

Characterizing Phenotypes of Zombified Mesenchymal Stromal Cells



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BACKGROUND:
Over time, our stem cells become dysregulated and take on a senescence-associated secretory phenotype (SASP), which may contribute to aging and autoimmune diseases. They are often called “zombies” because they are dysregulated and take on large, strange shapes, all while not dying. With this project, the goal is to produce and isolate these dysregulated “zombie” mesenchymal stem/stromal cells (MSCs) and characterize their phenotype using known oxidative stressors. This is an important step toward understanding their impact on the body, which may give us some insight as to how to begin treating diseases that may arise from them.

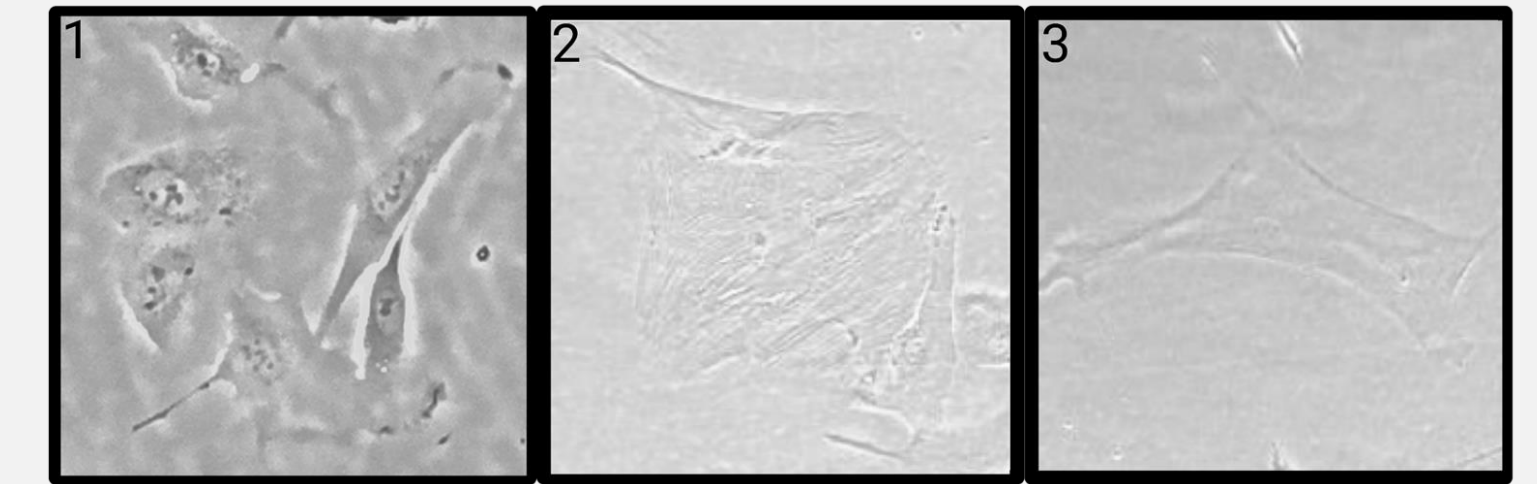


Figure 1. Panel 1: healthy bone marrow (BM)-MSCs, panels 2-3: naturally occurring zombie MSCs

METHODS
See Figure 2

RESULTS

- Cell death occurred at >1000µg/L of glyphosate and 22mM of glucose
- Treatment of human BM-MSCs with trace amounts of glyphosate causes accumulation of unknown vesicles.
- Glucose treatment increases cell size and slows cell division.

REFERENCES

- McHugh D, Gil J.. *J Cell Biol.* 2018;217(1):65-77.
- Canada, H. (2021, November 12). *Government of Canada.* Canada.ca. Retrieved March 7, 2022, from <https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management/public/consultations/proposed-maximum-residue-limit/2021/glyphosate/document.html>
- Wiese, D. M., Ruttan, C. C., Wood, C. A., Ford, B. N., & Braid, L. R. (2019). *Stem Cells Translational Medicine*, 8(9), 945–958.

Trace amounts of sugar or pesticides changes human MSCs

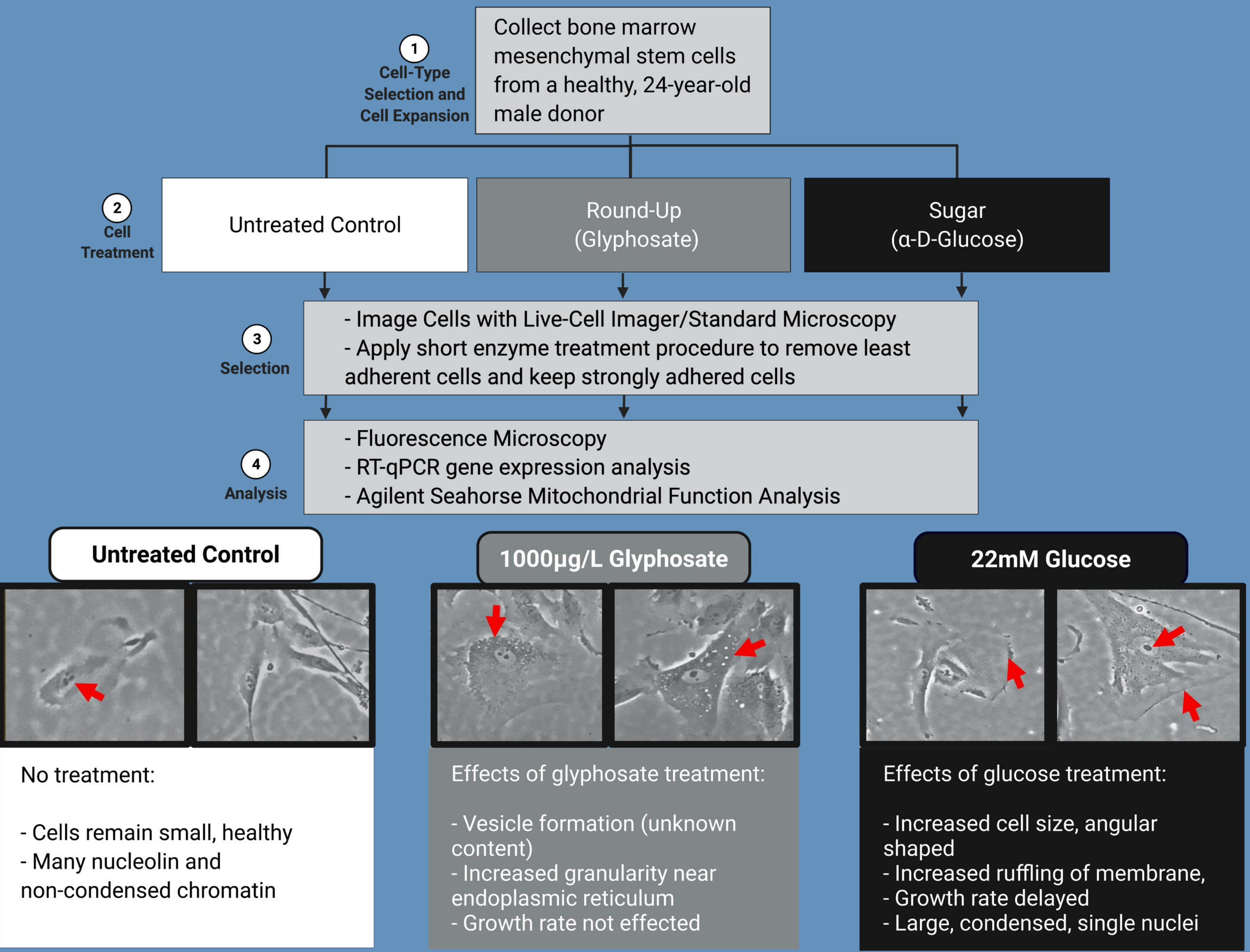
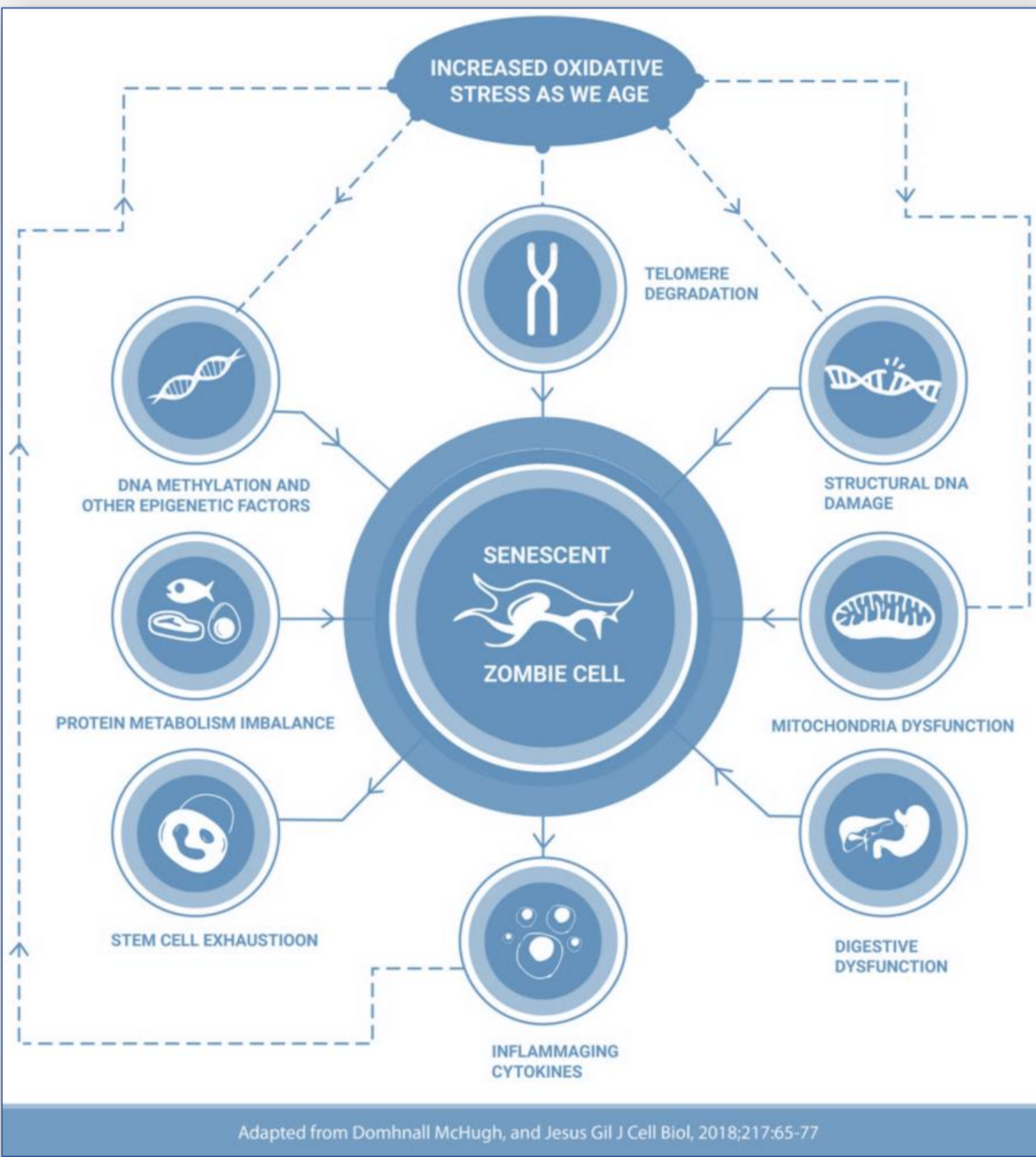


Figure 2. Flowchart for isolating “zombified” BM-MSCs

The concentration of glyphosate required to cause effects on the MSCs is 30-300x less than the legally allowable limit of 35,000µg/L (35ppm)² in Canada.

“No risks of concern to human health from current uses of glyphosate.”
– Environmental Protection Agency



DISCUSSION
Next steps:

- Measuring gene expression via RT-qPCR and ICC
- Assess changes in mitochondrial flux
- Genes of interest:
 - RGCC:** regulates cell cycle
 - MFAP5:** controls cell adhesion
 - CLN8:** conducts molecule transportation

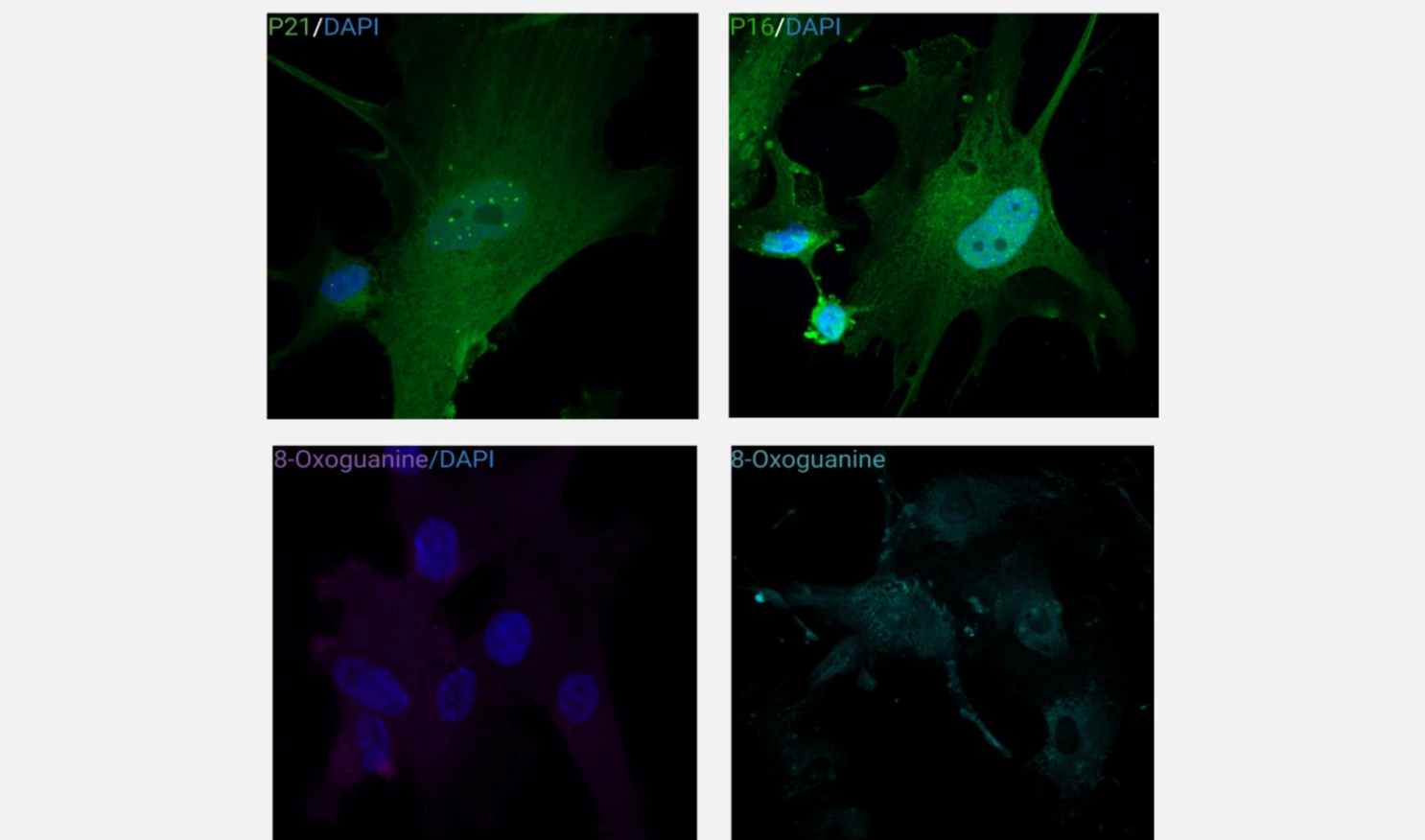


Figure 3. Fluorescent staining of p16, p21, and 8-oxoguanine

- P21 and P16** are upregulated under oxidative stress
- 8-oxoguanine** labels oxidative stress-induced DNA lesions

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