NATRIURETIC PEPTIDE SYSTEM GOVERNS DIVERSE

OSMOTIC ADAPTABILITY OF EELS

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The Natriuretic Peptide System in Eels

Three natriuretic peptides (atrial, ventricular, and C-type NP; ANP, VNP and CNP), and four NP receptors (NPR-A, -B, -C and -D) have been identified in eels, *Anguilla japonica* (Fig. 1). NPR-A and -B are guanylyl cyclase-coupled receptors that utilize cGMP as an intracellular messenger to exert

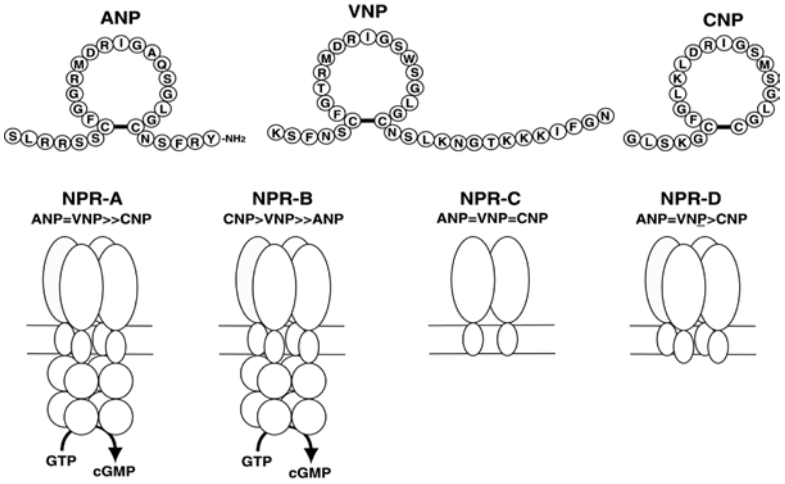


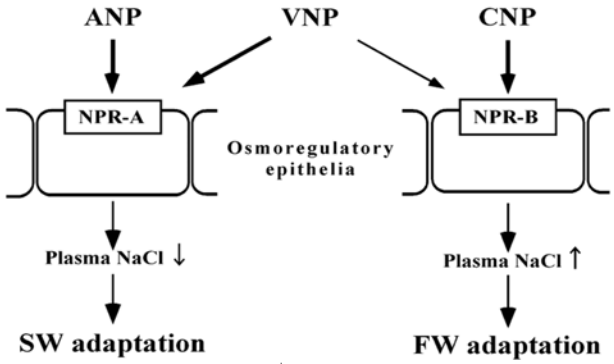
Figure 1. Natriuretic peptides and their receptors in eels.

biological actions. ANP and VNP have high affinity to NPR-A and CNP (and to a lesser extent, VNP) to NPR-B. The biological functions of NPR-C and NPR-D have not been fully elucidated. However, NPR-C may act as a buffer to regulate the peptide levels in plasma and at target tissues, since all three peptides bind NPR-C with equally high affinities and NPR-C is present in high densities in all tissues where NP effects have been demonstrated. NPR-D is expressed exclusively in the brain, thus indicating some biological function of guanylyl cyclase-deficient receptors

ANP Is a Seawater (SW)-Adapting Hormone

ANP is a volume-regulating hormone in mammals that is secreted in response to hypervolemia and itdecreases blood volume by stimulating the excretion of both water and NaCl (Fig. 2). In eels, however, ANP secretion is stimulated by hypernatremia and secreted ANP promotes SW adaptation by inhibiting the uptake and stimulating the extrusion of Na^+ ions specifically (Loretz and Pollina, 2001). The Na^+-specific effect in eels is supported by the fact that ANP infusion at physiological doses decreases urine flow but increases urine Na^+ concentration in SW eels (Takei and Kaiya, 1998). Actually, ANP is released upon transfer of eels to SW and released ANP inhibits drinking of environmental SW and subsequent intestinal absorption of NaCl from ingested SW. In this way, ANP

Figure 2. Interaction of natriuretic peptides for adaptation to diverse salinity



ameliorates a sudden increase in plasma Na^+ concentration and facilitates the survival of initial phase of SW adaptation. After the initial role, ANP disappears from blood quickly and participates in long-term adaptation to SW by stimulating cortisol secretion. Cortisol is known to differentiate branchial chloride cells to a SW type (McCormick, 1994).

CNP Is a freshwater (FW)-Adapting Hormone

CNP is a neuropeptide or a paracrine factor in peripheral tissues and is not involved in osmoregulation in mammals. In eels, however, CNP appears to be an important hormone for FW adaptation by stimulating the uptake of NaCl from media (Fig. 2). Supportive evidence is that considerable amounts of CNP is circulation in the plasma of FW eels, and that CNP-specific NPR-B is expressed abundantly in osmoregulatory organs of FW eels (Takei et al., 2001). In fact, infusion of CNP into FW eels increases plasma Na^+ concentration and increases ^{22}Na uptake from environmental water (J.C. Rankin and Y. Takei, unpublished data). This is opposite to the decrease of plasma Na^+ concentration observed after ANP infusion into SW eels (Fig. 2).

Natriuretic Peptide System and Euryhalinity

Eels are euryhaline, migratory species that readily adapt to both FW and SW environments. Judging from the data mentioned above, ANP and CNP are important for eel's excellent ability to adapt to diverse salinity environments. VNP is secreted constitutively into the circulation and its plasma concentration is relatively constant. Therefore, VNP may supplement the action of ANP and CNP for adaptation to SW and FW, respectively, as VNP has high affinity to both NPR-A and NPR-B (Fig. 2). Taken together, the natriuretic peptide system appears to play pivotal roles in diverse osmotic adaptability (euryhalinity) of eels (Takei and Hirose, 2002). It is somewhat surprising that the peptides in the same family that share more than 60% sequence identity act to promote adaptation to opposite environmental salinity.

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