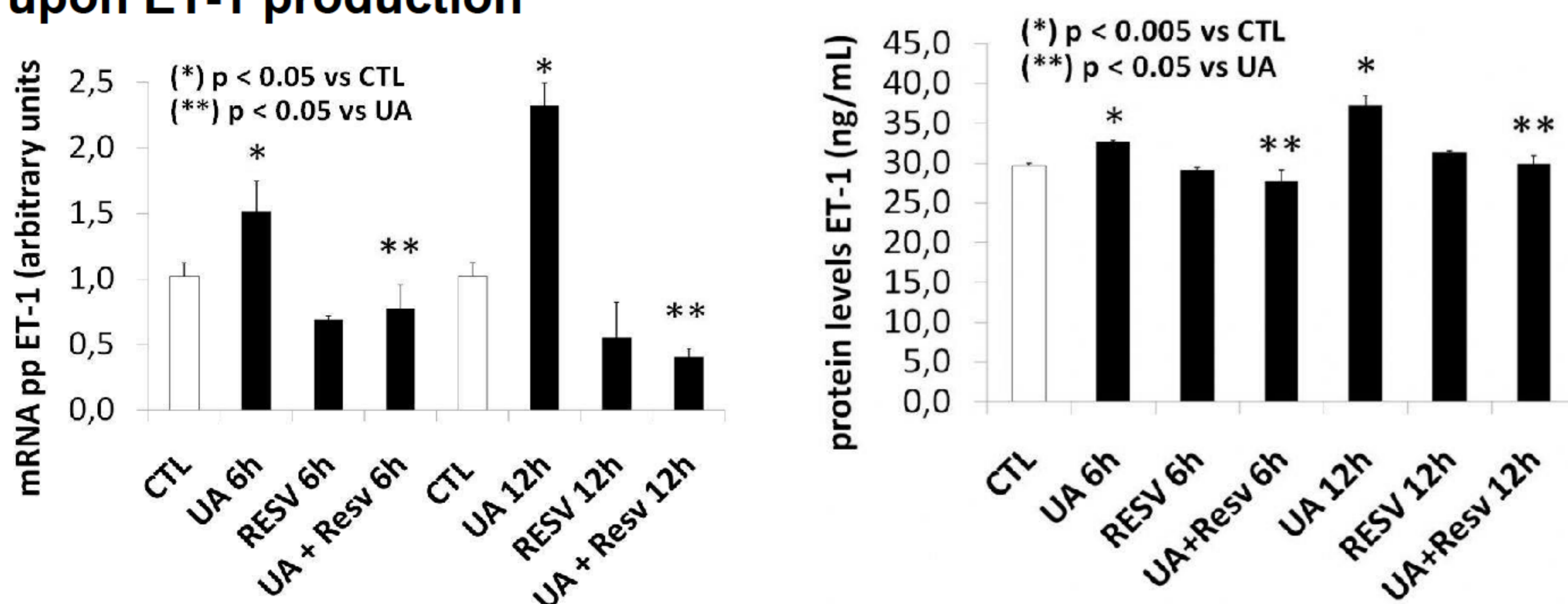


Figure 3. Effect of RESV in ihMCs treated with UA (10mg/dL) upon ET-1 production



UA significantly increased $[Ca^{++}]_i$ in 44% (8.14 ± 0.20 vs 5.65 ± 0.15 FI in the basal). The pre incubation with RESV significantly inhibited the increase in $[Ca^{++}]_i$ induced by UA (6.24 ± 0.01 vs 8.14 ± 0.20 FI in the UA). Figure 1. UA significantly increased AGT expression and All synthesis in comparison the control after 6 and 12h. When ihMCs were pre incubated with RESV, there was a significantly decrease in AGT expression and All synthesis in comparison the UA in both periods analyzed (Figure 2). Incubation of ihMCs with UA increased ppET-1 expression and ET-1 synthesis in comparison to control after 6h and 12h. When ihMCs were pre incubated with RESV, it was observed a significantly decrease in ppET-1 mRNA and ET-1 protein synthesis in comparison the UA (Figure 3).

CONCLUSIONS

Our findings constitute new evidence that the increased RAS associated with an increase in intracellular calcium could be minimized by use RESV preventing at least in part, for the glomerulosclerosis observed in hyperuricemia.

REFERENCES

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