Weill Cornell Medicine

HERV-K Expression as a Biomarker for Predicting Immunotherapy Response

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Background & Unmet Need

- Immune checkpoint blockade (ICB) therapies, such as anti-PD-1 and anti-CTLA antibodies, have demonstrated great success in a variety of cancers
- Despite eligibility for immune checkpoint blockade (ICB) therapy increasing over 30x, response rates continue to barely exceed 12%
- Biomarkers for predicting patient responsiveness currently in use, including PD-L1 expression, tumor mutational burden, and microsatellite instability fail consistently classify patients with high accuracy
- A variety of host factors influencing ICB efficacy have been proposed, including human endogenous retroviruses (HERVs), a type of transposable element contributing to oncogenesis
- **Unmet Need:** Additional biomarkers that enable more accurately prediction of patient responsiveness to ICB therapies

Technology Overview

- **The Technology:** HERV-K/HML2 provirus expression as a biomarker for predicting response to ICB therapy and identifying patients who may benefit from supplemental antiretroviral therapy
- **The Discovery:** An extreme boosted gradient machine learning model (XGBOOST) was developed to identify bacterial and viral signatures associated with ICB response among RNA from 139 melanoma, NSCLC, RCC, and GBM tumor samples
- HERV-K/HML2 expression was identified as a key factor for response to ICB therapy
- **PoC Data:** The XGBoost model identified 8 proviruses which classify participants by ICB response (AUC-ROC=0.801)
- HERV-K expression was found to be significantly higher in human cancer cell lines than healthy mouse cells
- Treatment of A375 melanoma cells with antiretroviral compounds suppressed HERV-K expression levels

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Patents:
Provisional Filed

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Cornell Reference:
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Weill Cornell Medicine

GBM: Glioblastoma; ICB: Immune checkpoint blockade
NSCLC: Non-small cell lung cancer; RCC: Renal cell carcinoma

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Technology Applications

- Method to identify patients who are likely to respond to ICB therapy in melanoma, NSCLC, RCC, and/or GBM
- Identification of patients who may may benefit from supplemental antiretroviral therapy in combination with ICB therapy
- Use as a biomarker for patient selection or stratification for ICB clinical trials

Technology Advantages

- Broad applicability across multiple solid tumor types
- HERV-K expression may provide an independent biomarker to complement existing biomarkers for ICB therapy, such as PD-L1 expression, microsatellite instability, and tumor mutational burden

Supporting Data / Figures

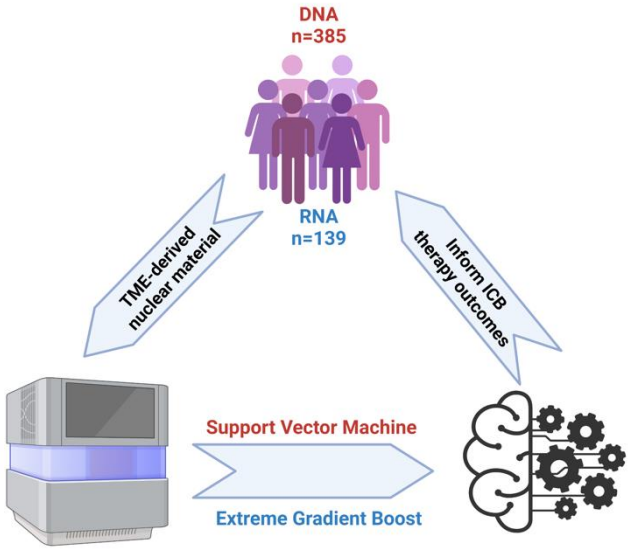

Figure 1: Graphical abstract of XGBOOST and SVM model development.

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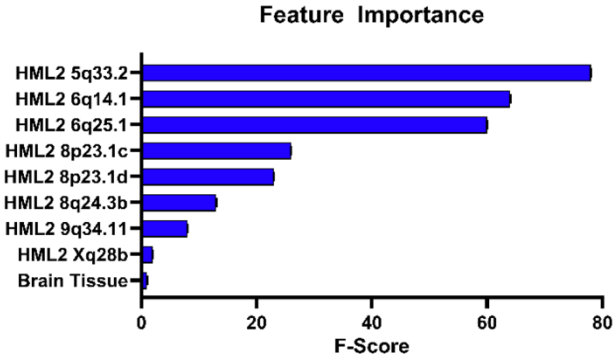

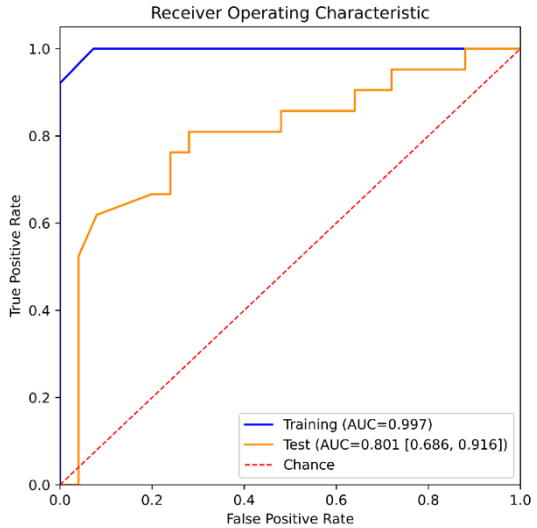

Figure 2: Left: 8 HERV-K/HML proviruses were identified by XGBOOST which classify participants by ICB response **Right:** AUC-ROC for ICB prediction using XGBOOST.

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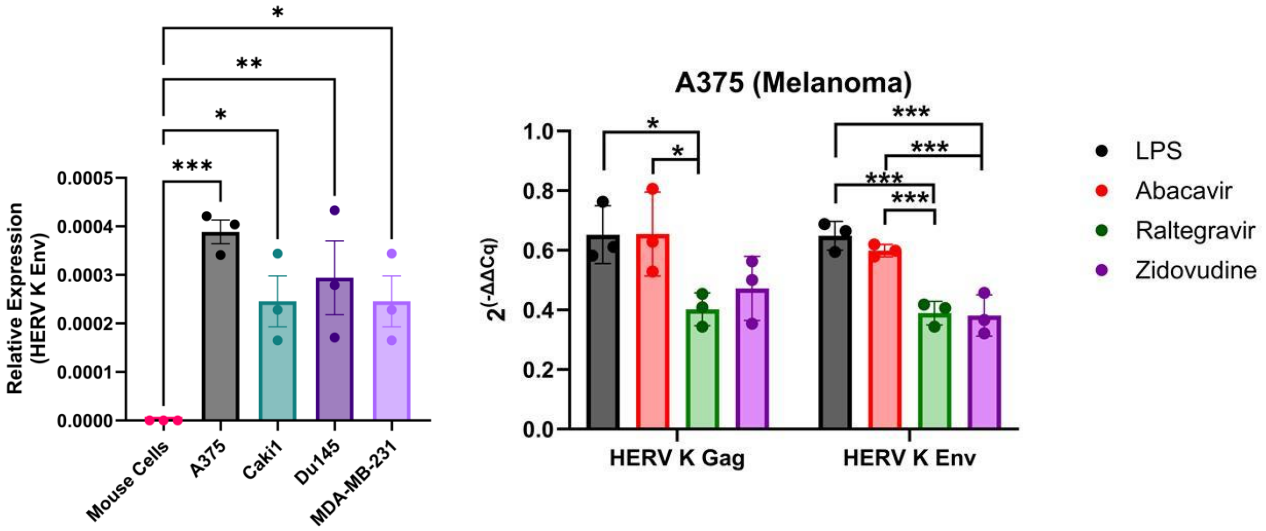

Figure 2: Right: HERV-K Env expression is significantly higher in human cancer cell lines than in control mouse cells: A375 (melanoma), Caki1 (renal cell carcinoma), Du145 (prostate cancer), MDA-MB-231 (breast cancer) **Right:** Antiretroviral compounds suppress HERV-K expression in A375 melanoma cells.

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