



# AML-Derived Extracellular Vesicles: Modulators of the Bone Marrow Microenvironment

Impact on BMSC survival, CTNNB1 signaling, and TGF- $\beta$ /VEGF expression

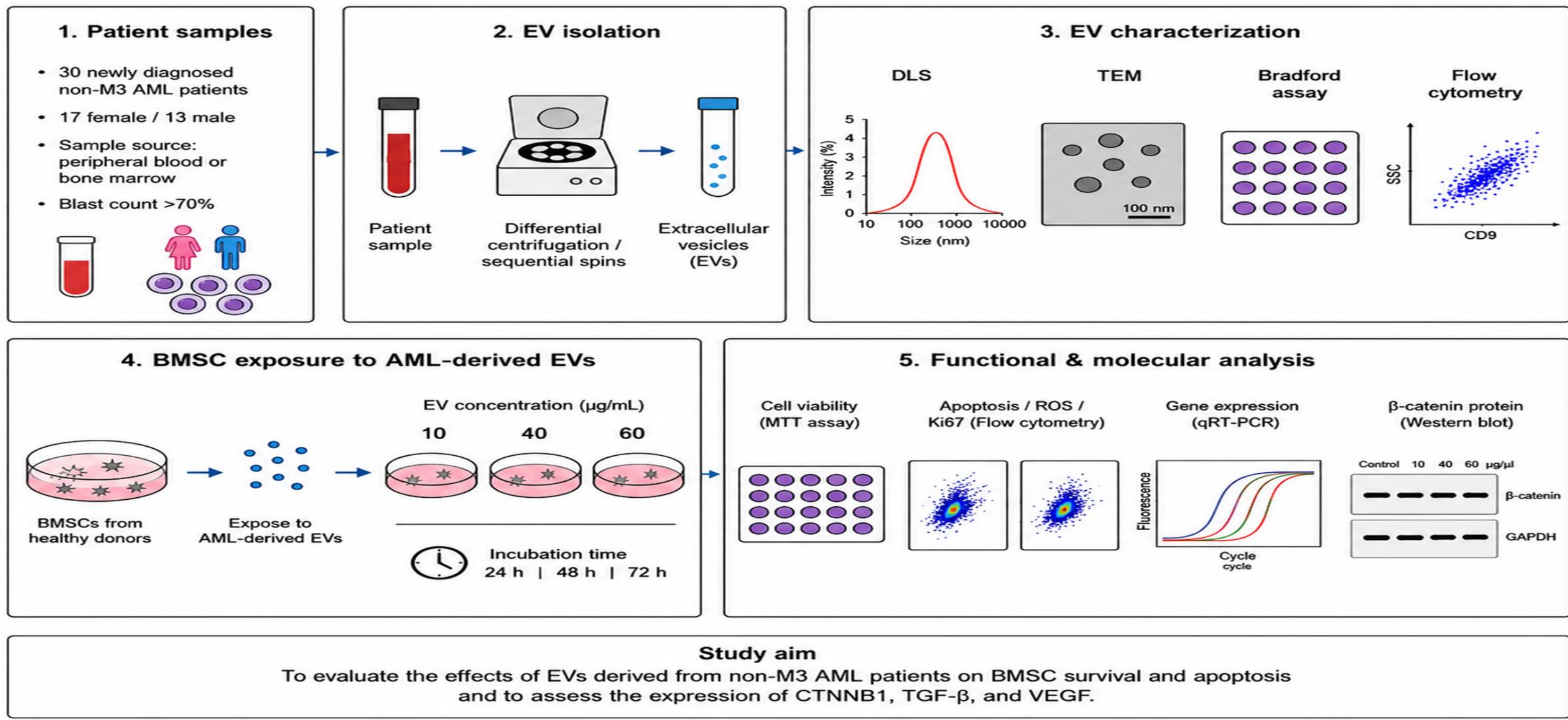
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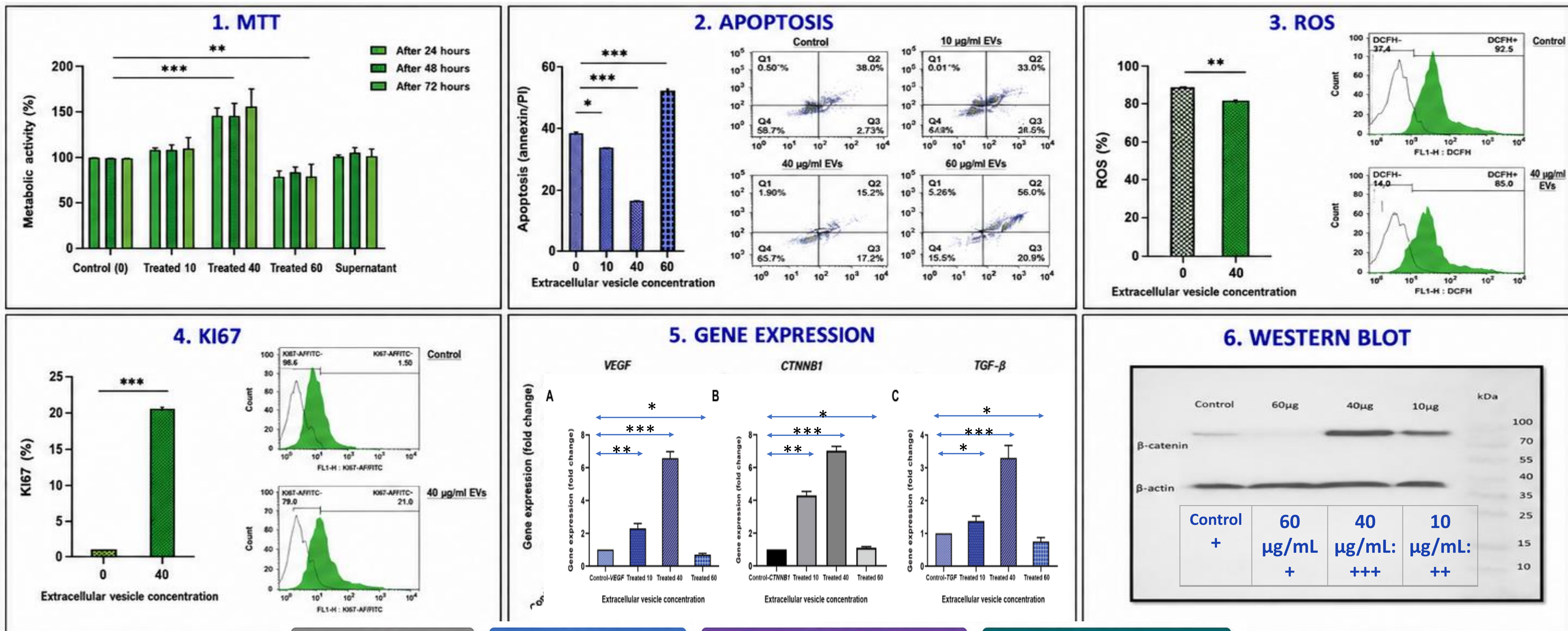
## Introduction:

**Acute myeloid leukemia (AML)** is sustained by reciprocal interactions between leukemic cells and the **bone marrow microenvironment**[1,2]. **Extracellular vesicles (EVs)** are emerging as important mediators of this crosstalk, transferring molecular cargo that can alter the proliferation, survival, and signaling programs of recipient cells [2,3] such as **bone marrow mesenchymal stromal cells (BMSCs)** [2,4]. This study show that AML-derived EVs can modify **BMSCs**, affecting BMSC survival and apoptosis and regulating CTNNB1, TGF- $\beta$ , and VEGF expression[5].

## Methods:



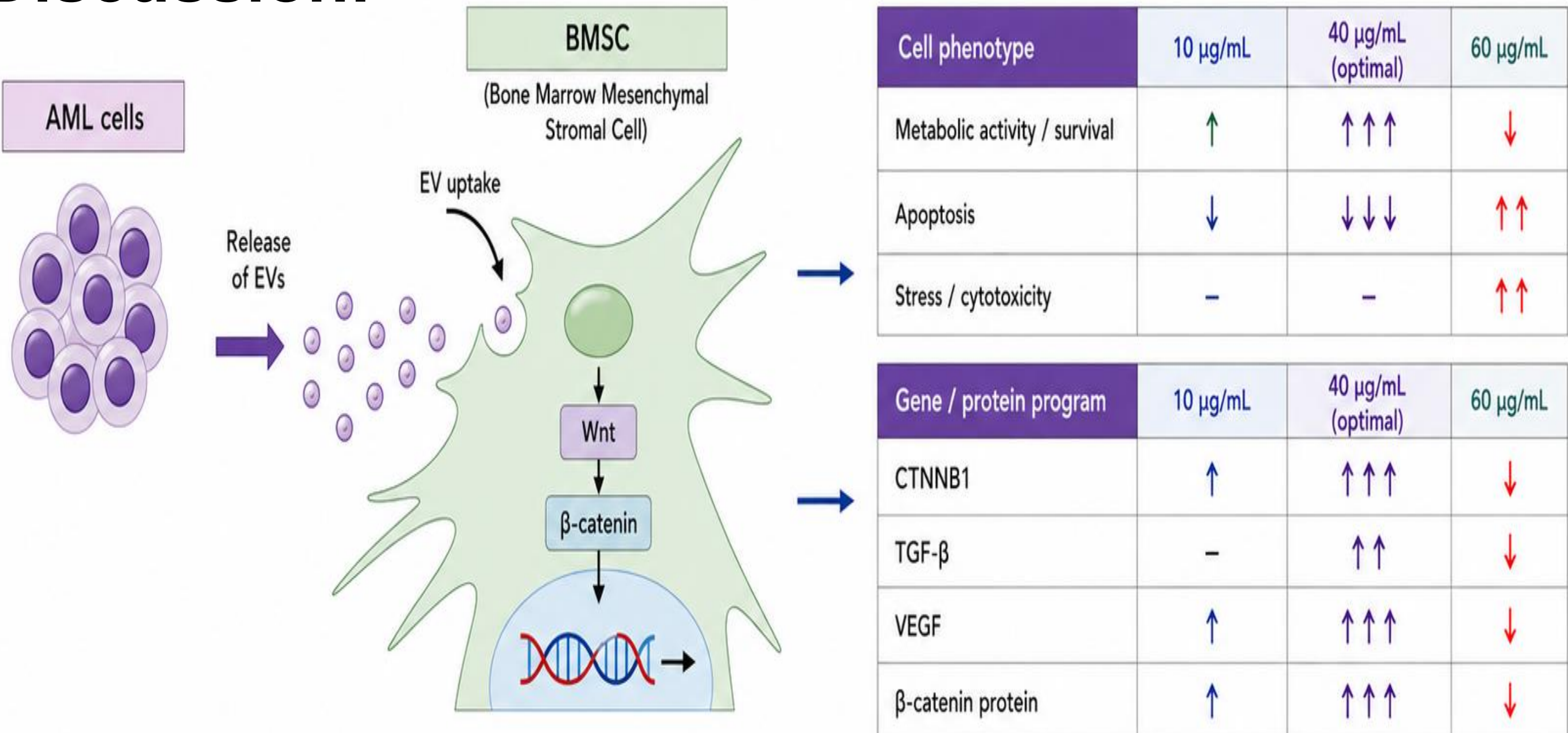
## Results:



| Control (baseline)               | 10 µg/mL (low dose)                | 40 µg/mL (optimal dose - strongest effect)       | 60 µg/mL (high dose)                |
|----------------------------------|------------------------------------|--------------------------------------------------|-------------------------------------|
| ✓ Baseline state                 | ✓ Mild pro-survival response       | ✓ Strongest pro-survival / pro-leukemic response | ✓ Stress / apoptotic shift          |
| ✓ Metabolic activity: baseline   | ✓ Metabolic activity / survival: ↑ | ✓ Metabolic activity / survival: ↑↑↑             | ✓ Metabolic activity / survival: ↓  |
| ✓ Apoptosis: baseline            | ✓ Apoptosis: ↓                     | ✓ Apoptosis: ↓↓↓                                 | ✓ Apoptosis: ↑↑↑                    |
| ✓ Gene/protein program: baseline | ✓ CTNNB1 and VEGF: ↑               | ✓ CTNNB1, TGF-β, VEGF, β-catenin: ↑↑↑            | ✓ CTNNB1, TGF-β, VEGF, β-catenin: ↓ |
| ✓ ROS: baseline                  | ✓ ROS / stress: ~ no major change  | ✓ Ki67: 1.4% → 21% ↑                             | ✓ Stress / cytotoxicity: ↑↑↑        |
|                                  |                                    | ✓ ROS: 92.5% → 85% ↓                             |                                     |

P<0.05:\*\*, and P<0.001:\*\*\*

## Discussion:



## Conclusion:

This study highlights AML-derived EVs as key mediators of bone marrow niche remodeling in a dose-dependent manner. By enhancing BMSC survival and activating CTNNB1/TGF- $\beta$ /VEGF-related signaling, particularly at 40 µg/mL, AML EVs may contribute to a leukemia-supportive microenvironment.

### Acknowledgments

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### REFERENCES

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40 µg/mL drives the strongest pro-survival / pro-leukemic reprogramming, while 60 µg/mL shifts toward stress and apoptosis.