Blocking the effect of inflammation-causing cells lowered prostate cancer cells invasion

April 8 2008

Recent studies have suggested an association between chronic inflammation and cancers of the prostate, colon, stomach and liver. Now scientists at Northwestern University Feinberg School of Medicine report success in blocking an early step in metastasis of prostate cancer cells by interrupting the communication between the cancer cells and other cells that promote inflammation.

Their success suggests new ways to control cancer spread and metastasis. The findings also provide an impetus to look more closely at existing inflammation-controlling drugs including non-steroidal anti-inflammatory drugs, cyclooxygenase inhibitors, antioxidants and statins. It is possible, says Dr. Paul Lindholm, that these widely available drugs could be used to control aggressive cancer cell growth and spread for these and other inflammation-associated cancers.

Dr. Lindholm presented results of the study on April 8 at the Experimental Biology 2008 meeting in San Diego. The presentation was part of the scientific program of the American Society for Investigative Pathology.

In earlier studies, Dr. Lindholm and his colleagues at Northwestern found that when compared to benign prostate tissues, prostate cancer tissue has a higher density of macrophages and the monocytes from which these immune system cells derive. These scavenger cells are vital to the regulation of immune responses and the development of inflammation. High grade and high stage prostate cancer tissues showed

significantly increased numbers of macrophages compared to low grade and low stage tumors. When the researchers added monocyte-like cell lines or monocytes obtained from the blood of normal people to less aggressive prostate cancer cell lines, these cancer cells became more invasive, indicating that the cancer cells and the monocytes were indeed communicating with each other. But how?

In the study reported at Experimental Biology, the researchers demonstrated that the monocyte-like cells stimulate the cancer cells' Nuclear Factor-kappaB, a gene regulating transcription factor able to stimulate gene activity. To test whether NF-kappaB activity was increasing the cancer cells' movement and invasive activity, the researchers then introduced into the cancer cells biological inibitors that blocks NF-kappaB activity. The treatments that block NF-kappaB activity reduced the cancer cell movement and invasion through the basement membrane (a thin, delicate layer of connective tissue underlying the epithelium of many organs).

The researchers now plan to study the effects of macrophages and inflammation and NF-kappaB inhibiting treatments in vivo, in a specially designed mouse model of invasive prostate cancer. They also plan to extend these experiments to include drugs currently used in humans to control inflammation.

If anti-inflammatory drugs block cancer cell NF-kappaB activity and spreading movement, as the researchers hope, these drugs may prove useful for patients whose cancers are discovered early but who are at risk for cancer spread. The results also could help identify biomarkers of early cancer, before it can be detected by current technology, and to monitor response to treatments designed to prevent cancer spread.

Source: Federation of American Societies for Experimental Biology