Bioengineered proteins: Trial confirms new way to tackle cancer

March 26 2009

Re-engineering a protein that helps prevent tumours spreading and growing has created a potentially powerful therapy for people with many different types of cancer. In a study published in the first issue of *EMBO Molecular Medicine*, Canadian researchers modified the tumour inhibiting protein, von Hippel-Lindau (VHL), and demonstrated that it could suppress tumour growth in mice.

When solid tumours grow they often have relatively poor and disorganised blood supplies. As a result, various regions including the centre of the tumour have low levels of oxygen and are said to be hypoxic. Cells in these hypoxic areas produce hypoxia-inducible factor (HIF) that helps them carry on growing. Consequently HIF is associated with aggressiveness in some of the most common types of cancer, including prostate, breast, colon and lung cancer. Under normal conditions VHL degrades HIF, but VHL is deactivated when oxygen levels are low. So, in hypoxic regions of a tumour, just where VHL is needed to inhibit cancer, it is ineffective.

The researchers, therefore, created a new version of VHL that does not stop working when oxygen is scarce. Introducing this newly engineered version of VHL into mice that had kidney tumours dramatically reduced levels of HIF, caused tumours to regress and limited the formation of new blood vessels within the tumours.

"We have genetically removed the Achilles' heel of VHL to permit unrestricted destruction of HIF," says lead researcher Professor Michael

Ohh, who works in the Faculty of Medicine at the University of Toronto. "The level of HIF is usually very high under conditions of low oxygen, but when we put in our bioengineered VHL its levels go right down to a level that would be comparable to that in normal oxygen levels."

Their findings could have implications for any type of cancer in which HIF plays a role. "We used kidney cancer as a model because it is one of the most resistant tumours to conventional radiation and chemotherapy, but our findings provide a novel concept that could potentially serve as a foundation for smarter anti-cancer strategy for a wide variety of cancers," says Ohh.

Source: Wiley (news : web)