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May 2nd, 12:00 AM

Investigating the Therapeutic Potential of Soursop in Treating Hematologic Malignancies

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Paparo, Sabrina Marie; Mendoza, Rebeca; Chitren, Robert; Al-Odat, Omar; Nelson, Emily; Jonnalagadda, Subash; Strair, Roger; and Pandey, Manoj, "Investigating the Therapeutic Potential of Soursop in Treating Hematologic Malignancies" (2024). *Rowan-Virtua Research Day*. 129.

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Investigating the Therapeutic Potential of Soursop in Treating Hematologic Malignancies

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Abstract

Acute Myeloid Leukemia (AML) and Multiple Myeloma (MM) are hematologic malignancies that originate in the bone marrow and account for approximately 1.3% and 2% of cancer cases, respectively. AML is characterized by an accumulation of myeloblasts, or immature myeloid cells, that have the potential to spread to the peripheral blood. There is an uncontrolled proliferation of plasma cells in the bone marrow in MM. While the current treatment options for both AML and MM show promise in achieving initial remission, it is unfortunately common for patients to experience relapse and develop drug resistance. There is a theory that relapse and resistance could be attributed to the survival of progenitor cells with stem-cell-like properties in the protective niches of the bone marrow. Our research suggests that the plant, soursop, may have potential in combating hematologic cancers by triggering apoptosis and potentially preventing drug resistance and relapse. Soursop, scientifically known as *Annona muricata*, is a plant that thrives in tropical and subtropical regions. Every component of the plant, including the leaves, fruit, seeds, and bark, exhibit preventative properties against a wide range of diseases. Our study focuses on examining the effectiveness and mode of action of an extract obtained from soursop leaves. We aim to determine its potential in exhibiting anti-cancer properties, specifically against AML and MM cell lines. Our findings reveal that the extract from soursop leaves has the ability to trigger apoptosis and reduce cell viability in HL-60 and MM.1S cells. Through our research, we have discovered the inhibition or downregulation of the JAK/STAT pathway.

Introduction

- According to the American Cancer Society 2024 estimation, approximately 20,800 new cases of AML will be diagnosed and 11,220 deaths will occur in the United States.
- According to this same estimation, approximately 35,780 new cases of MM will be diagnosed and 16,260 deaths will occur in the United States.
- Hematopoietic progenitor cells (HPCs) and stem cells (HSCs) bind to adhesion molecules on the surface of bone marrow stromal cells, which triggers cell proliferation, survival, drug resistance, and migration of AML and MM cells.
- Common pathways that are upregulated in cancer include the JAK/STAT pathway, where elevated STAT3 and STAT5 promote oncogenesis, the PI3K/AKT pathway, and the ERK/MAPK pathway.
- Despite the high efficacy of initial AML and MM cancer treatments, relapse will occur in a majority of cases. Compounds that target cancer stem cells in the bone marrow need to be studied.
- Soursop leaves contain acetogenins (AGEs) that were shown to have cytotoxic and anti-proliferative activity against cancer cells.

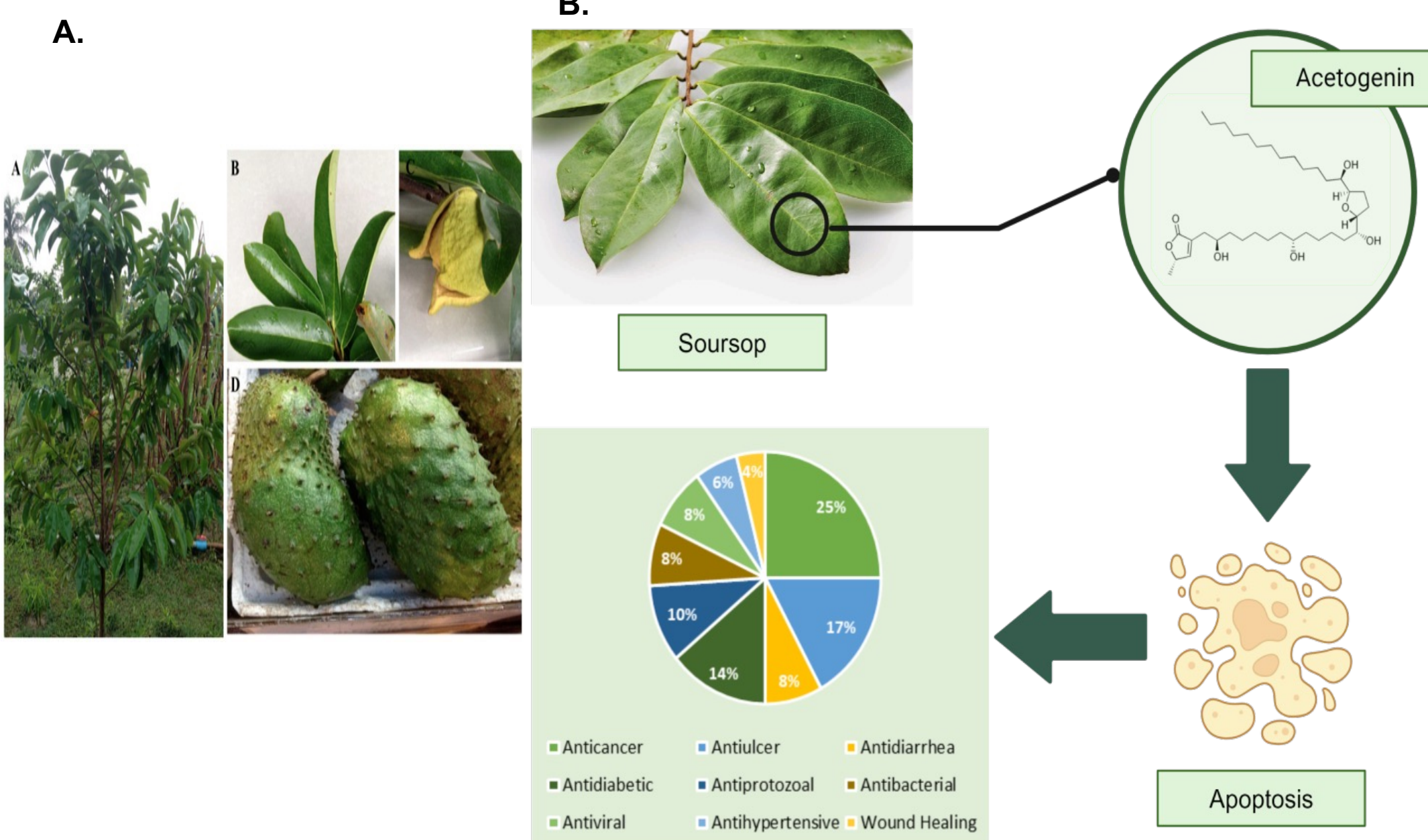


Fig 1. A, Image of *Annona muricata* published by Moghadamtousi, Soheil, et al. B, The main bioactive compound of soursop, acetogenins, induce apoptosis in cancer cells. The pie chart depicts the pharmacological activities of soursop. This image was produced in Biorender.com.

- This study was conducted to establish the hypothesis that soursop has anticancer effects that can induce apoptosis in hematologic cancers.
- We demonstrated that soursop induces apoptosis and reduces cell viability of AML and MM cancer cells.
- Soursop was shown to downregulate the JAK/STAT pathway.

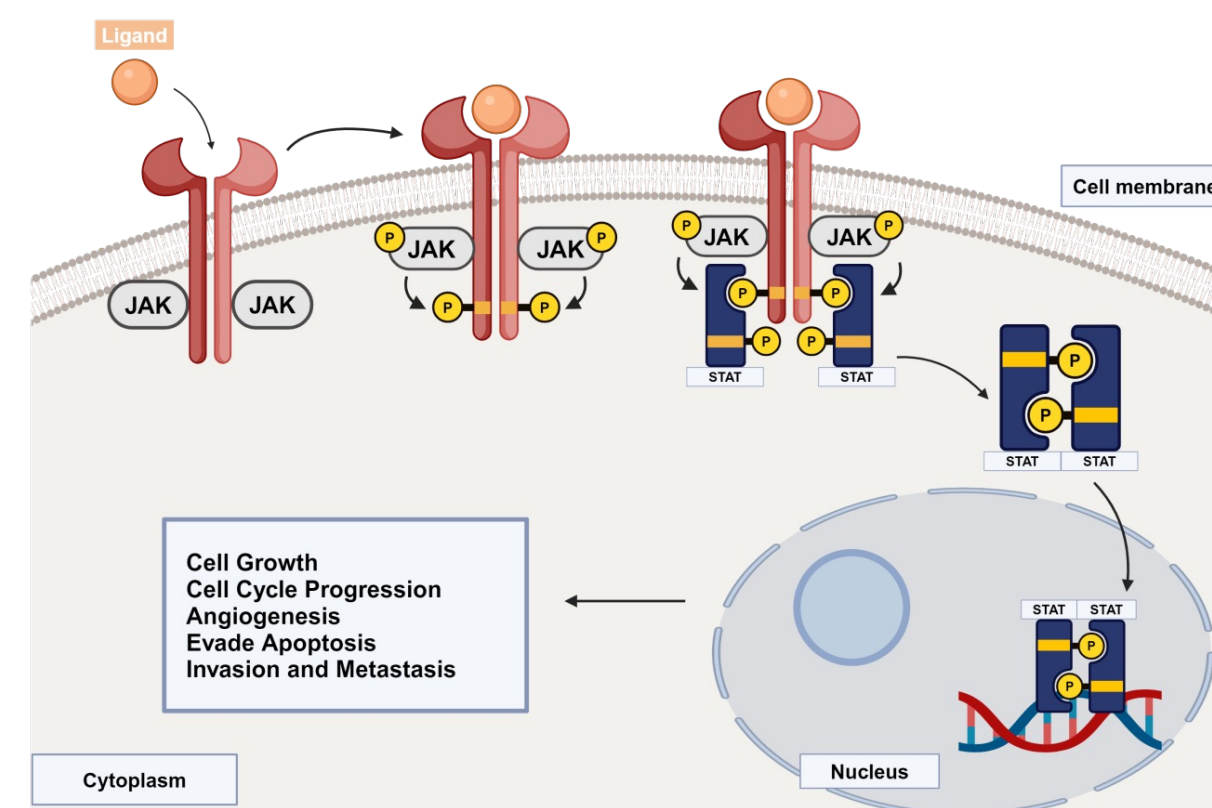


Fig 2. The mechanism of action of the JAK/STAT pathway and its function in oncogenesis. This image was produced in Biorender.com.

Results

Soursop Induces Apoptosis in AML Cells

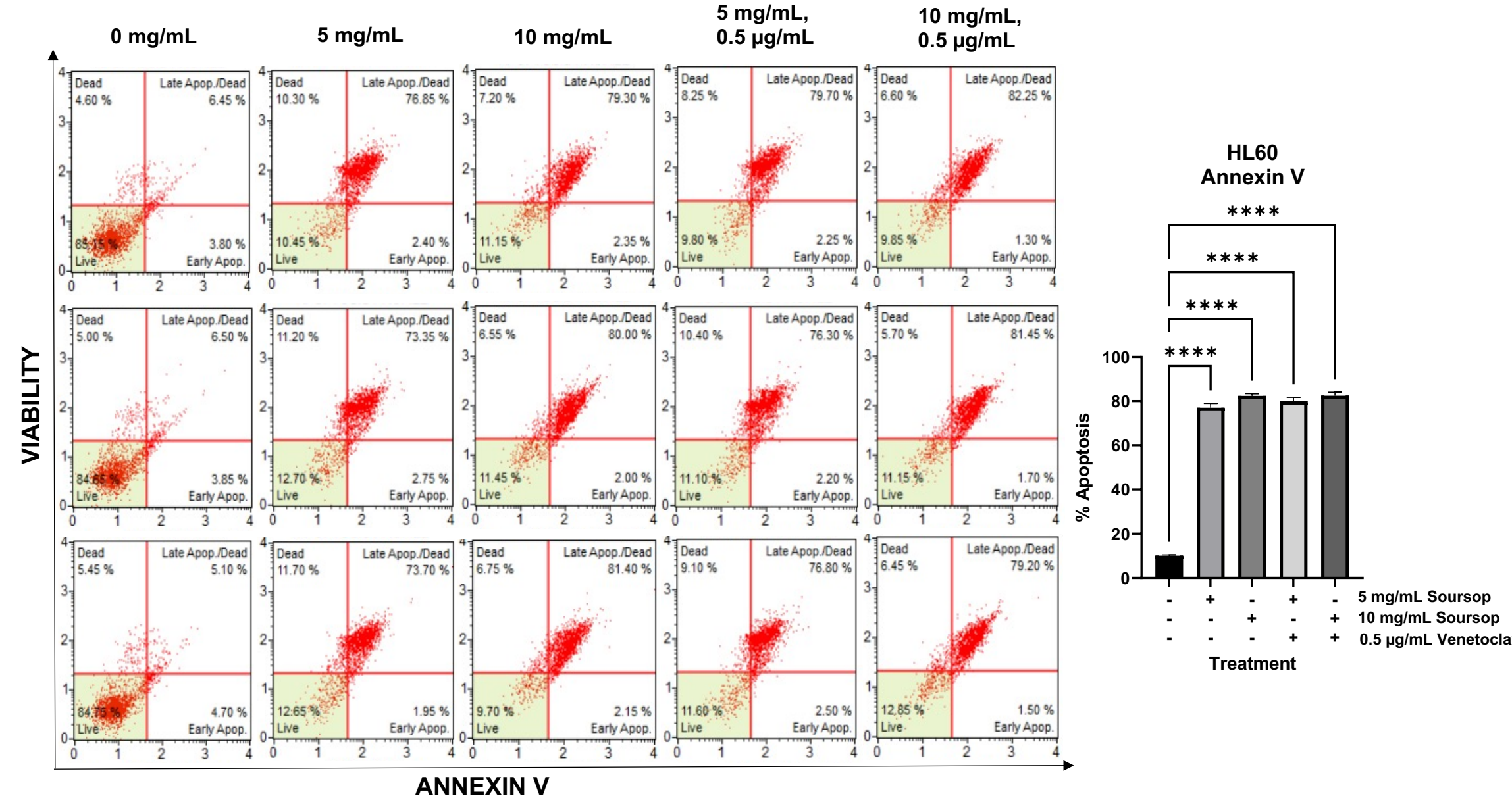


Fig 3. Annexin V experiment shows induction of early apoptosis in HL-60 AML cancer cell lines alone and in combination with Venetoclax.

Conclusion and Future Directions

- Drug resistance and relapse are major problems during treatment and management of AML and MM.
- In the literature, soursop has been shown to possess anti-cancer properties and presents as a potentially viable option for treatment.
- Soursop induces cell death in AML and MM cells and is a sufficient cell viability reducer via Annexin V and MTT.
- Soursop seems to downregulate a common pathway that is upregulated in cancer and contributes to survival, proliferation, and drug resistance.
- Our future studies will further uncover the mechanism of action of soursop and determine clinical efficacy via clinical trials.

Soursop Down-regulates STATs and Reduces Expression of P-STAT3

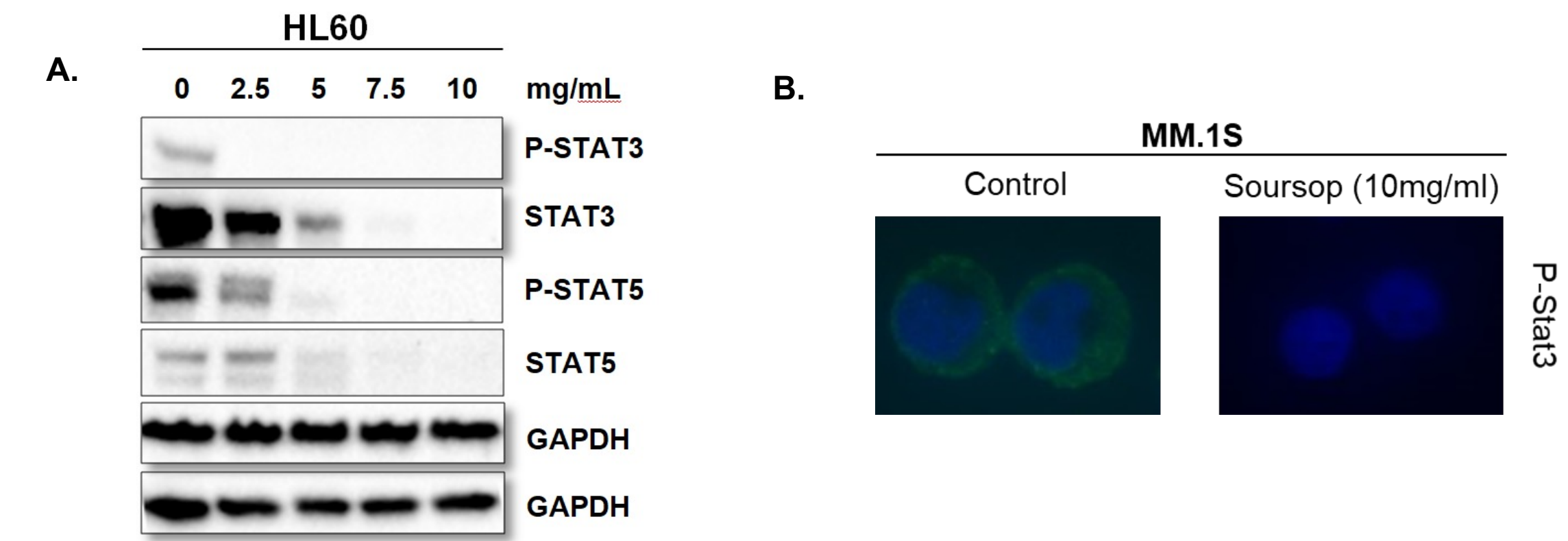


Fig 4. A, Western Blot of HL-60 AML cells treated with soursop at increasing concentrations. Soursop shown to decrease expression of STAT3 and STAT5. B, Immunocytochemistry (ICC) shows reduced expression of P-STAT3 in MM.1S MM cells at a soursop concentration of 10 mg/ml.

Soursop Induces Apoptosis in MM Cells

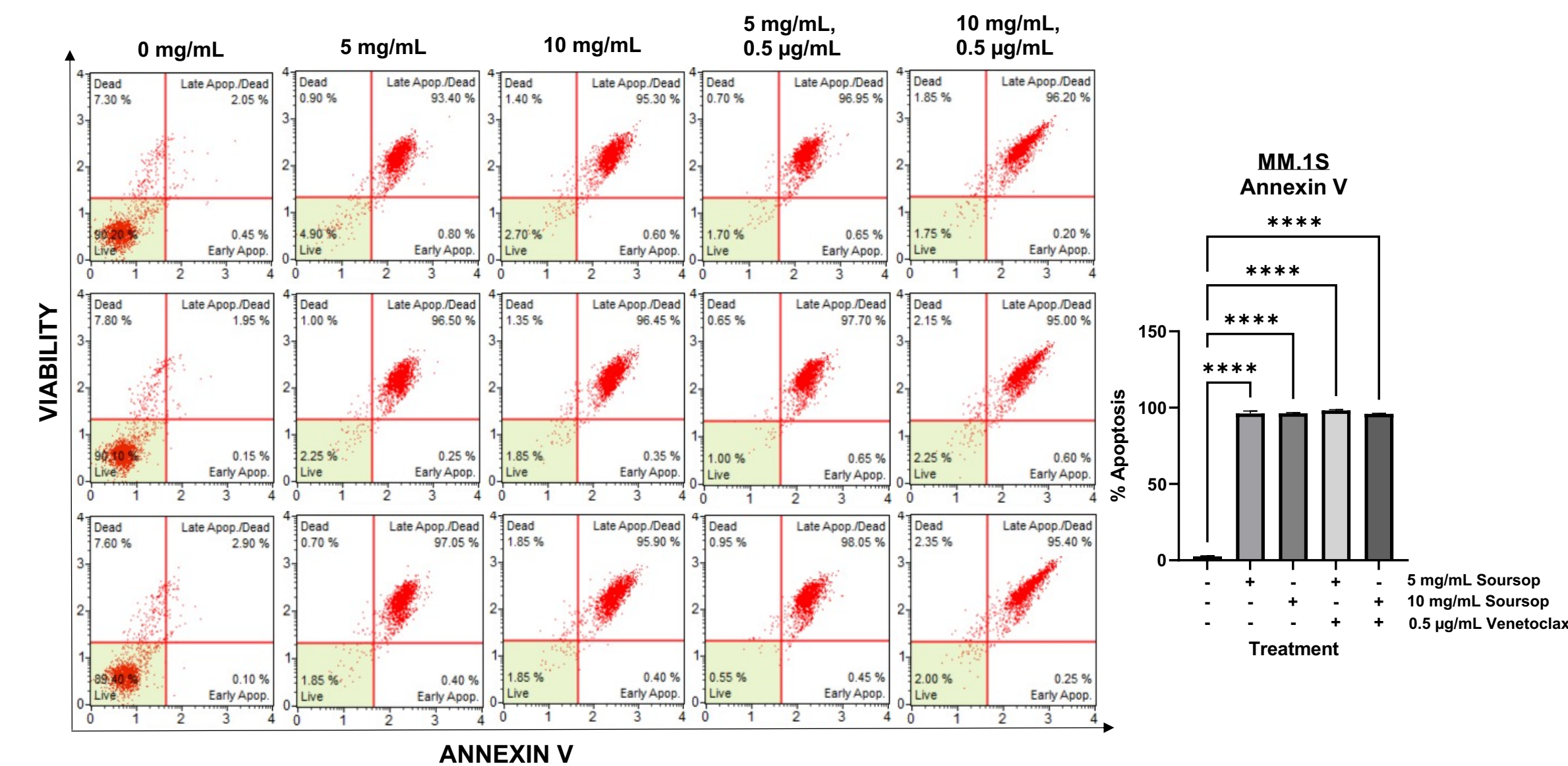


Fig 5. Annexin V experiment shows induction of early apoptosis in MM.1S MM cancer cell lines alone and in combination with Venetoclax.

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Acknowledgment

This work was supported by Camden Research Initiative fund (MP, TB-A, and SJ), New Jersey Health Foundation (SJ, MP), and inter department fund from Cooper Medical School of Rowan University, Camden, NJ (MP).