

Isotope research opens new possibilities for cancer treatment

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The triumphant research team during the acquisition of the first actinium X-ray Absorption Fine Structure analysis (on the screen). From left: Thomas Hostetler (SSRL), Chantal Stieber (former Los Alamos), Maryline Ferrier (Los Alamos), Juan Lezama Pacheco (Stanford) and Stosh Kozimor (Los Alamos).

A new study at Los Alamos National Laboratory and in collaboration with Stanford Synchrotron Radiation Lightsource greatly improves scientists' understanding of the element actinium. The insights could support innovation in creating new classes of anticancer drugs.

"The short half-life of actinium-225 offers opportunity for new alpha-emitting drugs to treat cancer, although very little has been known about actinium because all of its isotopes are radioactive and have short half-lives," said Maryline Ferrier, a Seaborg post-doctoral researcher on the Los Alamos team. "This makes it hard to handle large enough quantities of actinium to characterize its chemistry and bonding, which is critical for designing chelators."

The insights from this new study could provide the needed chemical information for researchers to develop ways to bind actinium so that it can be safely transported through the body to the tumor cell. "To build an appropriate biological delivery system for actinium, there is a clear need to better establish the chemical fundamentals for actinium," Ferrier said. "Using only a few micrograms (approximately the weight of one grain of sand) we were able to study actinium-containing compounds at the Stanford Synchrotron Radiation Lightsource and at Los Alamos, and to study actinium in various environments to understand its behavior in solution."

Medical Isotopes at Los Alamos

Medical isotopes have long been a product of the Los Alamos specialty facilities, which create strontium-82, germanium-68 and other short-lived isotopes for medical scans. Taking advantage of the unique multidisciplinary capabilities of the Laboratory, researchers use the linear particle accelerator at the Los Alamos Neutron Science Center (LANSCE) to provide rare and important isotopes to the medical community across the United States. The expansion into actinium

exploration moves the research forward toward treatment [isotopes](#), as opposed to only diagnostic materials, says Ferrier.

For the actinium work, a spectroscopic analysis called X-ray Absorption Fine Structure (XAFS) was used, a sensitive technique that can determine chemical information such as the number of atoms surrounding actinium, their type (i.e., oxygen or chlorine) and their distances from each other. To help understand actinium's behavior in solution and interpret the data obtained with XAFS, these experimental results were compared with sophisticated computer model calculations using molecular-dynamics density functional theory (MD-DFT).

The study showed that actinium, in solutions of concentrated hydrochloric acid, is surrounded by three atoms of chlorine and six atoms of water. Americium, another +3 actinide often used as a surrogate for actinium, is surrounded only by one chlorine atom and eight water molecules. It has been assumed in the past that actinium would behave similarly to americium.

"Our study shows that the two are different in a way that could help change how actinium ligands are designed," Ferrier said. "We're actively working to gather more fundamental data that will help understand how actinium chemically behaves."

Actinium Useful for Targeted Alpha Therapy

Perhaps the most potent impact of these studies will be on the application of the isotope actinium-225, which is used in a novel, attractive cancer treatment technique called targeted alpha therapy (TAT). TAT exploits alpha emissions from radioisotopes to destroy malignant cells while minimizing the damage to healthy surrounding tissue. "Our determination that actinium's behavior in solution is different than other nearby elements (such as americium) is directly

relevant to TAT in a biological environment, which is always a complex solution," said Ferrier.

Actinium-225 has a relatively short half-life (10 days) and emits four powerful alpha particles as it decays to stable bismuth, which makes it a perfect candidate for TAT. However, TAT with actinium can only become a reliable cancer-treatment if actinium is securely bound to the targeting molecule, as the radioisotope is very toxic to healthy tissue if it is not brought quickly to the site of disease.

More information: Maryline G. Ferrier et al, Spectroscopic and computational investigation of actinium coordination chemistry, *Nature Communications* (2016). [DOI: 10.1038/ncomms12312](https://doi.org/10.1038/ncomms12312)

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