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High chromosomal instability may predict which patients will benefit most from colorectal cancer drug

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Researchers at RCSI, along with international collaborators within the ANGIOPREDICT research consortium, have discovered that chromosomal instability (where whole human chromosomes or parts of chromosomes are duplicated or deleted) may predict which patients will receive most benefit from a key drug used to treat colorectal cancer (Avastin). By knowing in advance which patients would not benefit from Avastin, individuals could be spared the side-effects of the drug, and are more likely to receive optimal treatment with a minimum of delay, while reducing cost of care.

The study, led by researchers at RCSI (Royal College of Surgeons in Ireland) and the VIB-KU Leuven Center for Cancer Biology in Belgium is published this month in the prestigious international journal *Nature Communications*. It marks a further important advance in the global effort to move towards a more personalised treatment approach for colorectal cancer patients.

According to the World Cancer Research Fund, colorectal cancer is the third most common cancer worldwide with nearly 1.4 million new cases diagnosed annually. In 2014, almost 153,000 people died from colorectal cancer in the EU equivalent to 11 per cent of all deaths from cancer. Half of colorectal cancer patients develop metastatic cancer, where the cancer spreads to other parts of the body, for which Avastin is a key component of therapy.

Speaking on the significance of the discovery, Professor Annette Byrne, Associate Professor at RCSI's Department of Physiology and Medical Physics said: "We have drawn on knowledge emerging from global efforts to characterise the complex genetic alterations that underpin the progression of colorectal cancer. We have demonstrated that tumours with intermediate-to-high chromosomal instability have improved outcome after Avastin treatment, whereas tumours characterised by low chromosomal instability benefit less. This work further builds on our recent *Journal of Clinical Oncology* study and has identified a complementary biomarker strategy that could be used by doctors in the future to distinguish between patients who will benefit from Avastin and patients who will not respond."

"As always, our overall goal is to improve the standard-of-care for colorectal cancer and to make sure that patients only receive drugs that will work specifically in the setting of their own disease. This will reduce side-effects, treatment costs and improve patient outcomes", added Professor Lambrechts (VIB-KU Leuven Center for Cancer Biology).

More information: Dominiek Smeets et al. Copy number load predicts outcome of metastatic colorectal cancer patients receiving bevacizumab combination therapy, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06567-6

Erik van Dijk et al. Loss of Chromosome 18q11.2-q12.1 Is Predictive for Survival in Patients With Metastatic Colorectal Cancer Treated With Bevacizumab, *Journal of Clinical Oncology* (2018). DOI: 10.1200/JCO.2017.77.1782

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