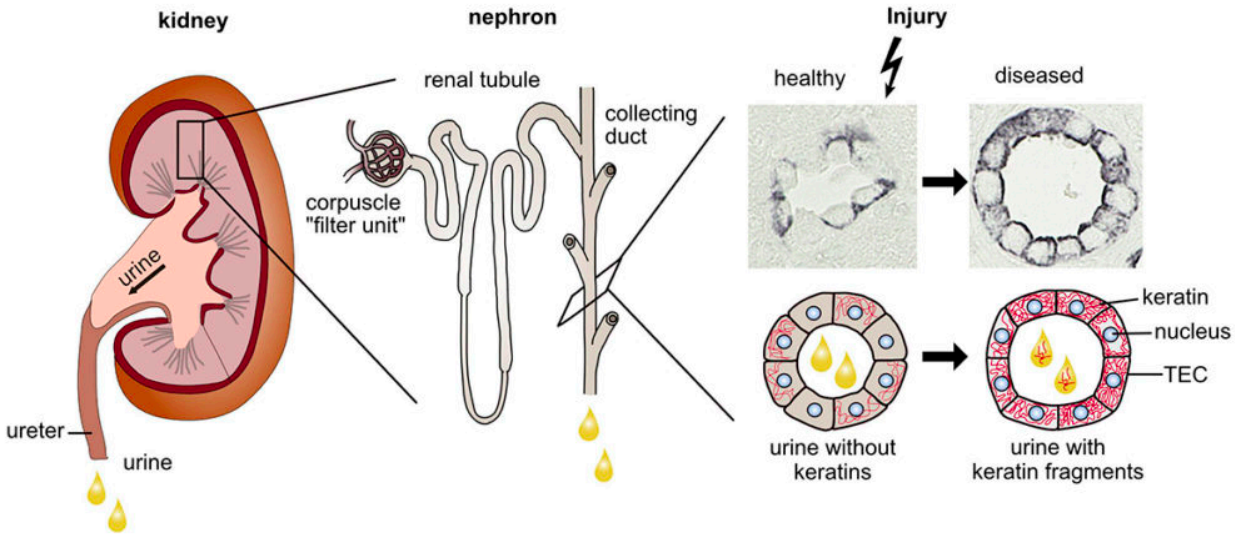
New way to detect kidney injury using keratins

As humans and animals have a skeleton supporting their structure, each cell has a similar microscopic skeleton termed cytoskeleton. Cytoskeleton also helps to maintain the shape and the internal organization of cells and is also involved in cell division and movement. Compared to the stable skeleton, the cytoskeleton is a dynamic structure, made of long (filamentous) molecules (proteins) which are divided into three major classes based on their size and composition. The largest are called microtubules with a diameter of about 25 nanometers formed by proteins called tubulin, the smallest are termed actin filaments with a diameter of only about 6 nanometers made of protein called actin, and the intermediate in size, i.e. about 10 nanometers in diameter, are called intermediate filaments, and are formed by several proteins including the keratins. All cells have intermediate filaments, but the specific proteins depend on the specific cell type. Keratins are found in epithelial cells, i.e. cells lining the cavities and surfaces of organs throughout the body, such as the skin, gut but also the kidneys.



The kidney consists of small unit, termed nephrons, that are responsible for the main kidney function, blood filtration. Nephron consists of a filter component (renal corpuscle) and a renal tubule. In the corpuscule, the fluid part of blood is completely filtered. The renal tubule is responsible for reabsorption of all necessary components, including water and minerals. At the end of the nephron, the final urine flows out of the kidney in the ureter. Keratins are a component of the cell cytoskeleton of tubular epithelial cells (TEC). After injury of tubular epithelial cells, the amount of keratins increases and they are also found in the urine. Detection of keratins could be used as a novel way to detect kidney diseases with tubular injury.

Kidneys filter the blood to remove waste products of metabolism and excess of water and also regulate blood pressure and produces hormones important for formation of blood cells. All these functions are lost in diseased and failing kidneys and would result in death if these functions would not be corrected. Kidney diseases affect a huge number of people around the world, e.g. the so called chronic kidney disease affect around 10% of the worldwide population. Epithelial cells of the kidney, in particular the so called tubular cells (TEC), are essential for the normal function of the kidneys. Tubular cells are exposed to a number of stress situations in various kidney diseases.

In the presented work we could show, that during various diseases, the keratins, and thereby the cytoskeleton of tubular cells, undergoes prominent changes. These include a different localization within a cell, modification e.g. by so called phosphorylation, and an increase in their production. Importantly, as injured or dying tubular cells might fall into the urine, we found that during injury, increased amount of keratins are found also in the urine. This could be exploited as a new way to detect kidney diseases, specifically characterized by injury to tubular cells. We have confirmed these results in several murine models of kidney diseases but also in renal tissue and urine from patients with kidney diseases. We also found that the increase in keratins is found already very early during the diseases course. Taken together, keratins could provide a new and early way to detect kidney diseases with tubular cell injury and help us to combat kidney diseases.

Sonja Djudjaj *and* ***Peter Boor***
Institute of Pathology, University hospital RWTH Aachen, Germany

Publication

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