⮕ DIAGNOSIS

Making DESI-MSI desirable

A new analysis method based on desorption electrospray ionization mass spectrometric imaging (DESI–MSI) of small metabolites and lipids might be an accurate and rapid method to identify prostate cancer cells and delineate surgical margins during prostatectomy, according to a report in *PNAS*.

DESI–MSI is a label-free, nondestructive imaging technique that enables *in situ* evaluation of a tissue metabolome. Molecules on the tissue surface are dissolved by a stream of charged microdroplets, which subsequently enter a high-resolution mass spectrometer for identification. A movable stage enables mapping and quantification of compounds present in the tissue surface with a resolution of ~200 μm. "Our group has used DESI–MSI before to distinguish between cancerous and normal tissue; for example, for the assessment of surgical margins of gastric cancers," comments corresponding author Richard N. Zare from Stanford University, California, USA. "The present work was a natural extension of what we had done before, inspired by discussion with urologists at the Stanford School of Medicine, who are coauthors of this paper."

The team tested the method in freshly frozen prostatectomy samples, mostly detecting small metabolites and glucose in the 50–200 m/z range and lipids in the 200–1,000 m/z range. The detected species included compounds in the Krebs cycle, as well as phosphatidic and free fatty acids, and glycerophospholipids. Following previous findings, they then tried to use lipidomic profiles to distinguish normal from malignant tissues, but found high cross-validation errors in training and validation data sets. However, in the 50–200 m/z range, the researchers had detected a large number of compounds that were differentially present in malignant and normal tissue. When including these compounds and developing a classifier based on the signal ratios of different species to estimate the probability that a specific DESI–MSI image pixel was malignant or normal their method had ~90% overall agreement with standard histopathological evaluation.

Low levels of citrate have previously been described in prostate cancer tissue. Hence, to speed up analysis while preserving accuracy, the researchers evaluated using the glucose:citrate signal ratio to identify cancer tissue. They found a distinct increase in the ratio at the border between normal and malignant prostate tissues, predominantly owing to a substantial drop in citrate levels in malignant areas, and could accurately classify areas by glucose:citrate signal ratios >1 and <0.5 for malignant and normal tissue, respectively.

"These findings could greatly aid surgeons in assessing cancer margins based on molecular information rather than tissue morphology; assessment takes ~1 minute with little to no sample preparation," concludes Zare. "We are keen to investigate whether we can distinguish Gleason grades, and indolent and aggressive cancers in biopsy samples. My goal is to make this method the 'standard operating procedure' in the future."

Clemens Thoma

ORIGINAL ARTICLE Banerjee, S. *et al*. Diagnosis of prostate cancer by desorption electrospray ionization mass spectrometric imaging of small metabolites and lipids. *Proc. Natl Acad. Sci. USA* http://dx.doi.org/ 10.1073/ pnas.1700677114 (2017)