VALIDATION OF AN FLT3 ACTIVITY SIGNATURE TO PREDICT FLT3 INHIBITOR RESPONSE IN ACUTE MYELOID LEUKEMIA

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INTRODUCTION

Emerging evidence suggests that patients with FLT3^{WT} AML may benefit from treatment with FLT3 inhibitors (FLT3i)[1] and the FLT3 mutation-like microarray-based gene expression signature[2] may help predict which patients with FLT3^{WT} AML are likely to benefit from FLT3i.

AIM

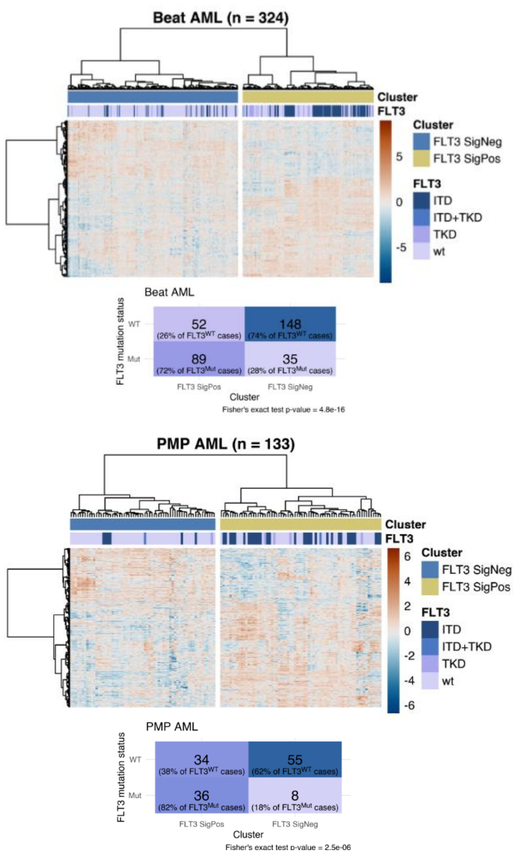
Validation of the FLT3-like gene expression signature among *de novo* AML patients from cohorts with **higher resolution RNA-seq data**.

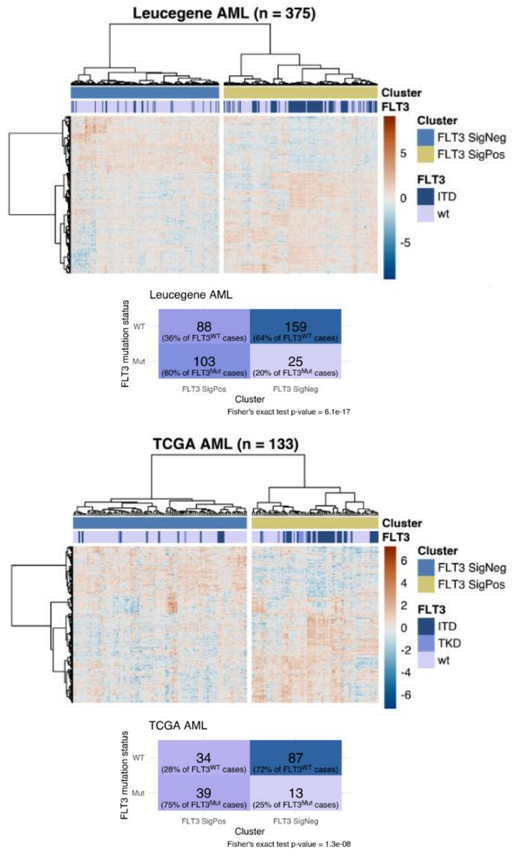
DESIGN

We accessed publicly available RNA-seq and clinical data for patients with *de novo* AML from: the **BEAT AML**, the **Québec Leucegene**, the **AML Personalized Medicine Program** (AML PMP) and **Cancer Genome Atlas** (TCGA AML) cohorts. We determined 572 unique genes corresponding to the 911 probes from the Orgueira signature. FLT3-ITD/TKD mutation status was assigned to as many patients as possible to optimize clustering.

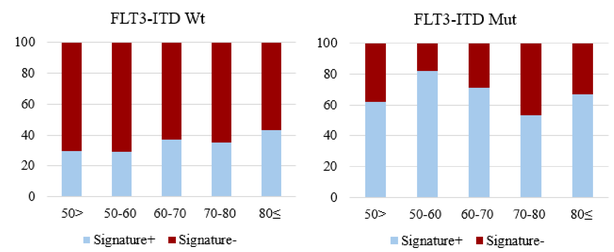
Gene signature was also correlated with response to FLT3i *in vitro* using the BEAT AML data.

RESULTS

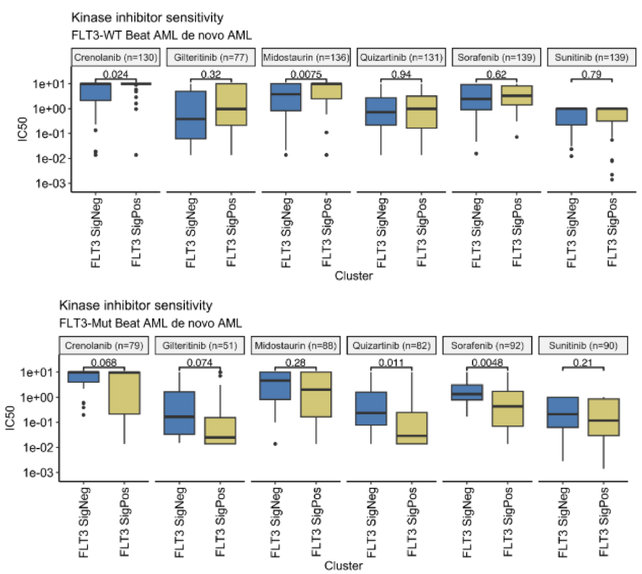




Age related effects on FLT3-like gene signature



In Vitro TKI drug sensitivity assays



CONCLUSIONS

- The FLT3-like gene signature can be applied to RNA-seq data with reproducible results.
- These findings support the feasibility and utility of applying the signature for optimal selection of FLT3WT patients eligible for intensive chemotherapy and FLT3i.
- Lack of in vitro sensitivity suggests another mechanism by which FLTi result in improved outcomes for FLT3WT patients.

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2 Mosquera Orgueira, A. et al. Gene expression profiling identifies FLT3 mutation-like cases in wild-type FLT3 acute myeloid leukemia. PLoS One 16, e0247093 (2021).