MedicalXpress

New model may help predict response to chemotherapy for colorectal cancer

January 17 2013

Scientists may be able to better predict which patients with colorectal cancer will respond to chemotherapy using a new mathematical model that measures the amount of stress required for a cancer cell to die without harming healthy tissue. The results of this study are published in *Cancer Research*, a journal of the American Association for *Cancer Research*.

"Our study demonstrates that systems medicine approaches (i.e., quantitative analysis of multiple factors in patients' samples combined with mathematical modeling) have a significant advantage over other approaches in predicting therapy responses in patients," said Jochen J.M. Prehn, Ph.D., director of the Centre for Systems Medicine at the Royal College of Surgeons in Ireland.

Apoptosis, or programmed cell death, is believed to be a hallmark of cancer resistance to chemotherapy. Prior research has shown that the key step in apoptosis, the process that leads to mitochondrial outer membrane permeabilization (MOMP) is controlled by different members of the BCL-2 family of proteins. Some family members promote apoptosis and some prevent it. In addition, those proteins that have the same effects on apoptosis work in parallel and can substitute for each other, which makes it difficult to predict whether cells are likely or unlikely to die.

To better inform decision-making in chemotherapy for colorectal cancer, Prehn and colleagues developed a tool that would incorporate

patient-specific, molecular data sets. They studied the BCL-2 proteins, determined levels of the individual proteins and put the levels into a mathematical model that calculated what genotoxic stress level is needed to achieve apoptosis.

"Resistance of colon cancer cells in culture, as well as treatment responses of patients with stages 2 and 3 colon cancer, were critically determined by the calculated stress level required to undergo apoptosis," Prehn said. "We found that individual patients had a high degree of heterogeneity in BCL-2 family protein levels and that this was a potential cause of the success or failure of adjuvant chemotherapy."

Prehn and colleagues tested a clinical decision-making tool that they call DR_MOMP to determine its use in predicting treatment responses in patients with colon cancer. Using DR_MOMP, they were able to robustly predict patient outcome.

"This finding may provide a clinical decision-making tool that enables predictions of treatment responses in patients with colon cancer," Prehn said. "As we provide a quantitative, dynamic analysis of the process of apoptosis, we can also calculate, for individual patients, the therapeutic window."

The model could help predict how much genotoxic stress is required for a cancer cell to die before normal tissue is affected. Prehn and colleagues hope to validate DR_MOMP in other cancers and in larger patient cohorts.

"We need to develop easy and accessible protein profiling and modeling platforms that enable the implementation of this new technology in clinical trials and in pathology laboratories," Prehn said.