



CONTACT	Lynn Shepherd	Ketura Lispi
	Vox Medica, Inc.	Vox Medica, Inc
	(267) 250-7378	(215) 925 9901
	lshepherd@voxmedica.com	klispi@voxmedica.com

***University of Miami Team Confirms Value of Monitoring Cell-Mediated Immunity
Pre- and Post-Transplant in Management of Kidney Transplant Recipients***

New data presented at annual American Transplant Congress in Toronto

EMBARGOED UNTIL 5:00 p.m. EDT, MONDAY, JUNE 2, 2008

Miami, FL – Manuel R. Carreno, MD, and colleagues in the Departments of Surgery and Pathology at the University of Miami Leonard M. Miller School of Medicine have confirmed the value of monitoring cell-mediated immunity (CMI) post transplant in recipients of kidney transplants using a regular laboratory assay of cell function (ImmuKnow[®]/Cylex). Their paper, entitled “Immune monitoring with Cylex ImmuKnow[®] in the management of post kidney transplant recipients,” will be presented on June 2 at the annual meeting of the American Transplant Congress in Toronto, Canada.

“The production of cyclic adenosine monophosphate (cAMP) by mitogen-stimulated peripheral CD4+ T-cells using the ImmuKnow assay has previously be shown to have utility in the management of several forms of organ transplantation,” stated Dr. Carreno, “In this study, we wanted to learn whether the ImmuKnow test data correlated with data from other tests and clinical findings in patients undergoing kidney transplantation.” Dr Carreno is the Assistant Director of Flow Cytometry and Cell Analysis in the UM Transplant Laboratories.

Patients undergoing kidney transplantation were immunosuppressed post-transplant and their immunosuppressed state was maintained with a combination of tacrolimus (Prograf[®]) and low-dose steroids. A total of 2,096 specimens were drawn from 339 transplant patients, and additional samples were provided by normal controls. Levels of CMI, as measured in terms of levels of ATP, were measured using the ImmuKnow assay and categorized according to the tests labeling: “low” (<225 ng ATP/mL), “moderate” (225-525 ng ATP /mL) and “strong” (>525 ng ATP /mL).

Several patterns of ATP level over time were noted in the patients and in the normal controls, as follows:

- The mean level of CMI for blood samples from normal controls (n = 20) was 432 ± 150 ng ATP/mL (generally well within the “moderate” range).



- Blood samples from patients prior to kidney transplant (n = 91) had a mean CMI level of 342.1 ± 155 ng ATP/mL, which was lower than that of the normal controls but significantly higher ($p < 0.005$) than the levels post transplant (see below).
- Blood samples taken from patients within four time periods post transplant had the following mean CMI levels
 - 1 to 30 days (Month 1): mean CMI = 203.7 ± 171 ng ATP/mL
 - 31 to 365 days (Months 2 to 12) mean CMI = 249.1 ± 162 ng ATP/mL
 - 366 to 730 days (Year 2) mean CMI = 278.3 ± 147 ng ATP/mL
 - 731 to 1,090 days (Year 3) mean CMI = 263.5 ± 136 ng ATP/mL

Patients whose pre-transplant CMI level tested in the “strong” ImmuKnow range (n = 10), and whose CMI level remained in the “strong” range post-transplant, showed no evidence of organ rejection. Several patients showed evidence of cellular (n = 8) or humoral (n = 2) rejection while under monitoring. The patients demonstrating cellular rejection all had increases in CMI > 200 ng ATP/mL, with rapid returns toward the mean post-transplant CMI level after good immune function as restored. The two patients demonstrating humoral rejections showed no changes in CMI. Finally, of the 23 patients who contracted infections, 21 (91 percent) demonstrated a drop in CMI level of > 150 ng ATP/mL.

“We believe that serial monitoring of blood samples from kidney transplant patients pre- and post-transplant is now an important aid in the clinical management of these patients,” said Phillip Ruiz, MD, PhD, the senior author of the paper, professor of surgery and pathology and head of the Division of Immunopathology and UM Transplant Laboratories. “CMI levels vary significantly, even among stable transplant patients. However, by establishing pre-surgical and post-surgical baseline levels, and monitoring the patients on a regular basis over time, we are able to watch for sudden, significant changes in the patients’ CMI levels, which are predictive of either infection or onset of cellular transplant rejection.”

The clinical research team further noted that among 29 patients with persistently low CMI levels (< 100 ng ATP/mL) they observed none of the major consequences reported by other investigators and that low absolute CD4+ T-cell levels did not impede the potential for “strong” ImmuKnow response levels.

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Founded in 1952, the University of Miami Leonard M Miller School of Medicine is Florida’s oldest medical school. The UM Miller School of Medicine now serves more than half a million patients with more than 1 million patient encounters every year. The Department of Pathology at the Miller School is world-



renowned for differential diagnoses and for the use of new technologies in disease diagnosis. The Miller School of Medicine is also home to the nation's top-ranked eye hospital, Bascom Palmer Eye Institute, as well as The Miami Project to Cure Paralysis, the Diabetes Research Institute, UM/Sylvester Comprehensive Cancer Center and nation-leading programs in organ transplantation, cochlear implantation, human genetics, digestive disorders and cardiovascular disease. To learn more, visit <http://med.miami.edu>.
