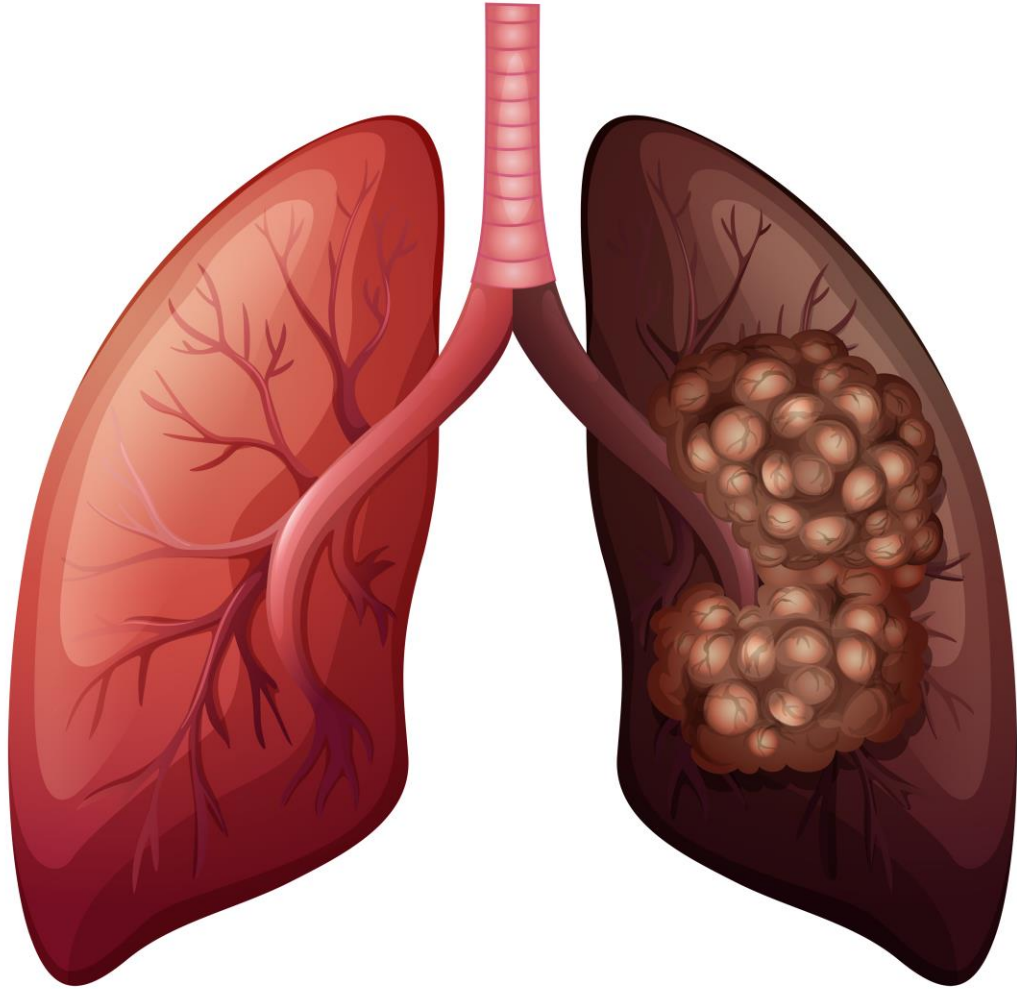




IMMUNOGENIC SENESENCE SENSITIZES LUNG CANCER TO LUNX-TARGETING THERAPY

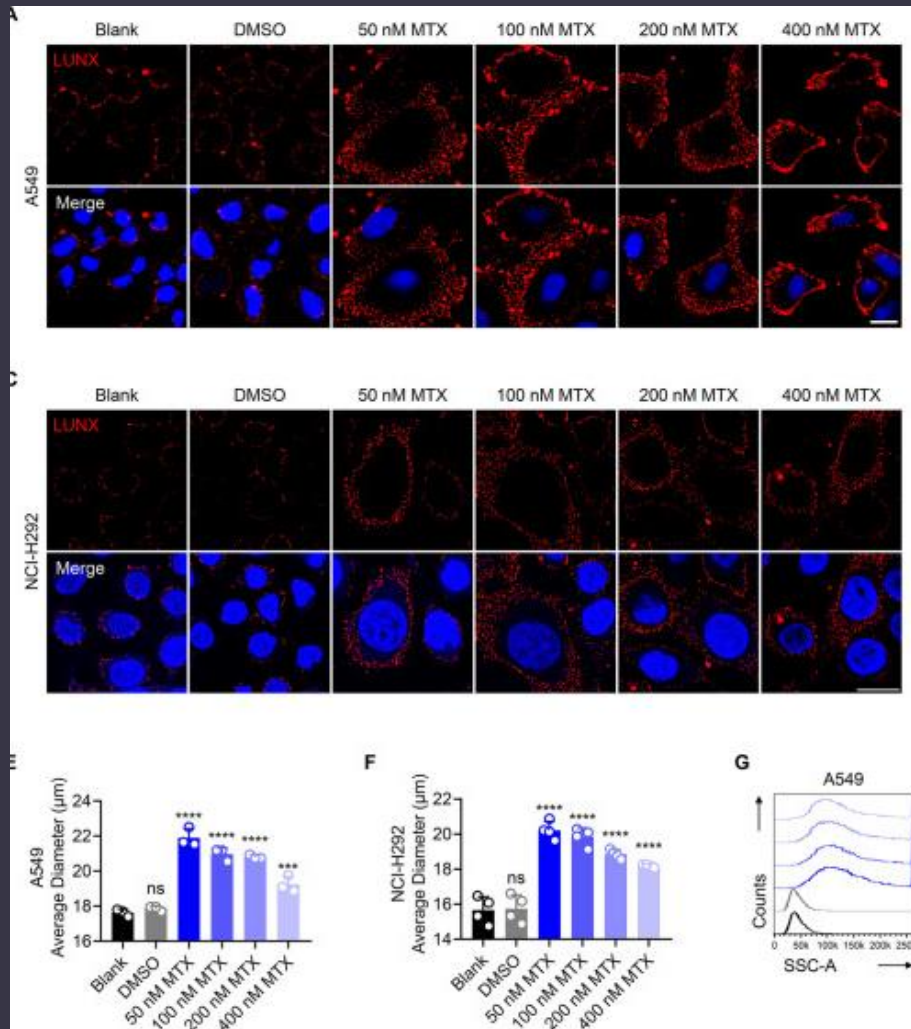
DEFENG JIAO , XIAOHU ZHENG , XIANGHUI DU , DONG WANG , ZIMING HU , RUI , ZHIGANG TIAN BINQING FU , HAIMING WEI

By Morena Basaly, Jiaqi Wang, Vraj Soni



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.



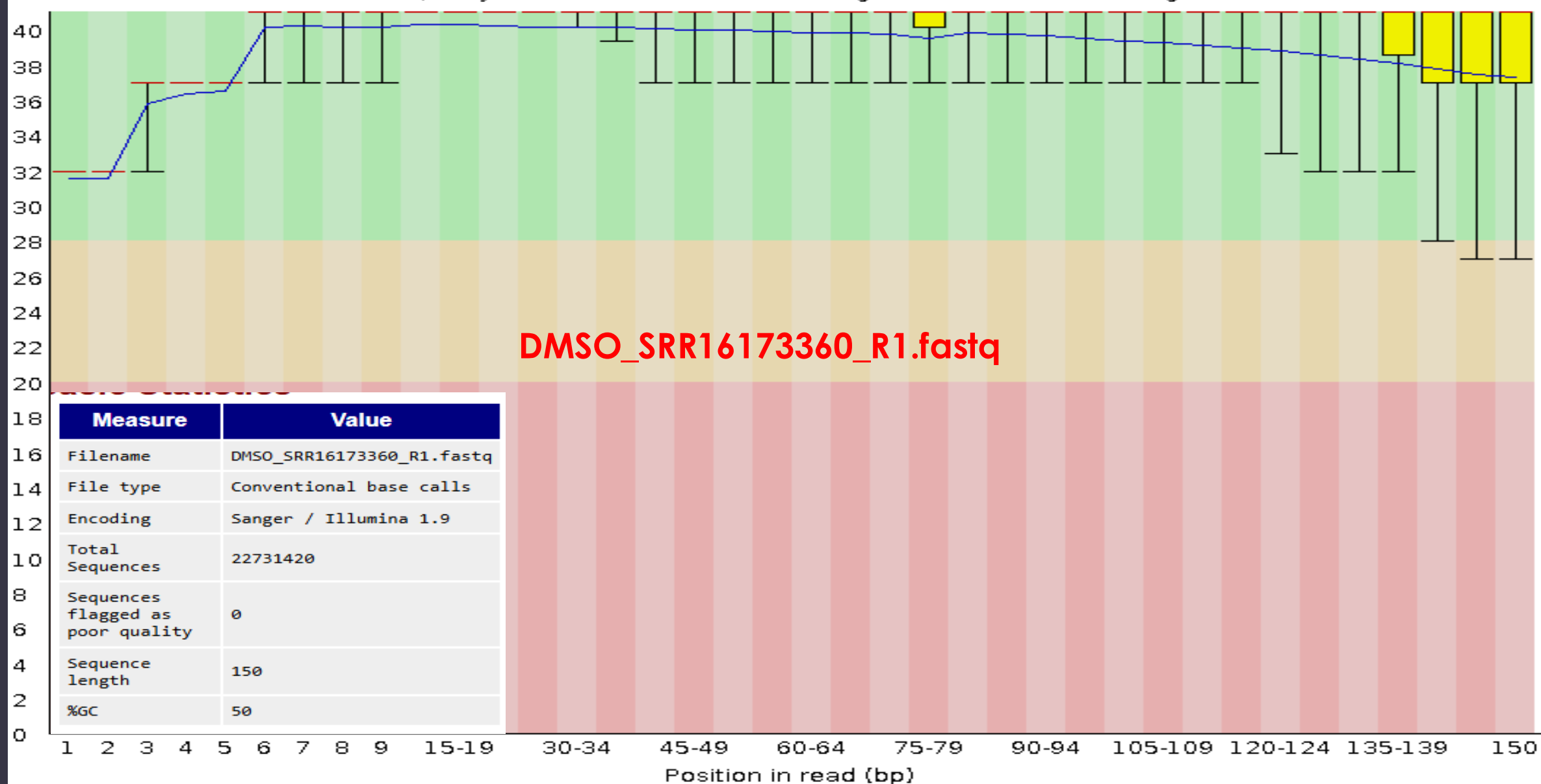
- **1. Introduction:** Lung cancer cells can evade the immune system, making treatment challenging.
- **2. Key Protein - LUNX:** found inside lung cells. During senescence, LUNX moves to the cell surface- ---- accessible target for therapies.
- **3. Inducing Senescence with Chemotherapy:** chemotherapy 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.

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

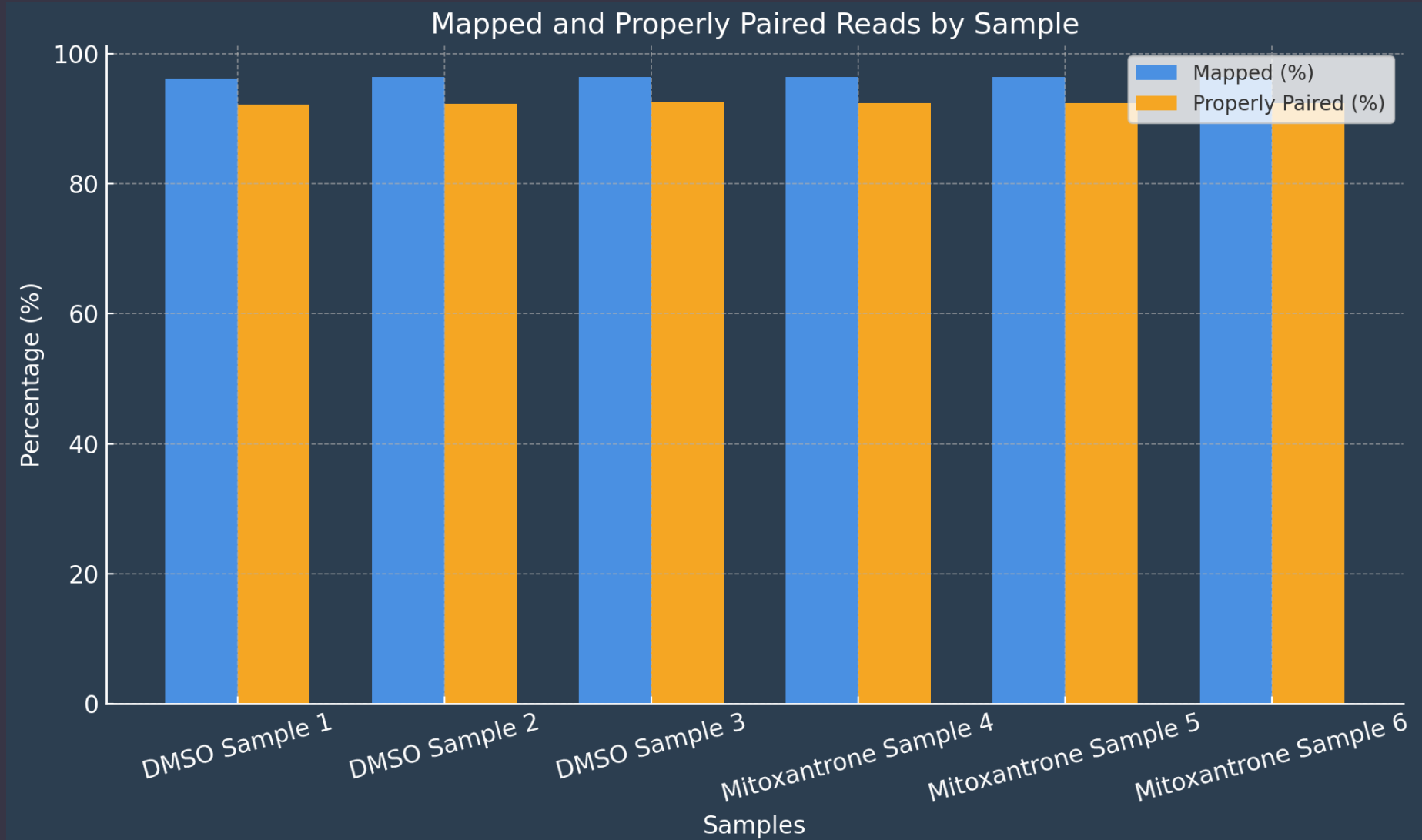
- **5. Role of Natural Killer (NK) Cells:** identification and destruction of harmful cells. LUNX-targeting antibodies enhanced the ability of NK cells to recognize and eliminate the senescent lung cancer cells.
- **6. Conclusion:** using chemotherapies to induce senescence in lung cancer cells + targeted antibody therapy against LUNX = promising strategy for treating lung cancer.



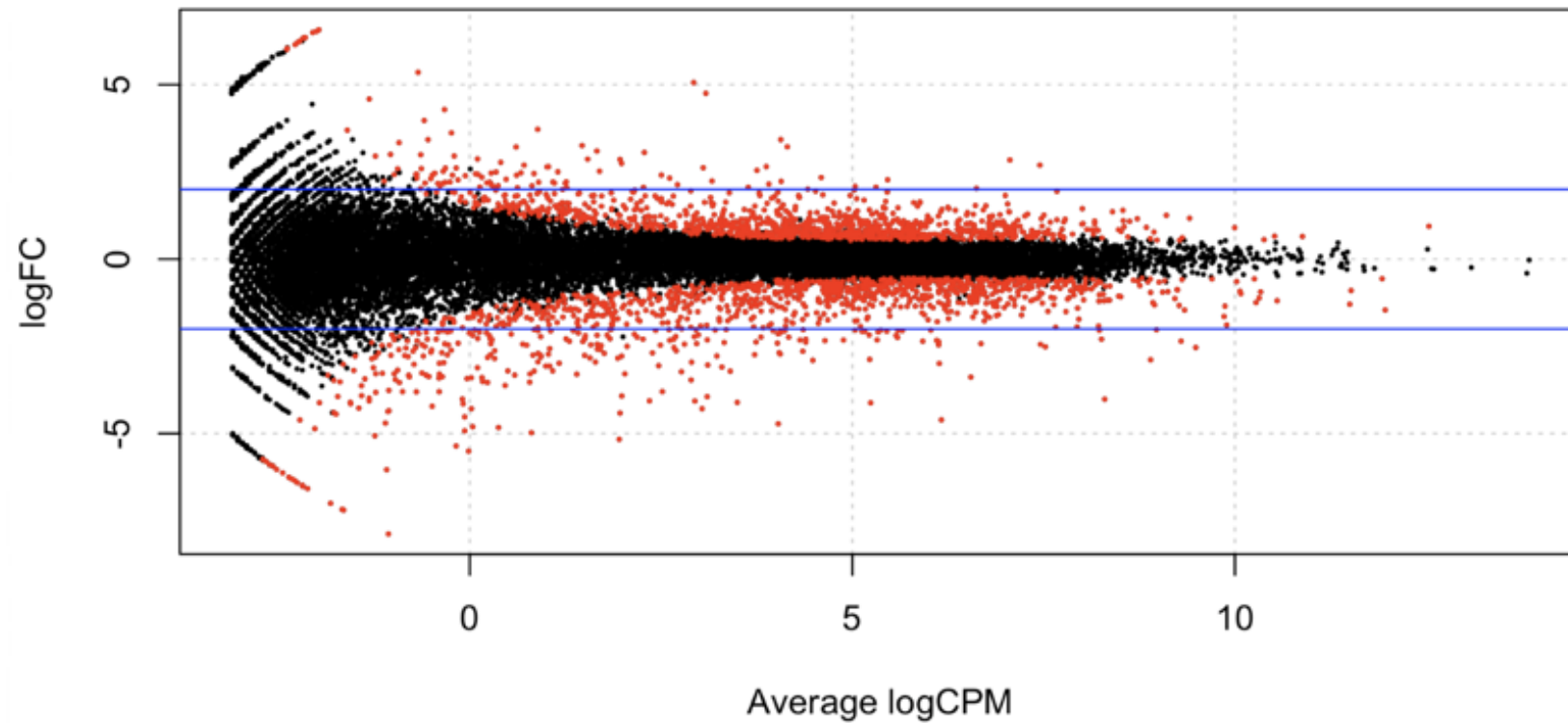
Quality scores across all bases (Sanger / Illumina 1.9 encoding)



Samtools flagstat report

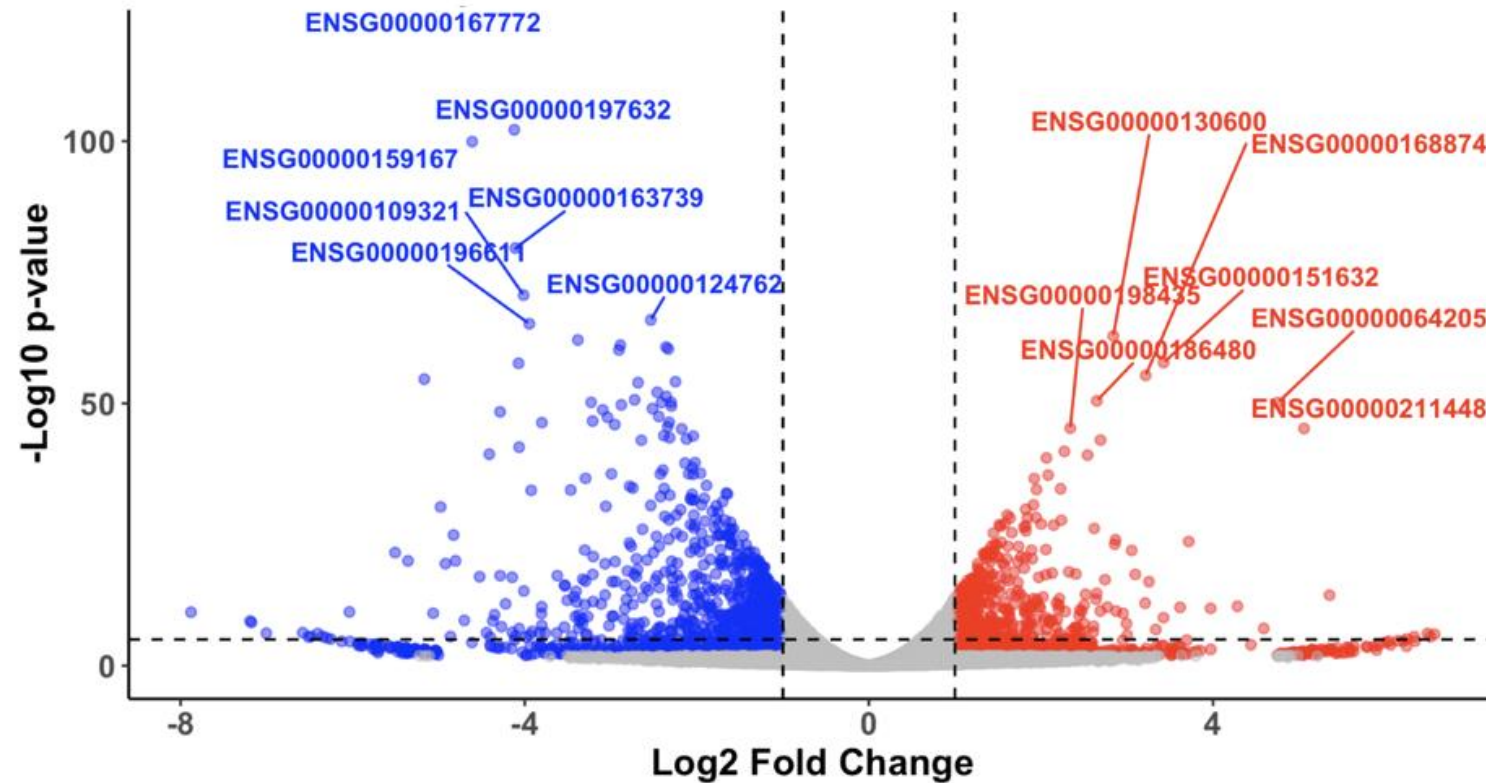


MA Plot



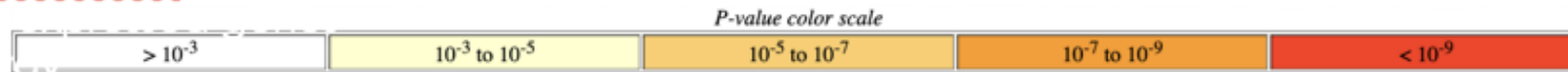
MA plot shows global expression patterns, highlighting significant changes in gene expression.

Volcano Plot

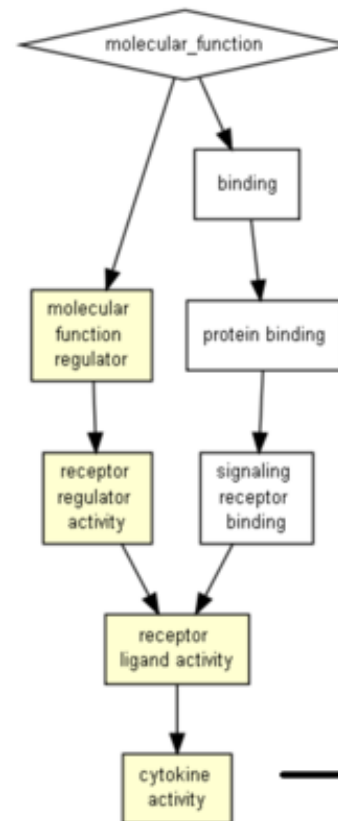


Volcano plot identifies significant upregulated and downregulated genes, including potential immune-related targets like ENSG000001030600.

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.

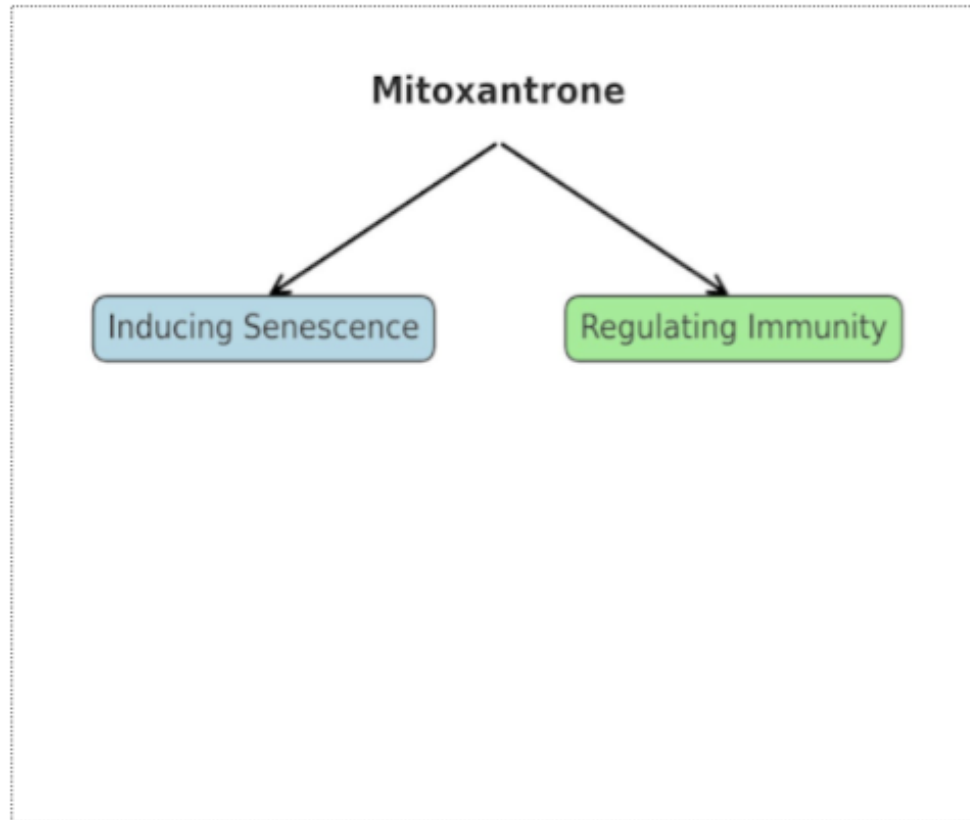
Linking Mitoxantrone to Cytokine Activity

- "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."

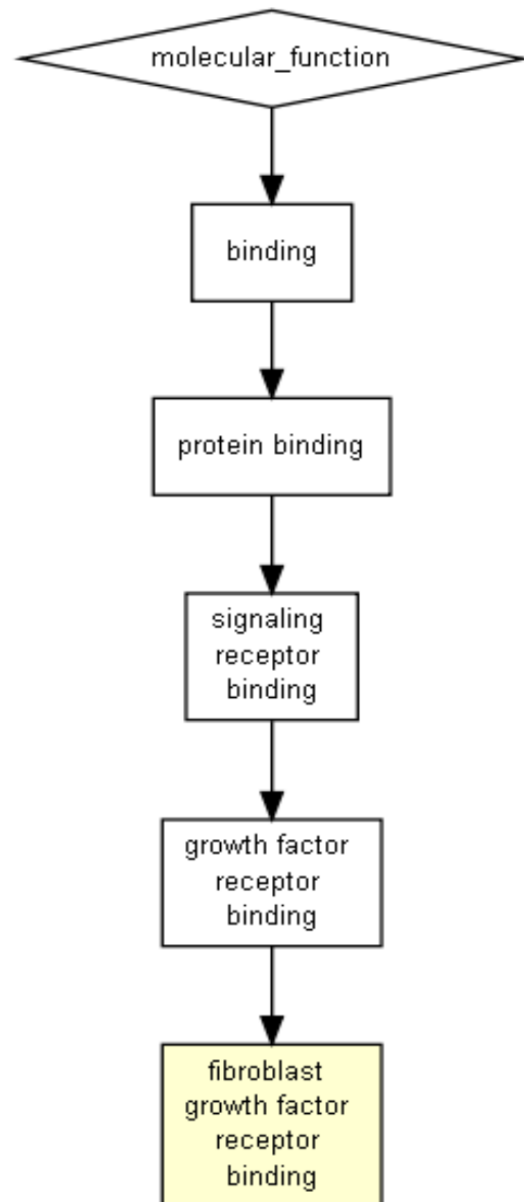
Fox, Edward J. "Mechanism of Action of Mitoxantrone." Neurology, 2004)

- 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.

Acknowledgement

- ITCGA: Integrated Training in Computational Genomics and Data Sciences NIH/NCI
Grant #3U54CA156734-1352