HIGHLIGHTS

HIGHLIGHT ADVISORS

ANTON BERNS
NETHERLANDS CANCER INSTITUTE, AMSTERDAM, THE NETHERLANDS

PETER BOYLE
EUROPEAN INSTITUTE OF ONCOLOGY, MILAN, ITALY

PETER CARMELIET
CATHOLIC UNIVERSITY LEUVEN, LEUVEN, BELGIUM

RON DEPINHO
HARVARD MEDICAL SCHOOL, BOSTON, MA, USA

STEPHEN W. FESIK
ABBOTT LABORATORIES, ABBOTT PARK, IL, USA

ELI GILBOA
DUKE UNIVERSITY MEDICAL CENTER, DURHAM, NC, USA

TOMAS LINDAHL
CANCER RESEARCH UK, LONDON RESEARCH INSTITUTE, HERTFORDSHIRE, UK

LANCE LIOTTA
NATIONAL CANCER INSTITUTE, BETHESDA, MD, USA

JANET D. ROWLEY
UNIVERSITY OF CHICAGO MEDICAL CENTER, CHICAGO, IL, USA

DAVID SIDRANSKY
JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, BALTIMORE, MD, USA

JÜRG TSCHOPP
UNIVERSITY OF LAUSANNE, EPALINGES, SWITZERLAND

BERT VOGELSTEIN
JOHNS HOPKINS ONCOLOGY CENTER, BALTIMORE, MD, USA

ROBERT A. WEINBERG
WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH, CAMBRIDGE, MA, USA

SAVIO WOO
MOUNT SINAI SCHOOL OF MEDICINE, NEW YORK, NY, USA

EARLY DETECTION

The ease of detection

The search for cancer markers is on, but finding non-invasive tests that are predictive of disease is not easy. Now, Andrew Feinberg and colleagues, reporting in the 14 March issue of *Science*, have moved a step closer to answering this elusive problem, as they show that a simple blood test could predict the risk of developing colorectal cancer.

Both genetic and epigenetic changes can initiate tumorigenesis, so detecting these could predict the risk or presence of cancer. Imprinting is epigenetic in origin and causes gene silencing; consequently, loss of imprinting (LOI) results in re-expression of previously silenced alleles of genes that could contribute to tumour formation. LOI of insulin-like growth-factor 2 (*IGF2*) has been found in several tumour types, but is it predictive of cancer?

LOI of *IGF2* is more common in the colonic mucosa of patients with colorectal cancer than in those without, and the authors investigated whether LOI was also more common in the peripheral blood lymphocytes (PBLs) of people with a family history or personal history of colorectal cancer. They found that LOI was 5.15 times more likely in those with a family history of colorectal cancer than without, and 4.72 times more likely if they had previously been diagnosed with adenomatous polyps or colorectal cancer. This indicates that LOI is strongly linked with colorectal cancer, and that it can be detected in the blood.

Further analysis showed that patients with a history of colorectal cancer were more likely to have LOI than those with a history of adenomas (21.7 times those with neither, compared with 3.46 times). This is consistent with the adenoma–carcinoma progression hypothesis of colo-rectal cancer, and indicates that LOI of *IGF2* could be associated with initiation or progression.

So, what is the association between LOI in the colon and in PBLs? If LOI was present in PBLs, it was also present in the colon, but there were cases in which LOI was only present in the colon. In these, however, there was no statistically significant association with cancer, so the use of detecting LOI in the blood is not undermined.

The ease of performing blood tests of risk assessment is improved if the test is based on DNA, rather than RNA. Fortunately, a differentially methylated region within *IGF2* is predictive of LOI. Its hypomethylation is associated with LOI in normal tissue and blood, as well as in colorectal cancer patients.

An LOI blood test might be a useful screening test in the general population, as it is predictive of colorectal cancer, and is more prevalent than other colorectal-cancer-predisposing mutations. However, large prospective trials must be performed before it could be introduced.

Emma Greenwood

References and links

ORIGINAL RESEARCH PAPER Cui, H. *et al.* Loss of *IGF2* imprinting: a potential marker of colorectal cancer risk. *Science* **299**, 1753–1755 (2003)

FURTHER READING Ransohoff, D. F. Developing molecular biomarkers for cancer. *Science* **299**, 1679–1680 (2003)

WEB SITE

Andrew Feinberg's lab:
http://www.hopkinsmedicine.org/geneticmedicine/Faculty/FacultyProfile.cfm?ProfileID=3