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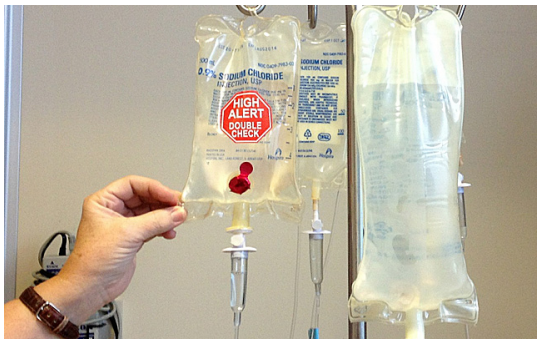
New Biomarkers Might Help Personalize Metastatic Colorectal Cancer Treatment

Low levels of two genes predicts positive response to chemotherapy and longer survival times

Metastatic colorectal cancer patients tend to live longer when they respond to the first line of chemotherapy their doctors recommend. To better predict how patients will respond to chemotherapy drugs before they begin treatment, researchers at University of California, San Diego School of Medicine conducted a proof-of-principle study with a small group of metastatic colorectal cancer patients. The results, published June 17 in *PLOS ONE*, revealed two genes that could help physicians make more informed treatment decisions for patients with this disease.



Metastatic colorectal cancer is typically treated with two chemotherapy drugs, 5-Fluorouracil in combination with either oxaliplatin or irinotecan. A new study uses genetic markers to determine whether oxaliplatin or irinotecan is best for individual patients.

Metastatic colorectal cancer, the third deadliest cancer in the Unites States, is typically treated with two chemotherapy drugs, 5-Fluorouracil in combination with either oxaliplatin or irinotecan.

“Several large trials compared oxaliplatin and irinotecan head-to-head and concluded that the response rate is about equal. How an oncologist bases his or her treatment decision can be based on experience, comfort level prescribing and the patient’s health,” said senior author Paul Fanta, MD, assistant clinical professor of medicine and oncologist at UC San Diego Moores Cancer Center. “But in reality, the two drugs are very different. For any individual patient, one might be better than the other. As an oncologist, how do I know which is better for my patient? That’s where this study comes in.”

Fanta and his team used a commercially available test to analyze levels of the genes ERCC1 and TS in 41 patients with metastatic colorectal cancer. These genes encode proteins involved in building and repairing DNA.

The researchers found that 33 of their 41 patients had low ERCC1 levels. These same patients also had significantly longer average survival times (36 months) compared to patients with high ERCC1 levels (10 months). Similarly, 29 patients had low TS levels and significantly longer average survival times (36 months) than patients with high TS levels (15 months).

Twenty-two of the 41 patients had low levels of both ERCC1 and TS. Of that group, 20 — 91 percent — responded to oxaliplatin, suggesting that this should be the first treatment choice for patients with low ERCC1 and TS. Patients responded to irinotecan at the same rate whether they had low or high levels of these genes. This finding suggests that physicians might want to select irinotecan as the first-choice chemotherapy for patients with high ERCC1 or TS levels. These results are consistent with other studies evaluating the roles of ERCC1 and TS in metastatic colorectal cancer.

According to the authors, ERCC1 and TS profiling could help physicians better manage patients with metastatic colorectal cancer, individualizing and optimizing therapy for subsequent interventions such as surgical removal of metastatic tumors.

“Our study is small, retrospective and all of the patients were located at a single medical center, but it demonstrates that it’s possible to use molecular diagnostics to identify subgroups of patients more likely to respond to a given treatment,” said co-first author John Paul Shen, MD, senior clinical fellow and postdoctoral fellow. “Given this proof-of-principle, it’s our hope that molecular biomarkers will be included in future prospective clinical trials in metastatic colorectal cancer.”

Co-authors of this study also include Michel B. Choueiri, Andrew M. Gross, Justin K. Huang, and Trey Ideker, all of UC San Diego.

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