

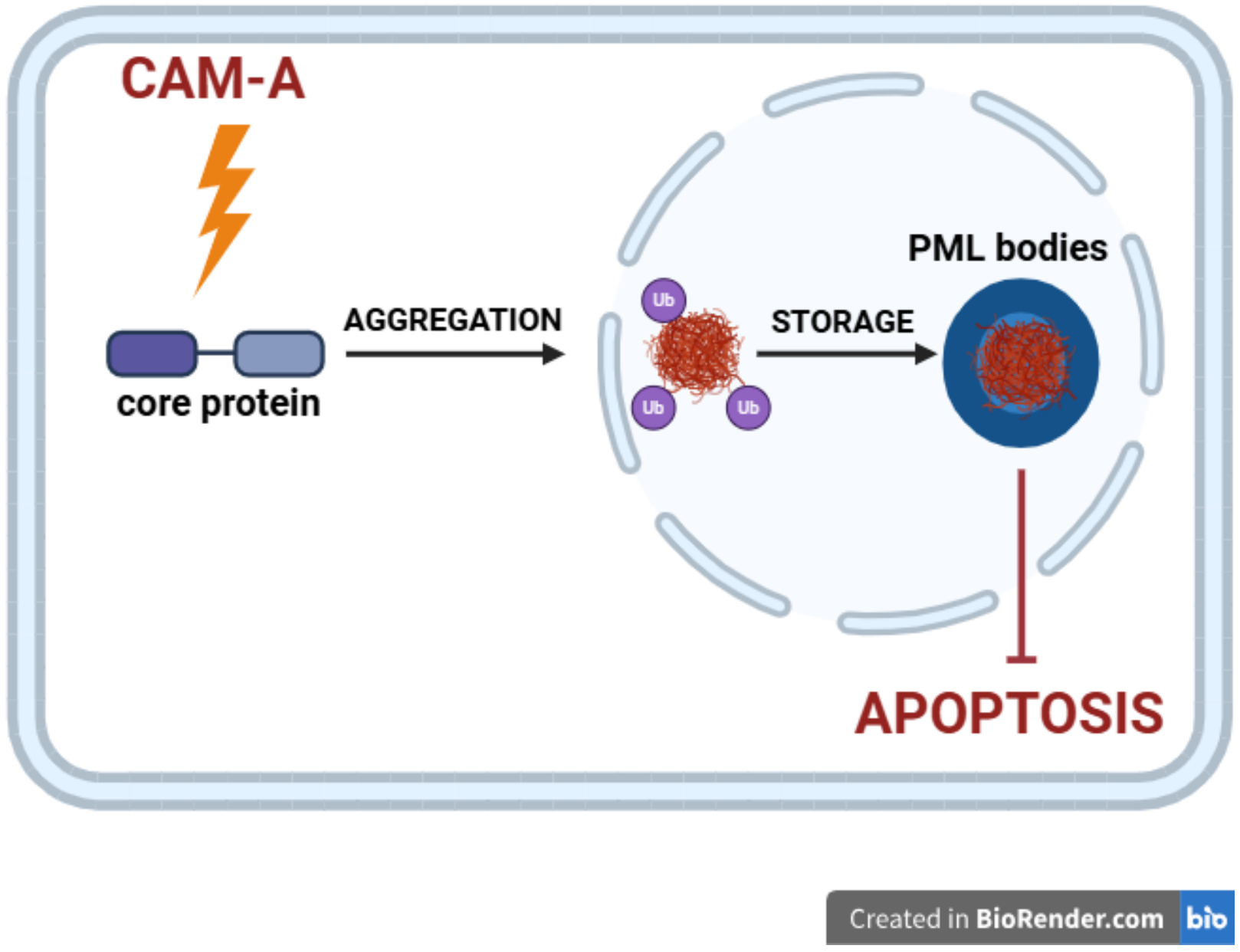
PML nuclear bodies store aggregated HBc and reduce CAM-induced apoptosis in HBc-expressing cells.

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INTRODUCTION

We recently described a subset of capsid assembly modulators (CAMs) that induce the formation of aberrant structures from the hepatitis B virus core protein (HBc) in the nucleus, leading to cell death via ANXA1 (Annexin A1)-driven apoptosis. CAM-A-induced apoptosis depends on *de novo* HBc expression and the amount of HBc, suggesting that cells possess the capacity to counteract the toxic effects of core aggregation. PML (promyelocytic nuclear protein) nuclear bodies have been described as sites of protein degradation, but their precise role in clearing HBc aggregates remains unclear. Therefore, we further elucidated the mechanism of core aggregation in the nucleus, paying particular attention to the interplay between core aggregates and PML nuclear bodies. In this study, we revealed a novel link between PML nuclear bodies and ANXA-1-driven apoptosis.



AIMS

- To elucidate the interplay between nuclear structures and CAM-A-induced core aggregates.
- To test the effect of nuclear structures targeting on CAM-A-induced ANXA-1-driven apoptosis.

CONCLUSION AND FUTURE PERSPECTIVE

- CAM-A-induces nuclear core aggregates that rapidly associate with PML nuclear bodies in HBc-expressing cells.
- The long-term treatment of HBV-infected cells with CAM-A-induced the formation of ring-shaped PML nuclear bodies, which store ubiquitinated core proteins.
- Targeting PML with siRNA potentiates ANXA-1-driven apoptosis in CAM-A-treated cells.
- A promising strategy for improving the CAM-A effect is to target PML nuclear bodies.

ACKNOWLEDGMENT

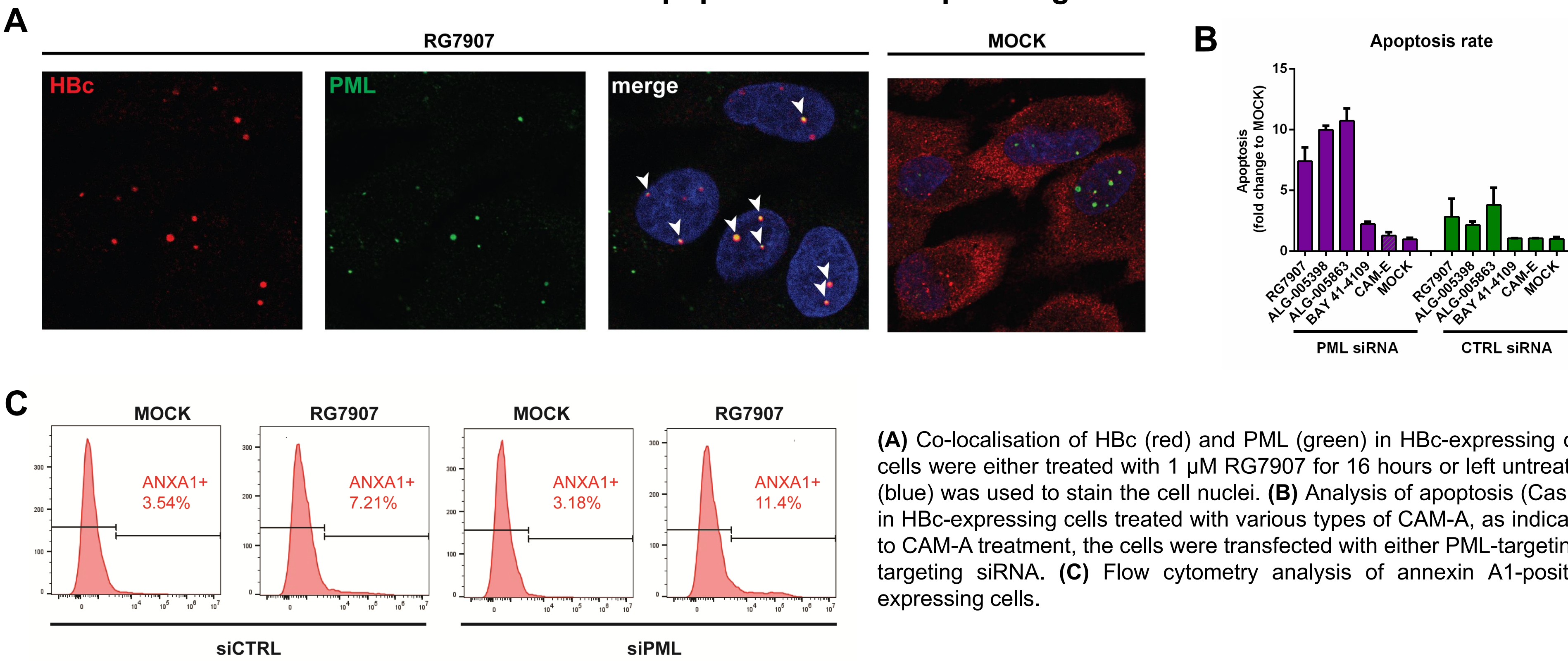
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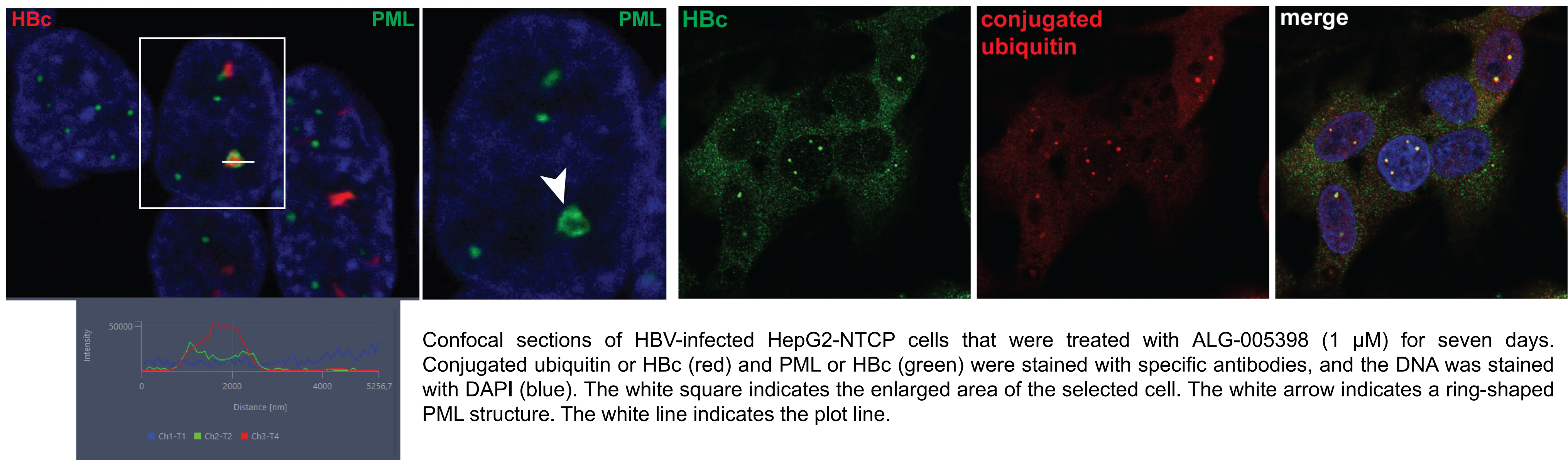
ALIGOS
THERAPEUTICS

RESULTS

PML nuclear bodies rapidly associate with CAM-A-induced aggregates and decrease ANXA-1-driven apoptosis in HBc-expressing cells.



Long-term CAM-A treatment of HBV-infected HepG2-NTCP cells induces the formation of PML nuclear bodies, which store aggregated core and ubiquitinated proteins.



Confocal microscopy reveals the formation of large, ring-shaped PML nuclear bodies in CAM-A-treated cells, with a size greater than 1 μ m.

