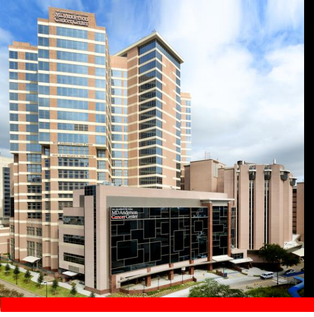

753B Efficacy in Acute Myeloid Leukemia

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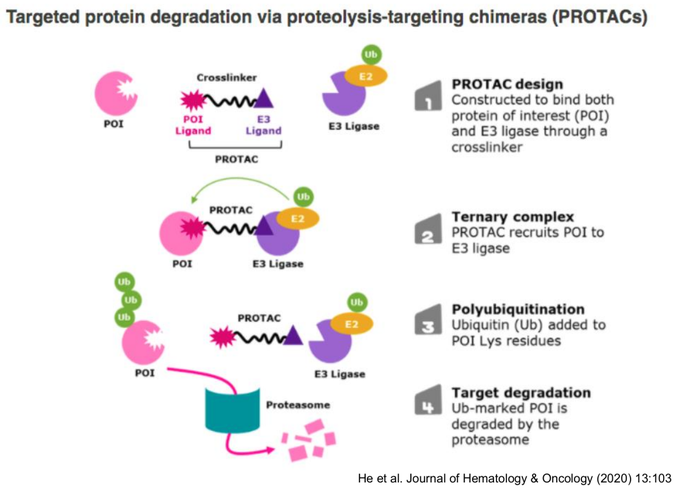
Background

- AML has been shown to be highly dependent on the expression BCL protein family
- BCL-2 inhibition has been shown to be a potent modailty in AML treatment
- Thrombocytopenia in myelodysplasmic syndromes range from 40-65%
- AML has a 30% 5-year prognosis
- 753B is a novel PROTAC bioengineered to degradate the BCL family, specifically BCL2 and BCLXL
- Coinically, 753B should have a greater affinity for targeting AML cells specifcially over other normal cell types, avoiding thrombocytopenia

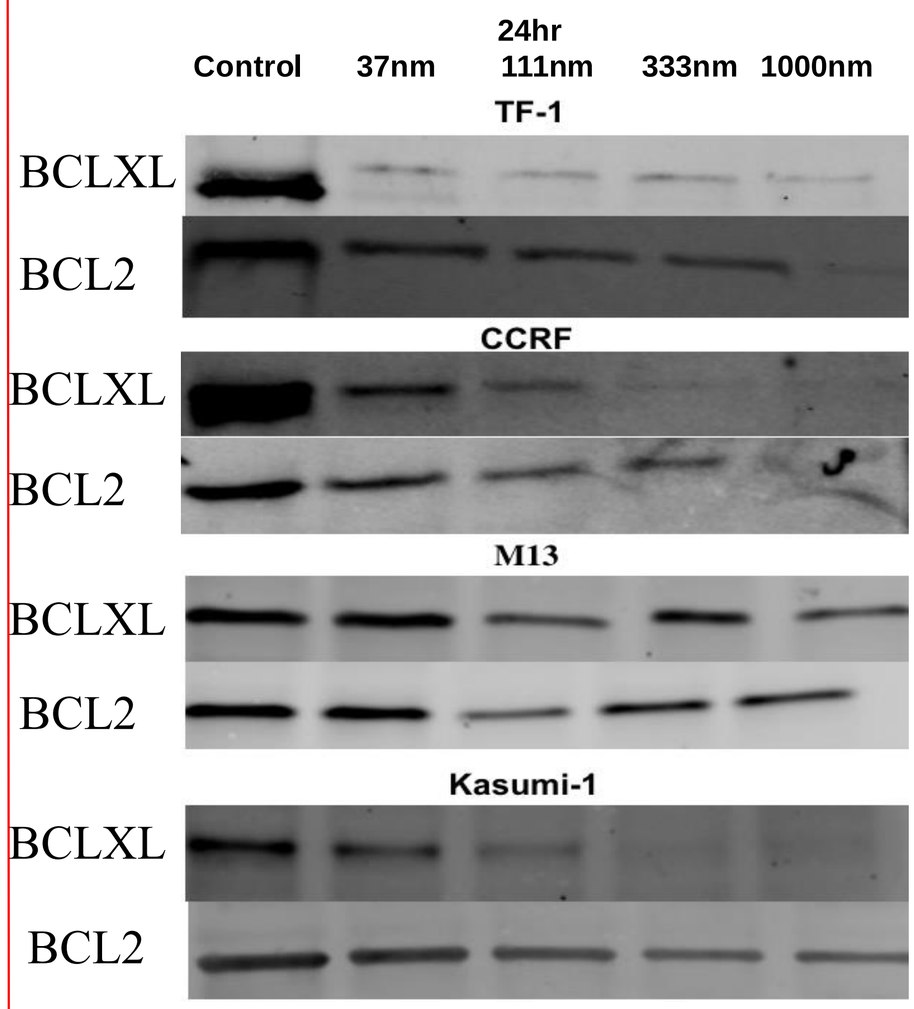


Methods

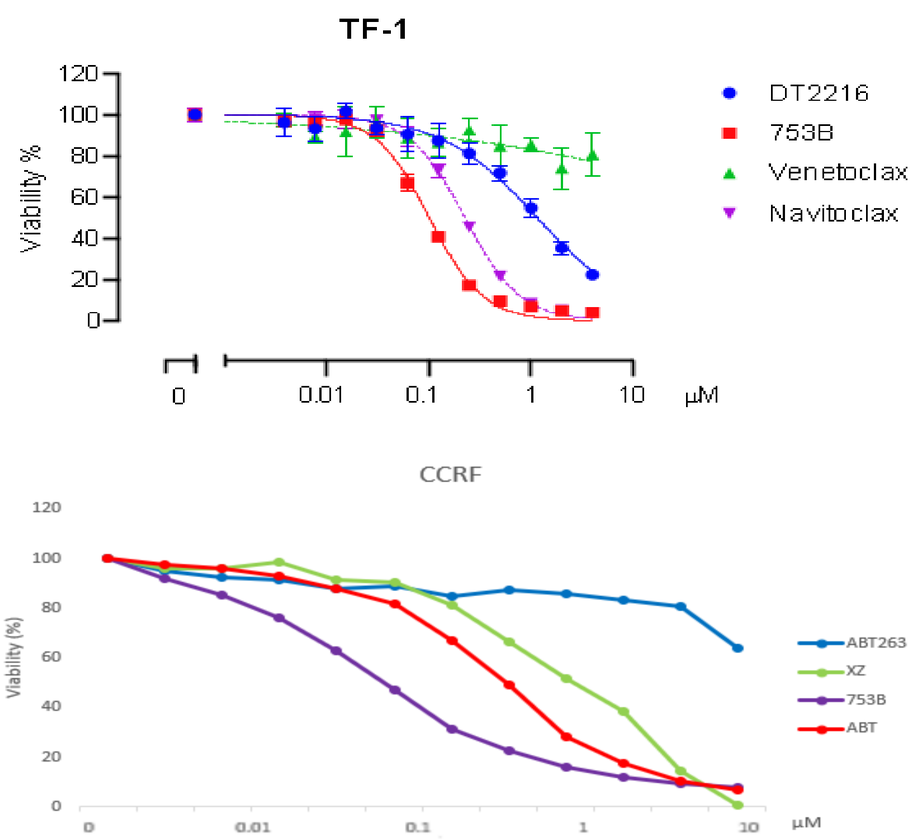
We treated various AML cell lines in vitro to observe the effects of introduction to 753B. We used the BioRad Western Blot system to observe the levels of protein expression degradation as different concentrations (0,37nm,111nm,333nm,1mm) in respective cell lineages. We then ultilized a CTG assay to observe rates of apoptosis induction in cell lines exposed to different drugs at identical concentrations. We used imagestudio and microsoft excel for data analysis and visulaization.

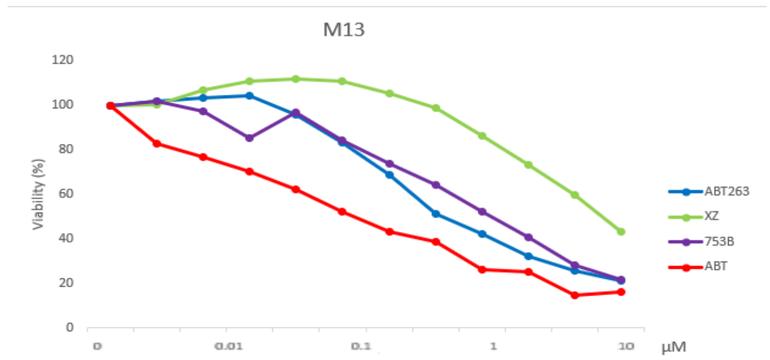
Results

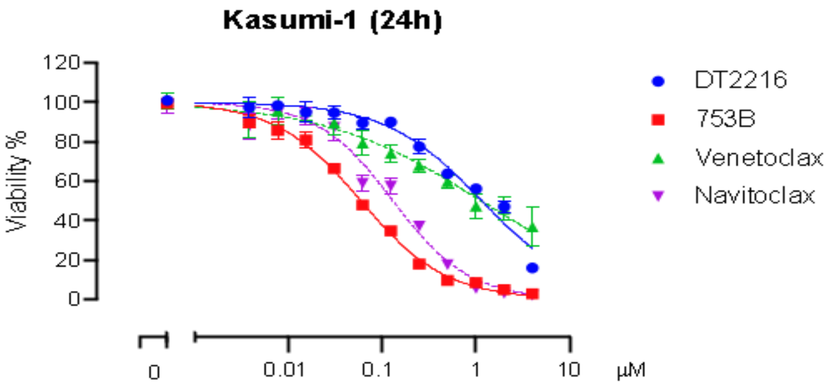
Aim 1: Prove that 753B is effective in BCL protein degradation



Aim 2: Indicate the efficacy of 753B in comparison to venetoclax, navitoclax, DT2216







Conclusions

Our experiments indicate that BCLXL is consitently degradated upon exposure to 753B. BCL2 seems to show moderate levels of degradation but tends to not be as significant or consistnent as BCLXL.The observed BCL2 resistance may be explained by current research, which suggests that certain cells lines which express highe levels of TP73 show BCL2 inhibition resistance. 753B also induces apoptosis at rates greater than or compareable to current drugs. Due to the specificity of 753B to AML cells, compareable apopotic induction may prove advantegous clinically, as the drug may avoid side efects, such as thrombocytopenia induction.

References

https://www.cancer.gov/types/leukemia/hp/adult-aml-treatment-pdq
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