CHARACTERIZATION OF VASOACTIVE INTESTINAL PEPTIDE RECEPTORS IN CANINE LIVER

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1. Vasoactive intestinal peptide (VIP) receptors in membranes from canine liver were studied using radioligand binding assays with [^{125}I]VIP, and the results were compared with those obtained in rat liver.
2. In canine liver membrane, the binding of VIP was specific, rapid, reversible, saturable, and dependent on time and temperature.
3. Guanine nucleotides increased the dissociation rate of the bound VIP and inhibited VIP binding in a dose-dependent manner. These data suggest that VIP receptors couple to G-proteins.
4. Scatchard analysis of competition binding experiments indicated the presence of two classes of VIP receptors with the following binding constants: canine liver, Kd=0.47 and 71.5 nM (corresponding Bmax=492 fmol/mg and 15.4 pmol/mg); rat liver, Kd=0.35 and 20.0 nM (corresponding Bmax=652 and 4,603 fmol/mg).
5. Various peptides with structural homology to VIP competed with the binding of [^{125}I] VIP. The rank order of competition potency was VIP>PACAP-27>PACAP-38>PHI>secretin in canine liver, and PACAP-27>PACAP-38>VIP>PHI>secretin in rat. With respect to PHI and secretin, appreciable differences were observed in competition potency between canine and rat liver.
6. In anesthetized dogs, the plasma VIP concentration was measured by radioimmunoassay. The VIP level in the hepatic vein was less than half of that in the portal vein, suggesting that liver VIP receptors may have a role in the removal of VIP from the circulation.
7. A canine liver cDNA library was screened under low stringency conditions using the nucleotide sequences of the rat lung VIP receptor. Six positive clones were isolated from 3×10^5 clones.
8. These results indicate that there are specific VIP receptors in canine liver, with high and low affinity binding sites. These receptors may act as clearance receptors. To determine the cause of species differences of VIP receptors between canine and rat liver, determination of the amino acid sequence of the canine VIP receptor is highly desirable.