LN from young (6 weeks old) mice and acquire LN from aged (11 month old) mice from a collaborator. We will section LN for ex vivo analysis, including quantification and localization of collagen I using immunofluorescent staining, analysis of microrheological properties using multiparticle tracking (MPT) with PEGylated fluorescent nanoparticles, and migration assays to track the movement of B and T cells. RESULTS/ANTICIPATED RESULTS: We hypothesize a positive correlation between collagen deposits and stiffness within murine LNs due to known mechanisms underlying age-related fibrosis. We also hypothesize that areas of increased stiffness (as revealed by MPT) will exhibit decreased cell migration due to physical hindrance to B and T cell mobilization. Furthermore, we hypothesize that aged murine LN will exhibit a significant increase in stiffness and resultant decreased cell mobility when compared to young murine LN, particularly in areas with increased collagen localization. DISCUSSION/SIGNIFICANCE OF IMPACT: These studies will elucidate structure–function relationships driving age-associated LN fibrosis and stiffness, and the resultant impedance to cell migration, thus clarifying some of the potential driving mechanisms behind immune aging and providing data capable of informing the development of relevant models and interventions.

426

Developing a Molecular Toolkit to define NEK functions in triple-negative breast cancer (TNBC) biology*

Julia Boehling[1], Jack R. Elliot[1,2], Elizabeth C. Martin[1,2], Bridgette M. Collins-Burow[1,2], David H. Drewry[3], Van T. Hoang[1,2], Sean Lee[4] and Matthew E. Burow[1,2]

[1]Department of Medicine, Section of Hematology and Oncology, Tulane University, New Orleans, LA; [2]Tulane Cancer Center, Tulane Univeristy School of Medicine, New Orleans, LA; [3]UNC Lineberger Comprehensive Cancer Center, School of Medicine, UNC at Chapel Hill, Chapel Hill, NC and [4]Department of Pathology and Laboratory Medicine, Tulane University School of Medicine, New Orleans, LA

OBJECTIVES/GOALS: The never in mitosis kinase (NEK) family regulates vital processes, namely cell cycle progression, but their potential as therapeutic targets in TNBC has not been fully explored. Our studies aim to develop a toolkit to investigate the functional roles of NEKs in pathologies including carcinogenesis. METHODS/STUDY POPULATION: To assess differential NEK expression in normal and tumor tissues and correlation of gene expression with patient survival, we used Gene Expression Profiling Interactive Analysis (GEPIA) and Kaplan–Meier Plotter (KMPlot) pan-cancer analysis, respectively. Basal NEK protein levels were determined by immunoblot across a panel of cell lines, including breast cancer, osteosarcoma, hepatocellular carcinoma, and non-cancerous cells, to identify appropriate systems for evaluation of NEK function. Doxycycline-inducible cell lines were generated by transduction with lentiviral stocks of NEK shRNA and overexpression constructs and antibiotic selection. Expression was analyzed by qPCR and immunoblot. RESULTS/ANTICIPATED RESULTS: Expression of NEK2, 4, 5, 6, 8, and 11 was higher in breast tumors compared to normal tissue by GEPIA analysis. Further examination using KMPlot showed a correlation between elevated NEK6 expression and decreased overall survival in patients with aggressive cancers. As an initial proof-of-concept study, we analyzed NEK6 protein expression in breast cancer cells. Levels of NEK6 were elevated in TNBC cells (MDA-MB-231) compared to hormone receptor positive (HR+) breast cancer cells (MCF7). Using complementary approaches to investigate the functional role of NEK6 in breast cancer, we depleted NEK6 expression using shRNAs in TNBC cells and expressed NEK6 in HR+ cells DISCUSSION/SIGNIFICANCE OF IMPACT: Because kinase dysregulation promotes oncogenesis and metastasis, targeting kinases is a key strategy in therapeutic development. A NEK-specific molecular toolkit allows researchers to elucidate NEK functions and contributions to carcinogenesis, promoting advancement of novel therapies.

427

Integrating Implementation Science into the Wake Forest Clinical and Translational Science Award

Alexandra Peluso[1], Justin B. Moore[2], Kristie Foley[2], Sarah Birken[2] and Gary Rosenthal[3]

[1]Wake Forest Clinical and Translational Science Institute; [2]Wake Forest University School of Medicine Department of Implementation Science and [3]Wake Forest University School of Medicine Department of Internal Medicine

OBJECTIVES/GOALS: To develop and deploy an academic learning health system (aLHS) Bridge Program to capitalize on our unique organizational strengths in Implementation Science (IS) and to overcome the gap between science and practice that threatens the success of an aLHS. The aLHS Bridges includes an IS Shared Resource, intended to advance IS to practice. METHODS/STUDY POPULATION: The new IS Shared Resource is built on our expertise in dissemination and implementation science, pragmatic, and adaptive trials and the CTSI's prior success in integrating academic and clinical missions. We also leveraged our existing experts to co-lead the aLHS Bridge including Kristie Foley, PhD, inaugural Chair of the Department of Implementation Science, and Gary Rosenthal, MD, Chair of the Department of Internal Medicine. Specifically, the new IS Shared Resource builds on the capacity of the Department of IS, comprised of 36 faculty members (19 primary and 17 secondary/adjunct appointments) with expertise in qualitative and mixed-methods research, stakeholder engagement, participatory research, digital health, and organizational theory. RESULTS/ANTICIPATED RESULTS: The IS Shared Resource is primed to aid faculty with dissemination and implementation needs, including shortening the time of intervention adoption and using implementation science to inform sustainable and effective implementation practice. The IS Shared Resource is equipped to provide consultation services to faculty members to understand their specific request and match IS faculty members who are expertly trained in specific strategies or contexts. DISCUSSION/SIGNIFICANCE OF IMPACT: Leveraging current resources and our first-of-its-kind Department of Implementation Science, our CTSI was able to stand up the IS Shared Resource to support the goals of the CTSA and our greater institution mission. Using a multidisciplinary approach was essential to the success of the IS Shared Resource.

https://doi.org/10.1017/cts.2024.1033 Published online by Cambridge University Press