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PrC210 as a Cytoprotective Scavenger in Sulfur Mustard Exposure: An In Vitro Toxicological Analysis

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1. Introduction

- Sulfur mustard (SM) induces DNA alkylation, oxidative stress, and persistent DNA damage responses driving apoptosis and stress-induced premature senescence.
- Reactive oxygen species (ROS) exacerbate SM toxicity and represent a viable therapeutic target.
- WR1065, the active dephosphorylated metabolite of amifostine (WR- 2721), is the prototypical aminothiol countermeasure but has demonstrated inconsistent efficacy against SM.
- PrC210 is a next-generation aminothiol ROS scavenger that does not require enzymatic activation.
- We compared 5-minute scavenger pre-treatment with untreated SM-exposed cells at single-cell resolution.

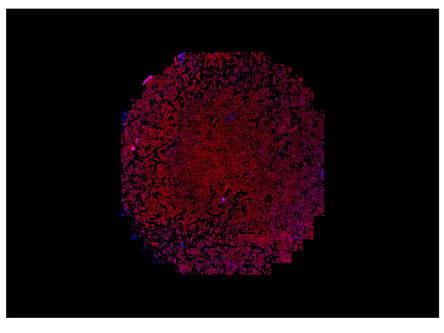
2. Materials & Methods

- Human keratinocytes
- SM: 50 µM and 500 µM +- PrC210 or WR1065
- 5 min pre-incubation (pre-treatment)
- N7-guanine DNA adducts detected by 2F8 antibody IF + DAPI
- Single-cell high-content imaging

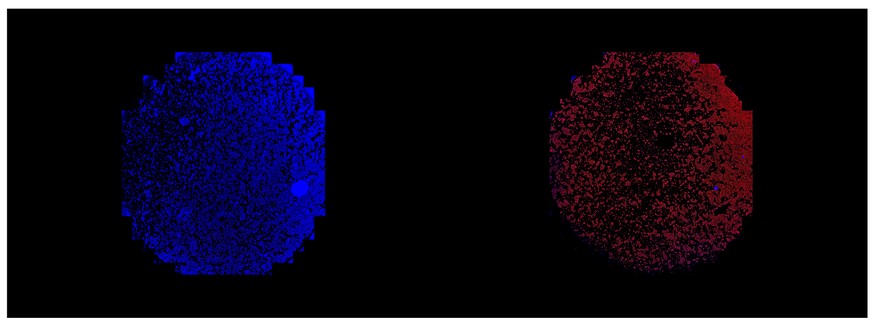
- Log2 fold-change (lfc) relative to untreated controls
- Mann–Whitney U test (cell and slide level)
- Effect sizes (Cohen's d)
- Univariate logistic regression (slide level) for discriminability (ROC analysis)

3. Results

PrC210

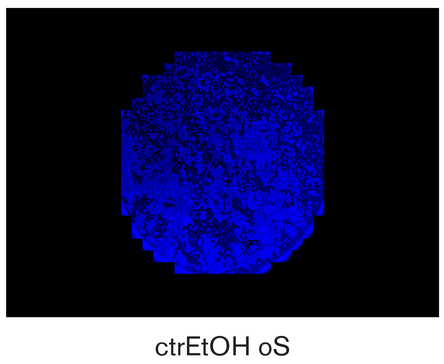


50 µM SM oS

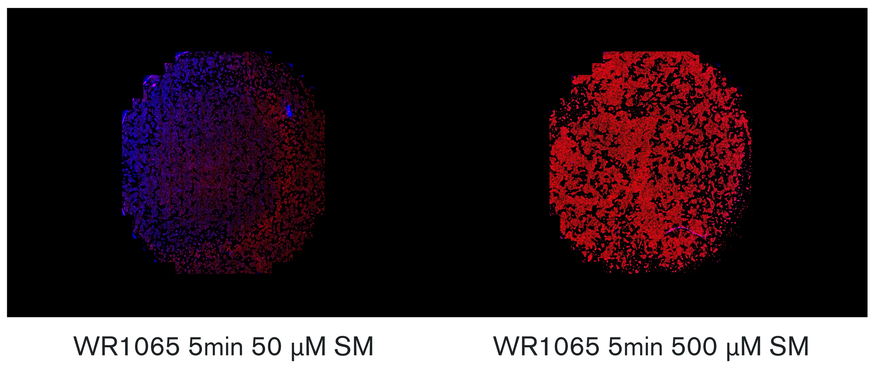


Prc210 5min 50 µM SM Prc210 5min 500 µM SM

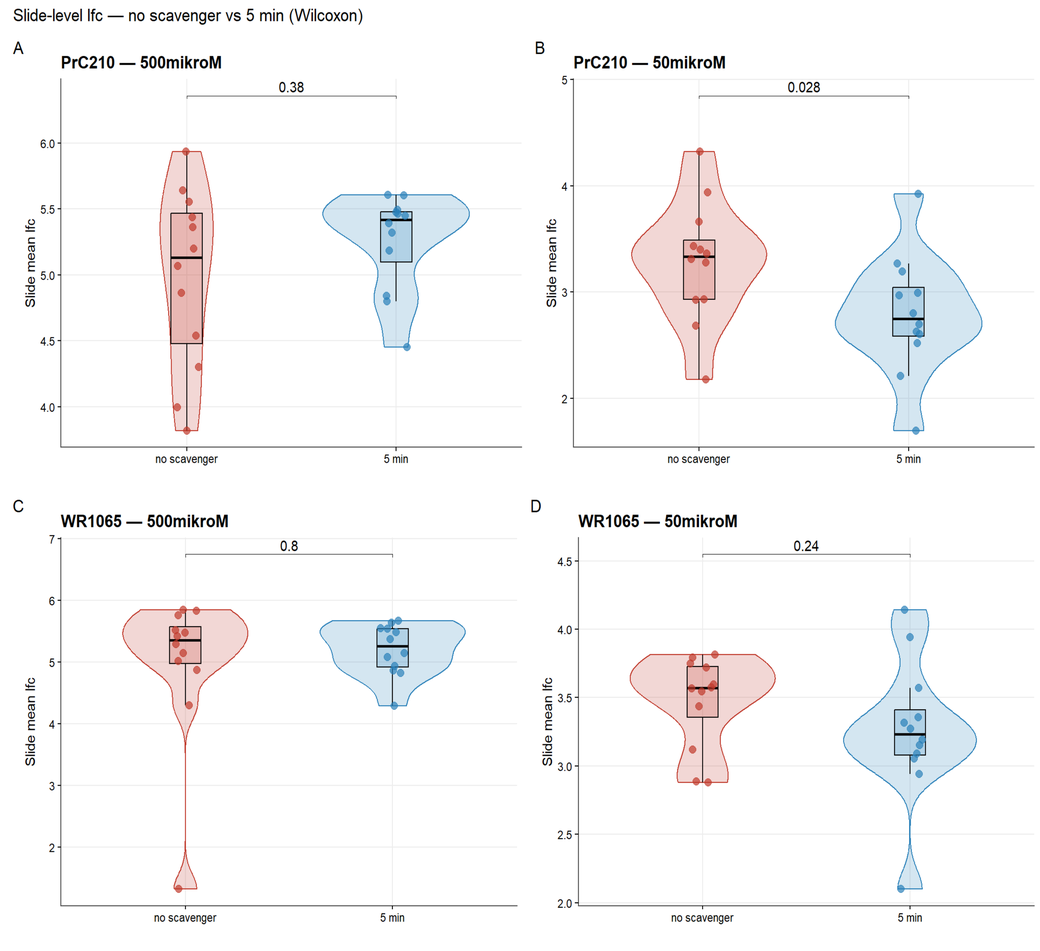
WR1065



ctrEtOH oS



WR1065 5min 50 µM SM WR1065 5min 500 µM SM



4. Discussion

- PrC210 at 50 µM significantly reduces SM-induced N7-guanine adduct burden after 5-min-pre-treatment, with a large slide-level effect size.
- WR1065 shows only a small, non-significant effect at 50 µM.
- At 500 µM, neither scavenger provides protection (negligible effect size).
- Log10(2F8) intensity discriminates treated from untreated slides for both scavengers (AUC > 0.60).
- PrC210 demonstrates potential as an improved, enzyme-independent countermeasure.

5. Conclusion

PrC210 at 50 µM significantly reduces SM-induced N7-guanine adduct burden after 5-min pre-treatment, with a large slide-level effect size confirmed by Mann–Whitney U testing.

These findings support PrC210 as a candidate medical countermeasure against vesicant-induced DNA damage.

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