

# Laser ablation-inductively coupled plasma-mass spectrometry 2D elemental bioimaging of cisplatin-induced nephrotoxic side effects

Thibaut Van Acker<sup>1</sup>, Stijn J.M. Van Malderen<sup>1</sup>, Marjolein Van Heerden<sup>2</sup>, Filip Cuyckens<sup>2</sup> and Frank Vanhaecke<sup>1\*</sup>

<sup>1</sup>Department of Analytical Chemistry, Ghent University, Krijgslaan 281 - S12, 9000 Ghent, Belgium

<sup>2</sup>Preclinical Development and Safety, Janssen Research and Development, Turnhoutseweg 30, 2340, Beerse, Belgium

\*Corresponding author. E-mail: Frank.Vanhaecke@UGent.be

Cisplatin is a chemotherapeutic drug, which is used predominantly to treat ovarian, colorectal, cervical and testicular cancer due to its ability to induce DNA crosslinks, resulting into potential cell damage.<sup>1</sup> Unfortunately, cisplatin administration can lead to severe side effects, such as nephrotoxicity, neurotoxicity, vomiting and ototoxicity.<sup>1</sup> Blood filtration and cisplatin excretion occurs inside the kidneys, but due to partial cisplatin reabsorption in epithelial cells of tubular segments, especially Proximal and Distal Convoluted Tubules (PCTs and DCTs), accumulation can take place, causing tubular damage.<sup>1</sup> This research focusses on nephrotoxic side effects in *Cynomolgus* monkeys, treated with different doses of cisplatin. Therefore, adjacent 5  $\mu\text{m}$  thin slices of Formalin-Fixed Paraffin-Embedded (FFPE) kidney tissue were stained with Haematoxylin and Eosin (H&E) and left unstained, enabling the combination of histopathological examination with the cisplatin distribution obtained by monitoring and mapping the Pt distribution using Laser Ablation-Inductively Coupled Plasma-Mass Spectrometry (LA-ICP-MS). Figure 1 shows that epithelial cells of PCTs and DCTs contain cisplatin and tubular lumens contain very low concentrations. The cortical region with tubular necrosis is positively linked to cisplatin accumulation according to the highest Pt signals. This work clearly shows the benefits of LA-ICP-MS by revealing patterns of cisplatin distributions on a cellular level.

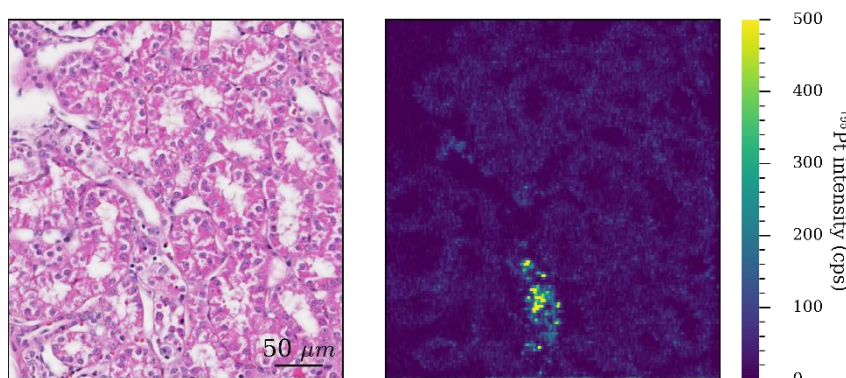


Figure 1. Image of a cortical region with tubular necrosis on a H&E stained kidney section (left) and corresponding 3  $\mu\text{m}$  spatial resolution Pt distribution map (right).

1. Yao, X., Panichpisal, K., Kurtzman, N. & Nugent, K. Cisplatin nephrotoxicity: a review. *Am. J. Med. Sci.* **334**, 115–124 (2007).