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Prevalence of cell-free DNA mutations in patients with renal cell carcinoma: Preliminary findings

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Increasing quantity of circulating cell-free DNA (cfDNA) has been shown to correspond to many solid tumors. Circulating cell-free DNA is elevated in patients with renal cell carcinoma (RCC), and limited data suggests potential utilityof cfDNA quantificationin RCC prognosis. While there are select studies analyzing hypermethylation or microsatellite alterations of cfDNA, many studies in RCC analyze total amount and/or length of cfDNA.As there are other non-malignant causes of elevated cfDNA, including endothelial dysfunction, trauma, and autoimmune disease, a more specific method to detect RCC-associated cfDNA would be advantageous.

Somatic mutations in a number of genes are associated with RCC. Furthermore, mutations in BAP1, SETD2, PRBM1, and KDM5C may have prognostic utility. Our group is using deep genetic sequencing of 14 genes associated with RCC, including those above, to detect whether urine and/or circulating cfDNA mutations may be useful as a biomarker and/or prognostic indicator in patients undergoing nephrectomy for suspicious renal mass.

At least one of our 14 selected genes are mutated in 84.7% of cases of RCC in The Cancer Genome Atlas (TCGA). Compared to buffy coat leukocyte DNA as a control for inherited mutations, we found somatic mutations in the selected genes in 8 of 9 (88.89%) patient tumor samples. Cell-free DNA from serum and/or urine in 7 of the 9 RCC patients (77.78%) revealed mutations. Continued sample accrual and further analysis should provide insight regarding utility of cfDNA in detecting tumor-specific mutations in patients with renal cell carcinoma.

Biography

Chris Keith received his B.S. in biology from Duke University. Afterward, he performed a postbaccalaureate research fellowship at the National Cancer Institute investigating inflammatory side effects of anti-EGFR medications. He is currently a fourth year medical student at Emory University, where his research efforts have includedprojects in urologic oncology, association of cigarette-smoking and pancreatic insufficiency, and utility of peer medical education. He is currently investigating biomarkers of renal cell carcinoma in the lab of Dr. John Petros and hopes to pursue a career in urology.

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