Tumor wizardry wards off attacks from the immune system

July 14 2006

Like the fictional wizard Harry Potter, some cancerous tumors seem capable of wrapping themselves in an invisibility cloak. Researchers at Washington University School of Medicine in St. Louis have found that pancreatic tumors hide from the body's immune surveillance by surrounding themselves with cells that make it hard for the immune system to detect them.

The tumor-protecting cells are white blood cells called regulatory T cells, or T-reg for short. Under ordinary circumstances, T-reg cells inhibit immune components responsible for killing unwanted cells -- this allows T-reg cells to help prevent autoimmune reactions.

The scientists discovered that cancerous cells take advantage of T-reg cells' suppressor ability, enlisting them to keep the immune system at bay. Their report appears in the July/August issue of the Journal of Immunotherapy.

"Earlier, we found that T-reg cells are much more prevalent in patients with breast cancer and pancreatic cancer than in healthy patients," says David C. Linehan, M.D., associate professor of surgery and a researcher with the Siteman Cancer Center. "The new findings show that tumors are directly responsible for the increase of T-reg cells and can attract T-reg cells to their vicinity. This could be one way for tumors to evade immune surveillance."

Linehan believes this could explain the failure of many experimental anti-

cancer vaccines. Such vaccines are designed to rev up the immune response to cancer cells so that the immune system can attack tumors. But a tumor shielded with T-reg cells could potentially circumvent the immune system's attack and remain safe.

In mice implanted with pancreatic cancer, the researchers demonstrated that tumor growth caused an increase in T-reg cells in both the blood stream and in lymph nodes leading from the tumors.

When the research team blocked a signaling molecule that pancreatic tumors secrete in abundance, T-reg cells were no longer present in the tumor-draining lymph nodes, suggesting that this signaling molecule, referred to as TGF-beta, has an important role in weaving a tumor's cloak of invisibility. Such information could lead to a method for blocking tumors from using T-reg cells for protection. Other research by Linehan and colleagues showed that in mice with pancreatic cancer, simply depleting T-reg cells slowed tumor growth and increased survival time.

"We're looking at several potential ways to interfere with tumor recruitment of T-reg cells," Linehan says. "We'd like to see these findings advance cancer immunotherapy. We want to find a way to actively suppress T-reg cells and at the same time actively evoke an immune response to tumor-specific antigens."

In collaboration with other researchers at the School of Medicine, Linehan is planning to set up a clinical trial that pairs T-reg depletion with anti-cancer vaccine as a therapy for pancreatic cancer patients.

"We're attacking the problem from different angles hoping to translate these findings to our patients," Linehan says. "Right now, no effective treatment exists for pancreatic cancer."

Source: Washington University School of Medicine