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Low Dose Doxorubicin Inhibits Immune Checkpoint Upregulation In Acute Leukemias

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INTRODUCTION

- Chemoresistant leukemia stem cells (LSCs) can cause relapse in leukemia
- Doxorubicin (DXR) has been identified as an inhibitor of an immune checkpoint (IC) mechanism of resistance
- Objective: determine the DXR doses that inhibit IC expression upregulation in vitro

METHODS

- Kasumi and Jurkat cell lines were treated with low and high doses of DXR determined by previous kill curve experiments
- Cells were collected at 12h timepoints over the course of 48h and analyzed for expression of CTLA-4, PD-1, PD-L1, TIGIT, and TIM-3 via flow cytometry
- Statistical analysis was done using Tukey's multiple comparisons test

Multiple immune checkpoints show significantly lower expression in low dose doxorubicin treated leukemia cells compared to cells treated with chemotherapeutic dose doxorubicin.

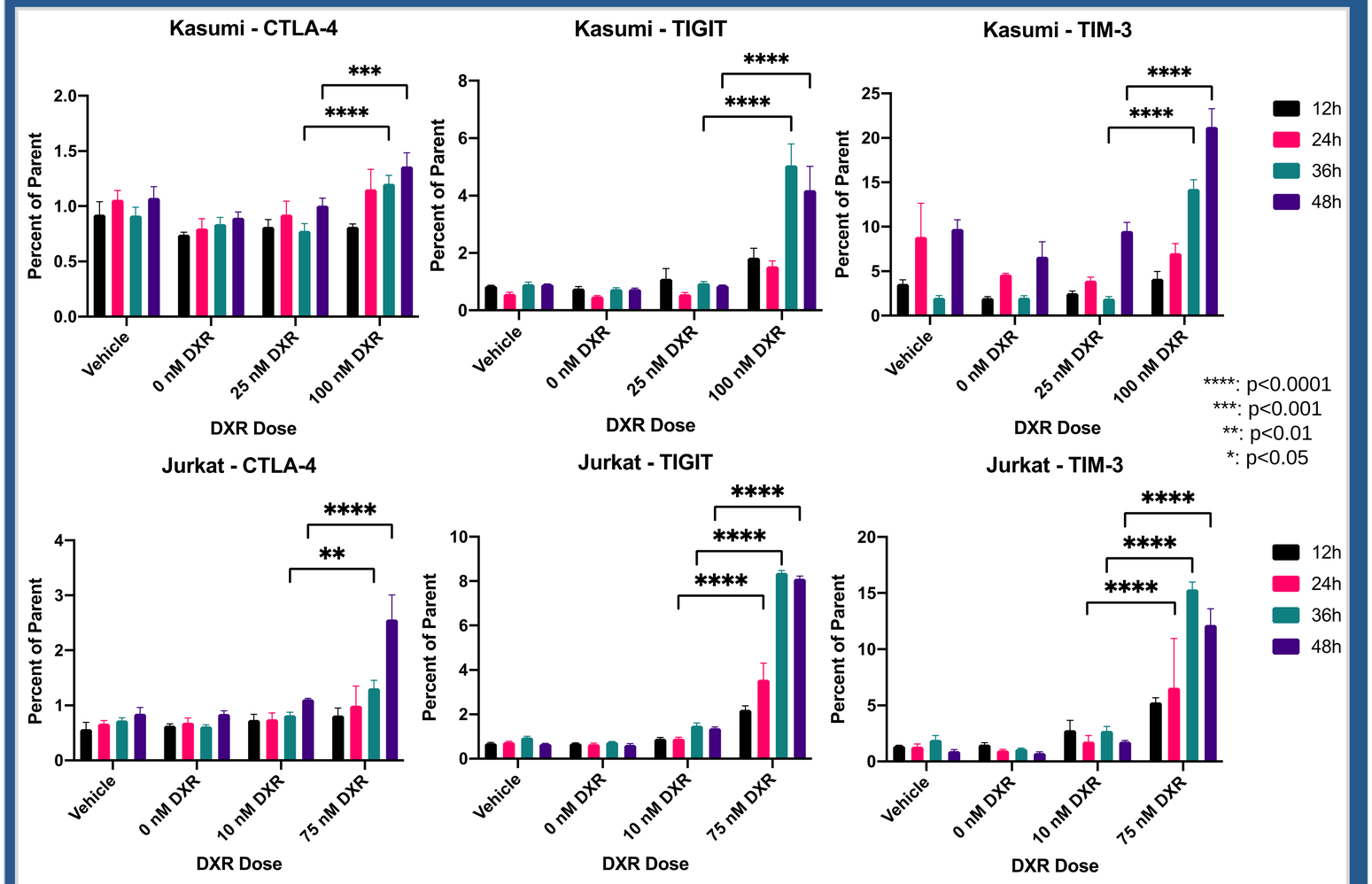

Figure 1: Bar graphs showing expression of CTLA-4, TIGIT, and TIM-3 immune checkpoints in Kasumi and Jurkat cells. Expression is measured as the percent frequency of the parent cell population detected.

RESULTS

- 25 nM DXR treated Kasumi cells showed significantly lower CTLA-4, TIGIT, and TIM-3 expression at 36h ($p<0.0001$) and 48h ($p<0.001$)
- 10 nM DXR treated Jurkat cells showed significantly lower CTLA-4, TIGIT, and TIM-3 expression at 36h ($p<0.01$) and 48h ($p<0.0001$)
- TIGIT and TIM-3 also showed lower expression at 24h ($p<0.0001$)

DISCUSSION

- Results show that in mixed cell populations, low dose DXR prevents the upregulation of multiple ICs within the first two days of treatment
- Overall, this presents a promising strategy for preventing a mechanism of resistance using an established chemotherapeutic agent

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