America's Oldest Public Medical School
UNIVERSITY OF MARYLAND MEDICAL CENTER

Division of Molecular Pathology, Department of Pathology, University of Maryland School of Medicine
Molecular Diagnostics Laboratory, Laboratories of Pathology, University of Maryland Medical Center

Molecular Profile

A newsletter of Molecular Diagnostics & Molecular Pathology

"Individualized Molecular Testing for Personalized Medicine" will be the theme of the 4th annual symposium; date is set on October 14, 2008

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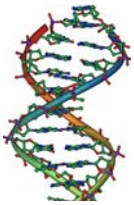
News highlights

- Division of Molecular Pathology concluded its third annual symposium
- New molecular diagnostic tests for monitoring kidney transplantation
- New gene array test for monitoring heart transplantation
- Individualized testing for arterial and venous thromboembolic disorders
- New AmpliPrep TaqMan Cobas system HIV-1 viral load testing



Inside this issue:

Division of Molecular Pathology Concluded Its Third Annual Symposium

The Third Annual Symposium on Translational Research in Molecular Pathology has concluded in late October of 2007. Theme of the symposium was "Clinical Applications of Genomics". The symposium was held at the Davidge Hall and was part of the School of Medicine's bicentennial celebrations. The symposium highlighted the most recent developments and clinical applications of genomic research from genomic medicine to translational research in breast cancer. Dean E. Albert Reece, MD, PhD, MBA, Vice President for Medical Affairs, University of Maryland John Z. and Akiko K. Bowers Distinguished Professor and Dean, School of Medicine delivered introductory remarks and emphasized the importance of this symposium. Dr. J. Craig Venter (top photo), founder and president of The J.

Craig Venter Institute, and founder and former president of Celera Genomics, gave the keynote lecture on "From Humans to the Environment." Celera Genomics is well known for its parallel effort with the National Institutes of Health in the first sequencing of the human genome. Venter's contribution to this project was recently celebrated by his inclusion on the 2007 *Time* magazine's "The *Time* 100: The People who Shape our World" list. Besides Venter, seven other nationally and internationally renowned scientists Drs. Andrea Califano (Columbia), Nir Barzilai (Albert Einstein), Angela Brodie (UMB), Claire M. Fraser-Liggett (UMB), Stephen B. Liggett (UMB), Alan R. Shuldiner (UMB), David Sidransky (JHU) and Todd C. Skarr (Indiana U) gave lectures in this symposium. Over 300 people represented 22 academic institutions, governmental agencies and private sectors participated in this symposium. symposium.

New Molecular Diagnostics Tests are offered for BK / JC viral load quantification

A new BK/JC multiplex real-time PCR assay has recently been included to the Molecular Diagnostic Laboratory (MDL) testing menu. These new tests offer rapid and quantitative detections of two human polyomaviruses, i.e., BK virus (BKV) and JC virus (JCV) in urine and plasma compartment of blood samples. To order these tests, 5 mL fresh urine collected in a sterile container and/or 3-5 mL whole blood collected in an EDTA tube (purple top) are required.

Infection of the BKV or JCV at present represents a diagnostic and therapeutic challenge in the transplant patient (TP). Most of the primary BKV infection occurs in the early childhood without specific symptoms and remains latent in renal cells, urinary tract epithelium and B lymphocytes for life, its reactivation arises largely due to the use of new and potent immunosuppressive drugs that often cause severe clinical complications such as tubulointerstitial nephropathy (BKVN) in the renal TP and hemorrhagic cystitis in bone marrow transplant patients. Different from BKV, reactivation of JCV mainly affects the nervous system and has been associated with progressive multifocal leukoencephalopathy (PML) in the HIV+ patients although JCV has also been implicated in BKVN.

Between 1-10% of the renal TPs develop BKVN and about one-half of them lose their graft. Therefore, the mainstay of the viral therapy is the reduction rather than intensification of the immunosupression treatment to allow the successful antiviral immune response of the TP. Although extensive clinical data on these viral infections are now available, successful management of the renal TPs depends on the early detection (normally in urine) and continue monitoring of the viral infection in blood by quantification of the viral load by real-time PCR. For example, detection of high viral load in urine (≥10 million copies/mL) or blood (≥10,000 copies/mL) may indicate potential high risk of BKVN.

With this new detection system, the BKV or JCV can be detected either together or separately. The detection limit of these new tests will be 7,000 copies/mL for plasma and 15,000 copies/mL of for urine with the linear dynamic range between 7,000 copies and 10 billion copies. To order these tests, please contact Cynthia Glaser, Supervisor of the MDL, extension 8-8539 or Dr. Richard Zhao, MDL Director at 6-6300/8-0054 [Luis Rubio].

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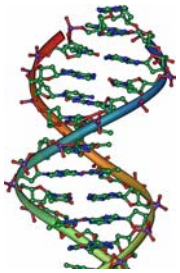

Our goal is to meet the molecular diagnostic needs of physicians and to improve our patient care at the UMMC community, your feedback is important to us

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A publication of the Molecular Diagnostics Laboratory at the University of Maryland Medical Center (UMMC), and the Division of Molecular Pathology, Department of Pathology, University of Maryland School of Medicine

Current test menu of molecular diagnostics laboratory at UMMC

Infectious Diseases	BK/JC Quantitative Multiplex PCR	Ashkenizi Familial Dysautonomia (FD)*
HIV-1 Quantitative RT-PCR	EBV Quantitative PCR**	Factor V Leiden Mutation Analysis by PCR
HIV-1 Genotyping	Toxoplasma gondii Qualitative PCR	Factor II Mutation Analysis by PCR
HIV-1 Virtual Phenotyping	**Genetic and Familiar Disorders**	**Hematology/Oncology**
HCV Qualitative RT-PCR	Cystic Fibrosis (CF)*	Immunoglobulin Gene Arrangement by Southern hybridization
HCV Genotpying	Ashkenazi Canavan Disease (CD)*	Immunoglobulin Gene Arrangement by PCR (VDJ PCR)
HSV-1/2 Qualitative PCR	Ashkenazi Gaucher Disease*	T-cell receptor (TCR) gene arrangement by Southern hybridication
CMV Qualitative PCR	Ashkenazi Tay-Sachs (TS)*	T-cell receptor gene arrangement analysis by PCR
CMV Quantitative PCR	Ashkenazi Niemann-Pick (NP)*	* special request; **available soon

For specific specimen requirement of each test, please log on "http://intra/ummc/index.htm

Implementation of New AmpliPreP TaqMan/ Cobas HIV-1 Viral Load Testing

The Molecular Diagnostics Laboratory has successfully completed its transition from the old Roche's Cobas System to a new and automated AmplicoPreP Cobas/Taqman System for HIV-1 viral loading testing. This transition will improve work efficiency of HIV-1 viral load testing and allow better performance of the assays. As results, we have eliminated the old STANDARD and ULTRASENSITIVE assays. Instead we now have a single test with an improved detection sensitivity of 48 copies/mL of plasma. The new linear detection dynamic range is from 48 copies/mL to 1 million copies per mL. Other viral detection tests such as HCV and HBV will also be implemented in the near future.

To ensure we have adequate amount of blood samples for these tests, a minimum of 3 mL (6 mL is preferred) of whole blood should be collected in sterile tubes using EDTA (lavender/purple-top) as the anticoagulant. PPT tube will no longer be accepted for this testing.

PPT tube will no longer be accepted for HIV-1 viral load testing.

Upon blood draw, store whole blood at 2-25°C for no longer than 6 hours. Separate plasma from whole blood within 6 hours of collection by centrifugation at 800-1600 x g for 20 minutes at room temperature. Transfer plasma to a sterile polypropylene tube and send it to us for testing.

For additional information, call 8-2969/8-8539.

Individualized testing for anti-cancer drug Warfarin/ Coumadin® under development at UMMC Warfarin/ Coumadin®, which is one of the most widely prescribed drugs for the prevention and treatment of arterial and venous thromboembolic disorders. Major risk of using this drug is bleeding that occurs in 1.2-7/100 patients. One solution to avoid bleeding is to lower the dose by identifying those patients who are sensitive to Warfarin/ Coumadin®. This can be accomplished by genetic polymorphic analysis of the *CYP2C9* (CYP2C9*2 and CYP2C9*3) and *VKORC1* (–1639/3673) genes. MDL is currently working with several vendors to implement this test in house.

New gene array test helps heart transplant patients at UMMC It is imperative to monitor sign of rejection of heart transplantation. This monitoring is traditionally carried out by invasive biopsies. An AlloMap test™, offered by the XDX Inc., is now used at UMMC to predict cardiac allograft rejection. This is a simple blood test that is based on a 20 gene panel gene expression profile. For more information or to call this test, Call Dr. Zhao at 6-6300.