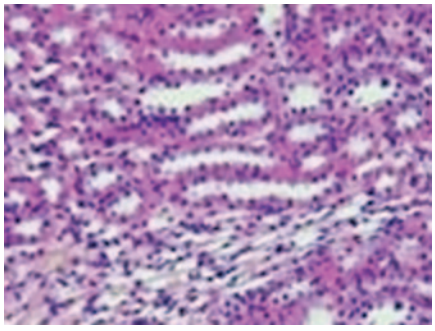
Kidney International (2012) **82**, 615. doi:10.1038/ki.2012.310

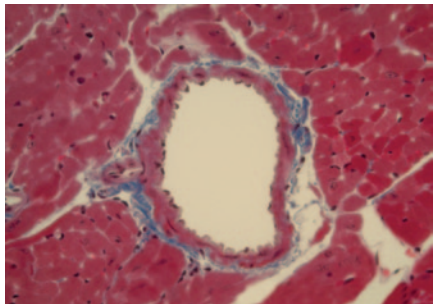
Cilastatin protects against cisplatin-induced nephrotoxicity without compromising its anticancer efficiency in rats



Cisplatin is a chemotherapeutic medication with strong activity against many solid malignancies; however, its use is often limited by acute kidney injury (AKI). Although numerous studies have examined the mechanism of cisplatin-induced AKI, there are no effective options to prevent or treat this complication. Humanes and co-workers demonstrate that cilastatin, a small-molecule inhibitor of renal dehydropeptidase I, prevents cisplatin-induced AKI in rats. Cilastatin prevented cisplatin-induced decline in glomerular filtration rate, renal histologic injury, tubular-cell apoptosis, and renal oxidative stress. Crucially, cilastatin exerted these protective effects without decreasing systemic cisplatin levels or inhibiting cisplatin-induced death of cancer cells, raising the exciting possibility that cilastatin may protect patients from cisplatin-induced AKI without reducing its efficacy. **See page 652.**

Aldosterone signaling mediates Ang II toxicity

Angiotensin II (Ang II) antagonists are protective in many types of kidney disease, and these effects are mediated, in part, via reduced aldosterone receptor signaling. As they report in this issue, Luther *et al.* studied whether endogenous aldosterone synthesis is necessary for Ang II-induced renal injury. Aldosterone synthase knockout and normal mice were subjected to Ang II infusion and high-salt diet with or without aldosterone receptor blockade with spironolactone. The investigators found that aldosterone synthase knockout mice had reduced blood pressure and renal, cardiac, and vascular injury and that injury was further reduced by the addition of spironolactone.



This important study demonstrates that aldosterone receptor antagonism protects against Ang II–mediated injury via aldosterone synthase–dependent and independent pathways. **See page 643.**

The serum anion gap is altered in early kidney disease and associates with mortality

Elevated serum anion gap (AG) is known to occur in advanced kidney disease, but the prevalence of elevated AG in earlier stages of chronic kidney disease (CKD) is unknown. Abramowitz and colleagues analyzed data from National Health and Nutrition Examination Survey 1999–2004 (NHANES) to determine the prevalence of AG elevations using three different formulas in patients with estimated glomerular filtration rate (eGFR) values greater than 15 ml/min/1.73 m^2. They report that the traditional AG formula only identified elevated AG in patients with eGFR less than 45 ml/min/1.73 m^2, whereas the albumin-adjusted and fully adjusted (potassium, calcium, albumin, and phosphate) formulas identified elevated AG at much higher levels of eGFR. Importantly, patients with elevated albumin-adjusted and fully adjusted AG—including those with early-stage CKD—had higher mortality than those with normal AG. **See page 701.**