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POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

Molecular Biomarkers of Aging to Predict Clinical Frailty in Newly Diagnosed Hematologic Malignancy

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Introduction: Older adults with hematologic malignancy (HM) are a growing demographic with wide-ranging therapeutic options. With aging, patient health and treatment decision-making are heterogenous. Treatment decisions are impacted by chronological age, performance status, and comorbidities. An approach to treating older adults based on objective measures of health may better personalize therapy by focusing on physiologic parameters. Here we examined the relationship of a blood-based aging biomarker, p16 ^{INK4a} (p16), with clinical frailty.
Methods: Newly diagnosed patients with HM were enrolled in a prospective study capturing fitness measures and peripheral blood T lymphocyte (PBTL) p16 levels pre-treatment. Clinical phenotypes of fitness included 11 measures: ECOG performance status, Patient-Reported Outcome Measurement Information System (PROMIS) Global Health Scale Short Form v1, Older Americans Resources and Services (OARS) instrumental activities of daily living (IADL), Medical Outcomes Study (MOS) physical function, patient-reported Karnofsky Performance Status (KPS), social activity and social support (MOS) scores, Mental Health Index (MHI), and cognition (Blessed Orientation-Memory-Concentration). Physical function was measured using the Short Physical Performance Battery (SPPB). PBTL p16 was measured using the OSU_Senescence Nanostring CodeSet, which includes 74 additional T cell markers and five controls. PBTL were also examined for DNA methylation. PBTL were extracted, bisulfite converted, and methylation was quantified using the Illumina 850K EPIC methylation array at the TruDiagnostic core laboratory. Raw data was processed using the *minfi* pipeline, followed by normalization, batch correction, and KNN-based imputation using the *GMQN* and *impute* R packages. Principal-component (PC) PhenoAge measures were calculated using the processed methylation values.
Results: Patients newly diagnosed with HM (n=33) (acute leukemia n=13, 39.5%, plasma cell dyscrasia n=13, 39.5%, lymphoma n=4, 12.1%, chronic lymphocytic leukemia=3, 9.1%) and complete p16 analysis with geriatric deficits were included. The mean p16 score was 32.6 (range 1.7-259.7). We quantified a composite deficit index defined as a frailty score higher than the third quartile using the aggregate score of the above fitness measures (range 0 to 11). Using a threshold for p16 $\geq$31.9, the model had 80% sensitivity and 79% specificity to identify frailty. The positive predictive value was 0.40, the negative predictive value was 0.96, and the accuracy was 0.76. The area under the ROC curve (AUC) for frailty versus p16 was 0.725. PBTL p16 was also explored in relation to other biomarkers of interest including epigenetic age (n=50). PBTL p16 correlated with PhenoAge r=0.38, p=0.0067.
Conclusion: Aging biomarkers provide a novel means to quantify physiologic age in newly diagnosed HM. PBTL p16 levels showed a significant relationship with a composite metric of clinical fitness and accelerated aging in patients with different HM. PBTL p16 was both a sensitive and specific blood-based biomarker to identify clinical frailty in this preliminary analysis.

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Figure 1 A. PBTL p16 score of ≥31.9 has a sensitivity of 80%, specificity of 79% to detect clinical frailty in newly diagnosed HM. B. PBTL p16 levels correlate with PBTL epigenetic age as measured by mPhenoAge.

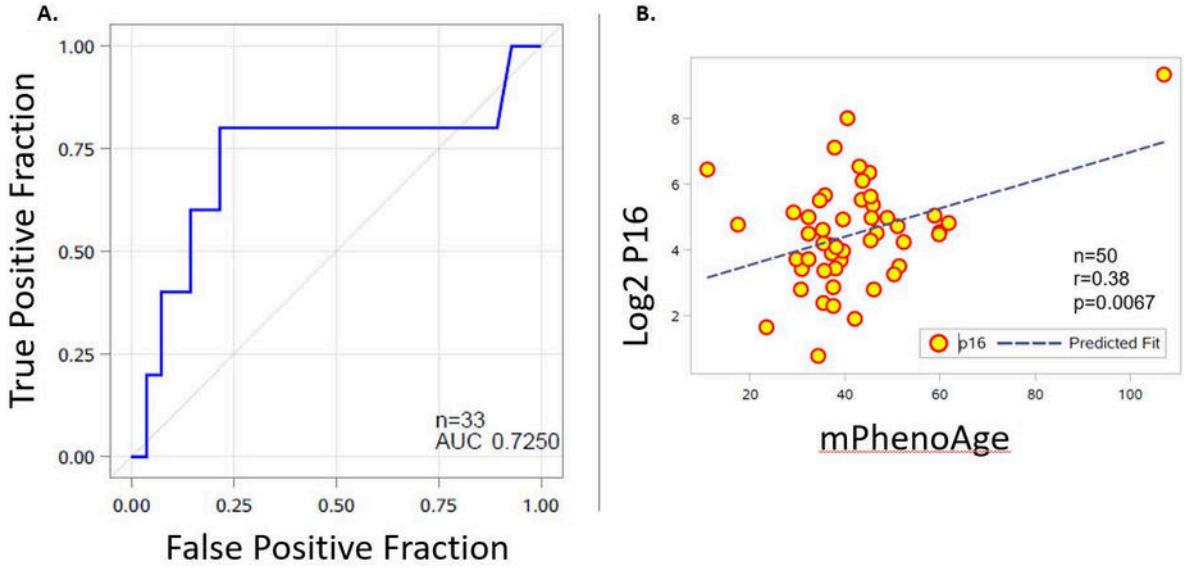

Figure 1

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