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Researcher aim to 'unmask' cancer cells to trigger body's immune system

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Cancer cells are deadly traitors, good cells gone bad. They evade the body's defense systems, passing themselves off as organisms that pose no threat.

But researchers at the University of North Carolina at Chapel Hill's Eshelman School of Pharmacy are working on a way to blow their cover.

Moo J. Cho, Ph.D., an associate professor of molecular pharmaceutics, is creating a delivery system that would embed bacterial elements in a cancer tumor in order to encourage the body's immune system to recognize and attack the tumor.

"It's like planting a big red flag on the tumor to attract the attention of the body's immune system, which normally ignores cancerous cells," Cho said. "It's a great idea. We just don't know how to do it yet."

To support his work, Cho, who is also a member of UNC's Lineberger Comprehensive Cancer Center, has received a five-year grant from the National Cancer Institute worth more than $1.5 million.

The goal of the research is to develop a unique way to intravenously administer a nucleic acid derived from bacteria and deliver it to a tumor. While it is possible to inject some tumors directly, many are relatively inaccessible and can be better reached through the body's own pathways, Cho said.

The bacteria's nucleic acid would normally be excreted very rapidly from the body when delivered via IV. Cho plans to add a molecule to the nucleic acid that will allow it to latch on to a class of proteins called IgG immunoglobulin that occur naturally in the body.

"We will ask the IgG antibodies to carry the bacteria-derived nucleic acid as a guest throughout the body," Cho said. "This will allow the nucleic acid to circulate for days, which is different from how antibodies have been used in classical targeted delivery."

Cho believes that eventually enough nucleic acid will be carried to the tumor to attract the attention of nearby immune cells, which recognize the nucleic acids as an invading pathogen, triggering an anti-tumor immune response. This approach differs from the classical method of actively targeting a tumor based on specific markers.

"Rapidly growing solid tumors are surrounded by imperfect, almost chaotic, blood flow," Cho said. "The tissue is very leaky. Because of this unusual permeability, the antibody-nucleic acid complex should become lodged in the tumor periphery. This should mimic a local infection, which the body will work to eliminate."

Infecting a tumor so that the body can see it and kill it is one element of immunotherapy, a cancer-treatment option that has been used since the late nineteenth century but has fallen out of favor since the development of radiation therapy and chemotherapy. Radiation and chemotherapy are well understood and relatively predictable, but they can kill healthy cells as well as cancerous ones, suppress the immune system, and come with unpleasant and often dangerous side effects.

"You can use a sledgehammer to kill a fly," Cho said. "But I prefer to try a lighter touch."

However, getting immunotherapy to be consistently effective has been a challenge to science throughout the years, Cho said. Success or failure varies wildly depending on successfully infecting a tumor and the patient's reaction to the infectious agent. Cho's research focuses on the first step of developing a reliable delivery method.

Source: University of North Carolina at Chapel Hill