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Novel personalized medicine trial launched for metastatic colorectal cancer

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Imagine if treatments for disease could be based not on a patient's diagnosis but instead on the characteristics of their tissue. By identifying and decoding the cryptic messages hidden deep inside the human proteome, scientists and physicians who study personalized medicine are seeking more effective treatments and disease management for patients.

Lance Liotta, MD, and Emanuel Petricoin, III, professors of life sciences and co-directors of George Mason University's Center for Applied Proteomics and Molecular Medicine (CAPMM), are pioneers in the field of patient-tailored research and personalized medicine. The two are studying biomarkers (or indicators of disease in tissue and bodily fluids) related to cancer, heart disease, liver disease and obesity.

They recently launched a unique clinical trial in partnership with oncologists and co-principal investigators Kirstin Edmiston, MD, medical director of cancer services at Inova Health System, and Alexander I. Spira, MD, director of Fairfax Northern Virginia Hematology Oncology Research Program, to treat patients with late-stage colorectal cancer, a fatal cancer that starts in either the colon or the rectum.

The three-year trial will accommodate up to 50 men and women who have late-stage colorectal cancer that has spread to the liver. Striking more than 150,000 men and women each year in the United States, colorectal cancer is the nation's third most commonly diagnosed cancer and third leading cause of cancer death according to the American

Cancer Society.

"Traditionally, all colon cancers have been lumped together and given similar treatments. The novelty about this is that we can, in a very minimally invasive way, start to treat the metastatic tumor based on its unique protein makeup. If we're going to be successful in treating the metastatic disease, which is what kills people, then we need to focus on using therapies targeted towards the individuality of a patient's disease state. This clinical trial is the first step toward doing that," says Edmiston.

Trial participants will be treated with standard metastatic colon cancer therapy and will test the addition of Gleevec, a medicine that is typically prescribed for certain forms of leukemia and gastrointestinal tumors. Gleevec targets disease pathways in tumor cells that previous CAPMM research revealed were among those found in typically fatal liver metastasis in colorectal cancer patients.

Because the primary tumors in the colon are removed in most colorectal cancer patients as soon as they are diagnosed, this study will focus on treating the often fatal secondary tumors or metastatic lesions that appear when the disease spreads to the liver, causing death through destruction of that organ.

Using a new drug target mapping technology called "reverse phase protein microarray" that was developed by CAPMM's scientists, the researchers will sample these lesions and create a unique molecular profile or "fingerprint" that shows which protein pathways or drug targets are activated in the lesion. This process will allow the researchers to determine whether specific drugs such as Gleevec might be an effective treatment for this particular patient before it is even administered.

By monitoring the drug target activity in trial participants' tumors and basing their treatment on those characteristics, the researchers are hopeful that this clinical trial will lead to more effective and individualized treatment for patients who suffer from this devastating disease.

"The exciting aspect of this trial is that an established drug is being considered for a new indication, and that's one of the promises of personalized therapy--that a patient's molecular portrait would be considered as the rationale for choice of therapy rather than based on the site or the kind of cancer alone," says Petricoin. "Until now, the most cutting edge clinical trials utilize genomic profiling of the tumor to select patients. This is the first trial that uses a direct proteomic approach that maps the drug target activation networks that are in use in each patient's tumor--just technologically being able to do this in a real clinical trial is a first."

Provided by George Mason University