Breakthrough in cancer vaccine research

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Researchers at the University of Cambridge hope to revolutionise cancer therapy after discovering one of the reasons why many previous attempts to harness the immune system to treat cancerous tumours have failed.

New research, published today in the journal *Science*, reveals that a type of stromal cell found in many cancers which expresses fibroblast activation protein alpha (FAP), plays a major role in suppressing the immune response in cancerous tumours – thereby restricting the use of vaccines and other therapies which rely on the body's immune system to work. They have also found that if they destroy these cells in a tumour immune suppression is relieved, allowing the immune system to control the previously uncontrolled tumour.

Douglas Fearon, Sheila Joan Smith Professor of Immunology of the Department of Medicine at the University of Cambridge, said: "Finding the specific cells within the complex mixture of the cancer stroma that prevents immune killing is an important step. Further studying how these cells exert their effects may contribute to improved immunological therapies by allowing us to remove a barrier that the cancer has constructed."

Vaccines created to prompt the immune system to attack cancerous cells in tumours have shown to activate an immune response in the body but have, inexplicably, almost never affected the growth of tumours. Immunologists who specialise in tumours have suspected that within the tumour microenvironment the activity of immune cells is somehow suppressed, but they have thus far been unable to fully reverse this

suppression.

The new research, funded by the Wellcome Trust and the Sheila Joan Smith Professorship endowment, sheds light on why the immune response is suppressed. The Cambridge study found that at least one immune suppressive component is contained within normal tissue cells (called stromal cells) the cancer has coerced to assist its survival. The cell they studied specifically expresses a unique protein often associated with wound healing - fibroblast activation protein alpha (FAP). The FAP expressing cells are found in many cancers, including breast and colorectal cancers.

In order to determine if FAP expressing stromal cells contribute to the resistance of a tumour to vaccination, the researchers created a transgenic mouse model which allowed them to destroy cells which expressed FAP. When FAP-expressing cells were destroyed in tumours in mice with established Lewis lung carcinomas (of which only 2% of the tumour cells are FAP-expressing), the cancer began to rapidly 'die'. The Fearon lab now hopes to collaborate with scientists at the CRUK Cambridge Research Institute to evaluate the effects of depleting FAP-expressing cells in a mouse model that more closely resemble human cancer, and to examine FAP-expressing cells of human tumours.

Professor Fearon continued: "These studies are in the mouse, and although there is much overlap between the mouse and human immune systems, we will not know the relevance of these findings in humans until we are able to interrupt the function of the tumour stromal cells expressing FAP in patients with cancer.

"It should be noted, however, that the FAP-expressing stromal cell was actually first found in human cancer by Lloyd Old and his colleagues 20 years ago."

More information: The paper 'Suppression of Antitumour Immunity by Fibroblast Activation Protein – α – Expressing Stromal Cells' will be published in the 05 November 2010 edition of *Science*.

Provided by University of Cambridge