Luo et al. (1) recently showed that central adiposity may largely account for the link between obesity and the risk of renal cell carcinoma. The possible biologic mechanisms of this link discussed in their article include elevated levels of insulin, insulin-like growth factor-1, and sex steroids. However, we believe an additional important mechanistic possibility is chronic hypoxia. Genetic syndromes that predispose to renal cell carcinoma, such as the von Hippel-Lindau (VHL) syndrome, and some epidemiologic risk factors both lead to perturbations in hypoxia detection (2), which may be a common link in causing renal cell carcinoma. These mechanisms may all reflect the kidney’s physiologic mechanism of hypoxia detection that has gone awry. VHL is physiologically involved in hypoxia detection, leading to an increase in erythropoietin production and an increase in red blood cell production (3). Chronic hypoxia may lead to a similar tumorigenic mechanism as VHL mutations, in oxygen-detecting tissues, such as the kidney. In addition to the metabolic changes noted by Luo et al., obesity can lead to chronic hypoxia through sleep apnea. Furthermore, central adiposity, in particular, predisposes to sleep apnea (4, 5), which may explain the findings of Luo et al. Although our hypothesis is speculative, we believe that the potential link between sleep apnea, as well as other causes of chronic hypoxia, and renal cell carcinoma merits epidemiologic study.

ACKNOWLEDGMENTS

This research was supported in part by the Intramural Research Program of the National Institutes of Health and by the Center for Cancer Research, National Cancer Institute.

Conflict of interest: none declared.

REFERENCES