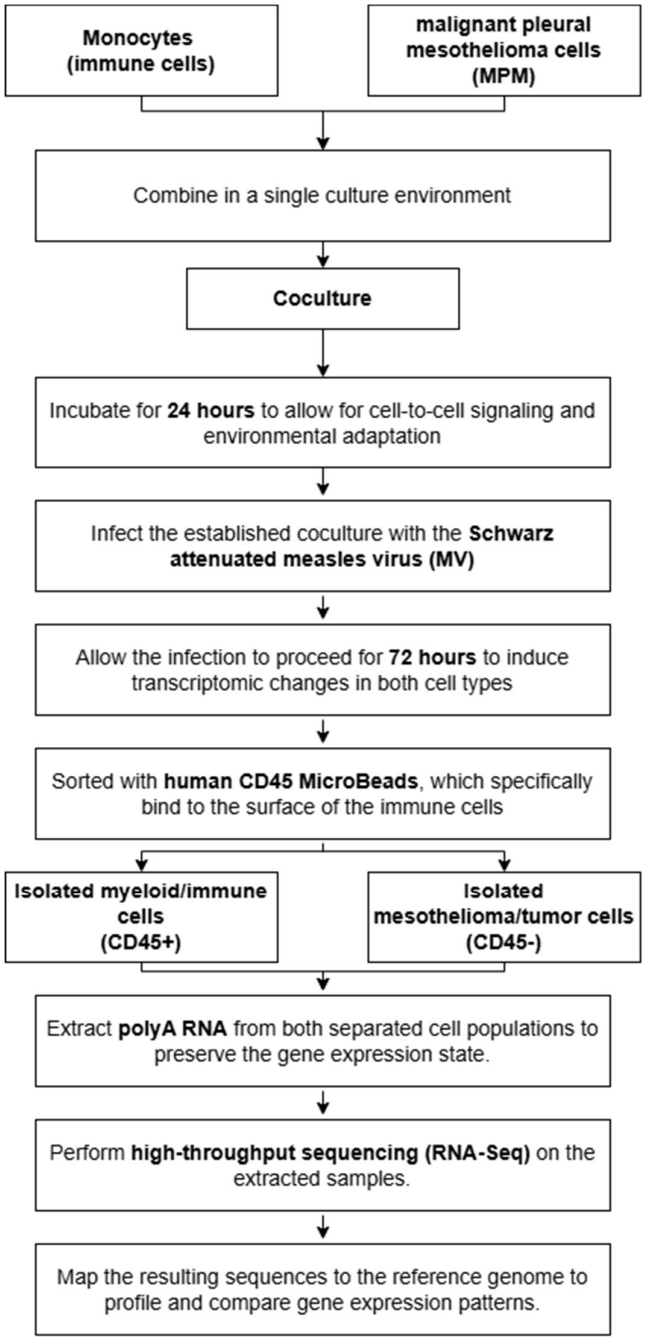
Genome-wide analysis of deregulated gene expression by tumor cells (CD45-) or myeloid cells (CD45+) in cocultures infected with measles virus (MV) – GEO2R Analysis

I. INTRODUCTION

Malignant Pleural Mesothelioma (MPM) remains one of the most difficult skin cancers to treat due to its aggressive growth and its ability to create an environment that evades natural body defenses. To overcome this, Chatelain and Fonteneau (2023) are exploring the use of the Schwarz attenuated measles virus as a strategic oncolytic agent. By exploiting the fact that MPM cells overexpress the CD46 receptor, the virus can selectively infiltrate the tumor microenvironment. This approach transforms the viral infection into a therapeutic tool

II. METHODS



III. RESULT

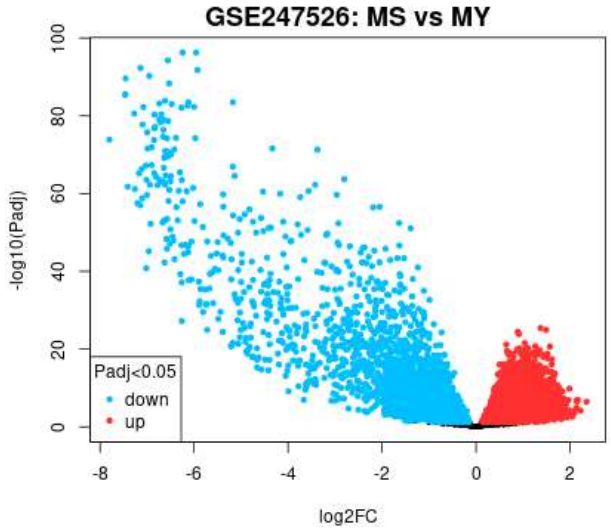
a. Analysis focused on the **250 most differentially expressed genes of 10,804 genes** based on the highest adjusted P-values.

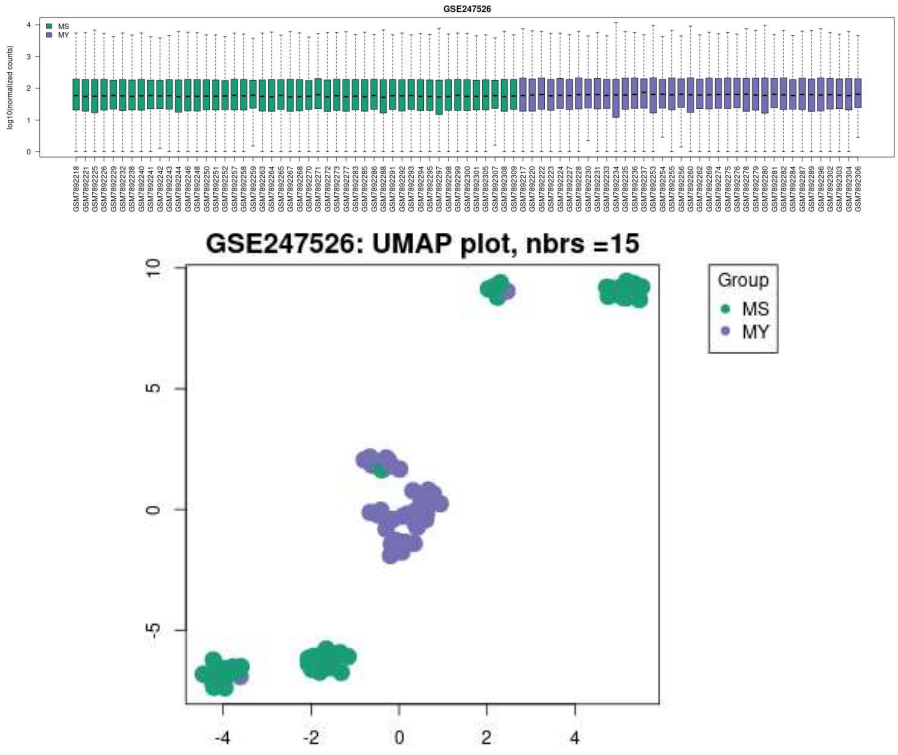
b. **The most statistically significant genes identified are:**
   - ***C1orf162*** (Chromosome 1 Open Reading Frame 162);
   - ***HLA-DMA*** and ***HLA-DRA*** (Major Histocompatibility Complex, Class II); and
   - ***VMO1*** (Vitelline Membrane Outer Layer 1 Homolog).

c. **Direction of Gene Expression Change**
   - Upregulated (Increased Expression):
     - ❖ Significant genes (***HLA-DRA*** and ***HLA-DMA*****)** typically show increased expression in the immune cell fraction.
     - ❖ This indicates an upregulation of antigen presentation pathways, showing that the immune cells are being activated to recognize the tumor.
   - Downregulated (Decreased Expression):
     - ❖ Genes associated with the cell cycle and DNA replication (found in the CD45- tumor fraction) are typically downregulated.
     - ❖ This suggests that the viral treatment is effectively slowing down or stopping the growth of the mesothelioma cells.

d. **Virus Mechanisms in Cell**
   - The Schwarz attenuated measles virus (MV) uses the ***CD46*** receptor (highly expressed on tumor cells) to enter and infect the mesothelioma. The results show that the virus doesn't just kill the cancer, but also triggers a inflammatory response.
   - The expression of ***Major Histocompatibility Complex II*** genes (***HLA-DRA/DMA***) proves that the virus helps activate the immune system around the tumor environment, potentially making the cancer more vulnerable to further treatment.

e. **Graphic Result**





IV. CONCLUSION

Measles virus can act as a potent immunovirotherapy against Malignant Pleural Mesothelioma (MPM). By targeting the overexpressed CD46 receptor, the virus selectively infects the tumor environment into immunogenic, so immune system can detect it. The analysis confirms a dual therapeutic effect. First is the direct suppression of cancer growth (downregulation of cell cycle genes). Second is the activation of the host immune system (upregulation of HLA-DRA/DMA for antigen presentation). This evidence supports the use of oncolytic viruses to break tumor defenses and prime the immune system for cancer eradication.

V. REFERENCES

Chatelain, C. and Fonteneau, J. 2023. Genome-wide analysis of deregulated gene expression by tumor cells (CD45-) or myeloid cells (CD45+) in cocultures infected with measles virus (MV). (GSE 247526).