

# Pathogen engineered to self-destruct underlies cancer vaccine platform

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A team of investigators has developed a cancer vaccine technology using live, attenuated pathogens as vectors. A feature of the vaccine causes these bacteria to self-destruct once they've done their job, making it safe for use in humans. The research is published in *Infection and Immunity*, a journal of the American Society for Microbiology.

Unlike "prophylactic" vaccines that protect people from the becoming infected with diseases such as measles, influenza, tetanus, or hepatitis, the new vaccine is "therapeutic," that is, designed to treat existing infections or, in this case, prostate and [colorectal cancer](#). It might also be used against hard-to-treat infectious diseases such as malaria or tuberculosis.

Using a bacterium in a platform for a vaccination has several benefits, said principal investigator Pete Lauer, Ph.D., formerly Executive Director, Molecular Biology at Aduro Biotech, Berkeley, CA. "Listeria is a little biological factory... it replicates itself in both the lab and after vaccination. This makes manufacturing as easy as inoculating a culture, and growing it for about a day."

Using a pathogen is useful because it "induces the type of immune response that is required to treat cancer—a CD8 T cell response," said Dr. Lauer. Using a non-pathogen, "we would have had to try to modify the bacterium to be more pathogenic in the right way, which can be really tricky."

The platform, known as "L. monocytogenes recombinase-induced intracellular death," or Lm-RIID for short, is a live recombinant, but highly attenuated (weakened) derivative of the common food-borne pathogen, *Listeria monocytogenes*. The strain on which Lm-RIID was based showed promise as a [therapeutic vaccine](#) in [clinical trials](#) in advanced cancer patients as early as 2009. But more [safety precautions](#) were needed, because *Listeria* can be life-threatening in people with weakened immune systems.

Early feedback on safety from regulatory experts at the Food and Drug Administration, as well as physicians treating cancer patients, was daunting, said Dr. Lauer. Experts from both groups were skeptical about injecting live bacteria into the veins of cancer patients."

That feedback was highly motivating. "Whereas *Listeria*-based vaccines have shown promise as therapeutic vaccines in clinical trials for various cancers, we have gone even further and developed a modified version of *Listeria* that upon entering host cells, deletes essential genes, rendering the bacterium incapable of replication," which in bacteria is tantamount to death, said Dr. Lauer. Besides enabling cancer vaccines, "This additional layer of safety may allow further development of this platform for use in vaccines for a variety of viral and parasitic (e.g. malaria) diseases that currently lack effective vaccines." Cancers of the cervix, lung, and liver, as well as melanoma are also possible targets, said Dr. Lauer.

The other major element of the recombinant *L. monocytogenes* is an antigen that is specific to the

cancer type the vaccine is designed to combat. After vaccination, Lm-RIID is engulfed by immune cells, said Dr. Lauer. Therein, this platform expresses the target antigen. Then, these immune cells, called "antigen presenting cells," deliver the target antigen to their surface. There, CD8 T cells—also immune cells—recognize the antigen. That recognition activates the CD8 T cells to find and destroy the [cancer](#), which Dr. Lauer explains is an immunotherapeutic effect, rather than an oncolytic effect.

Provided by American Society for Microbiology

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