UNC HOSPITALS

MEMORANDUM#10

TO: UNC Hospitals Attending Physicians, Housestaff, Nursing Coordinators, Department Heads and Supervisors

FROM: MLG MRB Margaret L. Gulley, MD, Director of Molecular Pathology
Mark Brecher, MD, Director, McLendon Clinical Laboratories

DATE: June 27, 2008

SUBJECT: New Molecular Test to Predict Irinotecan Toxicity and to Confirm Gilbert's Syndrome

The UNCH Molecular Genetics Laboratory now offers a molecular test to detect heritable variants in *UGT1A1* that are associated with altered drug metabolism and risk of toxicity with the antineoplastic agent, irinotecan (CPT-11, Camptostar). The same assay is used to evaluate patients for Gilbert's syndrome.

Clinical indications for testing:

1. To predict toxicity and adjust drug dose accordingly in a patient being considered for high dose irinotecan (>250mg/m^2).
2. To investigate Gilbert's syndrome as a potential cause of unconjugated hyperbilirubinemia in a patient with mildly elevated serum bilirubin.

Sample requirements: 3ml EDTA blood (purple-top tube), may be refrigerated up to 2 days before receipt in laboratory.

Turn around time: Assays are performed weekly.

Method and Reporting: DNA is extracted, amplified using PCR primers flanking the *UGT1A1* promoter sequence followed by capillary electrophoresis to detect length polymorphisms reflecting the number of TA-repeats within the TATA box. Results are reported as heterozygous or homozygous for 5, 6, 7, or 8 TA repeats, along with an interpretation of the clinical implications.

References:

1. Hoskins JM, Goldberg RM, Qu P, Ibrahim JG, McLeod HL: UGT1A1*28 genotype and irinotecan-induced neutropenia: dose matters. *J Natl Cancer Inst* 2007, 99:1290-1295
2. Liu CY et al: UGT1A1*28 polymorphism predicts irinotecan-induced severe toxicities without affecting treatment outcome and survival in patients with metastatic colorectal carcinoma. *Cancer* 2008, 112:1932
3. Huang CK, Dulau A, Su-Rick CJ, Pan Q: Validation of rapid polymerase chain reaction-based detection of all length polymorphisms in the UGT1A1 gene promoter. *Diagn Mol Pathol* 2007, 16:50-53

For further information, consult the McLendon Clinical Laboratories Manual of Pathology and Laboratory Medicine Clinical Services (Website= http://labs.unchealthcare.org/directory/molecular_pathology/index_html), or contact the Molecular Genetics Laboratory at 966-4408 or Dr. Gulley at margaret_gulley@med.unc.edu.