Lessons from analysis of a single urinary biomarker, Ngal

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To obtain new insights into understanding of physiology and pathophysiology of the kidney and renal disorders, we have identified and analyzed a novel urinary biomarker, neutrophil gelatinase-associated lipocalin (Ngal or LCN2). Our candidate molecule approach may be opposite but should be complimentary to proteomic approach.

In renal ischemia–reperfusion injury of mice, Ngal mRNA expression was elevated by 1,000-fold at 36 h after reperfusion. Analysis of the contra-lateral control kidney at 24 h after unilateral ureteral obstruction revealed that increased protein expression of Ngal does not necessarily reflect enhanced protein synthesis of Ngal in the kidney. In diabetic mice, marked increase in urinary Ngal excretion was mainly caused by impaired reabsorption of Ngal derived from circulation.

By also reviewing the findings reported for other urinary biomarkers, we would like to propose 3 major mechanisms for the appearance of biomarkers in the urine: (1) increased renal synthesis and direct excretion, or indirect excretion after systemic circulation and glomerular filtration; (2) impaired reabsorption of circulating proteins at proximal tubules caused by direct stress upon tubules, or by protein overload due to glomerular injury; (3) luminal exocytosis, or release of protein or cellular fragments into urinary space.

In acute kidney injury following cardiopulmonary bypass surgery, urinary Ngal levels may be peaked immediately after surgery and 24 h later. This multi-phasic nature of urinary biomarkers during the course of kidney injury should make it very difficult to interpret data from biomarker panel and proteome analysis.

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