Study finds potential key to immune suppression in cancer

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In a study investigating immune response in cancer, researchers from Moffitt Cancer Center in Tampa, Fla., and the University of South Florida have found that interaction between the immune system's antigen-specific CD4 T cells and myeloid-derived suppressor cells (MDSC) – cells that play a major role in cancer-related immune suppression – dramatically change the nature of MDSC-mediated suppression. By contrast, the same effect was not observed when MDSCs interacted with the immune system's CD8 T cells.

Their study appeared in a recent issue of *Cancer Research*, published by the American Association for Cancer Research.

According to the authors, it has been established that inadequate immune response in cancer is a critical element in tumor escape, and that myeloid-derived suppressor cells (MDSCs) – cells that which normally keep the immune system in check and prevent it from attacking otherwise healthy tissue – can suppress the anti-tumor response and play a major role in tumor associated immune abnormalities.

In addition, research has shown that MDSCs block other immune system cells (such as CD 8 "killer" T cells) from binding with proteins that identify foreign antigens on the surface of unhealthy cancer cells and, in doing so, mark them as targets.

"To better understand the biology of immune defects in cancer, our study investigated the antigen-specific nature of MDSCs and their ability

to cause antigen specific CD4 T cell tolerance," said study corresponding author Dmitry Gabrilovich, M.D., Ph.D., who holds the Robert Rothman Endowed Chair in Cancer Research at Moffitt and whose research focus is on immunology. "We found that antigen specific CD4 T cells were able to dramatically enhance the immune suppressive activity of MDSC by converting them into powerful non-specific suppressors. But, to our surprise, we did not see the same response from CD8 T cells."

The researchers initially investigated several tumors modeled in mice but focused on two models of particular interest.

They reported that major histocompatability complex (MHC) class II molecules – found only on a few specialized cell types – played a role in this conversion to MDSC-mediated suppression when MHC class II and MDSC "cross-linked" through cell-to-cell contact. The effect, however, was dependent on the expression of MHC class II.

"This study showed for the first time that activated antigen-specific T-cells can potentiate the immune suppressive activity of MDSC by converting these cells to non-specific suppressors and, thus, limit the ability of the host to mount a potent immune response," concluded the authors.

The researchers suggested that their study might shed light on a mechanism that may act as a "negative feedback loop" aimed at controlling immune responses that become "dysregulated" in cancer.

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