Macula Densa Control of Renin Secretion

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Summary. Macula densa (MD) controls on renin secretion have recently been studied by examining the renin secretory response of the isolated perfused rabbit juxtaglomerular apparatus (JGA). Single JGAs, consisting of a segment of distal tubule including the macula densa, with adherent glomerulus and short vascular fragments, are dissected from rabbit kidney, and the tubule is perfused. Renin secretion from this preparation shows an inverse dependency on NaCl concentration in the tubular lumen. When perfused with a low NaCl solution, renin secretion is inhibited by addition of NaCl, choline Cl, and RbCl, but not by addition of Na acetate or Na isethionate. Renin secretion is stimulated by addition of $10^{-6}$M bumetanide to the tubular perfusate but not to the bathing solution. It is concluded that renin secretion is inversely related to the rate of tubular transport, and that the pattern of ion specificity is consistent with participation of the Na-K-2Cl co-transporter. Other studies examined possible stimulus-response coupling mechanisms. Renin secretion was found to be stimulated by the adenosine1 analog CHA (N6-cyclohexyladenosine), an effect that was blocked by the specific adenosine 1 blocker, CPX(8-cyclopentyl-1,3-dipropylxanthine). The inhibitory effect of a high luminal NaCl solution at the MD was markedly blunted in the presence of the A1 blocker CPX, but CPX did not significantly affect renin secretion when luminal NaCl was low, suggesting that adenosine formation is dependent upon luminal NaCl concentration, and supporting the hypothesis that variation in the local levels of adenosine may be at least partially responsible for macula densa signal transmission.

Introduction

The terminal end of the thick ascending limb of Henle, the site of the macula densa (MD), is a position uniquely suited for monitoring flow dependent changes of NaCl

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concentration. Along the proximal tubule, flow is not a major determinant of salt concentration. In more distal nephron segments, Na and Cl concentrations are largely determined by the actions of aldosterone and vasopressin. At the macula densa, however, NaCl concentration is primarily dictated by tubular flow rate. The transport properties of the thick ascending limb of Henle (TALH), and active NaCl transport by a water impermeable epithelium, result in the transformation of a flow signal into a change in salt concentration.

![Graph showing renin secretion rate under different NaCl conditions.](image-url)