Medical Xpress

Genetic 'hotspots' flag up opportunities for more personalised bowel cancer treatment

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(PhysOrg.com) -- Cancer Research UK scientists have identified the frequency of new genetic 'hotspots' which could help doctors to tailor therapies to as many as 3,000 additional bowel cancer patients each year, according to research published in the *British Journal of Cancer* today.

The team at the University of Dundee carried out a genetic analysis on 106 bowel cancer tumour samples to search for the frequency of known faults in a key gene called K-Ras. This gene is the blueprint for an important protein which acts as an 'on-off switch' in cells to control growth. It is already known that in some bowel cancers the K-Ras gene is faulty, leaving the switch permanently 'on'.

A subset of bowel cancer patients who have a normally functioning K-Ras 'switch' might in some circumstances benefit from new cancer drugs called cetuximab and panitumumab. But patients with faulty K-Ras will not benefit from these drugs and may even be harmed by them, making it especially important to be able to accurately test the K-Ras gene for faults.

The identification of these additional genetic 'hot-spots' could flag up additional patients who would not benefit from these types of treatments.

Each year more than 37,500 people are diagnosed with bowel cancer in the UK and scientists already knew that faults occur in three regions of the K-Ras gene in approximately 25 per cent of bowel cancer patients -

around 9,375 people. Three regions of the gene where these faults are found are at gene locations - called codons - 12, 13 and 61. But this new research shows that similar faults in other areas of the gene, most commonly at codon 146, occur in a significant number of additional patients. The study suggests that as many as 33 per cent of bowel cancer patients have a K-Ras fault - around 12,375 people in total - an additional 3,000 patients than previously assumed.

Study co-author, Professor Roland Wolf, director of the Biomedical Research Institute and the Cancer Research UK Molecular Pharmacology Unit at the University of Dundee, said: “Studies such as this clearly show us the importance of identifying faults in particular molecular pathways associated with drug response and tailoring drug therapy accordingly.

“These findings may in the future be relevant for selected patients with advanced bowel cancer as doctors will be able to more precisely target these treatments to the patients who will benefit and avoid treating those who won’t.”

Lead study author Dr Gillian Smith from the University of Dundee, said: “These results highlight additional gene faults which potentially could be tested for in bowel cancer patients to determine which people will respond best to which drugs.

“The next stage is to develop effective tests to screen for these mutation ‘hotspots’ to help doctors to plan the most effective treatment strategies for bowel cancer patients - and this will encourage scientists to also focus their efforts on finding new treatments for patients with faulty K-Ras genes to give them more options.”

Dr Lesley Walker, director of cancer information at Cancer Research UK, said: “This important study shows how the most fundamental

science can have a direct impact on the treatment of patients in the clinic. There is increasing interest in the identification of molecular markers to flag up the forms of cancer which would respond to a particular treatment and these findings could help health professionals plan and deliver more personalised and effective treatment for people with bowel cancer."

More information: Activating K-Ras mutations outwith hotspot codon in sporadic colorectal tumours - implications for personalised cancer medicine. G Smith et al. *British Journal of Cancer*.

Provided by University of Dundee