Histamine Receptors are Expressed in the Human Kidney

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Histamine is synthesized in mammalian glomeruli (Heald et al., 1976), increases second messenger levels in isolated glomeruli and influences renal hemodynamics, including microcirculation (Abboud, 1983; Sedor et al., 1984; Torres et al., 1978). The glomeruli has been demonstrated to express histamine H_1 receptors (H_1R) and H_2R in rats (Sedor et al., 1985). More recently, in our laboratory, the expression of the last discovered histamine receptor, H_4R, in the tubules of rat kidney and its overexpression in diabetic animals, have been reported (Rosa et al., 2013).

To characterize the functional role of the renal H_4R in humans, we investigated not only H_4R expression, but also the functional response to histamine agonism in human renal cells from different kidney regions and in specimens of healthy human cortex.

Three different human immortalized cell lines (podocytes, mesangial cells, a tubular epithelial cell line, iTEC), and a primary culture of human TEC (pTEC), isolated from kidney specimens of patients undergoing elective nephrectomy, were tested. Immunoblotting and RT-PCR analysis were carried out on cell cultures, and immunoistochemical detection was performed on human kidney specimens.

Histamine receptors resulted in being unevenly distributed among the different substrates. Mesangial cells and pTEC were positive for H_4R, while iTEC showed the expression of H_2R; H_1R was detected in all the cell types examined. These results were strengthened by second messenger assay, performed using LANCE® Ultra cAMP Kit. Histamine (1pM-1μM) increased cAMP accumulation in iTEC with a sigmoidal concentration-effect relationship (EC_{50} 21.6 nM). Differently, an inverse bell shaped concentration-response curve with the minimum at 3 nM was obtained in pTEC. In the mesangial cells, histamine caused a concentration-dependent reduction of cAMP accumulation with an EC_{50} at 15.8 pM.

In conclusion, pTEC and mesangial cells are suitable to evaluate the role of H_4R in the kidney. Finally, here we show a not yet reported distribution of the histamine receptor subtypes in the human kidney, that might exert different pathophysiological roles.

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