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Exploring the Inactivation Mechanisms of Human Adenovirus 2 in Solar Disinfection: The Role of Genome Repair in the indirect pathway

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Introduction

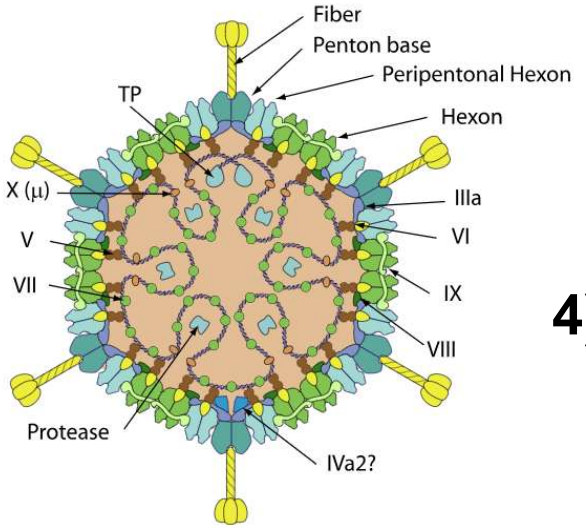
❖Human Adenovirus 2 (HAdV2)

1) Hazardness

- Respiratory illness
- Risky for children
- Contaminant candidate list 4

3) Structure

- Linear dsDNA
- Non-enveloped → stable
- Icosahedral capsid (~90 nm)
- Fiber → combine to host cell
- Replication in host nucleus



[Viralzone, accessed 29th May 2025]

2) Transmission via Water

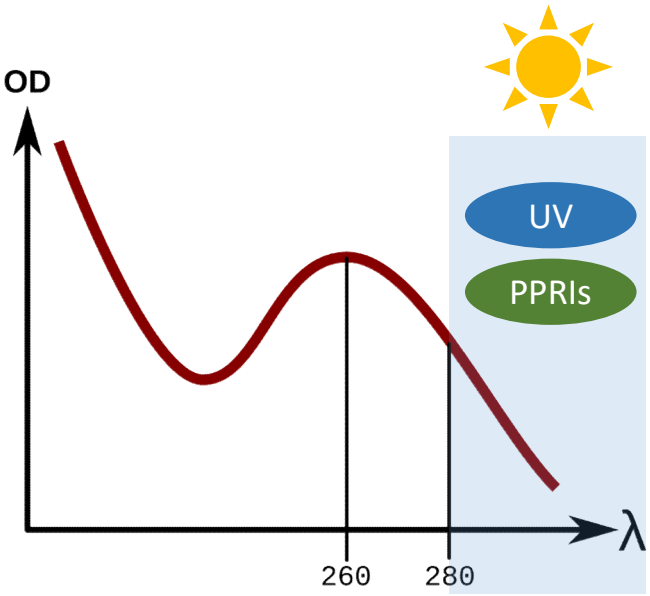
- Detected in various water sources
- Fecal-oral route

4) UV resistance

- > 180 mJ/cm^2 for 4 log inactivation
- Efficient **UV DNA repair** in host cell

Introduction

❖Sunlight disinfection of HAdV



High UV absorptivity of DNA

1) Direct pathway

: **DNA damage**

: **UV** absorption by TT site

: Cyclobutane pyrimidine dimer (CPDs), 64 photo-products (64PPs)

2) Indirect pathway

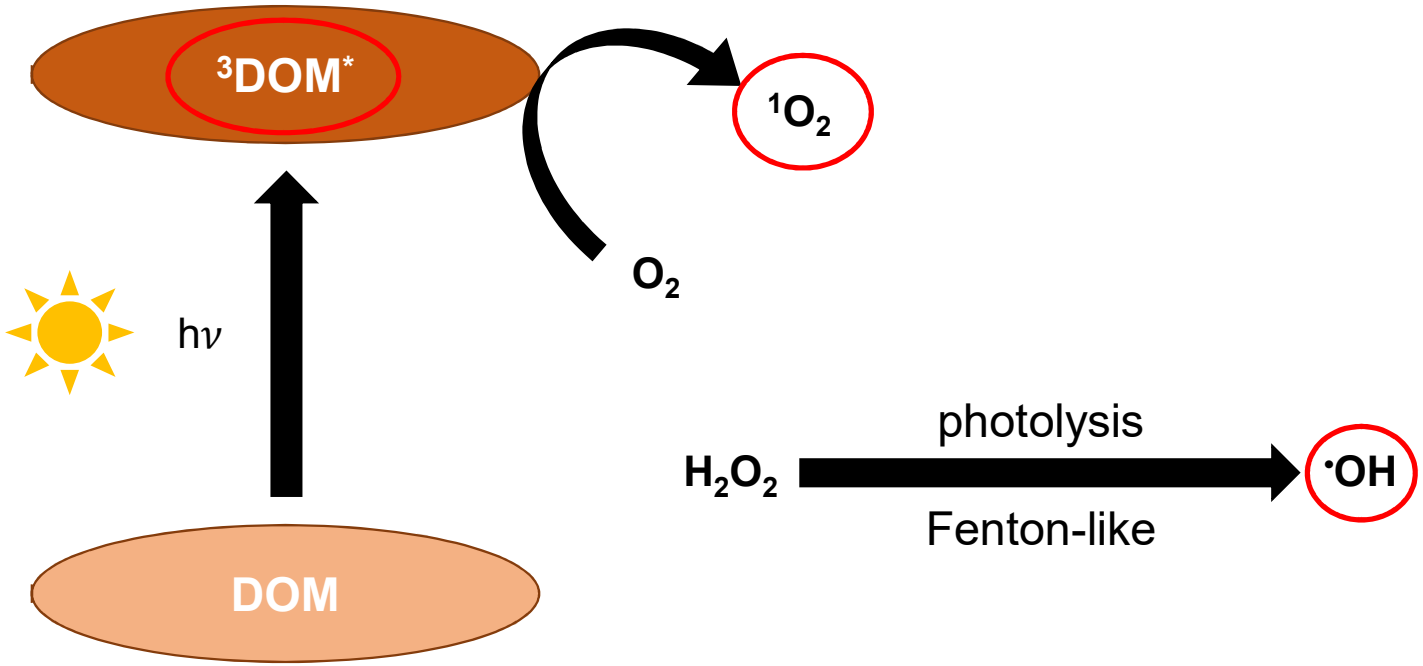
: **Protein damage**

: Photo-produced reactive intermediates (**PPRIs**)

Sunlight Disinfection mechanisms of HAdV *(UV and PPRI combined)?*

Material & Methods

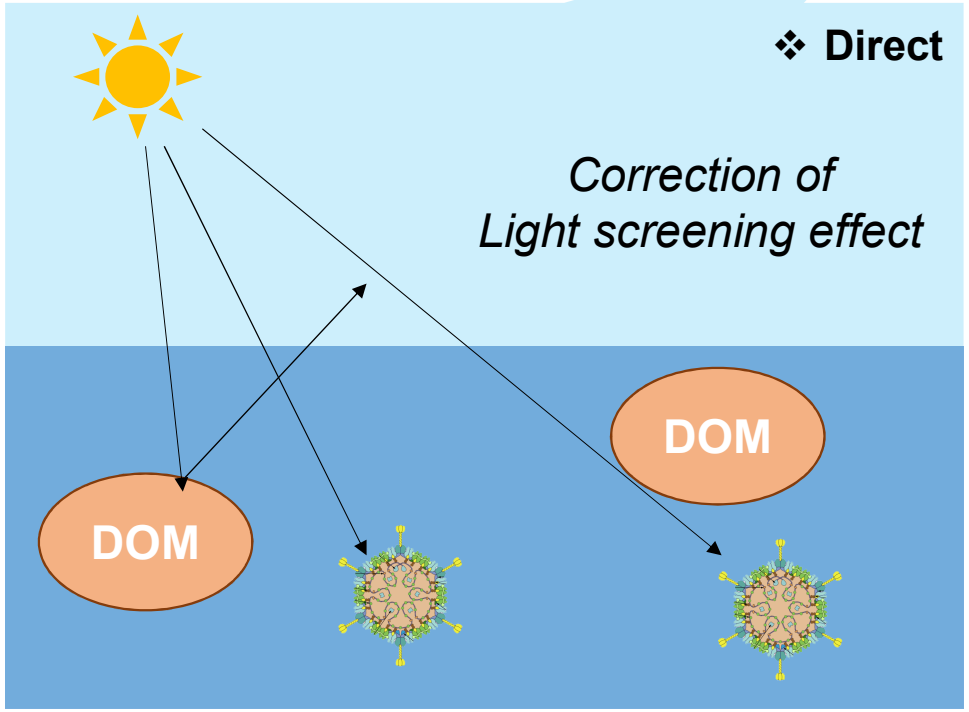
❖Dissolved organic matter (DOM): Natural Photosensitizer

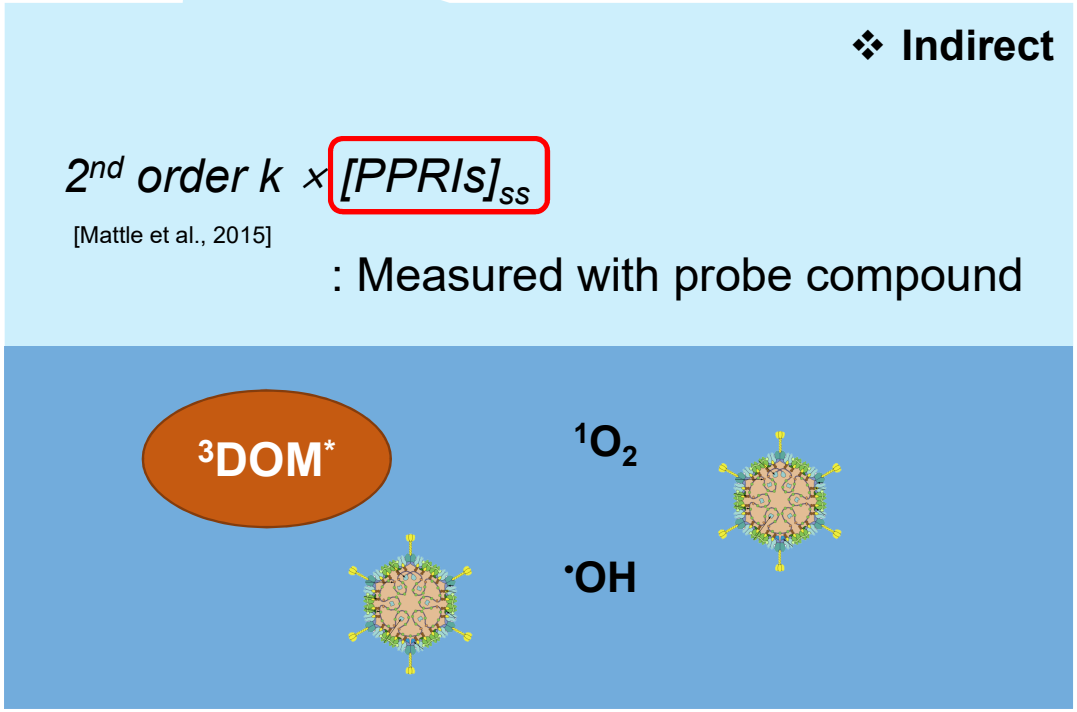


Material & Methods

❖Sunlight disinfection model

$$k_{overall,\ pred} = k_{direct} + k_{^1O2} + k_{\cdot OH} + k_{^3DOM^*}$$

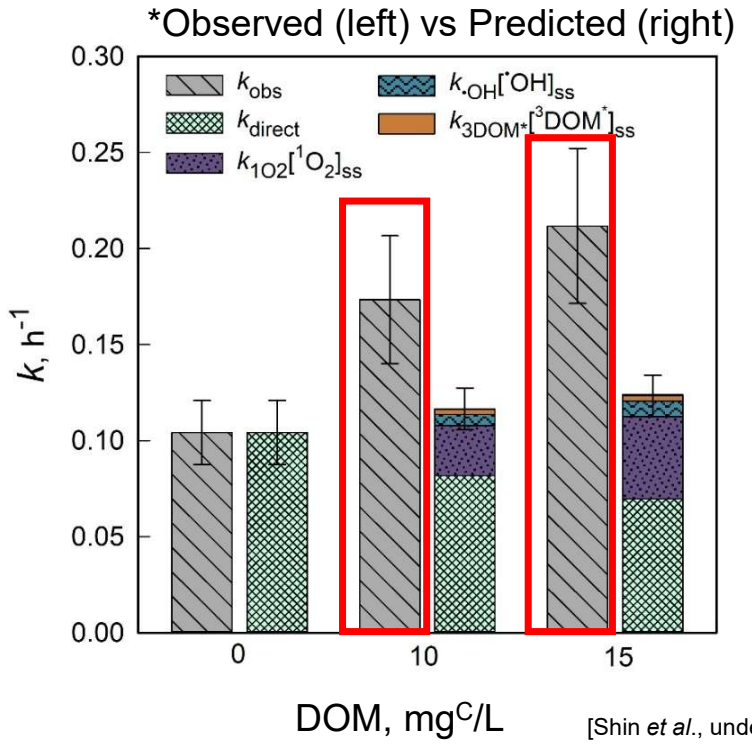




Results & Discussions

❖Can we predict HAdV2 sunlight disinfection?

$$k_{overall,\ pred} = k_{direct} + k_{1O2} + k_{\bullet OH} + k_{3DOM^*}$$



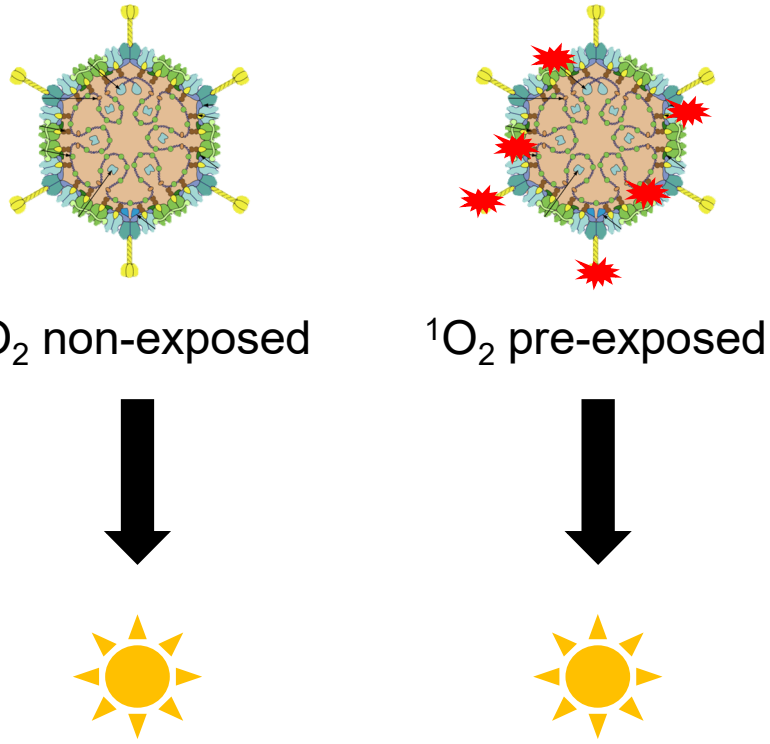
[Shin *et al.*, under review]

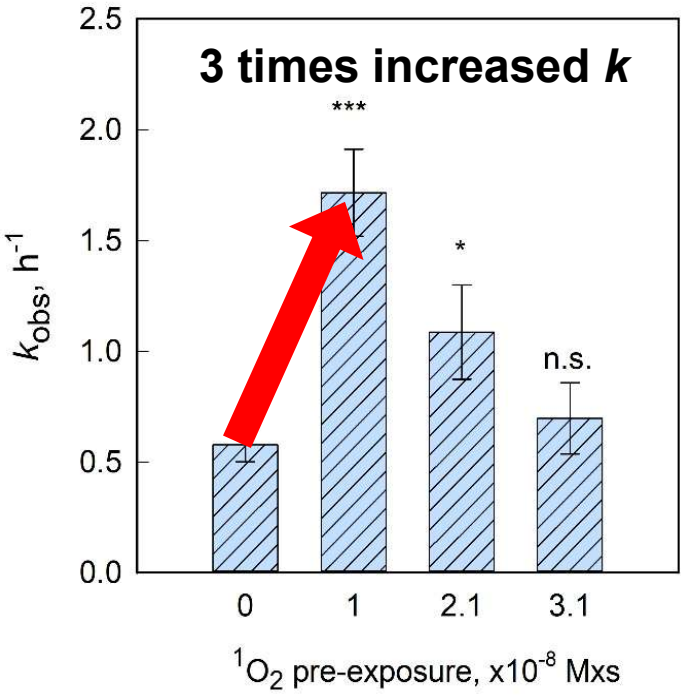
Figure 6-1. Sunlight inactivation rate constant of HAdV with DOM

- With DOM, k_{obs} increased while prediction didn't.
  : Light screening ↓ & PPRI formation ↑
  : $^1O_2$ played the dominant role among the PPRIs.
- Observed > prediction (1.5-1.7 fold)
  : **Unknown mechanisms of virus inactivation, other than direct and indirect.**

Results & Discussions

❖Is Direct and Indirect interlinked?





[Shin *et al.*, under review]

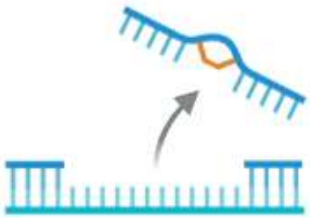
Figure 6-2. Sunlight inactivation rate constant of HAdV with pre-treatment of $^1O_2$.

Results & Discussions

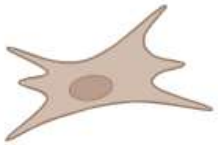
❖Does DNA repair efficiency change with PPRIs?

100 % repair

A549
: lung cancer cell

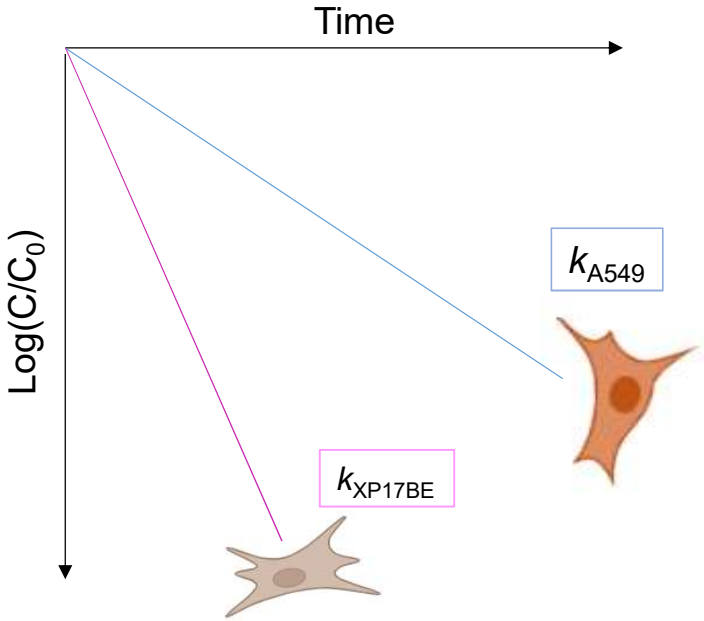


30-60 % repair



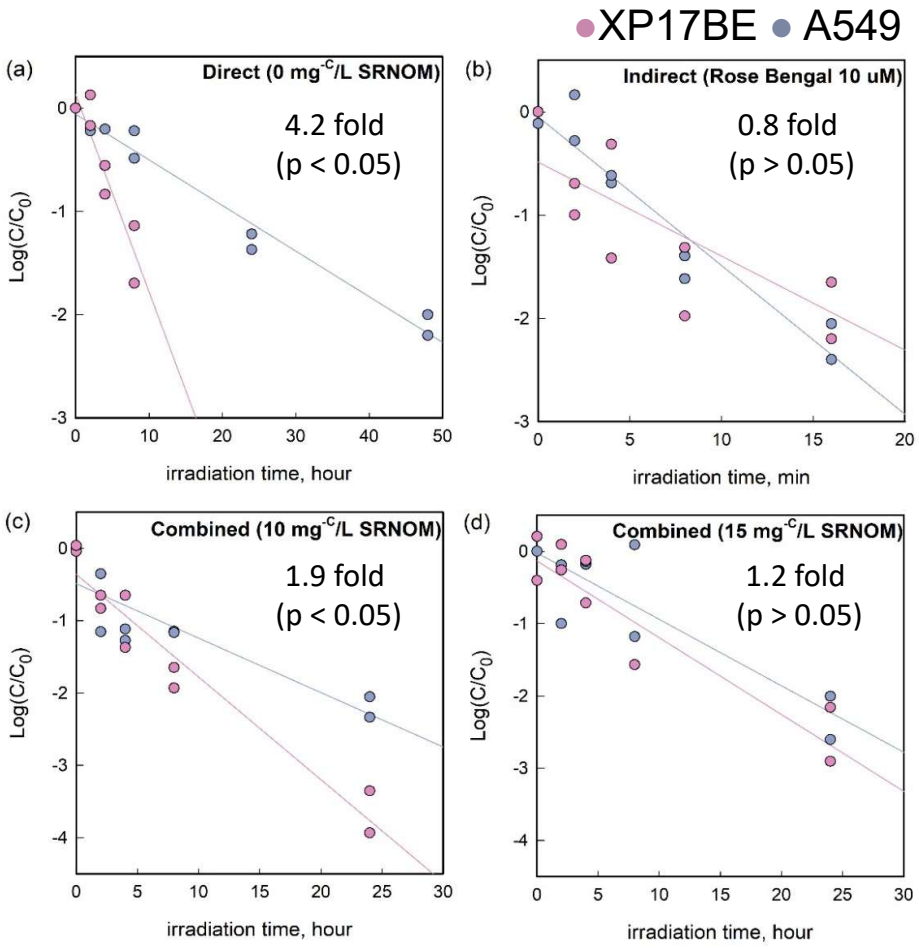
XP17BE
: skin cell
with Xeroderma Pigmentosum

HAdV inactivation rate



$$\frac{k_{XP17BE}}{k_{A549}} \propto \text{Amount of DNA repair}$$

Results & Discussions



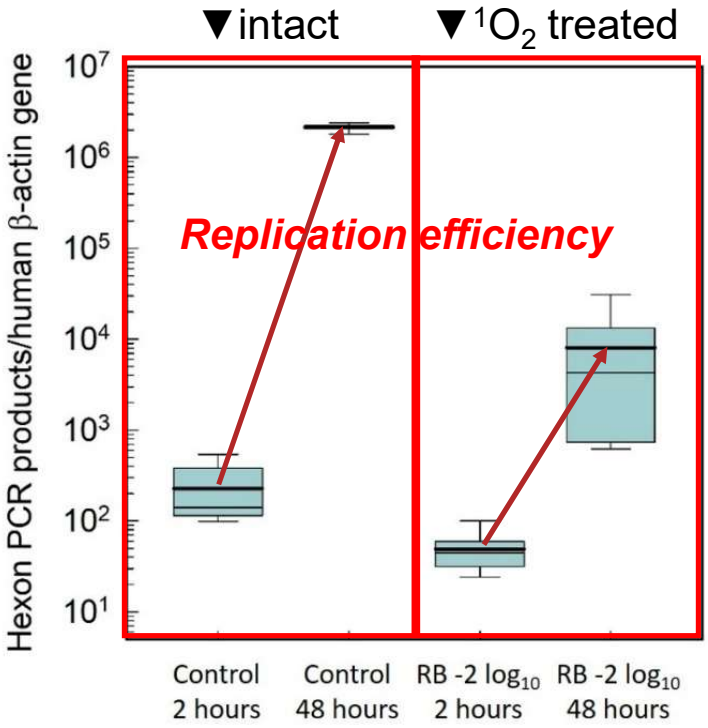
- ✓ In **Direct** only, XP17BE showed 4.2 fold faster inactivation than A549, due to active gene repair.
- ✓ In **Indirect** only, there's no difference between two (because there was few DNA damage to repair).
- ✓ In **Combined** system, the XP17BE/A549 has been reduced, but much larger than the UV light has been screened.
- ✓ **This means repair efficiency has been reduced as indirect pathway involved.**

Figure 6-3. Cell line comparison of HAdV sunlight inactivation rate (Direct, Indirect, Combined)

Results & Discussions

❖How does $^1O_2$ inactivate HAdV?

✓ The findings so far suggest…



…vation by inhibiting DNA repair when there's UV DNA damage. How?

…tivates HAdV

- Compared to the intact virus (control), $^1O_2$ treated virus showed up to 48 hours (one full replication cycle). **reduced replication efficiency** (-1.7 log).
- $^1O_2$ seems to damage core protein (histon like) which plays an important role in transcription/replication process.
- **Damaged protein seems to inhibit UV DNA repair.**

[Shin *et al.*, under review]

Figure 6-4. HAdV genome copies monitoring without and with $^1O_2$ treatment at 2 and 48 hours of incubation.

Conclusions

- **Research Goal:** Understanding sunlight disinfection mechanisms of HAdV2
- **Key questions & conclusions:**
  1. **Predictability of HAdV sunlight inactivation**

     : $k_{observed} > k_{predicted}$ in the presence of DOM

     : Interlinkage btw direct and indirect
  2. **Effect of indirect pathway to DNA repair efficiency**

     : Contribution of indirect pathway reduces the repair efficiency.
  3. **Inactivation mechanisms of HAdV by indirect pathway**

     : $^1O_2$ mainly reduced transcription/replication efficiency, which also affects DNA repair when there's UV DNA damage.
- **Implications**: For Hospital wastewater with high viral loads, UV based AOP is recommended.

  : Virus's history can affect its susceptibility to UV disinfection.

Acknowledgement

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- Laboratory of Environmental Virology (LEV), EPFL: visiting PhD student (8 months)