Scientists home in on reasons behind cancer drug trial disappointment

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Scientists based at the University of Helsinki, Finland, have discovered a 'hidden' mechanism which could explain why some cancer therapies which aim to block tumour blood vessel growth are failing cancer trials.

Numerous angiopoietin-blocking therapies, which work to starve the tumour of its blood supply, are currently in clinical trials for ovarian cancer and other cancers. But despite promising earlier results, some of these therapies are not improving patient survival as much as was expected.

Many current angiopoietin-blocking therapies work by inhibiting a specific cell pathway which promotes blood vessel growth. The pathway involves angiopoietin-1 and angiopoietin-2 proteins and also another protein, called Tie-2.

However this latest research, published in *Nature Communications*, suggests the existence of an alternative angiopoietin-mediated mechanism which 'bypasses' Tie-2.

Lead researcher, Dr Pipsa Saharinen, at the University of Helsinki said: "What we have found in our studies on cells and in mice, is another angiopoietin-2 mediated cell pathway, which usually works to destabilise blood vessels, but which also could promote blood vessel growth. This pathway is not necessarily targeted by current angiopoietin-blocking therapies, and this could help explain why some of the trials have not produced as much benefit as we might have hoped."

The same mechanism could play the role in the bacterial or viral septic shock - e.g. in Ebola fever - by destabilising the blood vessels, Dr Saharinen notes.

"We still need to confirm what we're seeing in normal cells is happening in tumors as well, and we have to figure out what actually happens inside the body. Then we can work out for sure how blocking this new angiopoietin 2 pathway affects tumour blood vessels," says Dr Saharinen.

"Ultimately, I think these results could help explain some of the confusing trial results we've seen."

More information:
http://www.nature.com/nrd/journal/v13/n12/full/nrd4509.html

Provided by University of Helsinki