Employee Spotlight: Jonathan Engle

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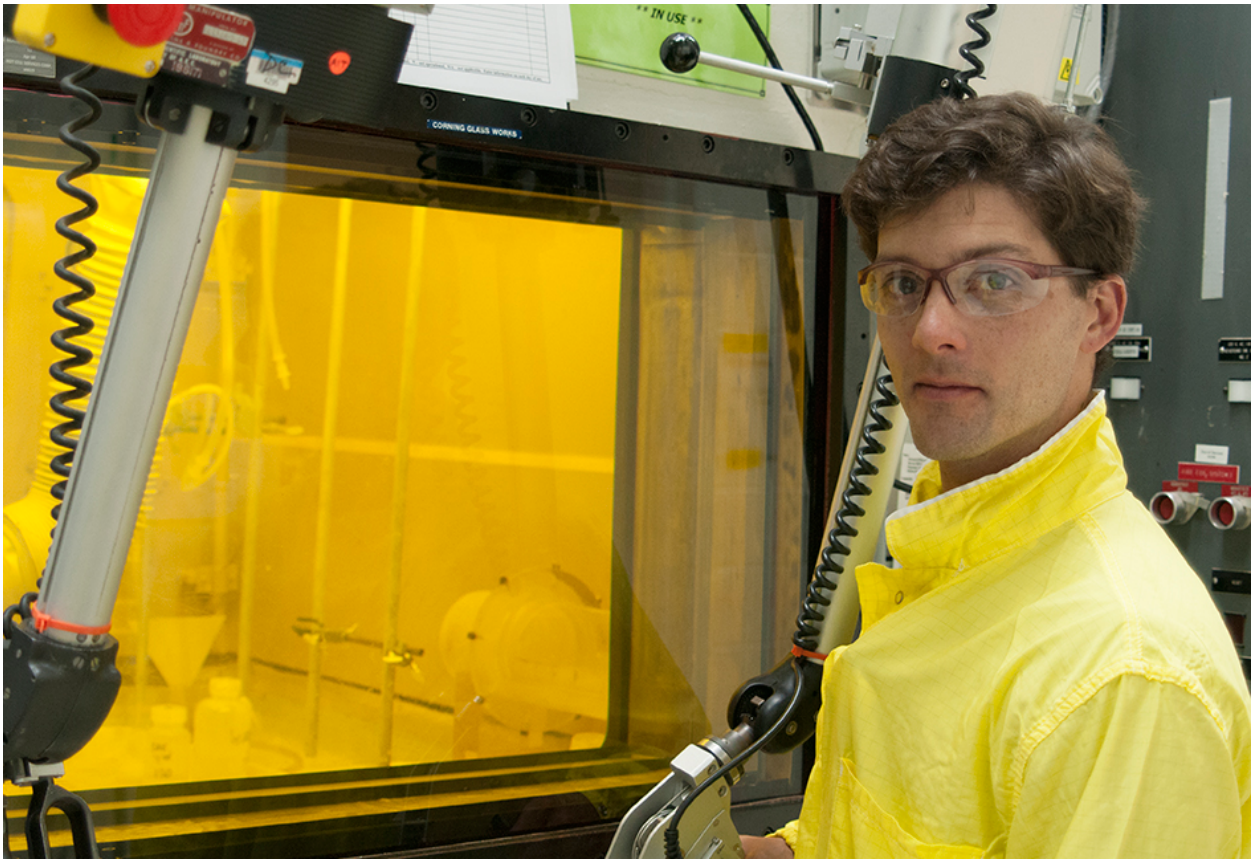

"You have cancer" are among the most feared words one can imagine hearing from one's physician, but if Jonathan (Jon) Engle, Reines Distinguished Postdoctoral Fellow at the Laboratory, has anything to do with it cancer patients may someday hope for a new and improved treatment option: Killing cancer cells from inside the body with the help of nuclear energy.

"The three cancer remedies primarily used today—surgery, chemotherapy and radiation therapy using an external particle beam—have advanced almost as far as they can," Engle suggests. "None of these options are sufficiently specific to cancer cells and all commonly fail to reach metastatic tumor sites, while the nuclear energy cancer treatment that my Los Alamos colleagues and I are working on promises a much higher level of specificity, leaving healthy tissues intact."

The treatment Engle is helping lay the scientific groundwork for uses the energy produced by radioactive isotopes—atoms with an unstable nucleus—inside the human body to zap and destroy diseased cells.

"Radioactive isotopes, often called 'radioisotopes' for short, sometimes occur naturally, but they also can be created artificially in nuclear reactors and particle accelerators," Engle explains. "We're particularly interested in the therapeutic potential of radioisotopes that emit alpha particles, because they deposit all their destructive energy in a very small volume near the site of radioactive decay, sparing nearby healthy tissue."

IPF target stack

Los Alamos has been making radioisotopes since the 1970s and today is a global leader in the production of high-energy, accelerator-produced radioisotopes for research applications and the commercial health care market thanks to the Lab's Isotope Production Facility (IPF). The IPF became fully operational in 2005 and is located near the front end of the proton beam at the Los Alamos Neutron Science Center (LANSCE). After the radioisotopes are created at the IPF, they go through an additional chemical separation and purification process.

But the attempt to treat cancer with accelerator-produced, alpha-emitting radioisotopes on a large scale is relatively new. Engle, who has a doctorate in medical physics, joined the Laboratory in early 2012 specifically because it is "one of very few entities worldwide that can even contemplate producing some of these isotopes at all, much less in useful volumes."

Research challenges

Long before clinical trials with cancer patients can begin, researchers like Engle need to create novel radioisotopes that meet a variety of crucial criteria: Their radioactive emissions must have a short range so only nearby cancer cells are zapped, their decay rates must be well-matched to the function of the biological systems that will be affected, they must be made in sufficient purity to not cause unwanted side effects and they must lend themselves to production on a large scale. The researchers need to then incorporate the isotopes into molecules that target specific malignant tumors and pursue pharmacological validation of the newly radioactive species for use in humans.

"Creating radioisotopes that have just the right characteristics is challenging," Engle admits. "Researchers have been working with nuclear material in medicine for decades, but it's only in the last couple of decades that we've started to really see the potential to combine biological selectivity with carefully chosen physical principles to selectively eradicate disease. And it takes a long time to move a molecule from the lab to the clinic."

Engle is young enough to invest his career in the development of radioisotopes suitable for effective cancer treatment, and he also has a deep commitment to experimental research.

"I vividly remember making a special, experimental radiotracer for a pediatric cancer patient at the University of Wisconsin," Engle recalls. "There wasn't another lab in

the Midwest that was producing this radiolabeled molecule, because it wasn't easy to make and involved irradiating fairly toxic gas mixtures with protons—not necessarily a 'fun' job. A surgeon in Milwaukee, an hour-and-a-half away, needed the diagnostic information it could provide to guide him during surgery. The tracer was labeled with fluorine-18, which has a two-hour radioactive decay window or half-life, which meant that no matter how well we did the chemistry at least half of our product would be gone by the time we delivered the dose."

Engle stops briefly before continuing. "We worked most of the day and my mentor white-knuckled it to the hospital as fast as he could drive, making it with just enough activity left for the scan. We heard the next day that the child's surgery went splendidly, and I found out later that my mentor decided not to charge for any of our time or materials. The feeling of accomplishment I derived from being part of that day is just as potent for me now as it was then, and I genuinely hope I can continue to be part of this kind of work for the rest of my life."

Engle works for the Chemistry Division's Inorganic, Isotope, and Actinide Chemistry group.

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More

- For additional information on the Laboratory's radioisotope cancer research project, you might enjoy watching the Isotope Cancer Treatment Research at LANL video on YouTube.
- For insights into the Lab's radioisotope production efforts, go to the Isotope Production and Applications website or see YouTube's Women Who Inspire: Eva Birnbaum video. Eva Birnbaum is one of Jon Engle's Los Alamos mentors.