



INTRODUCTION

- DIPG is a rare and aggressive pHGG primarily affecting children aged 5-10 in the brain's ventral pons.
- Current treatment is limited to radiation therapy, facing challenges with side effects and resistance.
- CDDO-2P-Im enhances radiation therapy, reducing doses and cognitive consequences in children.
- Targeting the CCL2/MCP-1 pathway impedes glioma progression and boosts immunotherapy response.
- Synthetic oleanane triterpenoids are studied as CCL2/MCP-1 inhibitors to improve radiation therapy outcomes and reduce toxicities.

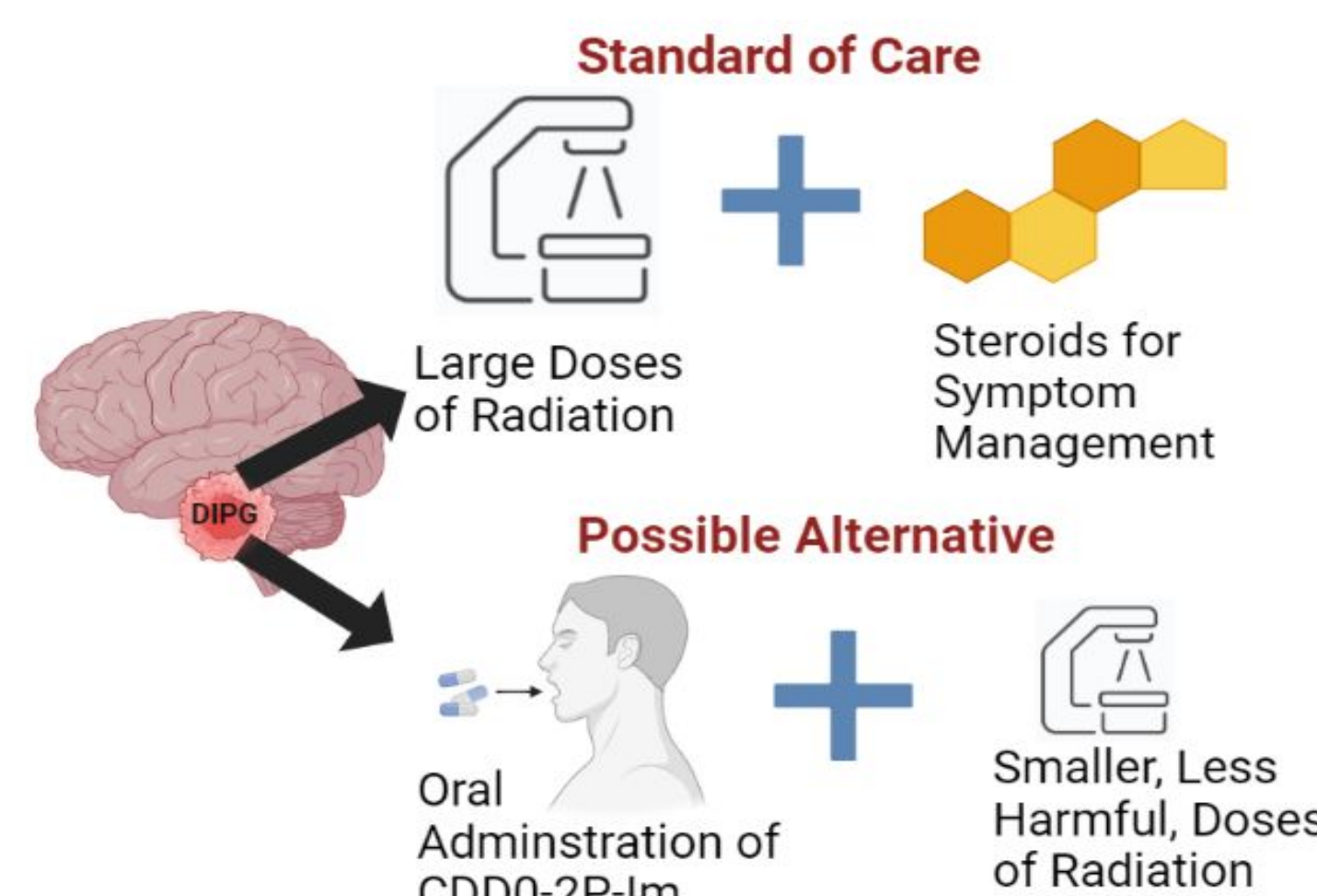


Figure 1. Alternative Treatment with CDDO-2P-Im and Radiation Therapy. (Created with Biorender)

PURPOSE

Investigate the efficacy of CDDO-2P-Im as a radiosensitizer in combination with radiation therapy through colony-forming assays, aiming to demonstrate a decrease in cell count at higher doses and thereby enhancing the treatment for DIPG

METHODS

- DIPG cell lines grown in T75 as confluency were monitored to ensure health of colonies
- Colony-forming assay (CFA) conducted using varying doses of CDDO-2P-Im, including control
- Process repeated, except with varying doses of radiation and a process that tested combination doses of radiation and CDDO-2P-Im
- DIPG cells stained using glutaraldehyde-crystal violet mixture
- Cells and number of colonies counted and statistical significance tests performed on the gathered data

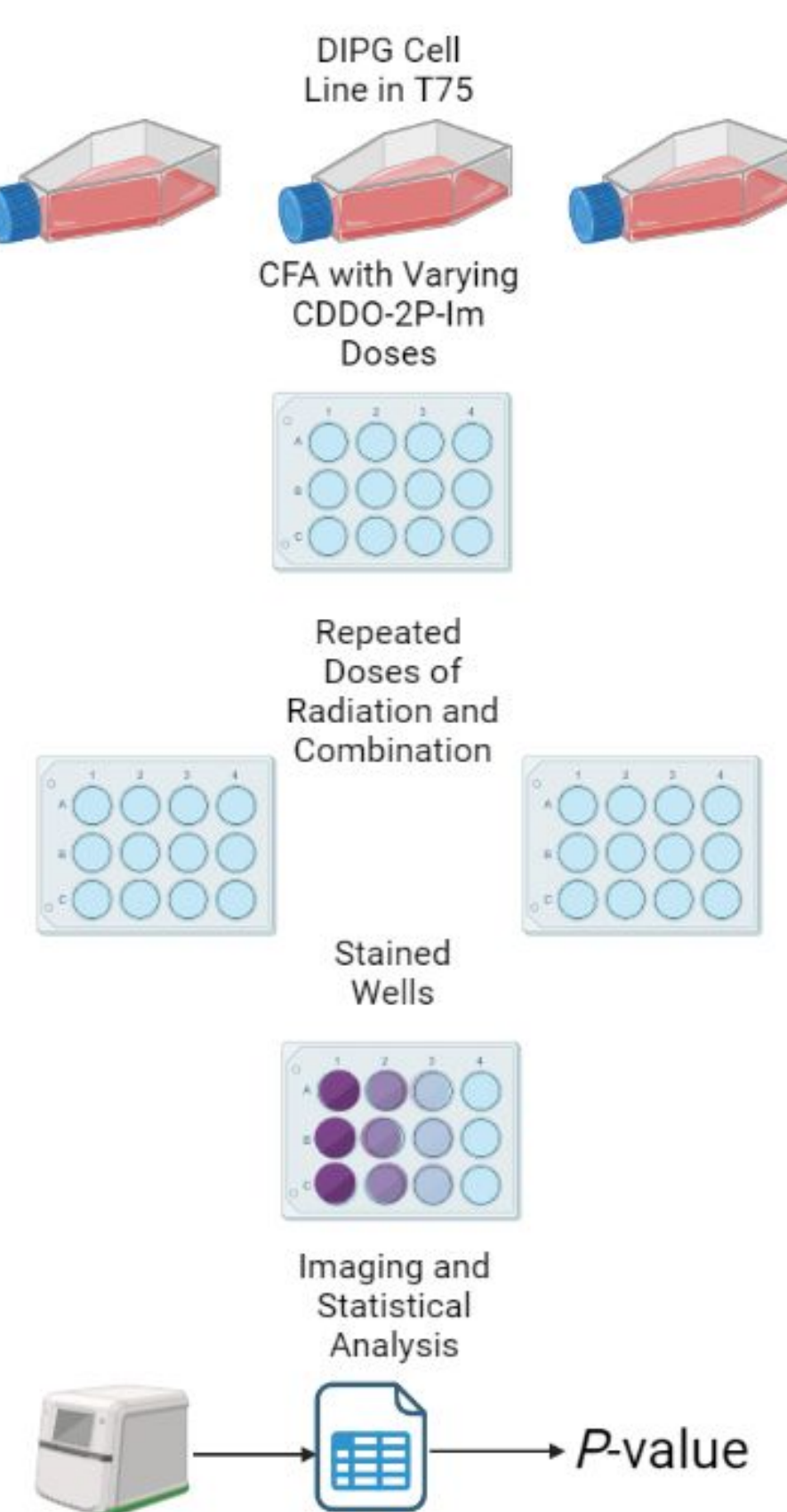


Figure 2. CFA and Analysis of Data. (Created with Biorender)

RESULTS

Figure 3. Imaging from Combination (Radiation + 2P-Im) Therapy.

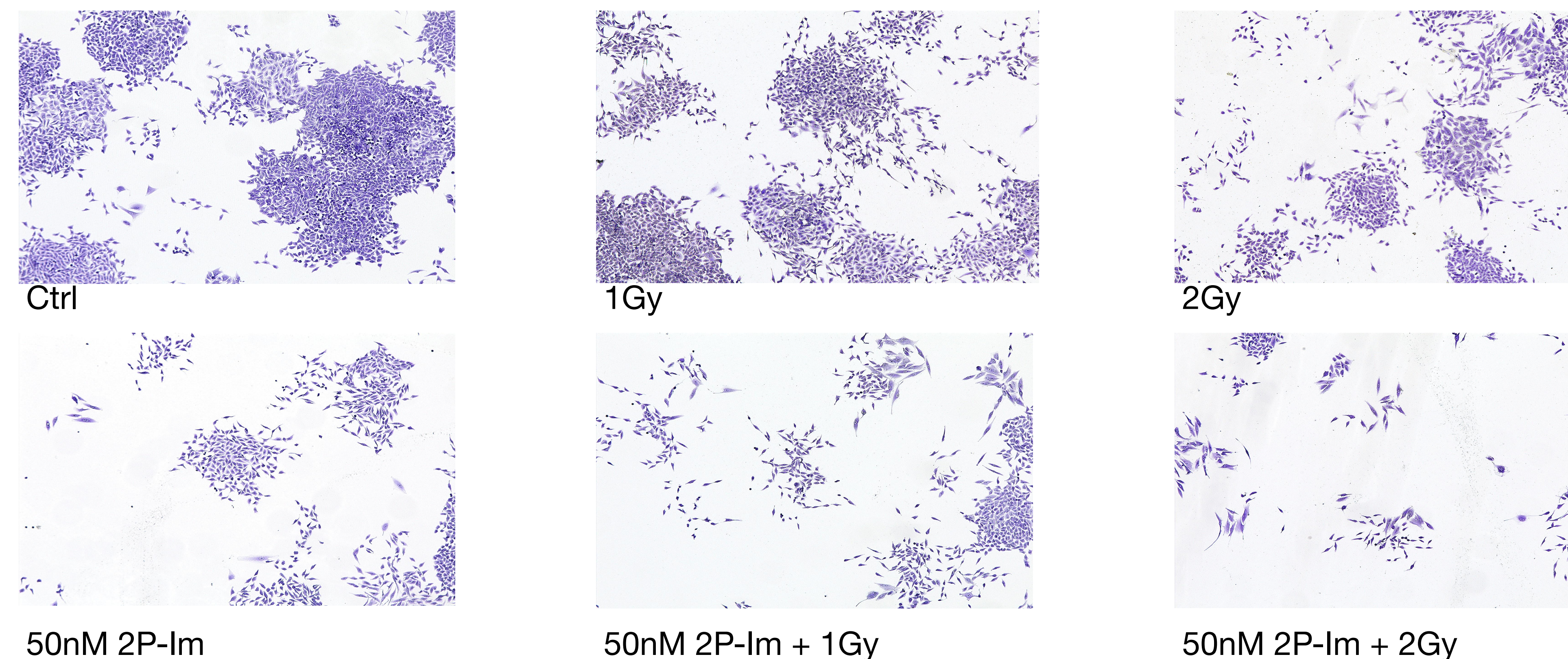
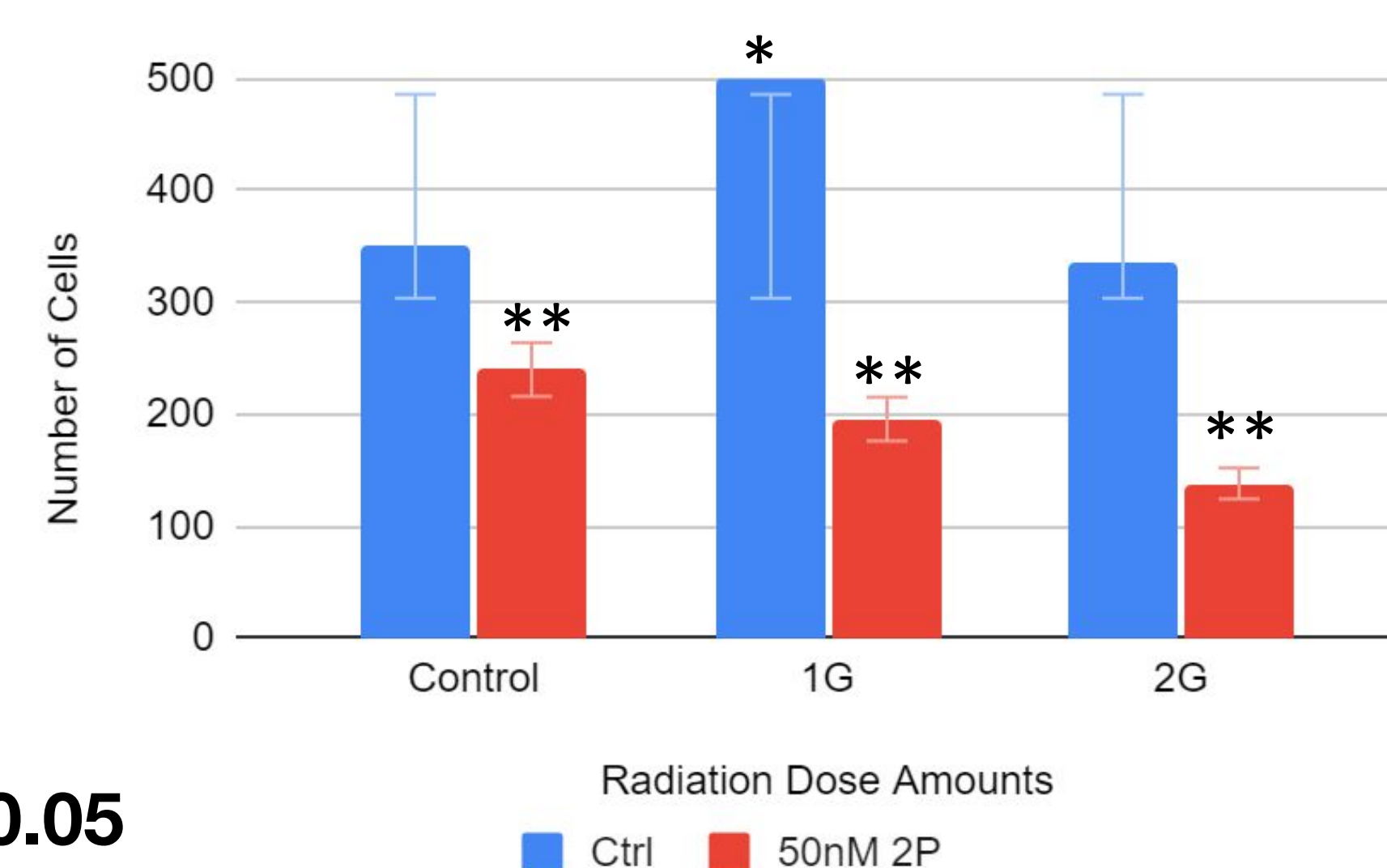


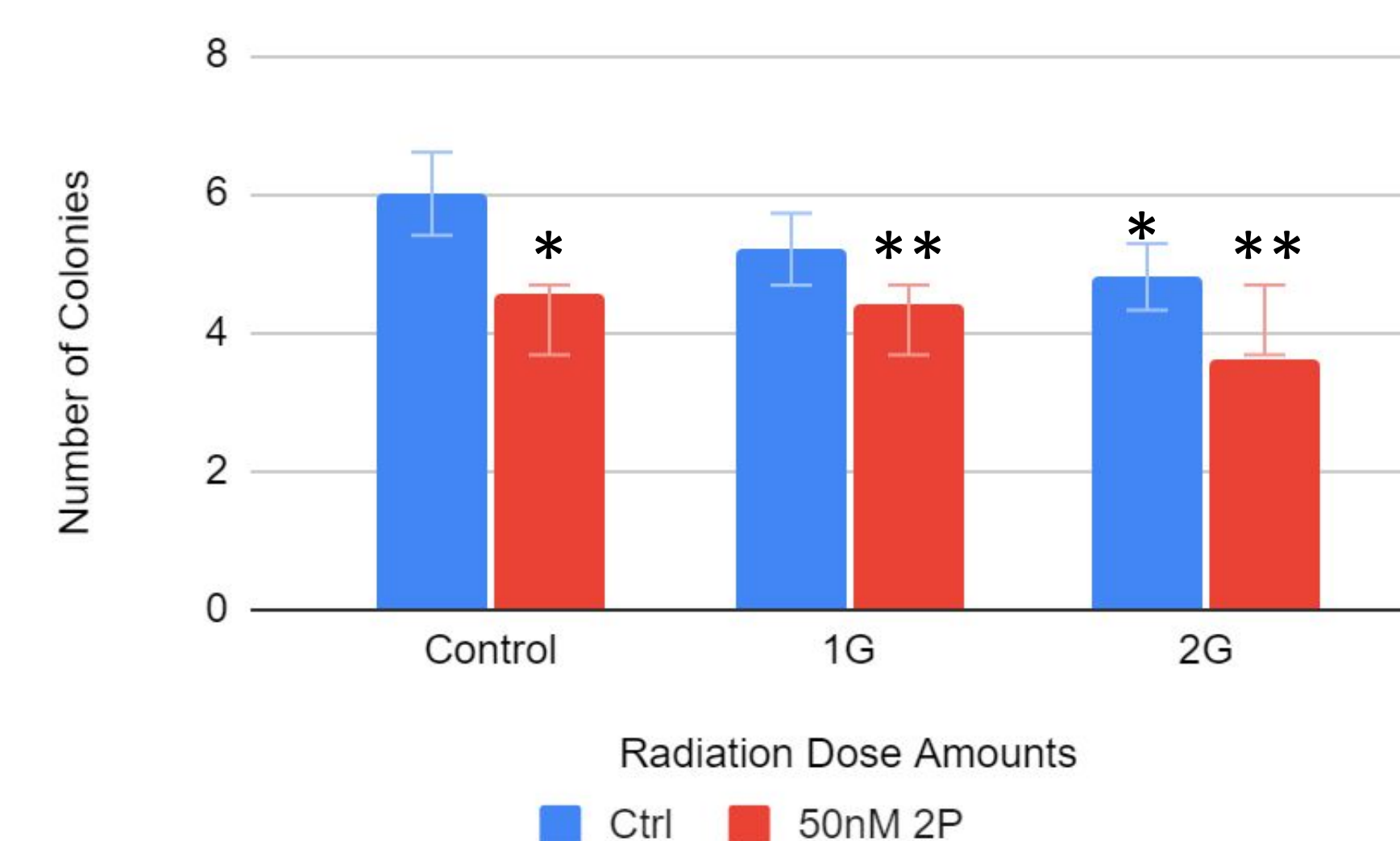
Figure 4. Average Cells per Colony.



*P<0.05

**P<0.01

Figure 5. Average Colonies per HPF.



DISCUSSION/FUTURE

- Investigate dose-dependent cytotoxicity of 2P-Im in animal models (mice) to determine optimal dosage and potential side effects
- Gain a deeper understanding of 2P-Im's mechanisms of action in treating DIPG to identify new targets for intervention
- Progress toward clinical trials to assess 2P-Im's safety and efficacy in human patients with DIPG for potential therapeutic use

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REFERENCES

- Pellot JE, De Jesus O. Diffuse Intrinsic Pontine Glioma. [Updated 2023 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK560640/>
- Franken NA, Rodermond HM, Stap J, Haveman J, van Bree C. Clonogenic assay of cells in vitro. Nat Protoc. 2006;1(5):2315-9. doi: 10.1038/nprot.2006.339. PMID: 17406473.
- Metselaar DS, du Chatinier A, Stuijver I, Kaspers GJL, Hulleman E. Radiosensitization in Pediatric High-Grade Glioma: Targets, Resistance and Developments. Front Oncol. 2021 Apr 1;11:662209. doi: 10.3389/fonc.2021.662209. PMID: 33869066; PMCID: PMC8047603.
- Akkari L, Bowman RL, Tessier J, Klemm F, Handgraaf SM, de Groot M, Quail DF, Tillard L, Gadiot J, Huse JT, Brandsma D, Westerga J, Watts C, Joyce JA. Dynamic changes in glioma macrophage populations after radiotherapy reveal CSF-1R inhibition as a strategy to overcome resistance. Sci Transl Med.