# Microgravity Modulates miRNA Networks to Enhance 5-FU Sensitivity in Colorectal Cancer

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## INTRODUCTION

Colorectal cancer (CRC) is a prevalent malignancy with increasing incidence in younger populations. Although 5-fluorouracil (5-FU) is a primary therapeutic agent for CRC, its efficacy is frequently compromised by drug resistance. Simulated microgravity has been demonstrated to improve the chemosensitivity of 5-FU on CRC organoids. Evidence also revealed microgravity-induced changes in microRNA expression, which play roles in regulating tumor proliferation and suppression.

## HYPOTHESIS

We hypothesize that simulated microgravity enhances 5-FU chemosensitivity in colorectal cancer by modulating microRNA expression. These changes disrupt the balance between tumor proliferation and suppression pathways, weakening survival signaling and thereby increasing chemotherapy effectiveness.

## METHODOLOGY

Literature review → Dataset mining → DEG analysis and miRNA filteration → Validated target genes → Predicted target genes → Enrichment analysis → Data visualization

## RESULTS

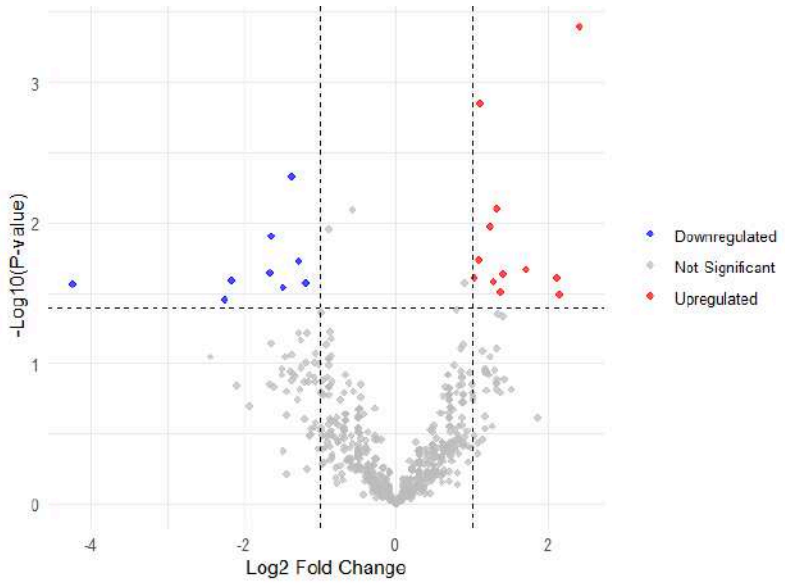


***Figure 1:*** *Volcano Plot of Differentially Expressed miRNAs*

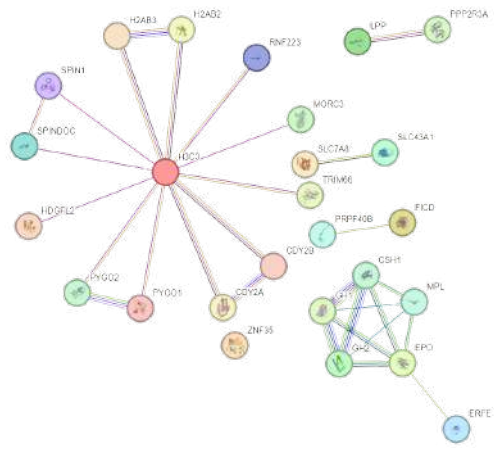

***Figure 4****: Protein interaction network of target genes and up to 20 neighboring proteins , generated by STRING*

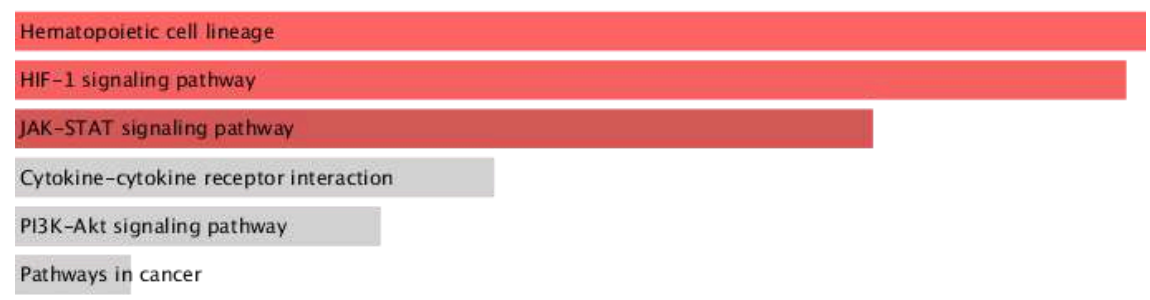


***Figure 2:*** *KEGG pathway enrichment of predicted miRNA target genes identified hematopoietic cell lineage, JAK-STAT, and HIF-1 signaling as the top enriched pathways. Erythropoietin (EPO), a central regulator of hematopoiesis and hypoxic response, was a key downregulated driver in our differentially expressed genes.*

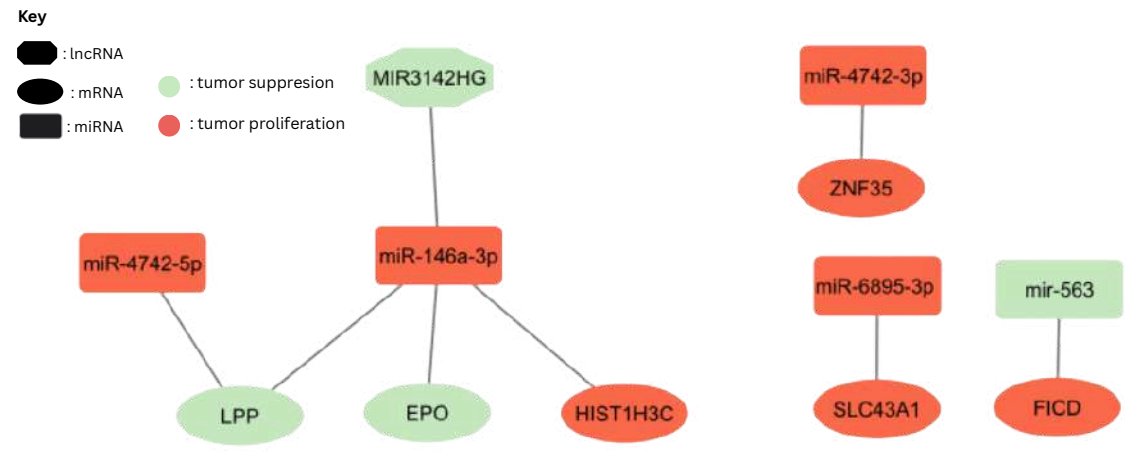


***Figure 4:*** *SLC43A1, although it shows tumor progression effects when upregulated, has been noted to determine the sensitivity of oxaliplatin in CRC cells.*

## CONCLUSION

We identified 5 miRNA–mRNA axes and 3 lncRNA–miRNA–mRNA axes. These were linked to both tumor-promoting (proliferation, immune evasion) and tumor-suppressive processes (growth inhibition, apoptosis), highlighting a dual regulatory role of these non-coding RNAs in colorectal cancer under simulated microgravity.

## WAY FORWARD

These findings provide a foundation for designing miRNA mimics to experimentally evaluate their potential to enhance 5-Fluorouracil chemosensitivity in colorectal cancer cells. Furthermore, this work opens promising avenues for investigating innovative cancer therapies within simulated microgravity environments on Earth.

## REFERENCES

1. Kim et al., 2024, Scientific Reports
2. Vidyasekar et al., 2015, PLoS One
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4. Rembiałkowska et al., Membranes (Basel), 2022

## ACKNOWLEDGEMENTS

I'd like to thank the Precision Medicine Summer Elective Program 2025, Madina Shirdel, Qurut ul ain, Arsalan Riaz for their help throughout the project.