Abstract

Erythropoietin (EPO) is a 30.4 kDa glycoproteic hormone mainly produced by the fetal liver and the kidney in adults. EPO promotes the proliferation and differentiation of erythrocyte precursors, however several studies have shown also a possible protective role in neural, cardiac, renal and vascular functions, indicating erythropoietin as a good candidate in therapy of nervous, cardiac and renal diseases.

The kidney regulates the erythropoiesis through EPO production. The precise location of renal EPO production has been intensively debated. Studies performed on anemic mice submitted to severe hypoxia presented disparate results, but the most convincing suggest that peritubular interstitial and proximal tubular epithelial cells are the erythropoietin-producing sites.

The aim of this study was the identification of the EPO-producing cells in adult human kidney, not submitted to hypoxia. The study was performed on 55 human renal biopsies from individuals without anemia and with normal renal function. Erythropoietin gene expression was detected by in situ hybridization using specific probes for the human EPO gene. The results demonstrated that EPO was expressed by epithelial distal tubular cells and cortical collecting tubules, and in a few biopsies, was also expressed by glomerular and interstitial cells. These results suggest that, in the normoxic human kidney, erythropoietin is mainly produced by distal and cortical collecting tubules. Since control of the body volume is regulated by the renin-angiotensin system, and given that renin is produced by the juxtaglomerular cells, which are in contact with macula densa cells and part of the distal convoluted tubule, the identification of distal tubular cells as EPO-producing locates the erythropoietin production and volume control in the same nephron segment. This result opens new perspectives to the study of kidney physiology and pathophysiology.