

'Super' enzyme may lead way to better tumor vaccines

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A "super" form of the enzyme Akt1 could provide the key to boosting the effect of tumor vaccines by extending the lives of dendritic cells, the immune-system master switches that promote the response of T-cells, which attack tumors.

"By keeping the dendritic cells alive longer, you extend the window of activation, promoting the desirable immune response, which in the case of cancer, is the expansion of T-cells," said Dr. David Spencer, associate professor of immunology at BCM. "The longer your dendritic cells are alive and active, the more likely you are to expand the appropriate T-helper repertoire and ultimately the desirable cytotoxic (cell killing) T-lymphocytes."

"The dendritic cells are the master switch in the immune system. They decide whether there will be a robust immune response or a tempered immune response to pathogens or cancer," he said.

Using a variety of sophisticated laboratory techniques, Spencer and his colleagues found that Akt1 "was in fact essential for dendritic cell survival," he said. Then they sought to develop a more potent form of Akt1 that would enable the dendritic cells to live longer, boosting immune response.

To do that, they altered the enzyme so that it targeted a particular domain on the plasma membrane of the cell where signaling occurred, making the action of Akt1 more specific. They then eliminated a small

part of the Akt1 molecule that had a negative or inhibitory effect.

"It turned out that the altered molecule was much more potent," Spencer said. He credited graduate student Dongsu Park with doing much of the work to develop the super form of Akt1.

Using specially designed adenoviruses, he and his colleagues put the modified "super" Akt1 molecule into the dendritic cells.

"As predicted, these dendritic cells lived longer and were more potent, both in the laboratory and in mice," he said. "It led to the elimination of some very aggressive tumors in the mice."

In the laboratory, they found that the "super" Akt1 also has a potent effect on human dendritic cells as well, although it has not been used to treat people yet.

He expects that when the enzyme is used in people, the first target will be prostate cancer – a long-standing interest of his laboratory. However, he said, it could be modified to attack other tumors as well.

Source: Baylor College of Medicine

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