Occasionally, an issue of Physiology will focus on a subdiscipline of physiology. This issue, which broadly focuses on the kidney, is such an example.

The first of the two Emerging Topics—by Komlosi, Fintha, and Bell—addresses the mechanism of tubuloglomerular feedback (TGF). TGF is an intrinsic renal mechanism that stabilizes glomerular filtration rate (GFR) at the single-nephron level. An increase in GFR will increase the flow of tubule fluid past the macula densa cells at the end of the thick ascending limb. This augmented NaCl delivery triggers a classical feedback mechanism that ultimately constricts the afferent arteriole and reduces GFR. Komlosi and colleagues discuss new insights into role of ATP and adenosine as paracrine mediators between macula densa cells and the afferent arteriole.

The second Emerging Topic—by Fleming, Kohlstedt, and Busse—examines the possibility that angiotensin converting enzyme (ACE), in addition to its classical vasoconstrictor role, may modulate intracellular signaling pathways. The mechanism may involve the ability of the cytoplasmic carboxy terminus of ACE to anchor several protein kinases. The authors also draw attention to the emerging role of ACE2, the carboxypeptidase activity of which leads to the formation of angiotensin 1-7. ACE2 anchors several protein kinases. The cytoplasmic carboxy terminus of ACE is likely to play important roles in all of these processes. Most of the channel information is based on work using patch-clamp studies of cultured MCs. Clarifying the physiological roles of these channels will require extending the studies to in vivo conditions.

Moving along the nephron, the article by Palacin and colleagues reviews recent developments in the physiology and pathophysiology of the heteromeric amino acid transporters (HATs). These proteins are unusual in that they are made up of two subunits, a “heavy” subunit from the SLC3 family and a “light” subunit from the SLC7 family of transport proteins. Genetic defects in these transporters can give rise to defects in the reabsorption of amino acids in the proximal tubule, as well as the absorption of amino acids in the small intestine. Examples include cystinuria and Hartnup disease.

Still in the proximal tubule, the review by Hediger, Johnson, Miyazaki, and Endou examines the molecular mechanisms of ureate transport. Deranged ureate metabolism can lead to gout and uric acid kidney stones. The interpretation of earlier work had been difficult both because of the intrinsic complexity of the transport events (e.g., simultaneous secretion and absorption) and marked species differences. Some clarification has now been provided by the identification of three transporters—URAT1, OAT1, and OAT3—that are members of the SLC22 family. The fourth, MRP4, is a member of the ABC transporter family that also transports cAMP and cGMP.

The final two reviews in this issue deal with the control of electrolyte transport in the distal nephron. The first—by McCormick, Bhatta, Poo, and Pearce—considers the role of serum- and glucocorticoid-regulated kinase 1 (SGK1) in mediating the action of aldosterone in stimulating transepithelial Na+ transport. Evidence from heterologous expression studies in cultured cells, as well as sgk1-knockout mice, suggests that aldosterone stimulates the synthesis of sgk1, which in turn phosphorylates the Nedd4-2 ubiquitin ligase. The phosphorylation interferes with the ability of the ligase to interact with the apical epithelial Na+ channel (ENaC), leading to the accumulation of the channel in the apical membrane. Thus, when challenged by Na+ restriction, the sgk1-knockout mouse is less able to conserve Na+.

In contrast to the previous review, which considers how Na+ depletion leads to a rise in Na+ reabsorption, the final article in this issue—by Lim, Sterling, and Wang—investigates how dietary K+ restriction inhibits the secretion of K+. Recent evidence suggests that principal cells sense diminished K+ intake and translate this signal into a stimulation of the Src protein tyrosine kinase. The subsequent phosphorylation of the main secretory K+ channel (ROMK) enhances the internalization of ROMK from the apical membrane, thereby reducing K+ secretion.

Although the subjects addressed in this issue of Physiology are of special importance for renal physiologists, each article has relevance for areas beyond the kidney. Whether you are a specialist looking for a critical review of the latest advances or a generalist taking a quick glance at what is new in renal physiology, we hope that you enjoy our April issue.