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Molecular profiling can accurately predict survival in colon cancer patients

Barcelona, Spain: Researchers in The Netherlands have developed a method of accurately predicting which patients with colon cancer are most likely to have their disease recur after surgery and who would, therefore, be likely to benefit from additional chemotherapy.

Led by Professor Rob Tollenaar at Leiden University Medical Center and Dr Laura Van 奏 Veer at The Netherlands Cancer Institute, they have analysed for the first time the different expressions of genes in the entire genome of tumour tissues from 121 patients with stage II colon cancer who had not received adjuvant chemotherapy.

Prof Tollenaar, who is head of sections endocrine, gastrointestinal and oncologic surgery in the department of surgery, told a news briefing at the European Cancer Conference (ECCO 14) in Barcelona, today (Tuesday) that the full-genome molecular expression profiling had identified two groups of patients that had distinct clinical outcomes.

Patients with stage II colon cancer have an overall five-year survival of about 80%,"he explained. So far, no randomised clinical trials has shown significant benefit from giving adjuvant chemotherapy. Three-quarters of patients are cured by surgery alone and, therefore, less than 25% of patients would benefit from additional chemotherapy.

Our analysis showed a cluster of 75% of the patients, of whom approximately 90% were likely to survive for at least five years with no distant metastases. In the second cluster of the remaining 25% of the patients, only about 65% of them had five-year survival without distant metastases, and this is the group who would be likely to benefit from adjuvant chemotherapy.

This is the first time that the identification of a poor survival group has been based on genome-wide expression analysis and, therefore, it relates tumour biology more accurately to the outcome of disease.

Further analysis of the results showed that patients in the poor outcome group were over three times (3.2) more likely to develop metastases than the patients in the good outcome group. This method of identifying poor outcome patients was better at predicting which patients should have adjuvant chemotherapy than the commonly-used method that follows recommendations from the American Society of Clinical Oncology (ASCO).

The researchers checked their findings against information from another set of colon cancer patients that had been published in the Journal of Clinical Oncology in 2005. Prof Tollenaar said: 的 n these stage II colon cancer patients, the five-year metastasis-free survival prediction was confirmed; for the good outcome group, five-year survival was 90% and for the poor outcome group it was 40%. This was important validation of our own results.

From the genome-wide analysis, the researchers identified a subset of 100 genes that were able to predict outcome equally as well as the full-genome molecular expression profile. Many of these genes are know to regulate the Epithelial-Mesenchymal transition (EMT) a programme of cell development that is thought to be a driving force behind the development of metastases in colorectal cancer.

Prof Tollenaar said that although his research predicted outcome of disease in patients who had not received adjuvant chemotherapy, more work would need to be done to identify the molecular profile for those patients who would actually benefit from chemotherapy.

Before the results of this research could start to be used in the clinic, Prof Tollenaar said two things needed to happen: current, ongoing validation studies required to confirm our findings have to be completed, and the test needs to be developed into a robust diagnostic device. The molecular profiling company Agendia BV of Amsterdam has taken this up and it is likely to be available in early 2008.

As to whether these findings would save large numbers of colon cancer patients from unnecessary chemotherapy, Prof Tollenaar said: this depends greatly on the current practice in different European countries. For example, in Spain 60% of stage II colon cancer patients receive adjuvant chemotherapy, while in The Netherlands only 20% do. So in some countries it will result in a decrease in the number of patients receiving chemotherapy and in others, an increase; but both outcomes will result in a more accurate selection of patients.

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