IMMUNOGENIC SENESCENCE SENSITIZES LUNG CANCER TO LUNX-TARGETING THERAPY

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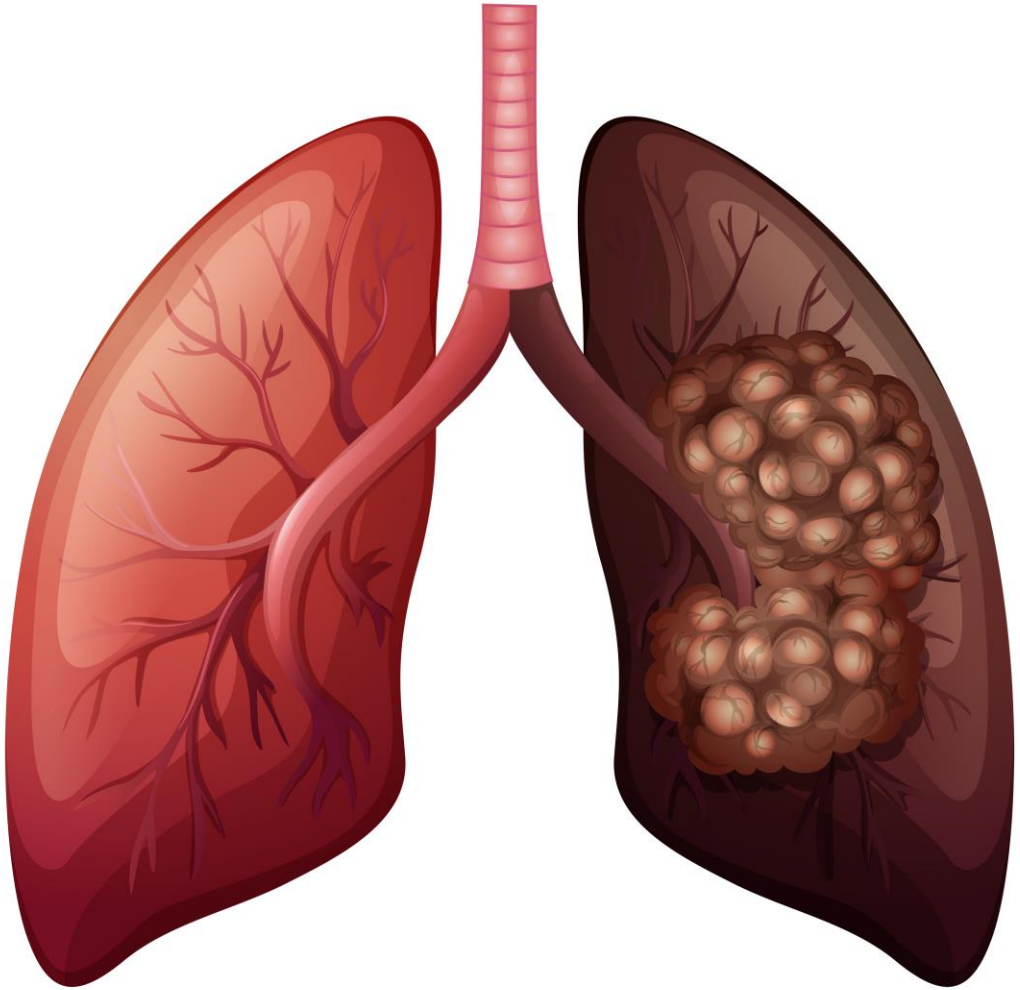
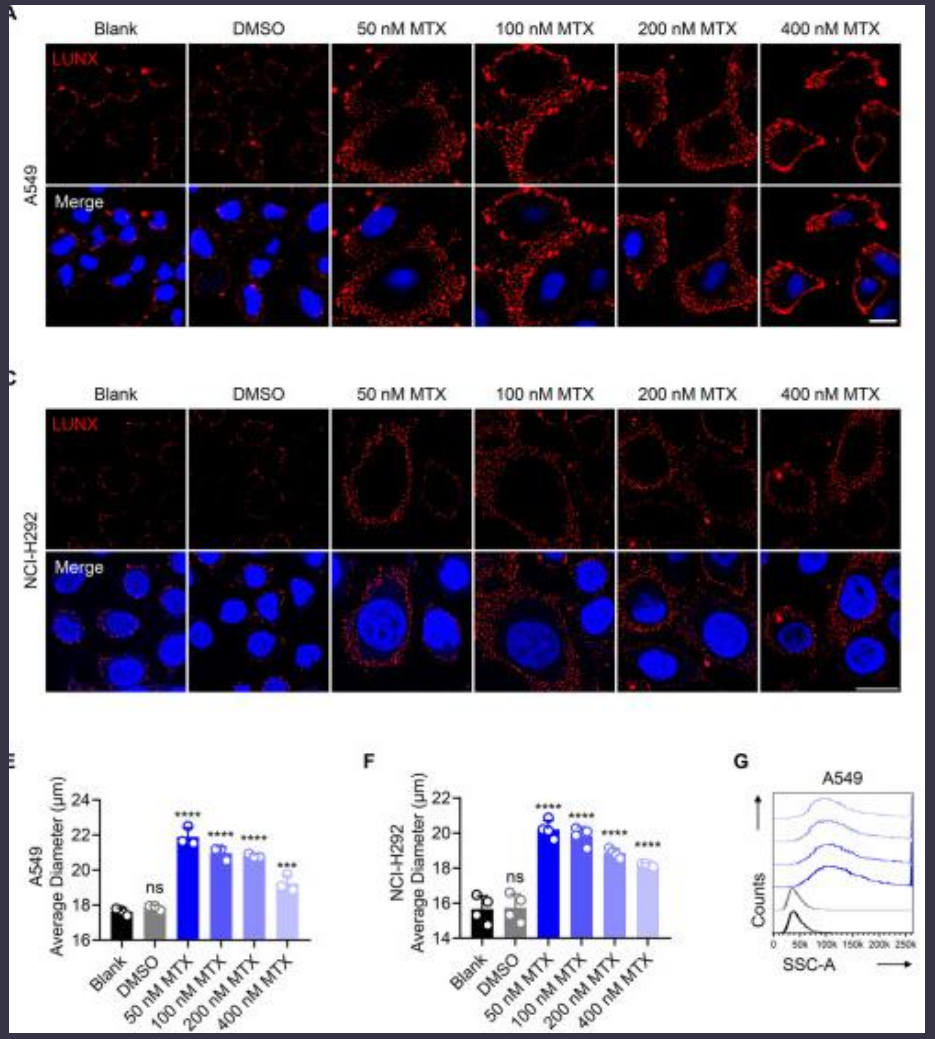


two-step treatment:

1. **use chemotherapy** to make lung cancer cells more visible to the immune system by bringing LUNX to the surface;

2. apply **LUNX-specific antibodies** to target and destroy these marked cells, with the help of the body's natural immune responses.

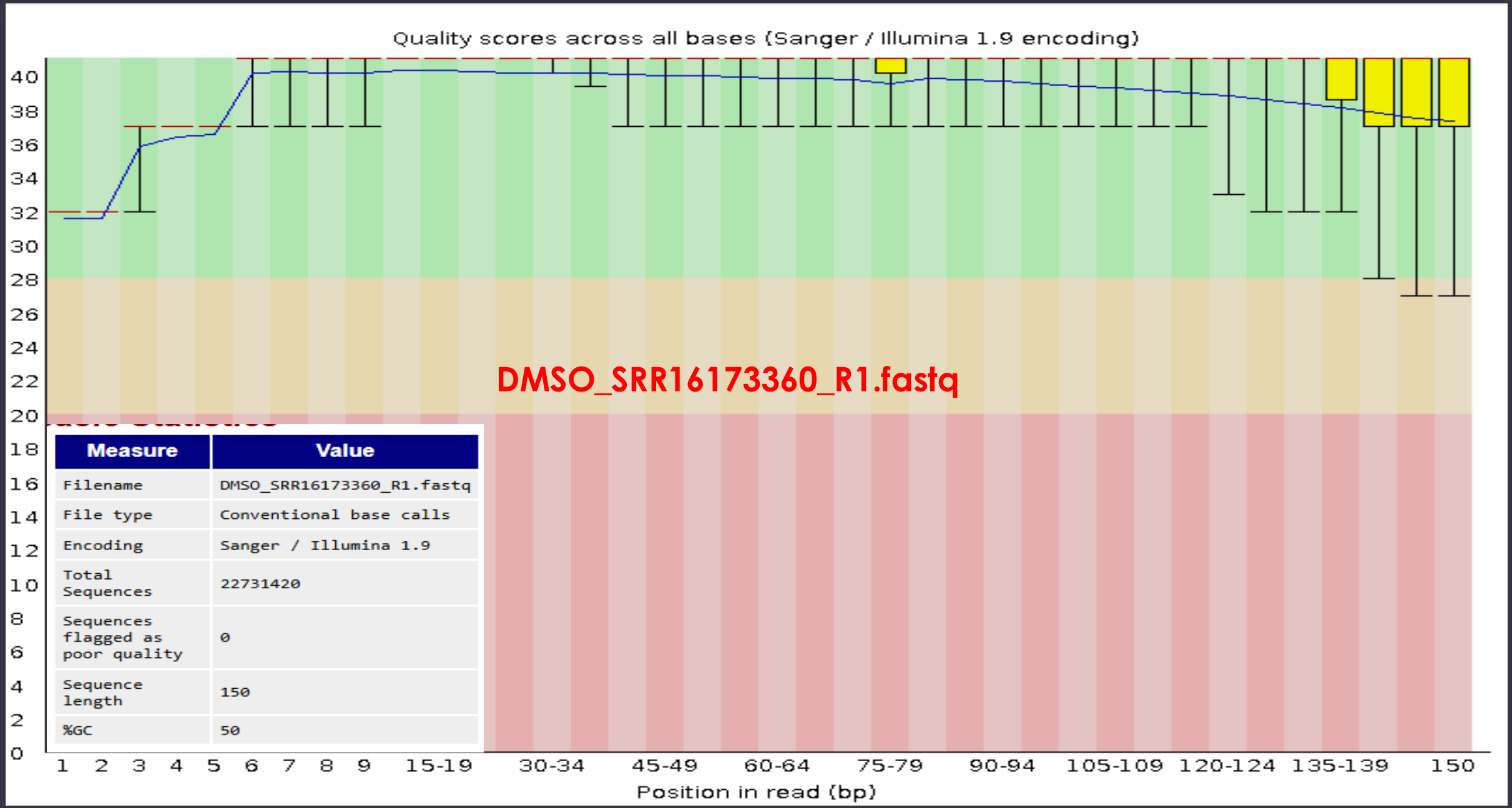


Cell-surface shuttling of LUNX after immunogenic chemotherapy (**A**–**D**) Surface exposure of LUNX was determined by immunofluorescence 48 h after treatment with the indicated concentration of mitoxantrone PMID: 34674012

- **1. Introduction:** Lung cancer cells can evade the immune system, making treatment challenging.
- **2. Key Protein - LUNX:** found inside lung cells. During senescence, LUNX moves to the cell surface----- accessible target for therapies.
- **3. Inducing Senescence with Chemotherapy:** chemotherapy drug, mitoxantrone, used to induce senescence in lung cancer cells. -----increase the presence of LUNX on their surfaces.
- **4. Targeting LUNX with Antibodies:** they effectively marked the senescent cancer cells for destruction.

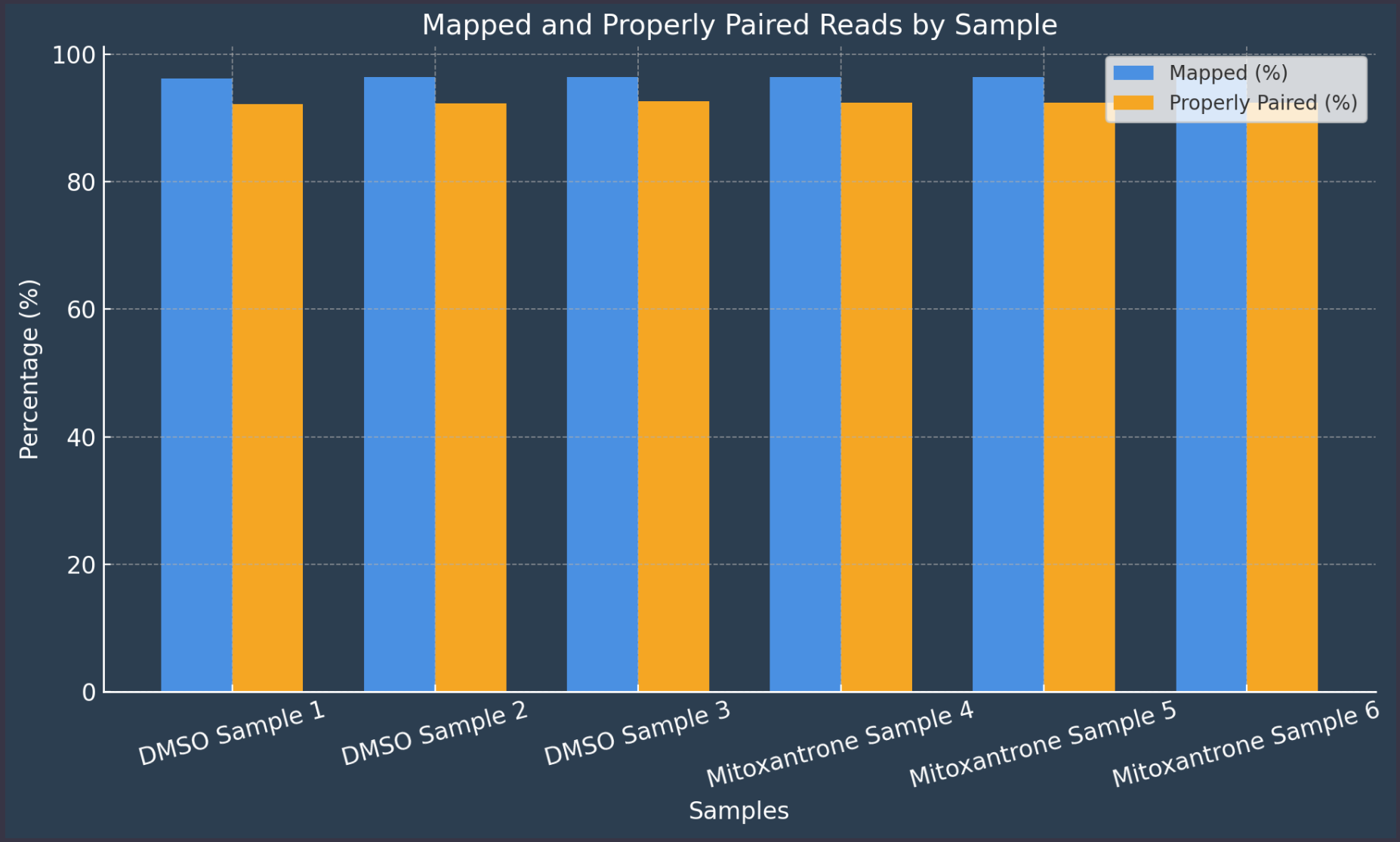
- **5. Role of Natural Killer (NK) Cells:** identification and destruction of harmful cells. LUNX-targeting antibodies enhanced the ability of NK cells to recognize and eliminate the senescent lung cancer cells.

- **6. Conclusion:** using chemotherapies to induce senescence in lung cancer cells + targeted antibody therapy against LUNX = promising strategy for treating lung cancer.

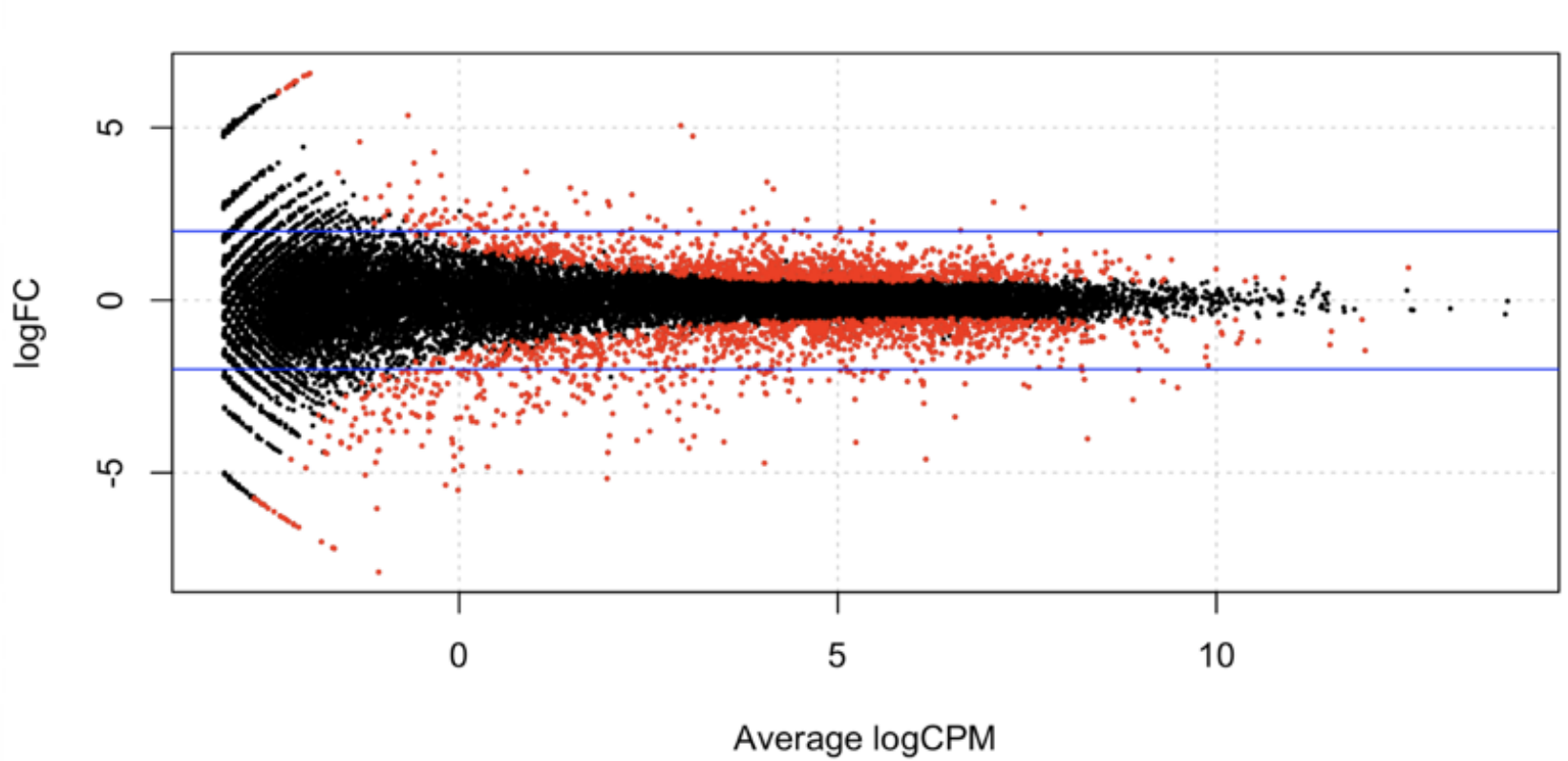


Measure	Value
Filename	DMSO_SRR16173360_R1.fastq
File type	Conventional base calls
Encoding	Sanger / Illumina 1.9
Total Sequences	22731420
Sequences flagged as poor quality	0
Sequence length	150
%GC	50

Samtools flagstat report

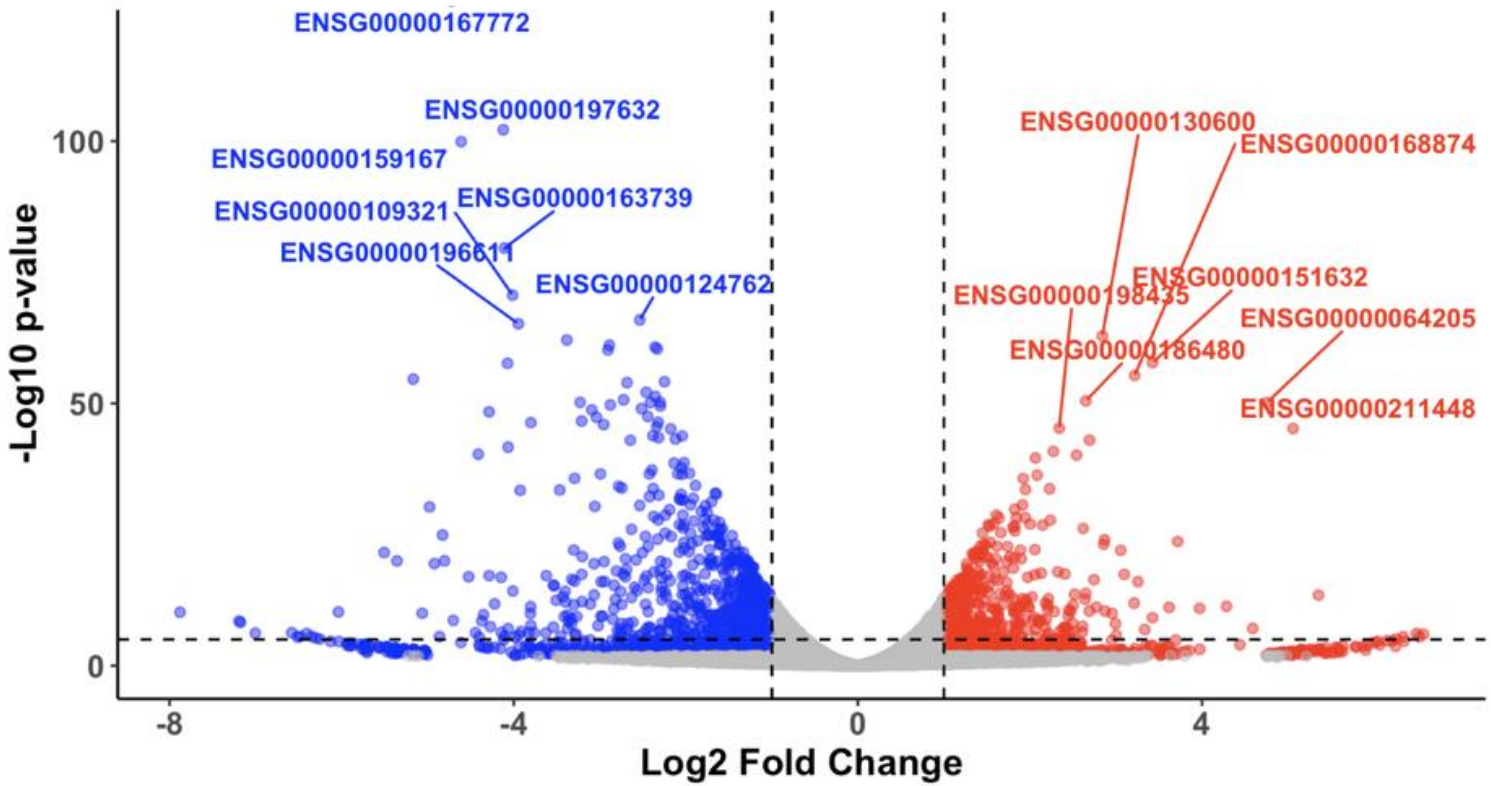


MA Plot



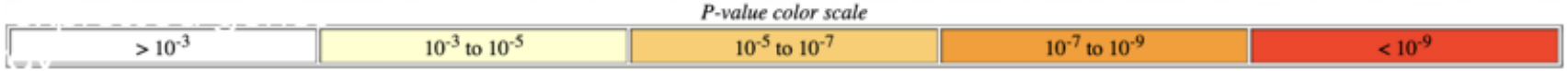
MA plot shows global expression patterns, highlighting significant changes in gene expression.

Volcano Plot

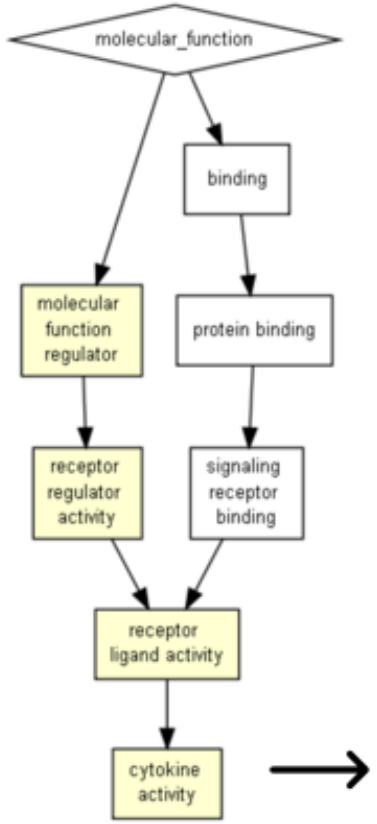


Volcano plot identifies significant upregulated and downregulated genes, including potential immune-related targets like ENSG000001030600.

GOrilla Analysis of Under-Expressed Genes



This pathway plays a crucial role in immune signaling and inflammation control.



Cytokine activity is the most enriched function, linking Mitoxantrone to immune regulation.

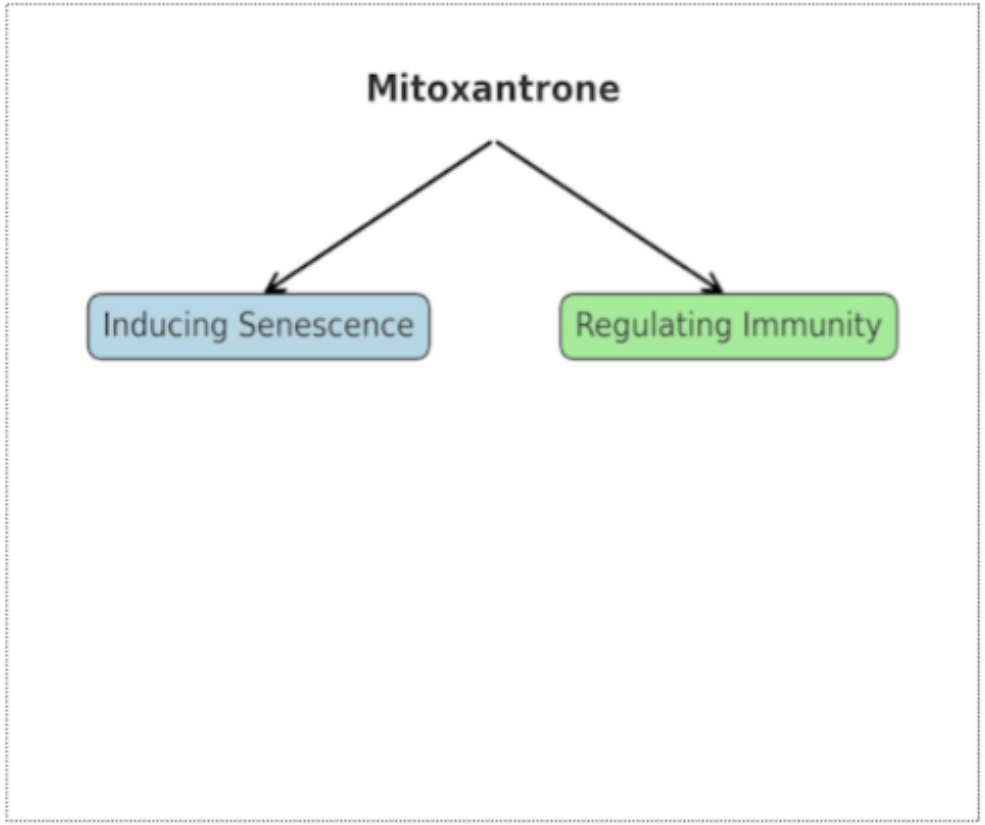
Linking Mitoxantrone to Cytokine Activity

- "Mitoxantrone is effective in reducing disease progression through a variety of different mechanisms of action. For example, it suppresses the proliferation of T cells, B cells, and macrophages. It impairs antigen presentation and decreases the secretion of pro-inflammatory cytokines."

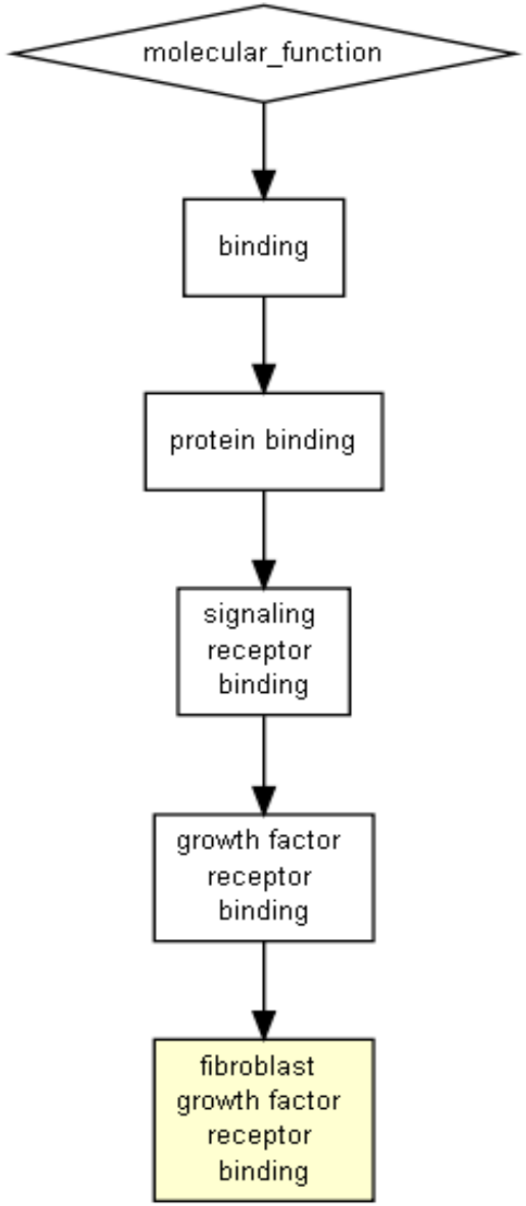
  Fox, Edward J. "Mechanism of Action of Mitoxantrone." Neurology, 2004)

- This mechanism aligns with the downregulation of cytokine activity observed in our analysis, suggesting that Mitoxantrone reduces inflammation and modulates immune responses by targeting key cytokine-related pathways.

A Dual Role for Mitoxantrone



- Mitoxantrone regulates immune responses by altering gene expression, reducing inflammation, and enhancing therapy. Its dual role in inducing senescence and modulating immunity highlights its potential as a comprehensive cancer treatment strategy.



FGFR Binding in Cancer Progression

Our study showed that combining **mitoxantrone-induced senescence** with **LUNX-targeting antibodies** significantly reduced lung cancer cell survival.

• **FGFR Overexpression in Lung Cancer:** FGFR signaling plays a key role in tumor growth, angiogenesis, and metastasis. In some cases, its overactivity may contribute to **resistance to chemotherapy** like mitoxantrone by promoting cell survival and repair of DNA damage.

• **Combination Therapy Opportunities:** This highlights the potential for combining FGFR inhibitors with mitoxantrone. Suppressing FGFR-driven survival signals could enhance the drug's effectiveness, particularly in patients with FGFR-overexpressing tumors.

References

Jiao D, Zheng X, Du X, Wang D, Hu Z, Sun R, Tian Z, Fu B, Wei H. Immunogenic senescence sensitizes lung cancer to LUNX-targeting therapy. Cancer Immunol Immunother. 2022 Jun;71(6):1403-1417. doi: 10.1007/s00262-021-03077-1. Epub 2021 Oct 21. PMID: 34674012; PMCID: PMC9123058.

Fox, Edward J. "Mechanism of Action of Mitoxantrone." *Neurology*, vol. 63, suppl. 6, 2004, pp. S15–S18, doi:10.1212/WNL.63.6.S15.

Awknowledgement

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