Autoimmune response can induce pancreatic tumor rejection

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Immune responses are capable of killing tumors before they can be directed toward normal body tissue, according to new scientific findings published in *Cancer Research,* a journal of the American Association for Cancer Research.

"There are extremely precise mechanistic methods augmenting the ability of the immune system to distinguish between normal tissues and tumors," said lead researcher Richard G. Vile, Ph.D. "Understanding the multiple checks and safeguards against autoimmunity should allow us to understand more closely how to generate antitumor immunity."

Vile, professor of immunology in the Department of Molecular Medicine and the Department of Immunology at the Mayo Clinic, Rochester, Minn., and professor of biological therapy at the University of Leeds, United Kingdom, along with other colleagues, induced pathological damage to a normal organ, in this case the pancreas, with the immune adjuvant hsp70. They investigated whether that damage could lead to the development of T-cell responses against the normal pancreas.

Inflammatory killing of the normal pancreas induced a Th-1-like, anti-self response to pancreatic antigens. Rapid suppression and damage to the pancreas induced a very strong suppressive regulatory T-cell response — Treg. Even after Treg cells were depleted, Vile and colleagues found that Th-1-like response was insufficient to induce significant ongoing autoimmunity.

"We believe that although there are additional mechanisms that prevent autoimmunity, simply removing the Treg uncovered a good antitumor response," Vile said. "We were not expecting that it would be possible to cure tumors without autoimmunity. Our prediction was that we would have to generate potent autoimmunity and then the tumors would be rejected."

Based on this study, the researchers suggested that it is more difficult than presumed to induce autoimmunity against the pancreas because multiple immune safeguards exist to prevent potentially autoimmune T-cells from destroying the normal pancreas. Further, when comparing the immunoprotective mechanisms of different tissues, profound differences exist in response to pathogen-like damage.

Cancer Research editorial board member Ivan Borrello, M.D., believes this study highlights several unique aspects of tumor immunology. The immune response toward normal elements and tumors in different organs are mediated through different mechanisms and may require different approaches to achieve a beneficial therapeutic outcome, he said. Further, in certain situations like the pancreas, it may not be sufficient to prime effective anti-tumor immunity.

"This study demonstrates the increasing complexity within which both normal tissues and tumors can protect themselves against destruction and underscores the complex network regulating immune responsiveness," said Borrello, an associate professor in oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins.

These findings may lead to a new approach for the development of a cancer vaccination, Vile said, whereby scientists link the autoimmune and antitumor fields more closely than ever before.

Additional research is underway to evaluate this approach for the

treatment of melanoma, as opposed to pancreatic cancer, and further studies are ongoing in prostate cancer. The field also needs to understand how to utilize and possibly sequence immune-mediated interventions in a more disease-focused and tailored manner, according to Borrello.

Source: American Association for Cancer Research (news : web)