BIOMARKERS

Taking out the trash

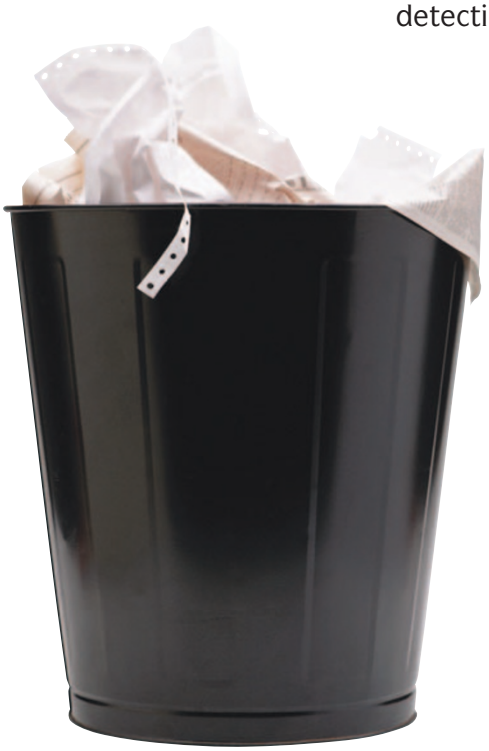
Despite years of intensive analysis, only a small number of plasma proteins have been validated as cancer biomarkers, such as prostate-specific antigen and cancer antigen 125. Now, Josep Villanueva and colleagues show that peptides in the serum of cancer patients that are generated as a result of tumour protease activity can be used for the detection and classification of cancer.

Many researchers have considered the thousands of proteolytically derived peptides — products that are the result of the high levels of active proteases that tumours produce — to be 'biological trash'. However, Villanueva *et al.* have developed a mass-spectrometry approach to identify tumour-specific peptidome patterns in serum samples. Although researchers have previously attempted similar approaches, their studies were not adequately validated. These authors set out with the goal of developing a mass-spectrometry-based system of serum analysis that could be reproduced in independent samples.

Villanueva *et al.* used an automated procedure for the simultaneous measurement of peptides in serum that used magnetic reverse-phase beads for analyte capture and matrix-assisted laser-desorption/ionization time-of-flight (MALDI-TOF) mass-spectrometry read-out — a more sensitive type of analysis than other mass-spectrometry-based approaches. To fully interpret their results, they developed a minimal-entropy-based algorithm that simplifies and improves statistical analysis of the data.

Using this system, the authors profiled 106 serum samples from patients with advanced prostate cancer, bladder cancer or breast cancer. On the basis of an analysis of 61 signature peptides, all of which were breakdown products, the authors were able to identify specific proteolytic patterns that were not only cancer-specific, but also cancer-type-specific. They then demonstrated that this signature could be used to discriminate between patients with advanced prostate cancer and control subjects in an independent validation set of serum samples.

> “the proteolytic degradation patterns in the serum peptidome might not only be used in cancer detection”



The authors propose that the proteolytic degradation patterns in the serum peptidome might not only be used in cancer detection, but also to distinguish indolent from aggressive tumours. Such tests are urgently needed to identify men with prostate tumours who might safely avoid surgery or radiation therapy. The findings also indicate that proteomic analysis should not involve inhibition of proteolysis in *ex vivo* samples, which could limit biomarker discovery.

Kristine Novak

ORIGINAL RESEARCH PAPER Villanueva, J. *et al.* Differential exoprotease activities confer tumour-specific serum peptidome patterns. *J. Clin. Invest.* **116**, 271–283 (2006)
FURTHER READING Coombes, K. R. *et al.* Serum proteomics profiling — a young technology begins to mature. *Nature Biotechnol.* **23**, 291–292 (2005)