Medical Xpress

Collagen clue reveals new drug target for untreatable form of lung cancer

August 29 2013

Collagen, the stuff of ligaments and skin, and the most abundant protein in the human body, has an extraordinary role in triggering chemical signals that help protect the body from cancer, a new study reveals.

Scientists at The Institute of Cancer Research, London, have uncovered a series of chemical signals sent out by collagen that appear to protect against cancer's growth.

Boosting those signals could act as an effective treatment for cancers that grow in the presence of collagen, including squamous cell lung cancer, for which no targeted treatments currently exist.

And the findings suggest that switching off these chemical signals, as some treatments for leukaemia do, is likely to be counter-productive in cancers where interaction with collagen plays an important role.

The study was funded by The Institute of Cancer Research (ICR), the Wellcome Trust and the Biotechnology and Biological Sciences Research Council (BBSRC).

The ICR team explored the role of signals triggered by collagen in human embryonic kidney cells, a type of cell often used in studies of this type. They analysed the role of a molecule called DDR2, which relays signals from collagen as a means of maintaining tissue structure and function, and is mutated in some forms of squamous cell lung cancer.

They treated cells with collagen, and found that DDR2 responded by activating a second protein called SHP-2, in a process that appears to be important in protecting against the growth of some cancers.

But a specific mutant form of DDR2 present in some squamous cell lung cancers seemed unable to signal through SHP-2, suggesting the loss of function had left the tissue vulnerable to cancer growth.

That finding offers an exciting opportunity to design the first targeted treatments for squamous cell lung cancer, perhaps by mimicking the action of SHP-2 to re-erect the normal controls against cancer's growth in the presence of collagen.

Dr Paul Huang, Team Leader in Protein Networks at The Institute of Cancer Research, said: "We knew collagen was capable of slowing the growth of some cancer types, presumably by maintaining the structure of tissues, but our new study for the first time identifies how this effect occurs in lung cancer.

"We sifted through data on 428 different proteins stimulated by collagen, and isolated just one we think can play a key role in protecting tissues from cancer. Identifying this molecular trigger opens up the prospect of targeted treatments for squamous cell lung cancer.

"Importantly, we also highlighted the duplicitous nature of this important signalling network. Although we know it directs a lot of cellular processes that can contribute to cancer—such as differentiation, proliferation and motility—in the presence of collagen, it actually seems to protect against cancer. That means we will need to treat cancers that develop in collagen-rich environments differently to blood cancers such as leukaemia."

Professor Alan Ashworth, Chief Executive of The Institute of Cancer

Research, said: "Survival rates for [lung cancer](#) remain extremely poor, and one of the ways to improve this is to discover new ways of targeting the disease with drugs. This new study is valuable for two reasons—it identifies an exciting new potential route for treating lung cancers, and it also shows us why some other approaches are unlikely to work.

"Scientifically, these results are very interesting as they demonstrate how one of the most common proteins in the human body plays a role not only in building the structure of tissues but also in cancer."

More information: Squamous cell cancer accounts for around 25 per cent of all lung cancer cases (Heist, R.S., et al., *J Thorac Oncol*, 2012. 7(5): p. 924-33).

Provided by Institute of Cancer Research