



RUNX1, General AML

AACR 2017: Poster LB-081/6 – RUNX1- targeted therapy for AML with RUNX1 mutation

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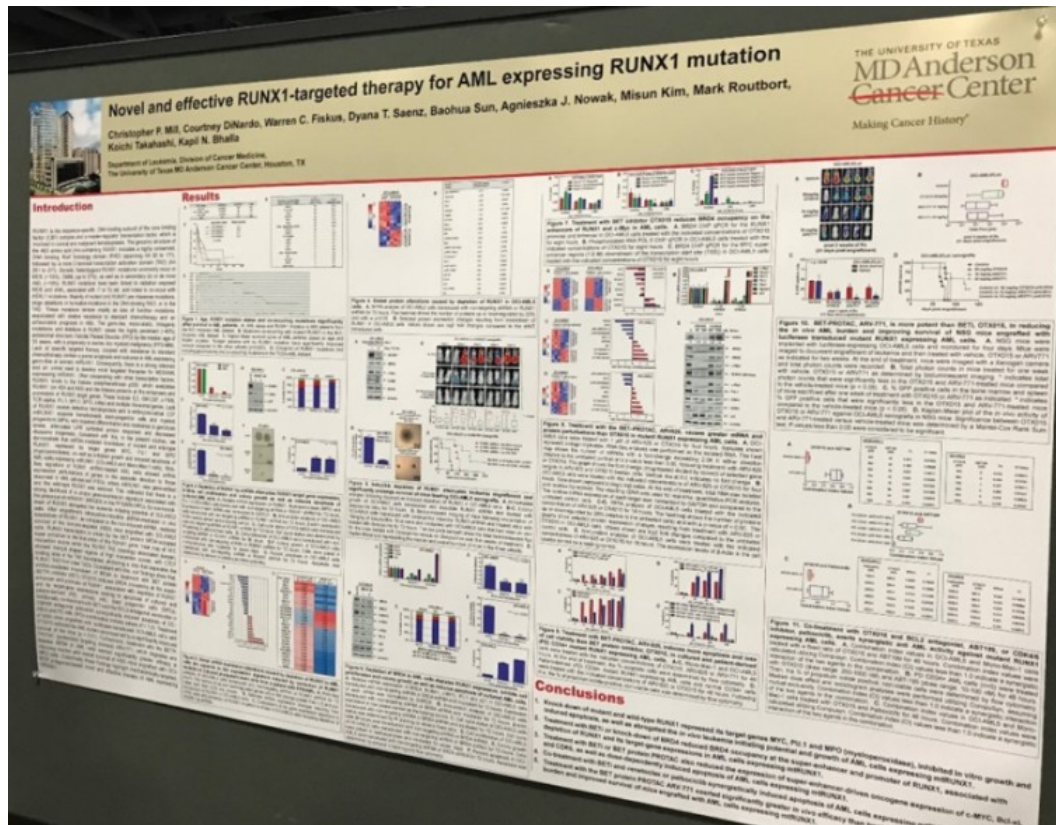
A late breaking research poster session titled “[Molecular and Cellular Biology 2](#)” took place at the [107th American Association for Cancer Research \(AACR\)](#) annual meeting in Washington, DC, USA, on Monday 3rd April. During this session, Mill *et al.* from the [MD Anderson Cancer Center](#) displayed their poster ([LB-081/6](#)) titled “Novel and effective RUNX1-targeted therapy for AML expressing RUNX1 mutation”.

Somatic mutations in *RUNX1* (mt*RUNX1*) are associated with resistance to standard chemotherapy and poor prognosis in Acute Myeloid Leukemia (AML) patients. Mill *et al.* aimed to develop a novel targeted therapy for AML expressing mt*RUNX1*.

The key results were:

- In OCI-AML5 cells (mutant *RUNX1* AML cell line), shRNA depletion of *RUNX1* led to an attenuation of *RUNX1* target gene expression, inhibition of cell proliferation, and an increase in apoptosis
- Depletion of Bromodomain-Containing Protein 4 (BRD4) in OCI-AML5 cells led to a decrease in *RUNX1* expression, inhibition of cell proliferation, and an increase in apoptosis
- OTX015 (Bromodomain and Extra-Terminal [BET] Protein [BETP] inhibitor) reduced BRD4 occupancy at the enhancer and promoter of *RUNX1* in OCI-AML5 cells
- Treatment of NSG mice engrafted with luciferase-transduced OCI-AML5 cells with OTX015 reduced the AML burden and significantly improved their survival ($P < 0.01$)
- Co-treatment with the OTX015 and ABT-199 (BCL2 inhibitor) or palbociclib (CDK4/6 inhibitor) or decitabine synergistically induced apoptosis of OCI-AML5 and PD AML BPCs

In summation, BETP antagonist-based therapy for AML expressing mt*RUNX1* was effective either alone or in combination therapy.



References

1. Mill C.P. *et al.* Novel and effective RUNX1-targeted therapy for AML expressing RUNX1 mutation [Poster]. In: Proceedings of the 107th Annual Meeting of the American Association for Cancer Research; 2017 Apr 1–5; Washington, DC. Philadelphia (PA): AACR; 2017. Poster nr [LB-081/6].