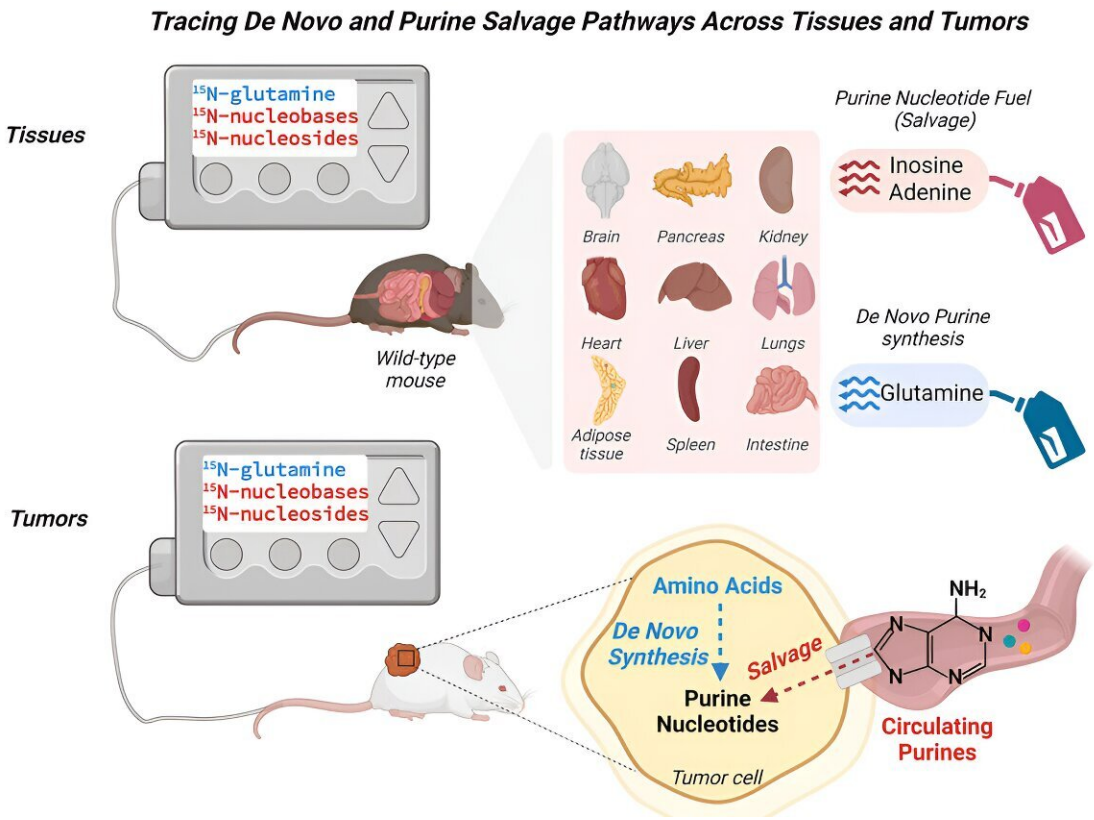
Study finds tumor growth fueled by nucleotide salvage

July 19 2024



Graphical abstract. Credit: *Cell* (2024). DOI: 10.1016/j.cell.2024.05.011

Cancer cells salvage purine nucleotides to fuel tumor growth, including purines in foods we eat, an important discovery with implications for cancer therapies from research by Children's Medical Center Research

Institute at UT Southwestern published in *Cell*.

CRI Assistant Professor Gerta Hoxhaj, Ph.D., and her team have challenged the long-standing belief that tumors primarily acquire purine nucleotides—building blocks for DNA, which is required for cellular growth and function—by constructing them from scratch via de novo synthesis. The Hoxhaj Lab's newest research shows tumors also significantly use the more efficient salvage, or recycling, pathway to acquire purines.

"For more than 70 years, drugs targeting purine nucleotides have been a cornerstone of cancer treatment, but these treatments have limitations, and drug resistance often develops," Dr. Hoxhaj said. "Our research illuminates the contributions of both pathways—de novo and salvage—and highlights the crucial, yet previously overlooked, role the salvage pathway plays in tumor growth."

Dr. Hoxhaj, with co-authors Diem Tran, Ph.D., Rushendhiran Kesavan, Ph.D., and Dohun Kim, B.S., used isotope tracing to follow the de novo and salvage purine pathways across normal mouse tissues and a variety of cancer types, including breast, kidney, colon, and liver cancers.

Normal tissue analyses showed the kidney salvaged the most purines, which could explain why people with kidney disease are at higher risk for gout. Gout, a type of arthritis linked to uric acid buildup, may be caused by the kidney's inability to process uric acid, a purine byproduct.

When conducting the same analyses on tumors, CRI researchers discovered cancer cells use both de novo and salvage pathways to fulfill their constant need for purines. Additionally, tumors grew faster in mice given a high dose of oral nucleotides, indicating purines from the diet contribute to cancer growth.

"While our food provides sugars, proteins, and fats, it also supplies purine nucleotides, especially from meat products. Our research could pave the way for doctors to include dietary interventions when creating a treatment strategy for cancer patients—restricting nucleotide availability could be a new tool to slow cancer progression," Dr. Hoxhaj said.

More information: Diem H. Tran et al, De novo and salvage purine synthesis pathways across tissues and tumors, *Cell* (2024). DOI: 10.1016/j.cell.2024.05.011

Provided by UT Southwestern Medical Center