Low Dose Doxorubicin Inhibits Immune Checkpoint Upregulation in Acute Leukemias

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Submitting/Presenting Author (must be a trainee): Bradley Stockard
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☐ Medical Student
☐ Resident/Psychology Intern (≤ 1 month of dedicated research time)
☐ Resident/Ph.D/post graduate (> 1 month of dedicated research time)
X Fellow

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Other authors/contributors involved in project: Jacqelyn Nemecheck, Kealan Schroeder, Jennifer Pace

IRB Number: study00000341 and IBC00008

Describe role of Submitting/Presenting Trainee in this project (limit 150 words):

Bradley has been responsible for establishing leukemic cell culture and maintaining cell lines for the project. He has reconstituted the various doses of chemotherapeutic agent used in this project and treated cell lines with these agents. Following treatment, he has conducted cell surface staining of immune checkpoint for flow cytometry analysis. Finally, he has performed statistical analysis of flow cytometry data received from the flow core.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background:

Evasion of drug and immune response in therapy-resistant leukemic stem cells (LSCs) is a major cause of relapse. A previous study has identified an alternative mechanism of action for low-dose doxorubicin (DXR) that inhibits upregulation of immune checkpoints (IC) in LSCs.

Objectives/Goal:

The objective of this study is to establish the DXR dose range that will achieve the inhibition of immune checkpoint expression in leukemic cell lines.
Methods/Design:

Cells were analyzed for expression of CTLA-4, LAG-3, PD-1, TIGIT, and TIM-3 via flow cytometry. Analysis was performed on days 3, 5, and 8 of treatment at concentrations identified as low, intermediate, and high from previously generated kill curve data.

Results:

These results show that low dose DXR inhibits upregulation of multiple ICs within the first few days of treatment. Follow up study will be necessary for replication, with particular focus on measuring IC expression within the first three days of treatment.

Conclusions:

Overall, this presents a promising strategy for treating resistant LSCs using an established chemotherapeutic agent.