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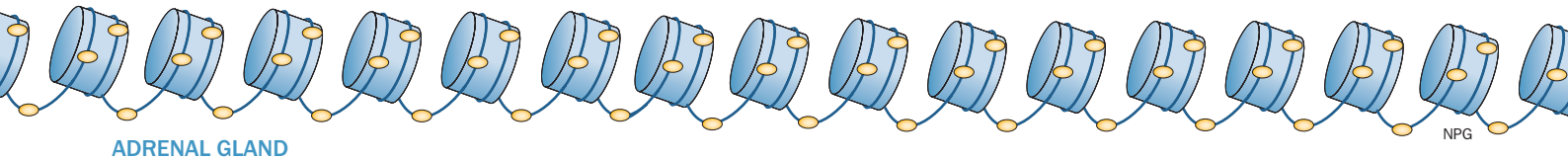

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ADRENAL GLAND

DNA methylation profiling—a new tool for adrenal tumour diagnosis?

DNA methylation profiling of adrenocortical tissue can be used to distinguish between benign and malignant adrenocortical tumours, according to results of a study published in the *Journal of Clinical Endocrinology & Metabolism*. "Methylation patterns were distinctly different and could distinguish normal, benign, primary malignant and metastatic adrenocortical tissue samples," says senior investigator Electron Kebebew of the National Cancer Institute, Bethesda, Maryland, USA.

Adrenocortical carcinomas are rare, having an annual incidence of 0.5–2 cases per million individuals. However, survival is very low, with only 15–45% of patients living 5 years beyond diagnosis. On the other hand, benign adrenocortical tumours are common (>14% of the population). Malignant and benign tumours are currently diagnosed on the basis of biopsied tissue morphology. "Methylation alterations have been implicated in tumour progression and in gene expression regulation," explains Kebebew, "so we were interested in determining if methylation differences were present when comparing benign and malignant adrenocortical tumours and normal adrenal cortical tissue samples." DNA methylation profiling could then potentially be employed as a molecular diagnostic tool and to identify therapeutic targets.

The researchers analysed a total of 86 adrenocortical tissue samples of which 19 were normal, 47 benign, eight from primary malignant tumours and 12 from metastatic tumours. The DNA methylation profile of each type of adrenocortical tissue was then determined.

> "...methylation alterations have been implicated in tumour progression..."

The DNA methylation profiles of normal tissue and benign tumours displayed the highest similarity among the different tissue types analysed. The DNA from primary malignant and metastatic tumours, however, was found to be hypomethylated overall when compared with DNA from normal tissue and benign tumours. Among benign tumours, the researchers found that aldosterone-secreting tumours displayed a different methylation pattern from those of cortisol-secreting and nonfunctional tumours. However, no significant differences in methylation patterns were found between cortisol-secreting and functional tumours. Nonetheless, the substantial differences in the DNA methylation state of normal and benign tumour tissues when compared with malignant tumour tissue could make methylation an important diagnostic marker.

Of particular interest, *IGF2* and other genes involved in its molecular pathway, whose dysregulation has been implicated in adrenal cancer progression, were hypermethylated in malignant tumours but not in normal tissue and benign tumours. Aberrant methylation of these genes might underlie differential expression patterns.

"We are currently evaluating the diagnostic accuracy of differential DNA methylation measurement in patients with adrenal tumours," says Kebebew. "Our future goals include studying the ability of demethylating drugs to reverse aberrant methylation patterns and determining the functional role of differentially expressed and methylated genes in adrenal tumour biology," he adds.

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Original article Rechache, N. S. *et al.* DNA methylation profiling identifies global methylation differences and markers of adrenocortical tumors. *J. Clin. Endocrin. Metab.* doi:10.1210/jc.2011-3298