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INTRODUCTION & AIM

Interstitial cystitis is a chronic inflammatory disease of the urinary bladder with no long-term effective treatment available to date.

The exact etiology and pathobiology of the disease remain unknown, however, **disturbed assembly of urothelial cell tight junctions, increased urine-blood barrier permeability, inflammation and oxidative stress** have been proposed to play crucial roles.

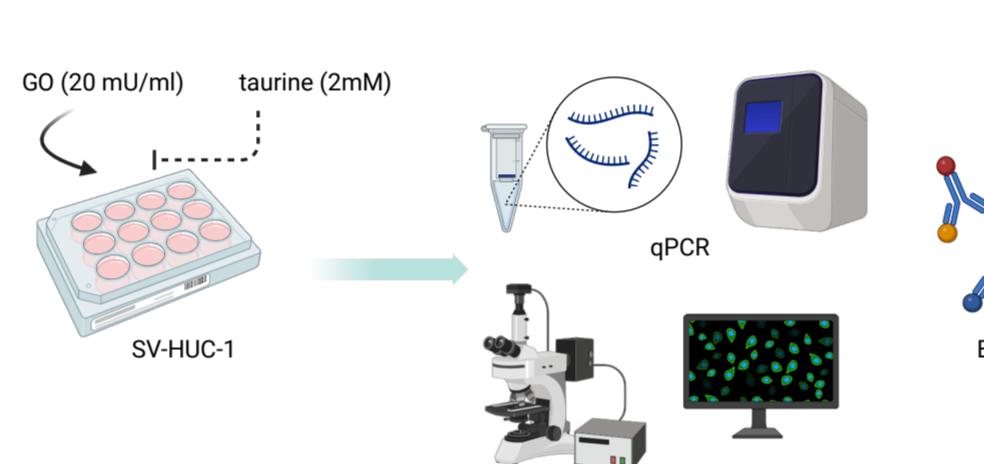
Agents that can simultaneously modulate all processes associated with interstitial cystitis will be of paramount importance for future therapy.

One such example is **taurine** (2-aminoethanesulfonic acid), the most abundant free amino acid in human. Taurine has already been shown to reduce inflammation as well as oxidative stress and improve integrity of various epithelial tissues.

Our aim was to look into the effects of taurine on inflammation, oxidative stress and blood-urine barrier function of urothelial cells in an *in vitro* model of interstitial cystitis.

METHODS

The *in vitro* model consisted of normal human urothelial cell line SV-HUC1, stimulated with glucose oxidase (GO; 20 mU/ml), which mimics prolonged low levels of oxidative stress. Cells were preincubated with taurine (2 mM) for 2h and then stimulated with/without GO for 24h. Untreated cells served as control. Cells were lysed for RNA isolation and subsequent qPCR analysis while protein levels were determined by ELISA and immunofluorescence (IF).

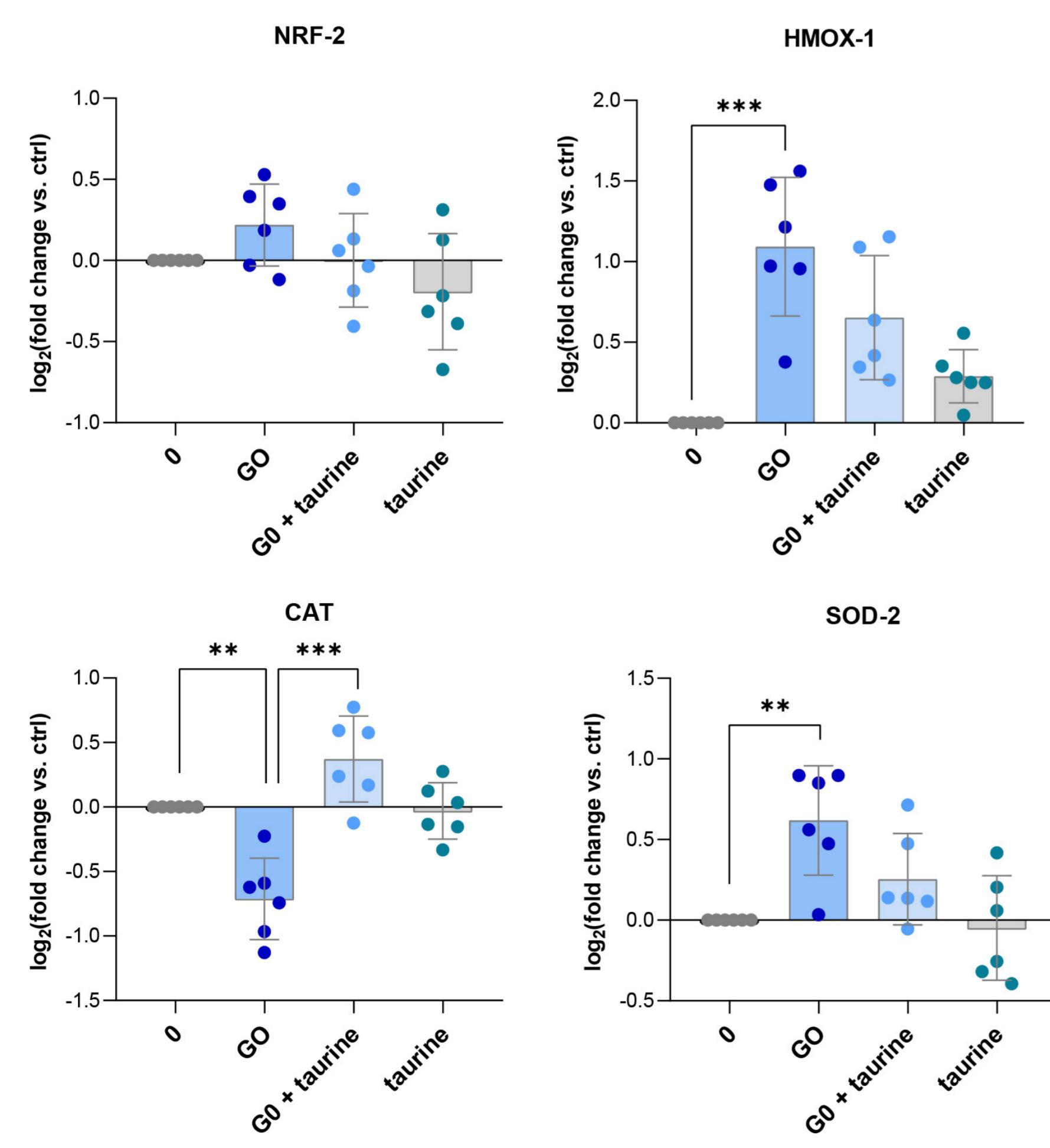


CONCLUSION

Our findings suggest that taurine has the potential to mitigate inflammation, oxidative stress as well as maintain the integrity of the urothelial barrier, all of which are implicated in the development and progression of interstitial cystitis.

Taurine upregulates catalase

Taurine upregulated the mRNA expression of the antioxidant enzyme catalase (CAT), downregulated by stimulation with GO. However, no influence of taurine on the expression of the redox sensitive transcription factor NRF-2 and the antioxidant enzymes SOD-2 and HMOX-1 were observed.



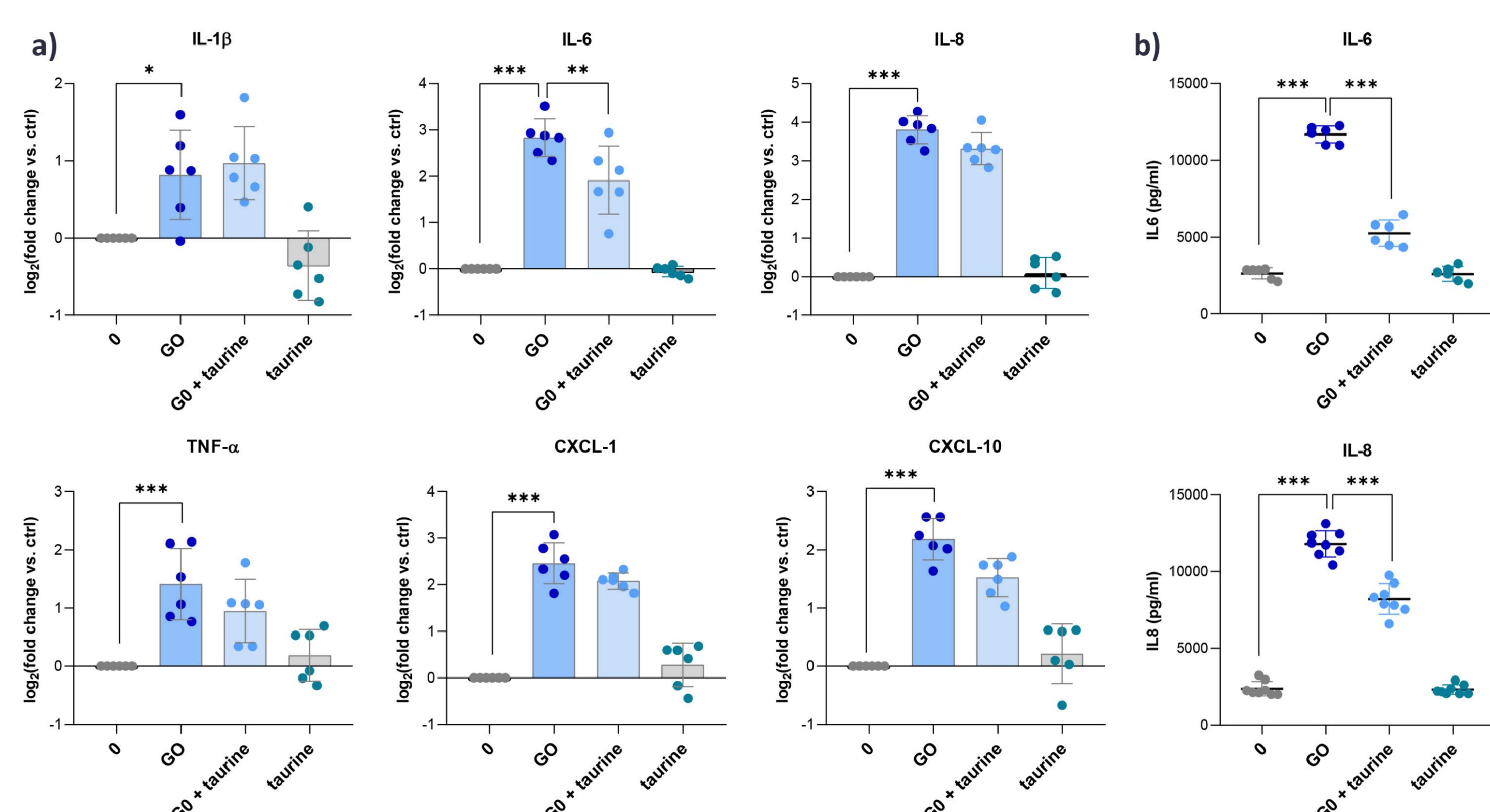
Effects of taurine on NRF2-activation pathway and antioxidant enzymes in GO-stimulated cells, determined by the qPCR method, normalized to the endogenous controls ACTB and GAPDH. Shown are means \pm SD for each group.

p<0.01; *p<0.001.

RESULTS

Taurine downregulates oxidative stress-induced inflammatory mediators

Taurine significantly downregulated the mRNA expression of the inflammatory cytokine IL-6, and the chemokines CXCL-1, and CXCL-10, which were upregulated by stimulation with GO. No significant effect of taurine was observed on the mRNA expression of IL-1 β and TNF- α . The protein levels of IL-6 and IL-8 released in the supernatants of urothelial cells incubated with taurine were also significantly lower compared to cells stimulated with GO.

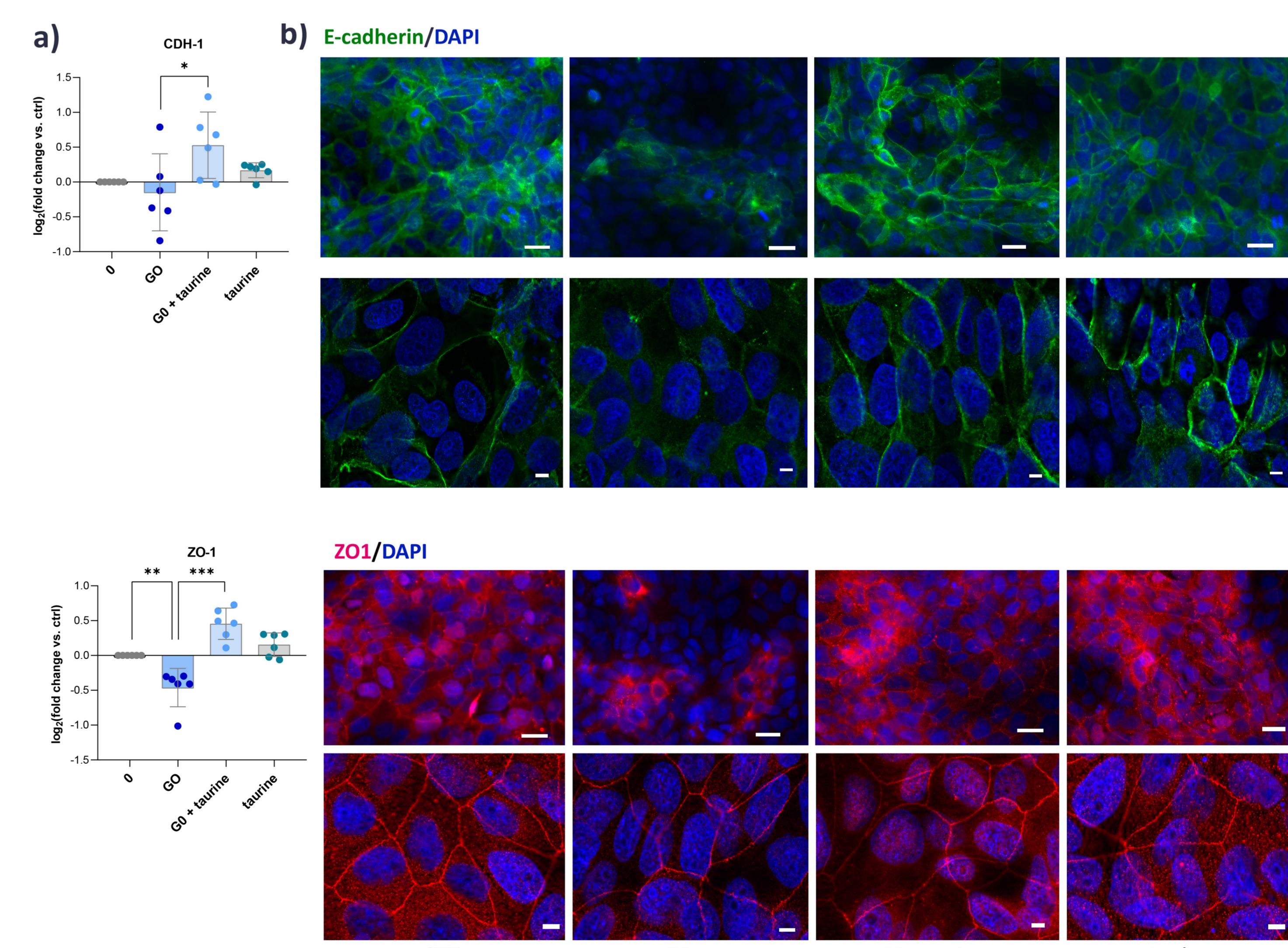


Effects of taurine on inflammatory mediators in GO-stimulated cells. a) mRNA expression of inflammatory cytokines and chemokines, obtained by the qPCR method, normalized to the endogenous controls ACTB and GAPDH. b) protein levels of IL-6 and IL-8, determined by ELISA. Shown are means \pm SD for each group.

*p<0.05; **p<0.01; ***p<0.001.

Taurine reverses the assembly of intercellular contacts disrupted by oxidative stress

Taurine significantly increased the mRNA expression of E-cadherin, encoding for adherent junction protein and zonula occludens-1 (ZO-1), encoding tight junction protein, which were downregulated in the presence of GO. This was subsequently confirmed also on protein levels showing altered assembly of adherens and tight junctions in the presence of GO, reversed by the addition of taurine.



Effects of taurine on intercellular junctions in GO-stimulated cells. a) mRNA expression of CDH-1 and ZO-1, obtained by the qPCR method, normalized to the endogenous controls ACTB and GAPDH. Shown are means \pm SD for each group. *p<0.05; **p<0.01; ***p<0.001. b) Representative images showing localization and distribution of E-cadherin (green) and ZO-1 (red). Nuclei are stained blue. Images were taken at the 20x and 63x magnification. Scale bars: 20 μ m and 5 μ m.