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Review highlights advances in kidney cancer research and care

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New insights into the biology of kidney cancer, including those informed by scientific discoveries that earned a Nobel Prize, have led to advances in treatment and increased survival rates, according to a review by UNC Lineberger Comprehensive Cancer Center's William Kim, MD, and Tracy Rose, MD, MPH.

Their observations, drawn from a meta-analysis of 89 studies published between January 2013 and January 2024, were published in *JAMA* Aug. 28.

"The Nobel Prize in Medicine or Physiology in 2019 was awarded for the discovery of how mammalian cells sense oxygen," said Kim, the Rush S. Dickson Distinguished Professor of Medicine at UNC School of Medicine and co-leader of the UNC Lineberger Cancer Genetics Research Program.

"One of the key components of this oxygen sensing pathway is the von Hippel-Lindau tumor suppressor gene, which is mutated in approximately 90% of kidney cancers. This deep understanding of kidney cancer biology has led to several important therapeutic advances in recent years."

Kim trained as a post-doc with William G. Kaelin, Jr., MD, who was jointly awarded the 2019 Nobel Prize for demonstrating how the von Hippel-Lindau gene influences cellular responses to changing oxygen levels.

The American Cancer Society estimates that more than 81,500 people will be diagnosed with kidney cancer in the United States this year, and the disease will cause 14,300 deaths. While the incidence of kidney cancer has been increasing by approximately 1.5% annually in recent years, deaths have decreased by about 2% each year from 2016 to 2020.

This decline in deaths is largely due to improved treatments and early detection. "The majority of kidney cancer cases are now detected incidentally, often before symptoms appear," said Kim.

He noted that the widespread use of abdominal imaging for unrelated issues has led to the incidental diagnosis of kidney cancer. "More cases

are being identified in earlier stages when the cancer is typically more responsive to treatment."

Cigarette smoking and being overweight are major risk factors for kidney cancer and are linked to nearly half of the cases in the United States. Other risk factors include high blood pressure, a family history of kidney cancer, workplace exposure to certain chemicals, and hereditary conditions, such as von Hippel-Lindau disease.

Current treatment approaches include surgery to remove part or all of the kidney, ablation using targeted heat or cold to destroy the tumor, or active surveillance with imaging technologies to monitor the tumor. For cancers that have metastasized, or spread beyond the kidney, newer treatment options include immune checkpoint inhibitors, tyrosine kinase inhibitors, or a combination of the two approaches.

"Advanced, metastatic kidney cancer is highly treatable with targeted therapy, immunotherapy or a combination of these newer therapies," said Rose, associate professor of medicine at UNC School of Medicine.

"Understanding the science underlying the disease has allowed for the rational development of therapies that have positively affected many patients the past two decades."

More information: Renal Cell Carcinoma: A Review, *JAMA* (2024). DOI: 10.1001/jama.2024.12848

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