EXPLORING SUBSTRATE STIFFNESS AND YAP/TAZ PATHWAYS IN NON-VIRAL GENE DELIVERY APPLICATIONS





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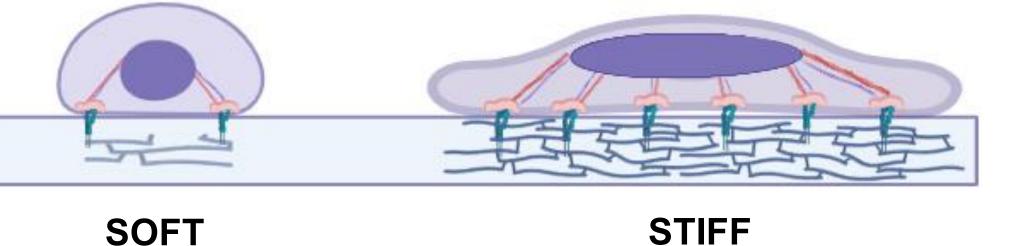
INTRODUCTION

Non-viral gene delivery systems hold great promise for therapeutic applications, but their efficiency remains limited by various barriers, including cellular uptake and nuclear entry [1]. This study investigates how substrate stiffness influences non-viral gene delivery by modulating YAP/TAZ mechanotransduction pathways. These pathways are pivotal in cellular adaptation to mechanical cues, thus potentially directly impacting transfection efficiency (TE) [2].

Impacting transfection eπiciency (TE) [2].

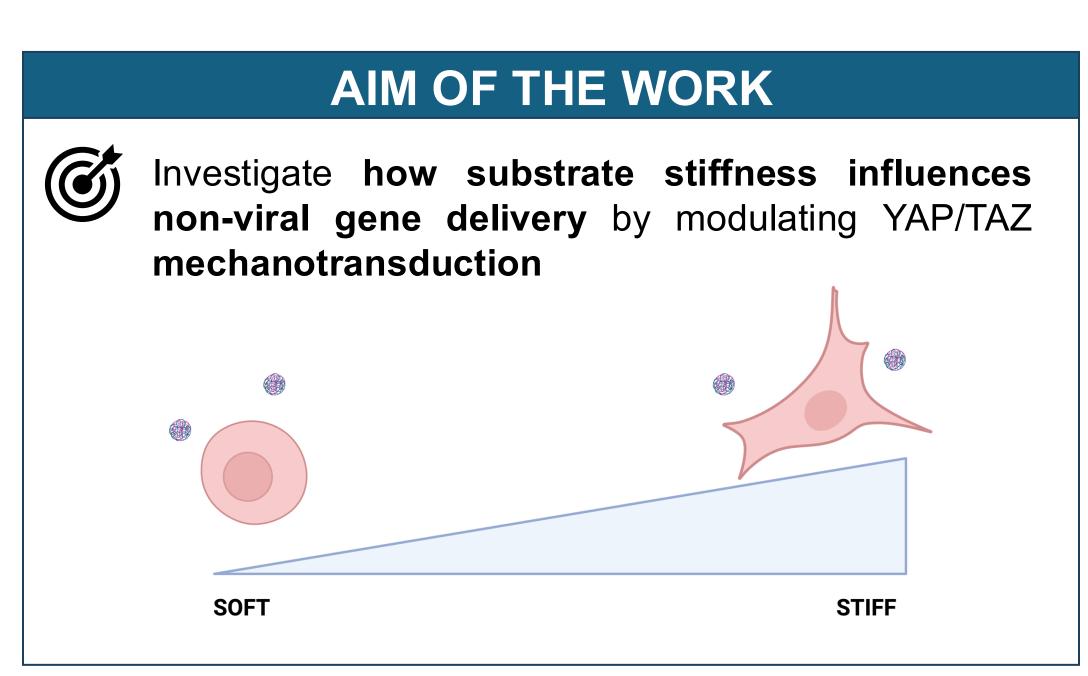
X Low proliferation

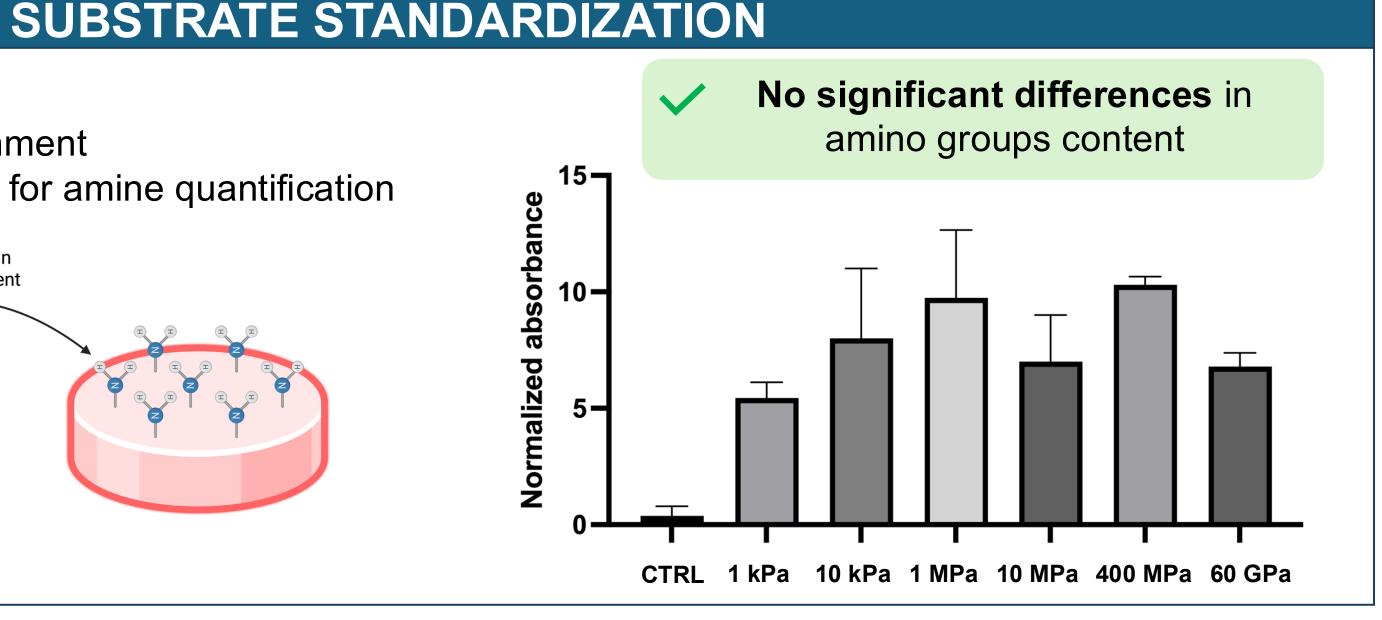
X Few focal adhesions

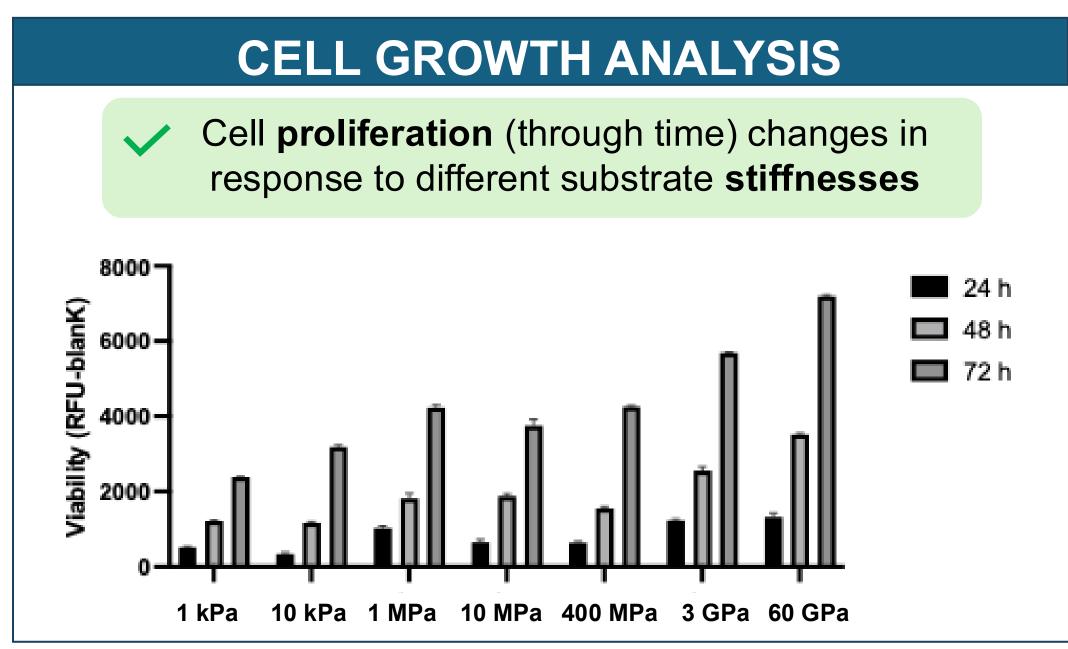


High spreading area

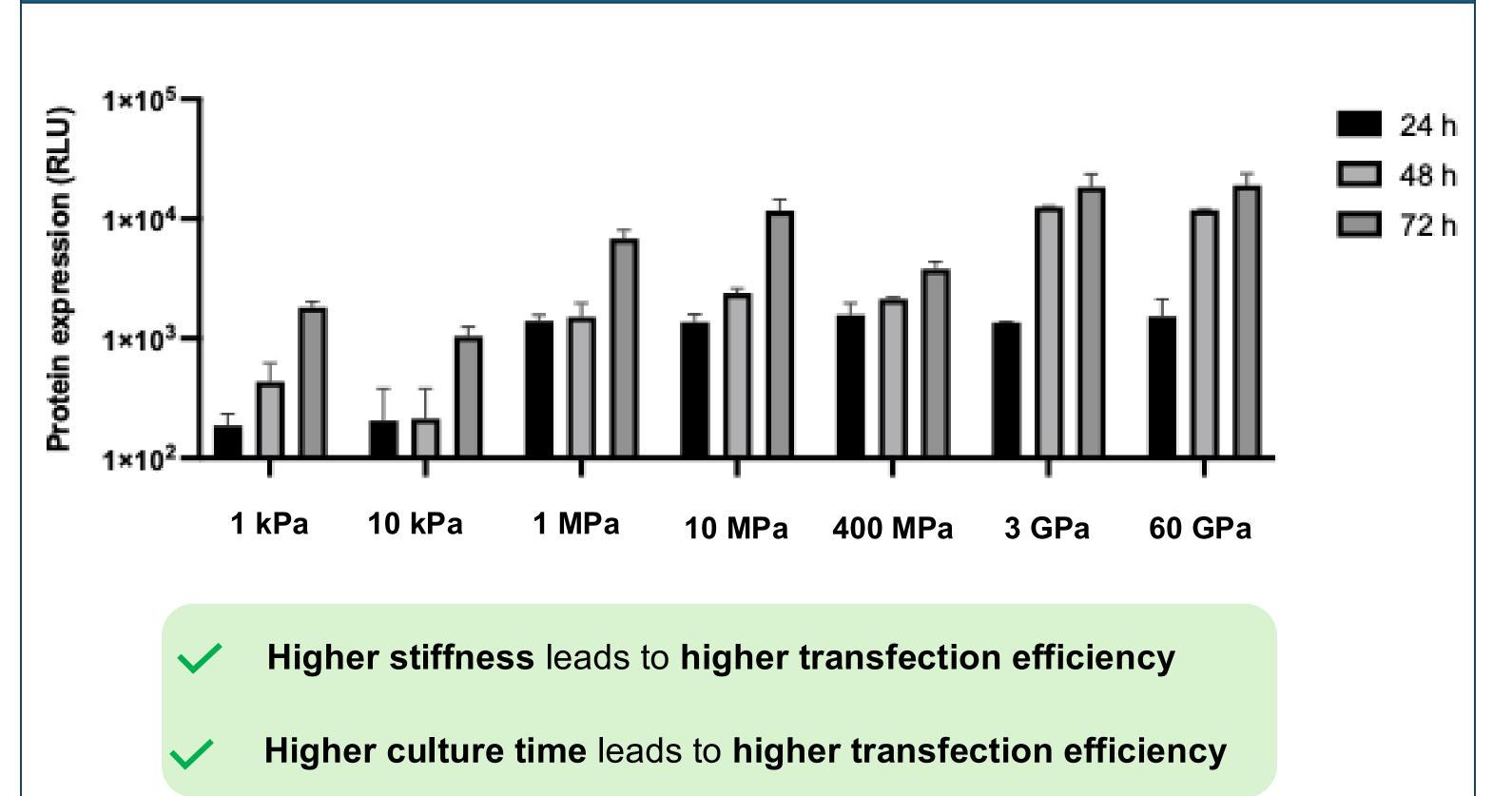
Actin stress fibres recruiting

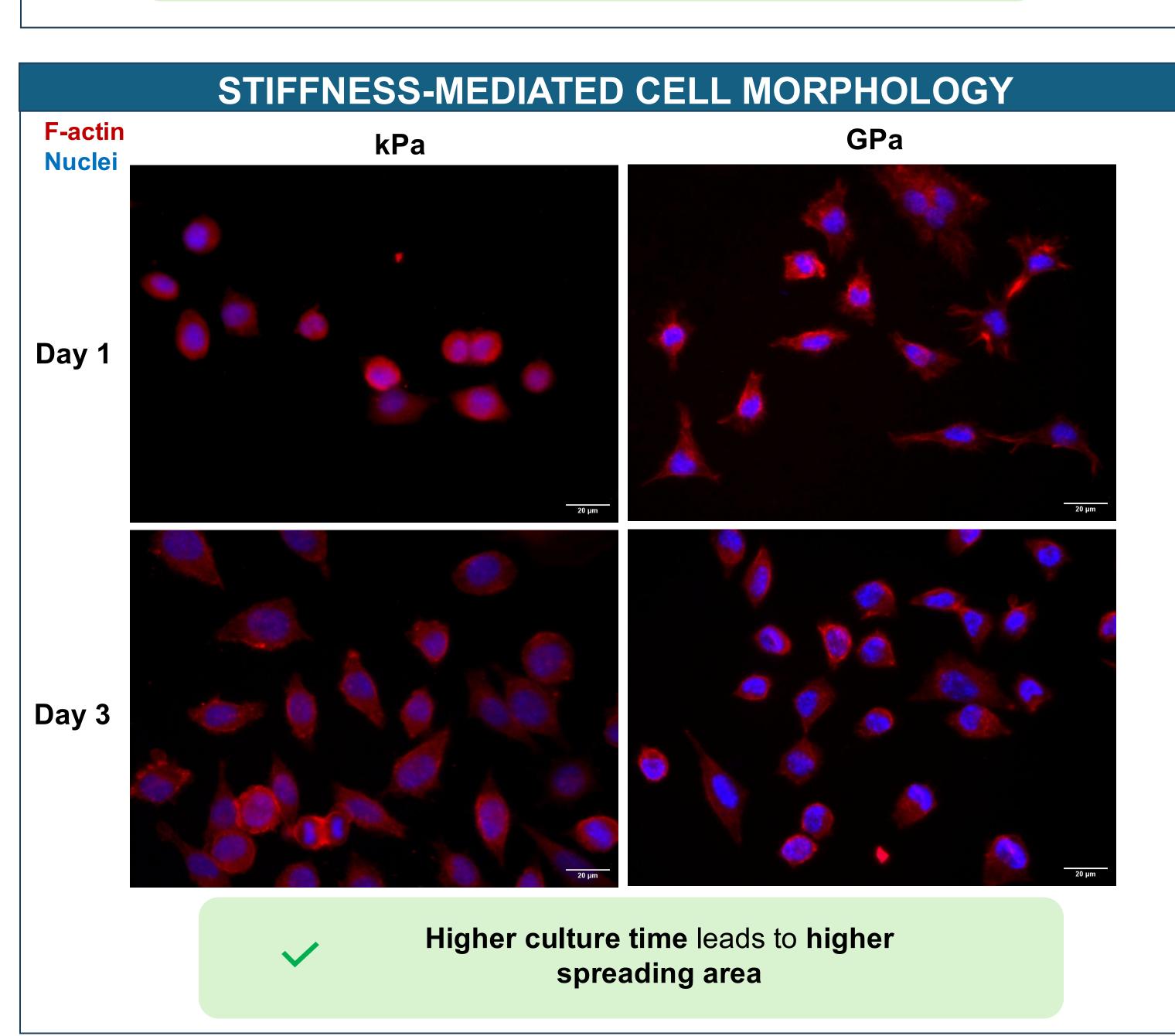






STIFFNESS-MEDIATED TRANSFECTION EFFICIENCY

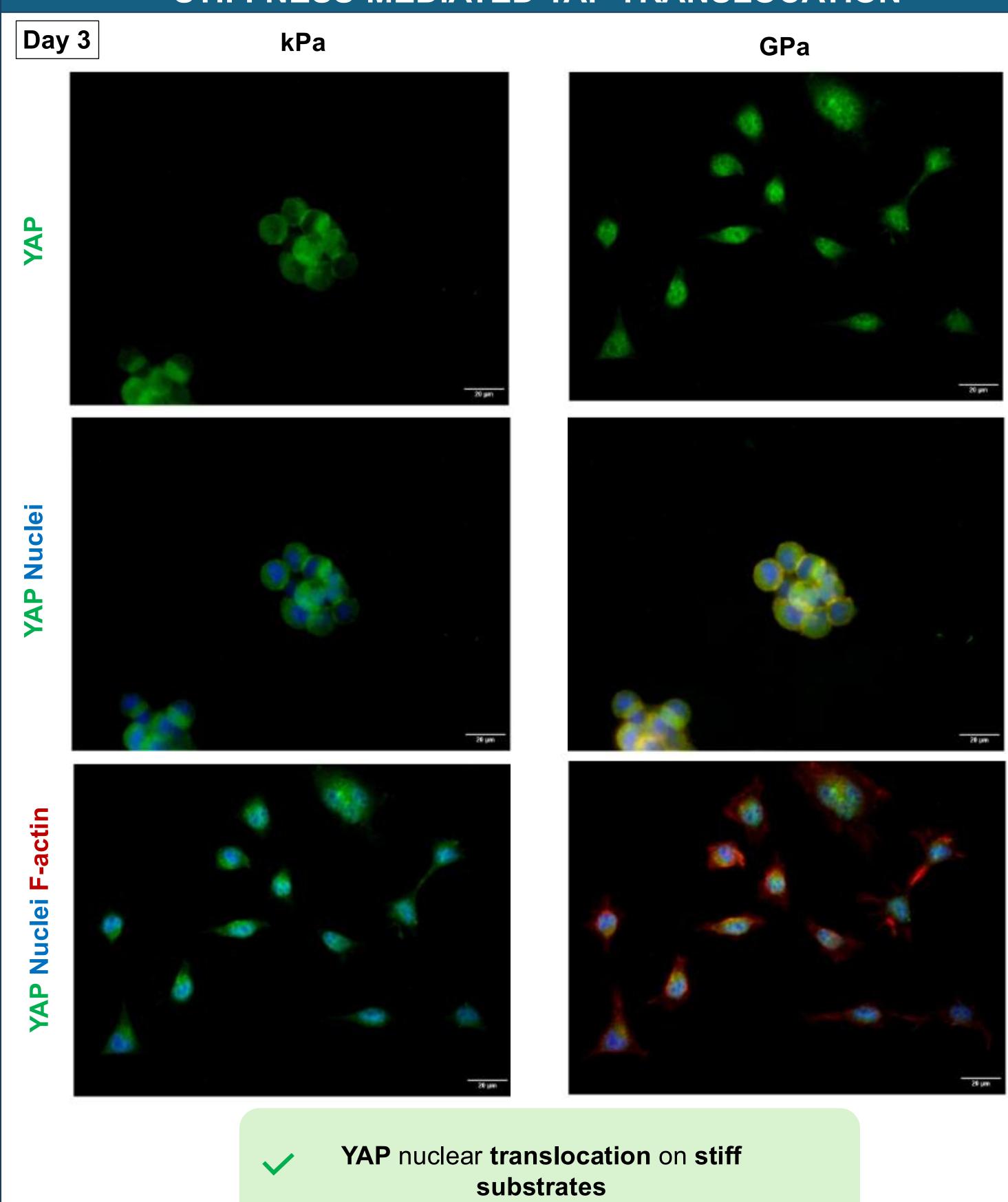




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[1] Bono, N.; Ponti, F.; Mantovani, D.; Candiani, G. Pharmaceutics 2020, 12, 183. [2] Nardone, G., Oliver-De La Cruz, J., Vrbsky, J. *et al.* YAP regulates cell mechanics by controlling focal adhesion assembly. Nat Commun 8, 15321 (2017).

STIFFNESS-MEDIATED YAP TRANSLOCATION



CONCLUSIONS

This study establishes a clear **link between substrate stiffness**, **nuclear morphology adaptation**, and **gene delivery outcomes**. These insights provide a foundation for designing biomaterials tailored to **improve non-viral gene delivery efficiency**.

