FACULTY SPONSOR'S NAME AND DEGREE: *Keri E. Lunsford , MD, PhD, FACS*
PHONE: (973) 885 - 0730
DEPARTMENT AND INTERNAL MAILING ADDRESS: *Surgery, MSB G586*
E-MAIL:*keri.lunsford@rutgers.edu*
PROJECT TITLE (200 Characters max):

Association of Pre-Transplant Immune Dysfunction with Early Mortality After Liver Transplant

HYPOTHESIS:
Severe pre-transplant immune dysfunction can be assessed through identification of biomarkers which predict the risk of death early after liver transplant, and these relate to immunometabolic derangements and development of immune paralysis.

PROJECT DESCRIPTION (Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)

Due to organ shortage, livers are transplanted in order of recipient medical urgency; however, ethical principles dictate avoidance of futile transplantation. The most common cause of death early after liver transplant (i.e. futility) relates to consequences of an immune system which is *frail* or dysfunctional prior to transplant. We have previously identified the ***Liver Immune Frailty Index (LIFI)***, a pre-transplant biomarker panel that predicts risk of early post-transplant death. In our discovery cohort of 279 liver transplant recipients, pre-transplant measurement of LIFI, based on HCV IgG, and plasma Fractalkine, and MMP3, can discriminate risk of death within one-year following liver transplant with a c-statistic of 0.84 and a false-positive rate of 4%. LIFI-low corresponds to 1.4% one-year mortality compared with 58.3% for LIFI-high. Multicenter validation is necessary to advance the LIFI as an objective clinical index to predict the risk of liver transplant futility. Mechanistically, our data suggest that immune frailty may relate to skewed intracellular energetics and immune cell exhaustion. These alterations likely result from severe cirrhosis-associated immune dysfunction. In preliminary studies, LIFI was determined at the time of transplant. Pre-transplant immune dysfunction is likely a fluid process and may also be responsible for decompensation and death on the waitlist. Ongoing studies related to this research include (1) multicenter validation of the LIFI index, (2) assessment of immunometabolic changes in the development of immune frailty, (3) analysis of mechanisms of immune paralysis associated with T cell and monocyte dysfunction with the development of immune frailty, (4) correlation of immunologic and physical frailty, and (5) longitudinal assessment of the evolution of immune frailty in the pre- and early post-transplant periods. Rotating student will be assigned to one of the areas of study. Research training may include in human subject research and informed consent, collection of patient data through chart review, patient sample collection and processing, immunologic methods such as flow cytometry, Luminex, ELISA, RNAseq, and Sea Horse Assay, and data analysis.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

1. Ayorinde, Tumininu, Guergana G. Panayotova, Anchal Sharma, **Keri E. Lunsford**. Clinical and biomarker assessment of frailty in liver transplantation. Current Opinion in Organ Transplantation. 2021 Oct 1; 26(5): 488-497. doi: 10.1097/MOT.0000000000000911. Epub ahead of print. PMID: 34343156.
2. Panayotova, Guergana G., Sopio Simonishvili, Duc T. Nguyen, Edward A. Graviss, Nikita Aware, Carl J. Manner, Laurie J. Minze, Tumininu Ayorinde, Yong Qin, Lianhua Jin, Linda W. Moore, Flavio Paterno, Ashish Saharia, Constance M. Mobley, Arpit Amin, Mark J. Hobeika, Nikolas Pyrsopoulos, Xian C. Li, James V. Guarrera, R. Mark Ghobrial, **Keri E. Lunsford**. Identification and Internal Validation of a Novel Pre-Transplant BiomarkerPanel

to Predict Mortality Following Liver Transplantation: The Liver Immune Frailty Index. Preprint. (Version 1) available at Research Square. 2022. Epub 05 October 2022. doi: 10.21203/rs.3.rs-2134172/v1 (Under Peer Review at *Nature Communications*)

3. Jin, Lianhua, Alexander Lemenze, Guergana Panayotova, Sopio Simonishvili,Yong Qin, Tumininu Ayorinde, Gagan Prakash, Laurie J. Minze, Flavio Paterno, Lloyd Brown, Arpit Amin, Xian C. Li, R. Mark Ghobrial, James V. Guarrera, **Keri E. Lunsford**. Early Mortality after Liver Transplant is Associated with Pre-Transplant Alterations in Monocyte Phenotype and Gene Expression. American Journal of Transplantation. 22 August 2022, 22(S3): 571. Conference Abstract #479, Presented at the American Transplant Congress 2022, Boston, MA.

4. Panayotova, Guergana G., Duc Nguyen, Edward Graviss, Laurie Minze, Sopio Simonishvili, Tumininu Ayorinde, Yong Qin, Gagan Prakash, Nikita Aware, Korie Cleveland, Carl Manner, Hersh Vyas, Flavio Paterno, Lloyd Brown, Arpit Amin, Xian C. Li, R. Mark Ghobrial, James V. Guarrera, **Keri E. Lunsford**. Internal Validation of a Pre-Transplant Biomarker Panel to Predict Post-Transplant Mortality: The Liver Immune Frailty Index. *American Journal of Transplantation*. 22 August 2022, 22(S3): 514-515. Conference Abstract #418, Presented at the American Transplant Congress 2022, Boston, MA.

THIS PROJECT IS: ☒**Clinical**   ☒**Laboratory**   ☐ **Behavioral**   ☐ **Other**

THIS PROJECT IS CANCER-RELATED ☐
Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED ☐
Please explain Heart, Lung, Blood relevance

THIS PROJECT INVOLVE RADIOISOTOPES? ☐

THIS PROJECT INVOLVES THE USE OF ANIMALS ☐
        PENDING ☐   **APPROVED** ☐   **IACUC PROTOCOL #**

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS? ☒
        PENDING ☐   **APPROVED** ☒   **IRB PROTOCOL #** Pro2019002643

THIS PROJECT IS SUITABLE FOR: Medical Students
UNDERGRADUATE STUDENTS ☐   ENTERING FRESHMAN   ☐
SOPHMORES   ☐   ALL STUDENTS   ☐

THIS PROJECT IS WORK-STUDY: **Yes** ☒   **or**   **No** ☐

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR
 FOR INTERESTED VOLUNTEERS: **Yes** ☒   **or**   **No** ☐

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
Students can expect to learn techniques in human subjects research and immunologic research methods as outlined above as well as data analysis.