Researchers study effect of chemotherapy combined with immunotherapy for advanced cancers

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Researchers at Moffitt Cancer Center and colleagues at the University of South Florida and Tianjin Medical University Cancer Institute and Hospital in China have discovered that combining chemotherapy drugs and immunotherapy cancer vaccines results in an enhanced anti-tumor effect. The results, achieved by testing cancer cells in a laboratory, are surprising because chemotherapy generally reduces immunity and could cancel out the benefits of immunotherapy when given together.

Their study appears in the Aug. 31 online issue of Cancer Research, a publication of the American Association for Cancer Research.

"Our question of interest for this study was 'Can immunotherapy be used in combination with conventional chemotherapy in patients with advanced cancer?' " said study lead author Dmitry I. Gabrilovich, M.D., Ph.D., senior member of Moffitt's Immunology Program. "The use of conventional cancer chemotherapy in combination with immunotherapy was previously not thought to be appropriate due to the immunosuppresive effects usually associated with chemotherapy. However, we identified a mechanism by which the two therapies could work together."

The mechanism involved was the dramatic upregulation of the mannose-6-phosphate receptor (MPR) to the tumor cell surface. According to the researchers, normally more than 90 percent of total

MPR is localized inside the cells, but after chemotherapy, large amounts of MPR localized on the cell membrane.

The researchers attributed this to autophagy.

"Autophagy is a reversible process than can contribute to both tumor cell death and survival," explained Gabrilovich. "When this pathway is initiated, cellular material is sequestered by autophagosome. The mechanism of autophagosome formation depends on the type of chemotherapy used."

According to the authors, the MPR upregulation effect was seen in every tumor model they tested and with all drugs they used. However, the effect of the combined treatment was seen only when chemotherapy was given within a specific window of time during which levels of MPR were observed on tumor cells. Much more about the mechanism needs to be clarified, researchers said.

"The relationship between autophagy and tumor immunity requires further investigation," Gabrilovich said. "Our study represents a novel concept relating to the interaction between cytotoxic T cells and tumor cells undergoing autophagy. We are suggesting that this process could be exploited during chemotherapy or radiation therapy, as well as with other treatments that cause autophagy of cells, although treatments need to be carefully timed."

The authors concluded that their data demonstrated that combining chemotherapy and immunotherapy for patients with advanced cancer has "a strong rationale."

More information: cancerres.aacrjournals.org/con … CAN-12-2236.full.pdf

Provided by H. Lee Moffitt Cancer Center & Research Institute