Killed in Cold Blood: An exploration of the efficacy of oncolytic adenoviruses in metastatic breast cancer

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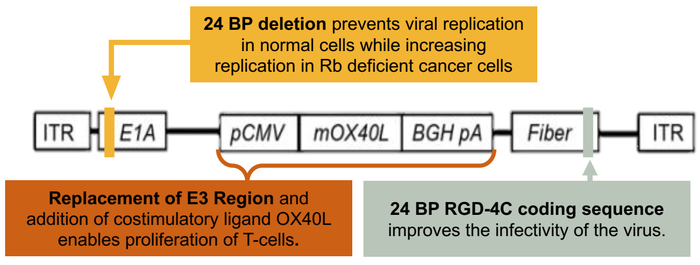
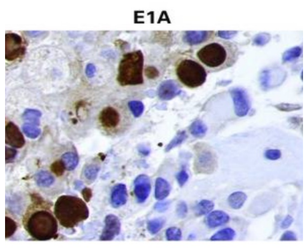
BACKGROUND

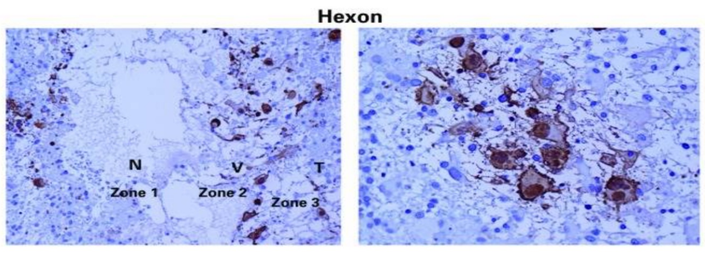
- **Metastatic breast cancer (MBC) is one of the most lethal cancer types worldwide.**
- **Current therapies include chemotherapy, radiotherapy, and surgery**. However, these methods are ineffective with regards to improving long-term survival rates for patients with MBC.
- **Delta-24-RGD has shown much success infecting and killing cancer cells in addition to inducing CD4⁺ T-Cell immune response.** The response from the immune system inadvertently initiates abscopal effects, as indicated in a phase 1 clinical trial.

▼ **Figure 1. Genomic structure of Delta-24-RGDOX**

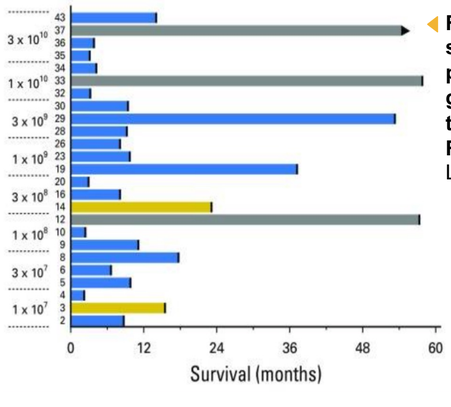




◀ **Figure 2. Immunohistochemical staining for E1A.** Indicative successful of viral infection in glioblastoma. Adapted from Lang *et al.*, *JCO*, 2018.



▲ **Figure 3. Immunohistochemical staining for Hexon protein.** Indicative successful of replication of Delta-24-RGD in glioblastoma. Adapted from Lang *et al.*, *JCO*, 2018.



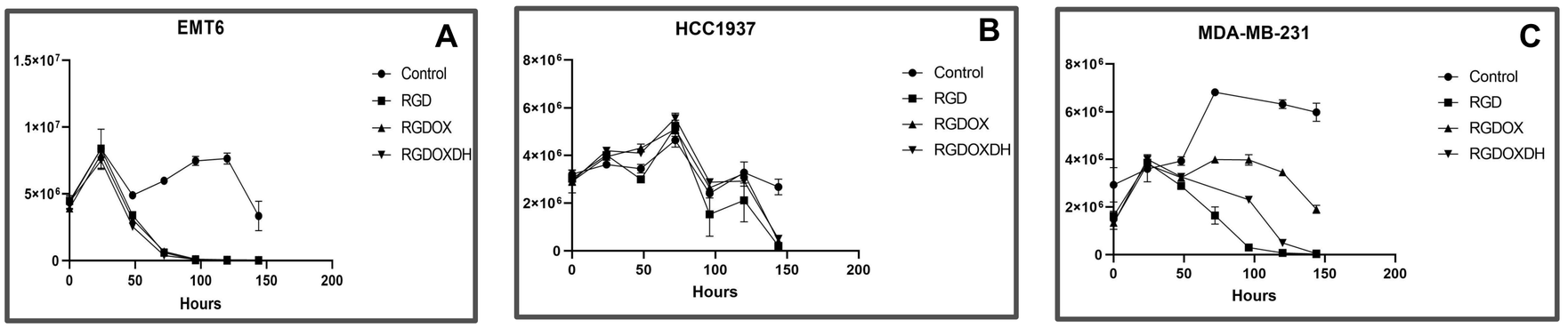
◀ **Figure 4. Long term survival rates in patients with glioblastoma, after treatment with Delta-RGD.** Adapted from Lang *et al.*, *JCO*, 2018.

HYPOTHESIS

In this study, we hypothesize that oncolytic virotherapy will elicit a robust antitumor immune response, which will exert abscopal effects and eradicate primary tumors and metastatic niches in metastatic breast cancer models.

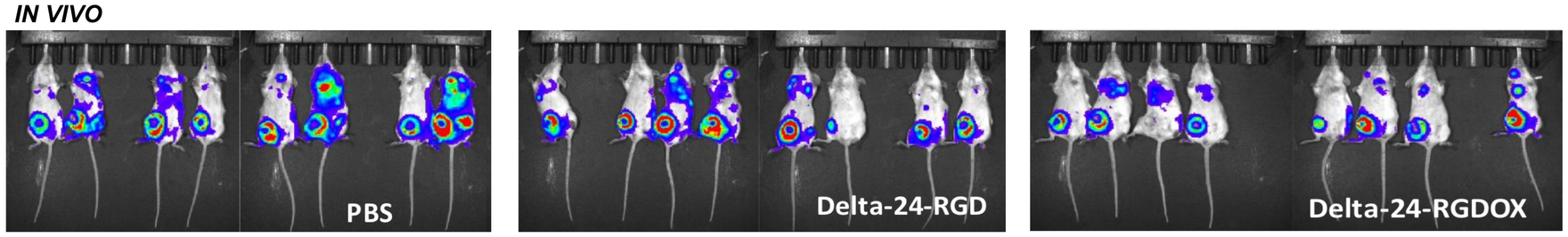
RESULTS

IN VITRO



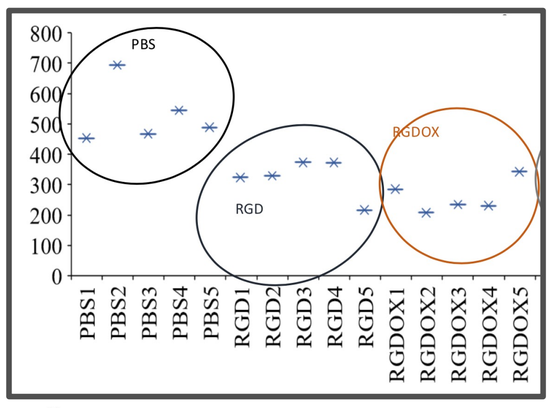
▲ **Figure 5. Viability assay for murine (A) and human (B,C) MBC cell lines *in vitro.*** Cell lines were infected with appropriate MOI of viruses and monitored over a period of 144 hours. Cytotoxic effects are measured using Viral ToxGlo™-Promega

IN VIVO

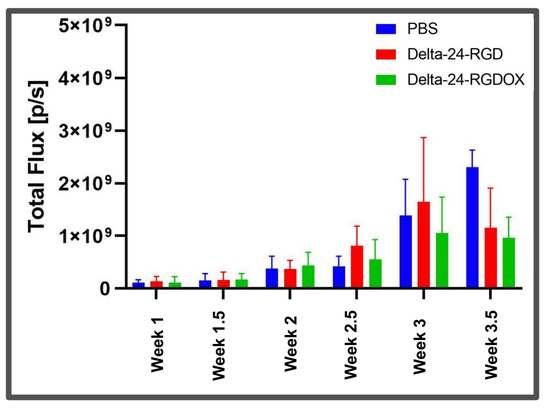


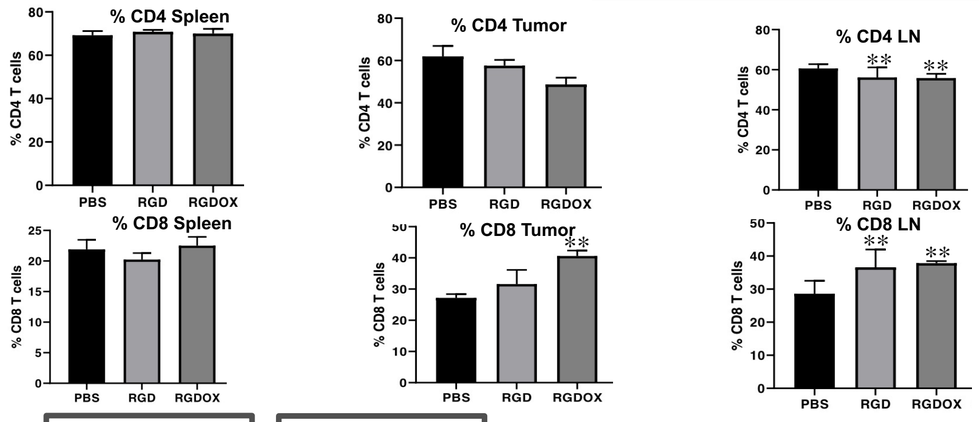
▲ **Figure 6. Observation of breast cancer metastasis in female BALB/c murine populations.** BLI imaging was performed more than 2 weeks after 1st dose (5 weeks after cell implant).

▼ **Figure 7. Tumor volumes in murine population (mm³).**



▼ **Figure 8. Intensity of 4T1 primary breast tumor in murine population (p/s).** Luciferin expression via BLI.





▲ **Figure 9. %CD4/CD8 T-Cell response in spleen, tumor, and lymph nodes.** Tissue samples were collected from live mice analyzed with Flow Cytometry. ** Statistically significant. Two-way ANOVA p<0.001

◀ **Figure 10. Percent lung (A) and brain (B) Metastasis in murine population after treatment.**

CONCLUSION

- Delta-24-RGD and Delta-24-RGDOX show great efficacy infecting and killing human and murine breast cancer cells *in vitro.*
- Treatment of murine models with armed oncolytic viruses increased T-cell specific anti-tumor responses and thus controls primary tumor growth and metastasis.

FUTURE INVESTIGATION:

The development of oncolytic viruses has introduced a paradigm shift in our approach to cancer treatment. Our data may constitute the basis for the development of virotherapy in patients with metastatic breast cancer.

ACKNOWLEDGEMENTS

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REFERENCES

Lang, F. F., et.al. Phase I Study of DNX-2401 (Delta-24-RGD) Oncolytic Adenovirus: Replication and Immunotherapeutic Effects in Recurrent Malignant Glioma. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *36*(14), 1419–1427. https://doi.org/10.1200/JCO.2017.75.8219