Cancer therapy may be too targeted

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Researchers have identified two novel cancer genes that are associated with the development of a rare, highly aggressive, cancer of blood vessels. These genes may now act as markers for future treatments and explain why narrowly targeted therapies that are directed at just one target fail.

Angiosarcoma is a rare cancer of blood vessels. It occurs either spontaneously or can appear after radiotherapy treatment. Although quite rare, with approximately 100 people diagnosed with the cancer in the UK each year, the survival outcomes for the cancer are poorer than many other cancer types.

Scientists have previously developed drugs against angiosarcoma that target specific cellular pathways involved in the formation of blood vessels. However, these drugs have had little or no success.

In this study, the team found that 40 per cent of angiosarcomas carry mutations in genes that control blood vessel growth, including two novel cancer genes, PTPRB and PLCG1.

"Because this cancer doesn't respond well to traditional chemotherapy and radiotherapy, it makes sense to develop drugs that target pathways that control blood vessel formation," says Dr Peter Campbell, co-lead author from the Wellcome Trust Sanger Institute "We found two novel cancer genes that control blood vessel formation which are mutated in this cancer and which could be targeted for treatment of this highly aggressive cancer."

However, in some patients, the team found multiple mutations in the pathway that controls blood vessel growth. These multiple mutations may make drugs developed for a single target ineffective in some patients. This study emphasises the need to take into account the effects multiple, co-operating mutations can have when designing targeted treatments for patients.

"This indicates that we may need to think more broadly to find a suitable treatment," adds Dr Campbell.

"This study really highlights the power that a limited number of samples can have to influence the clinical and biological understanding of a rare disease, in this case angiosarcoma," says Professor Adrian Harris, co-lead author from the University of Oxford. "Not only does our study change the way people view the biology of this tumour, it acts as a guide for future drug trials in angiosarcoma patients."

Because so few people are affected by angiosarcoma, clinical trials can be very difficult to conduct. With this new information researchers now need to determine if existing drugs could be effective against this detrimental cancer.

"It's extremely important to that we continue to study rare cancers such as angiosarcomas," says Dr Sam Behjati, first author from the Wellcome Trust Sanger Institute. "Not only will this help the many patients with these cancers and improve treatment strategies, but it will help us understand the full landscape of cancer-causing mutations and the underlying biology."

More information: Sam Behjati, Patrick S Tarpey, Helen Sheldon et al. (2014) 'Recurrent PTPRB and PLCG1 mutations in angiosarcoma' Advanced online publication in *Nature Genetics*, 16 March. DOI: 10.1038/ng.2921

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