



Saint Luke's Regional Laboratories Clinical Laboratory Letter



July 2010

Serum Autoantibody Testing for Lung Cancer

EarlyCDT-Lung™, a test offered by Oncimmune (USA) LLC, detects autoantibodies against six cancer associated antigens found in different types of lung cancer. An indirect enzyme-linked immunosorbant assay is utilized to detect antibodies to a panel of antigens that includes p53, NY-ESO-1, CAGE, GBU4-5, Annexin1, and SOX2. A positive result is reported if antibodies to any one of the six antigens are detected at a concentration above a defined cut-off (*Ann Oncol* 2010 Feb 2 [Epub ahead of print]).

In a study presented at the 2010 annual meeting of the American Society of Clinical Oncology (*J Clin Oncol* 2010;28(15_suppl):7032), this test was performed on 453 patients with newly diagnosed lung cancer and matched high-risk controls (samples collected from multiple sites in the USA, Canada, and Europe) and a second set of 211 small cell lung cancer patients and matched high-risk controls. The overall sensitivity of the test was 40%. Sensitivity for early stage non-small cell lung cancer was 35% (89/258) and for early stage small cell lung cancer was 46% (45/97). Overall specificity for all high-risk individuals was 88%.

This test is being marketed as an aid to risk assessment and early detection of lung cancer in high-risk, asymptomatic patients and for use in conjunction with imaging studies. It should be noted, however, that with 40% sensitivity and 88% specificity, the positive predictive value is only 10% even in the recommended high-risk patient population (<http://www.oncimmune.com>).

Therefore, most patients that test positive will not have cancer, although they may have to undergo additional testing, and high-risk patients with a negative test will still need to be followed regularly. Likewise, although a positive result in a patient with a lung nodule increases the likelihood that it is malignant; a negative test result does not exclude the possibility of malignancy. A biopsy is required for definitive diagnosis in either case.

This test is currently not approved by the FDA and cannot be ordered for inpatients. Saint Luke's Regional Laboratories (SLRL) patient service centers will collect specimens for outpatients with a physician's order. The patient must first obtain a collection kit from Oncimmune. SLRL will draw the specimen and give it to the patient, who will be responsible for mailing it to the company. SLRL will charge a venipuncture fee for this service. Oncimmune will bill the patient's insurance provider if they have Medicare Part B as their primary insurance or if they have private health insurance coverage. If the patient does not have insurance coverage, they must include payment with the collection kit. List price for the test is \$475.

BK Virus Quantitative PCR

BK is a type of polyomavirus that is ubiquitous in nature and infects most people in early childhood. Seroprevalence is 60-100% in epidemiologic studies. Following primary infection, the virus becomes latent in lymphocytes and renal epithelium. Intermittent viral shedding may occur in immunocompetent individuals (up to 20% incidence) and more frequently in immunocompromised individuals (up to 60% incidence). BK is so-named from the initials of the patient from whom the virus was first isolated. A related polyomavirus that infects humans is JC virus, which is associated with progressive multifocal leukoencephalopathy.

BK virus reactivation is a major concern for renal transplant and bone marrow transplant recipients. Reactivation has been linked to tubulointerstitial nephritis and nephropathy as well as ureteral stenosis in renal transplant patients, while bone marrow transplant patients are at risk for hemorrhagic cystitis. BK virus associated nephropathy is an important cause of allograft failure and affects renal transplant patients an average of 44 weeks post-transplant. Increasing degrees of immunosuppression are associated with increased risk for BK reactivation.

Quantitative PCR for BK virus DNA in blood or urine specimens is useful for monitoring and diagnosis of BK-associated complications in transplant recipients. In general, the levels of urinary BK virus DNA are 100 to 1000-fold higher than in blood, and the presence of urinary BK virus DNA precedes detection in blood specimens. Increasing viral load and sustained viremia have been associated with development of nephropathy post-renal transplant.

Beginning in August 2010, Saint Luke's Regional Laboratories Molecular Diagnostics will perform PCR testing for BK virus DNA. The lower reportable range will be 500 copies per mL. Specimen requirement is 1mL EDTA plasma or 1mL urine from a random collection. Turnaround time will be within 48 hours.

Can Genes be Patented?

The United States Patent and Trademark Office has issued over 40,000 patents on sequences of human DNA. Experts estimate that 20% of the human genome is now covered under patents held by academic institutions, private biotechnology companies and the diagnostic development industry.

Last year the American Civil Liberties Union (ACLU) filed suit against Myriad Genetics and the University of Utah on behalf of five cancer patients. Myriad holds exclusive patents on the BRCA1 and BRCA2 genes, which are linked to breast and ovarian cancers. The suit was prompted by patients who sought confirmatory testing for their BRCA1 and 2 test results. Myriad exercises exclusive patent rights, so they are the sole provider of BRCA1 and 2 analyses nationwide. The ACLU argued that Myriad's patents restrict patient access to genetic testing and create a monopoly that limits options and drives up costs. The suit further contends that such patents are contrary to patent law because genes are products of nature. The lawsuit is supported by prominent scientific organizations, including the Association for Molecular Pathology as lead plaintiff, and the College of American Pathologists, the American Society for Clinical Pathology and the American College of Medical Genetics.

On March 29 of this year, New York District Court Judge Robert Sweet ruled against Myriad Genetics, invalidating seven patents related to the two genes.

In a carefully rendered decision, Judge Sweet recognized the larger question of whether human genes can be patented even if, as Myriad argued, laboratory techniques are used to extract them from blood or tissues. Judge Sweet wrote, "DNA represents the physical embodiment of biological information, distinct in its essential characteristics from any other chemical found in nature. It is concluded that DNA's existence in an 'isolated' form alters neither this fundamental quality of DNA as it exists in the body nor the information it encodes".

Myriad intends to appeal and the case may ultimately reach the Supreme Court. A final decision will have major implications for both individuals and society. If Myriad's patents are upheld, most of the human genome will eventually be under patent protection. The availability, timeliness and cost of medical genetic testing would be controlled by large commercial laboratories and the diagnostic industry. Some patent holders would maintain exclusive testing services, such as Myriad does with BRCA1 and 2, and Clinical Data Inc does with long-QT syndrome. Others would develop and exclusively market diagnostic testing products that laboratories must use, whether or not the tests perform to the laboratory's quality standards. These scenarios currently exist and would proliferate as patent protection expands. The cost of developing tests for multiple genes covered by multiple patents could be prohibitive.

If Judge Sweet's decision is upheld by higher courts, most gene patents will ultimately be overturned. Patients and physicians would benefit from wider access to less expensive genetic tests. The quality of genetic testing in regulated clinical laboratories would be as good as or better than what is currently available, and inconsistent or questionable results could be confirmed. An unrestricted exchange of scientific information and ideas could produce innovative ways to apply genetic knowledge to the field of medicine. However, biotechnology and diagnostic companies that now base their business plans on gene patents maintain that denial of patent protection would stifle research and development.

The personal, medical and economic aspects of gene patenting will continue to be debated, but the basic question remains – who invented, discovered and owns our genes?