Background

- T-acute lymphoblastic leukemia (T-ALL) is a heterogeneous hematopoietic neoplasm of precursor T-cells.
- Ubiquitin is a small protein that marks proteins for degradation at the proteasome.
- Deubiquitinating enzymes (DUBs) remove ubiquitin, allowing targeted proteins to circumvent destruction.
- USP48 is overexpressed in T-ALL with 4% FBS.

Methods

- Cell culture: HPB-ALL cells, a T-ALL cell line, were maintained in RPMI-1640 medium supplemented with 4% FBS.
- PR-619 treatment: HPB-ALL cells were treated for 24 hours with varying doses of PR-619 (0 μM, 1.25 μM, 2.5 μM, 5.0 μM), a DUB inhibitor.
- shRNA knockdown: HPB-ALL cells were infected with an shRNA, knocking down the gene that encodes for USP48, and compared with cells infected with a control vector.

Hypothesis

USP48, if overexpressed in T-ALL, interacts with BRAT1 to increase cell proliferation and decrease apoptosis, thus contributing to leukemogenesis.

Results

- Prior research from this lab has shown that USP48 is overexpressed in T-ALL cell lines.
- Flow cytometry revealed that cells treated with PR-619 and shRNA showed elevated levels of apoptosis compared to control cells.
- Western blot revealed that BRAT1 expression increased with higher concentrations of PR-619, a DUB inhibitor.
- Western blot revealed decreased BRAT1 with decreased level of USP48, suggesting interaction.
- Immunohistochemical staining detected the expression of USP48 in T-ALL bone marrow specimens.

Conclusions

- Our results show a positive relationship between USP48 and BRAT1, suggesting a role in leukemogenesis.
- Higher levels of USP48 expression is correlated with poorer survival outcome.
- Knockdown and inhibition of USP48 shows increased apoptosis and decreased proliferation.
- Inhibition of USP48 may thus present new target therapy for patients with T-ALL.

References