

# Researchers isolate novel urinary biomarkers that may indicate adrenal cancer

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A global analysis of metabolites and small molecules in urine samples from patients with adrenal cancer has identified four biochemicals that, when measured together, can distinguish malignant from benign adrenal tumors, according to study results presented at the 2015 Annual Clinical Congress of the American College of Surgeons.

Findings from the study may help surgeons more confidently decide how to treat [patients](#) who have signs of adrenal masses on radiologic imaging but no symptoms of adrenal disease. Such patients are considered to have adrenal incidentalomas. Adrenal incidentalomas are the most common type of abnormality discovered on imaging studies that are performed for conditions unrelated to the [adrenal gland](#). The abnormalities are found in about 3 percent of people older than 50 years of age and about 4 percent of all computed tomography scans performed in the general population.<sup>1</sup>

Most adrenal incidentalomas can be managed conservatively because they are small and do not affect the release of hormones from the gland. However, about 5 percent of these lesions require prompt surgery because they are suspected to be cancerous. The 2009 guidelines of the American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons (AACE/AAES) on the management of adrenal incidentalomas recommend surgical removal of the adrenal gland when a lesion is 4 cm or larger in diameter or it exhibits radiologic characteristics suggestive of cancer, such as traces of calcium.<sup>2</sup>

These clinical signs are not definitively associated with cancer. Rather, they indicate the patient has an increased risk of an adrenal malignancy. "Up until now, there have been no metabolomic markers to tell us whether an adrenal lesion is cancerous or not," said Dhaval Patel, MD, a staff clinician at the National Institutes of Health,

Bethesda, Md.

Dr. Patel's team conducted a study to determine if a noninvasive urinary test could help diagnose [adrenal cancer](#) by detecting differences in [small molecules](#) in the body. Small molecules include genes, proteins, and end products of metabolism. This is believed to be the first study to focus on small molecules associated with this disease. "Researchers have done metabolic studies in patients with adrenal cancer, but they have looked at larger molecules, and they have targeted their investigations at specific steroids or gene profiles. This is the first untargeted, global look at all [metabolites](#) and molecules smaller than 800 Dalton," he said.<sup>3</sup>

The researchers obtained urine specimens from 19 patients with adrenal cortical carcinoma and 46 patients with benign adrenal tumors and ran a global analysis of all metabolites to detect differences in the two groups. A total of 67 biochemical features discriminated cancer from benign tumors in these samples, but only four specific metabolites could be considered as biomarkers for cancer: creatinine riboside, tryptophan, N?, N?, N?-trimethyllysine, and 3-methylhistidine. When these metabolites were present in characteristic patterns in [urine samples](#), they were highly sensitive and specific for carcinoma.

The metabolites could successfully identify cancer in 94.7 percent of cases and rule out the disease 82.6 percent of the time. In comparison, adrenal lesions greater than 4 cm in diameter have a sensitivity of 93 percent and a specificity of only 42 percent for cancer.<sup>4</sup>

The NIH study also found that the four metabolites had a high likelihood of predicting which patients had [cancer](#) and which did not. The positive predictive rate was 69.2, and the negative predictive rate was 97.4.

The researchers are obtaining more urine samples as well as serum to validate the results of this study. Down the line, they hope their investigations will lead surgeons to use global small molecule urinalysis as an adjunct to the standard radiologic workup of patients with incidental adrenalomas.

"When surgeons see changes in these metabolites, they may be more likely to lean toward surgery for patients with adrenal incidentalomas because the likelihood of malignancy will be much higher," Dr. Patel said.

**More information:** 1. Prashanth Kanagarajah et al. Current concepts in the management of adrenal incidentalomas. *Urol Ann*, 2012 Sep-Dec; 4(3): 137-144.

2. AACE/AAES Adrenal Incidentaloma Guidelines, *Endocr Pract*, 2009; 15(Suppl 1) 3.

3. A Dalton is a unit of atomic mass.

4. Anil Kapoor et al. Guidelines for the management of the incidentally discovered adrenal mass, *Can Urol Assoc J*, 2011 Aug; 5(4): 241-7.

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