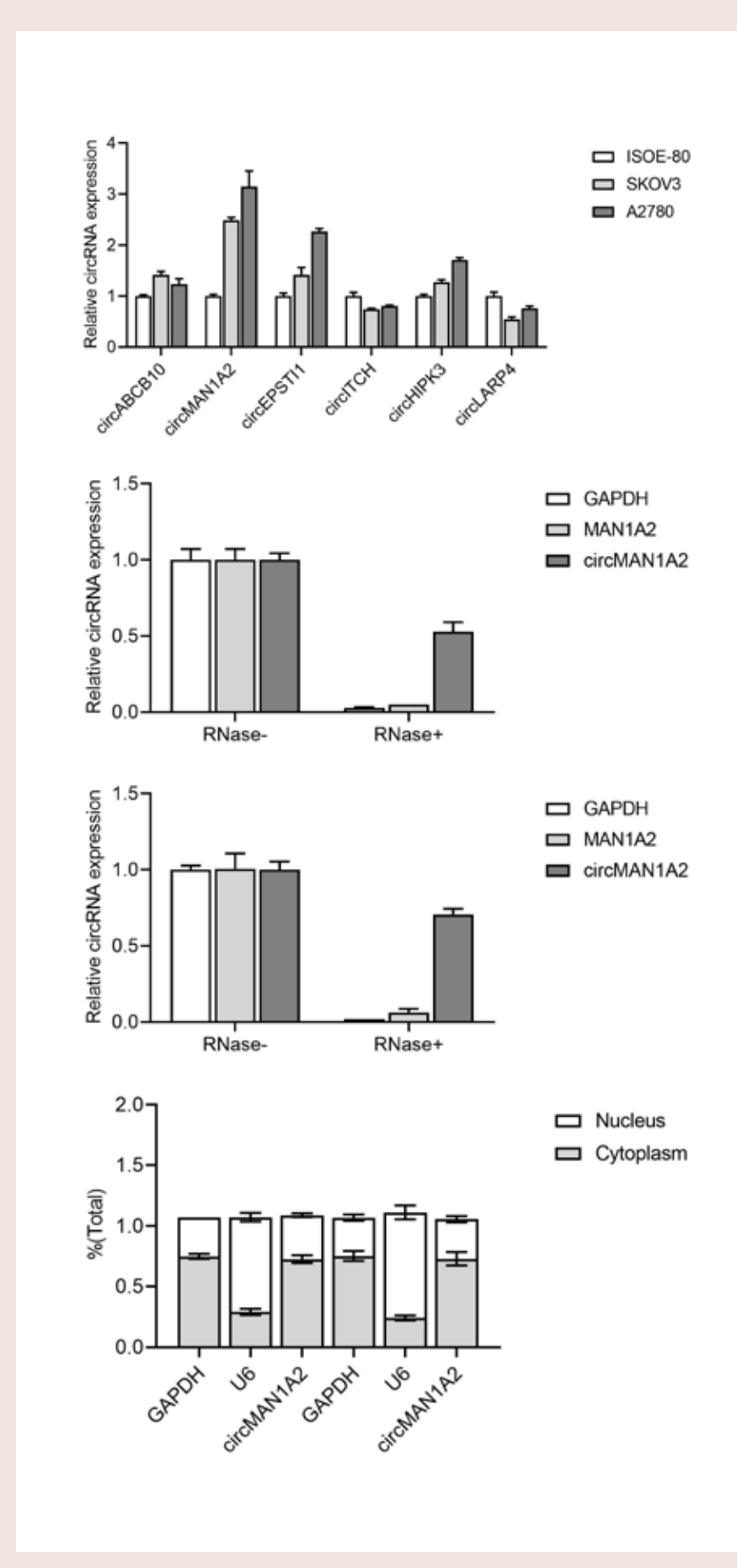
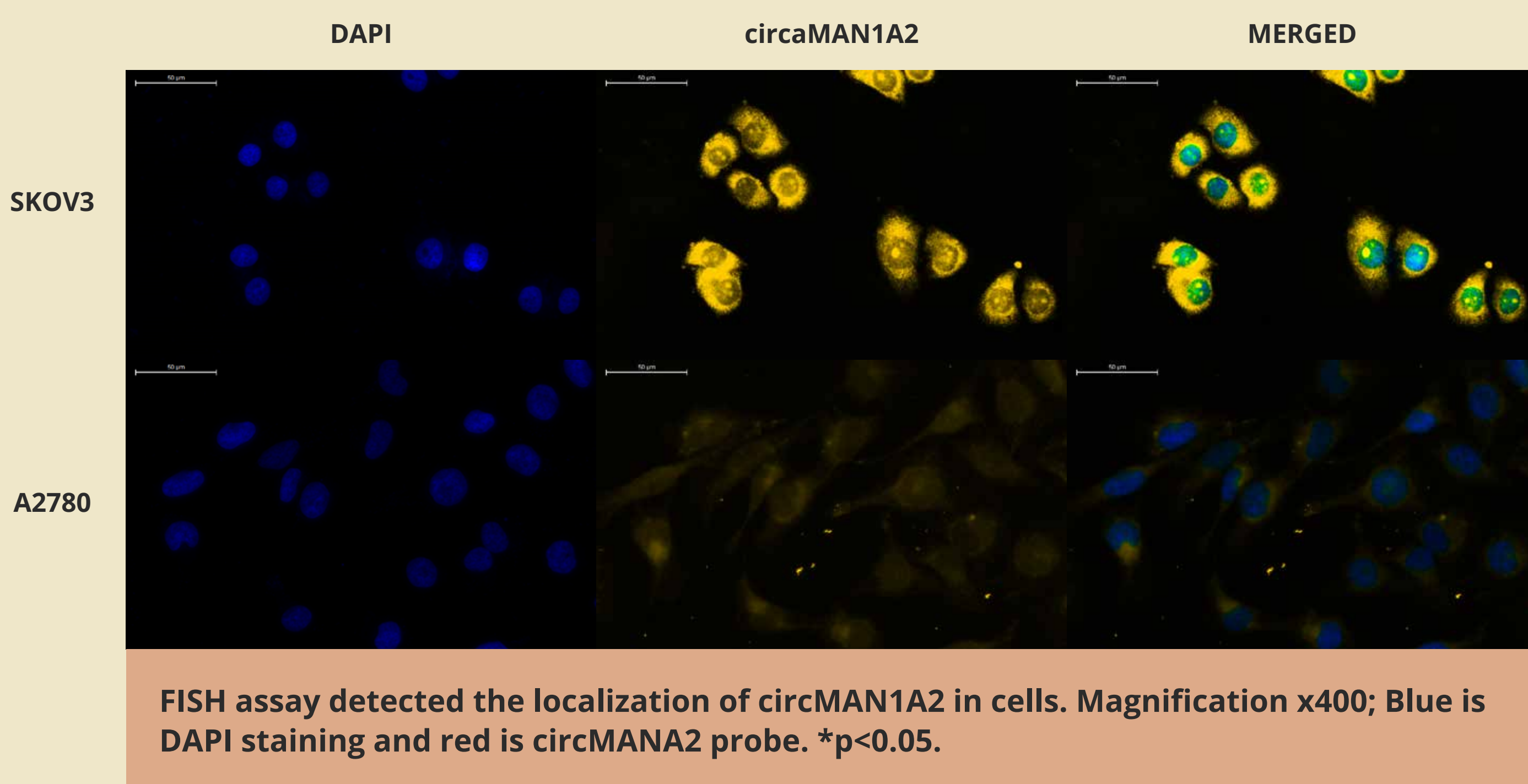


# Circular RNA circMAN1A2 promotes ovarian cancer progression through the microRNA-135a-3p/IL1RAP/TAK1 pathway

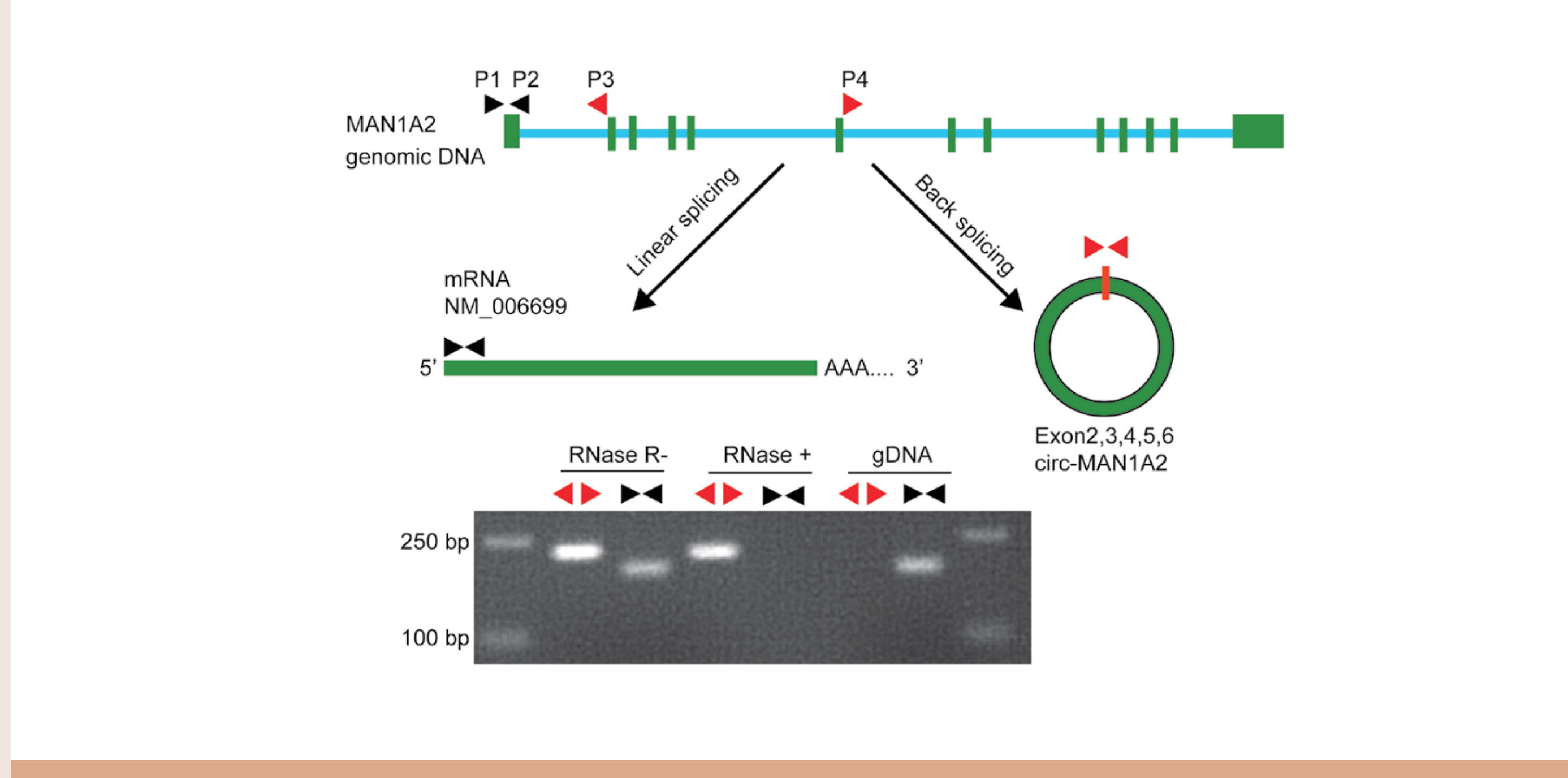
## BACKGROUND

Ovarian cancer (OC) is the most lethal malignancy in women owing to its diagnosis only at the advanced stage. Elucidation of its molecular pathogenesis may help identify new tumor markers and targets for therapy. Circular RNAs (circRNAs) are stable, conserved, and functional biomolecules that can be used as effective biomarkers for various cancers.



## METHODS

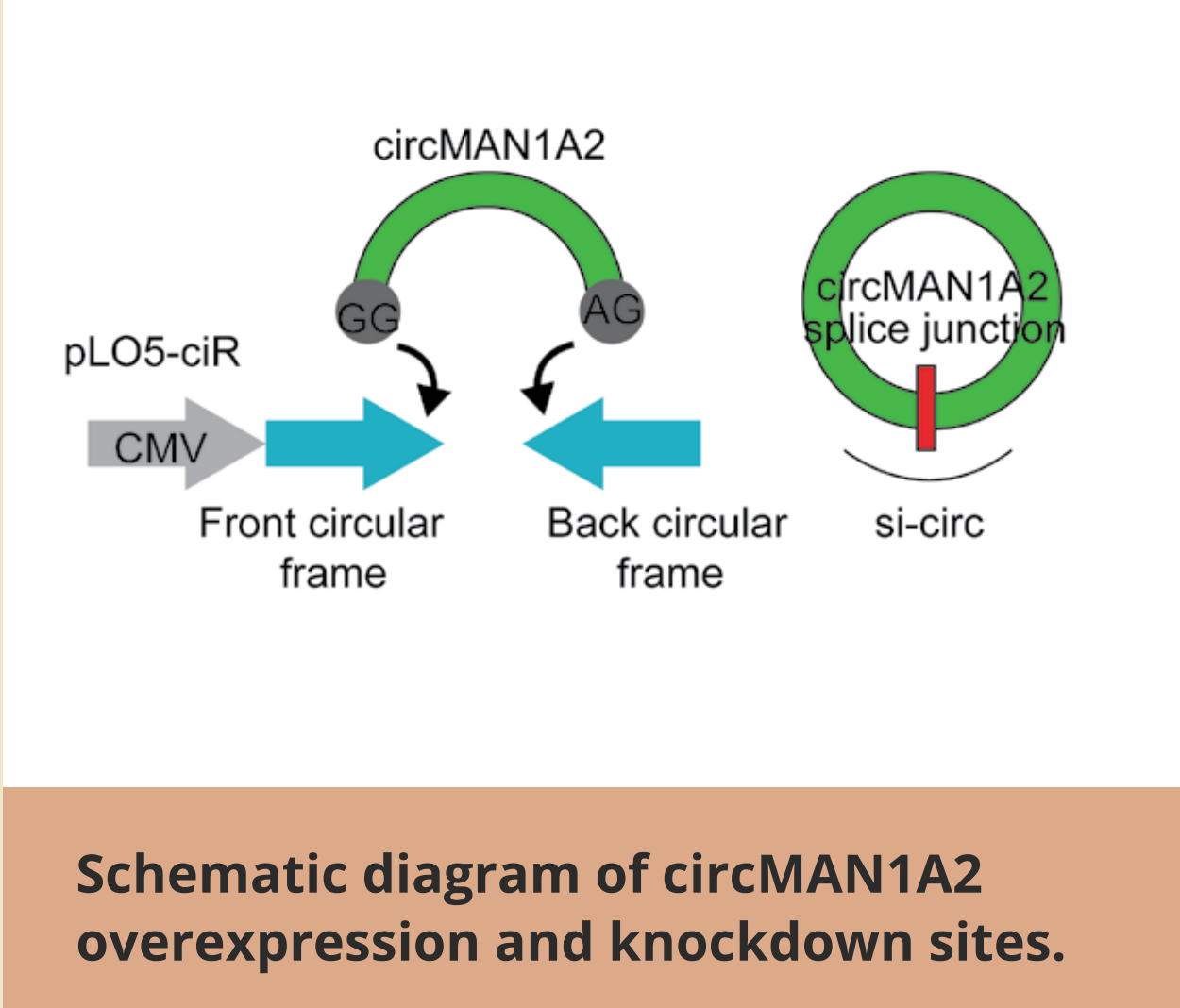
In this study, a potential circRNA related to early diagnosis of OC, circMAN1A2, was analyzed. Overexpression/knockdown of circMAN1A2 in OC cells was used to decipher its effects on cell proliferation with Cell Counting Kit-8, 5-ethynyl-2'-deoxyuridine (EdU), cell cycle, clone formation, and wound healing assay. RNA pull-down and Dual luciferase assay were used to explain the underlying mechanism by which circMAN1A2 regulates OC cell proliferation. *In vivo*, the effect of circMAN1A2 in OC was evaluated using nude mouse xenograft experiments.



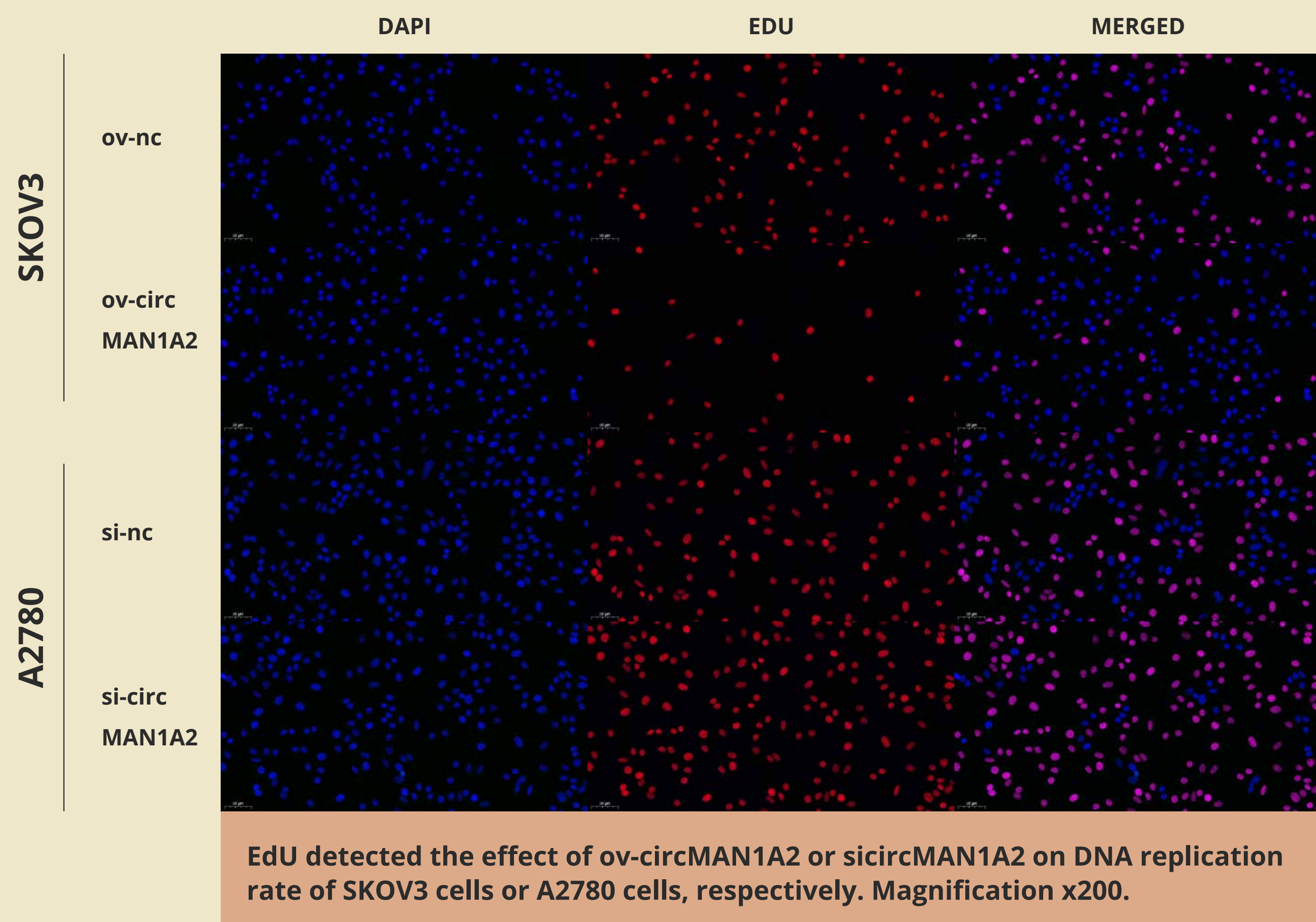
The looping site of circMAN1A2 was detected using agarose gel electrophoresis.

## RESULTS

CircMAN1A2 was highly expressed in OC and promoted proliferation, clone formation, and tumorigenicity of OC cells. In addition, we found that circMAN1A2 acted as a sponge for microRNA (miR)-135a-3p. miR-135a-3p directly targeted the 3' untranslated region of interleukin 1 receptor accessory protein (IL1RAP) in OC cells, thereby regulating the phosphorylation of transforming growth factor-beta activated kinase 1 (TAK1), resulting in the promotion of OC cell growth.

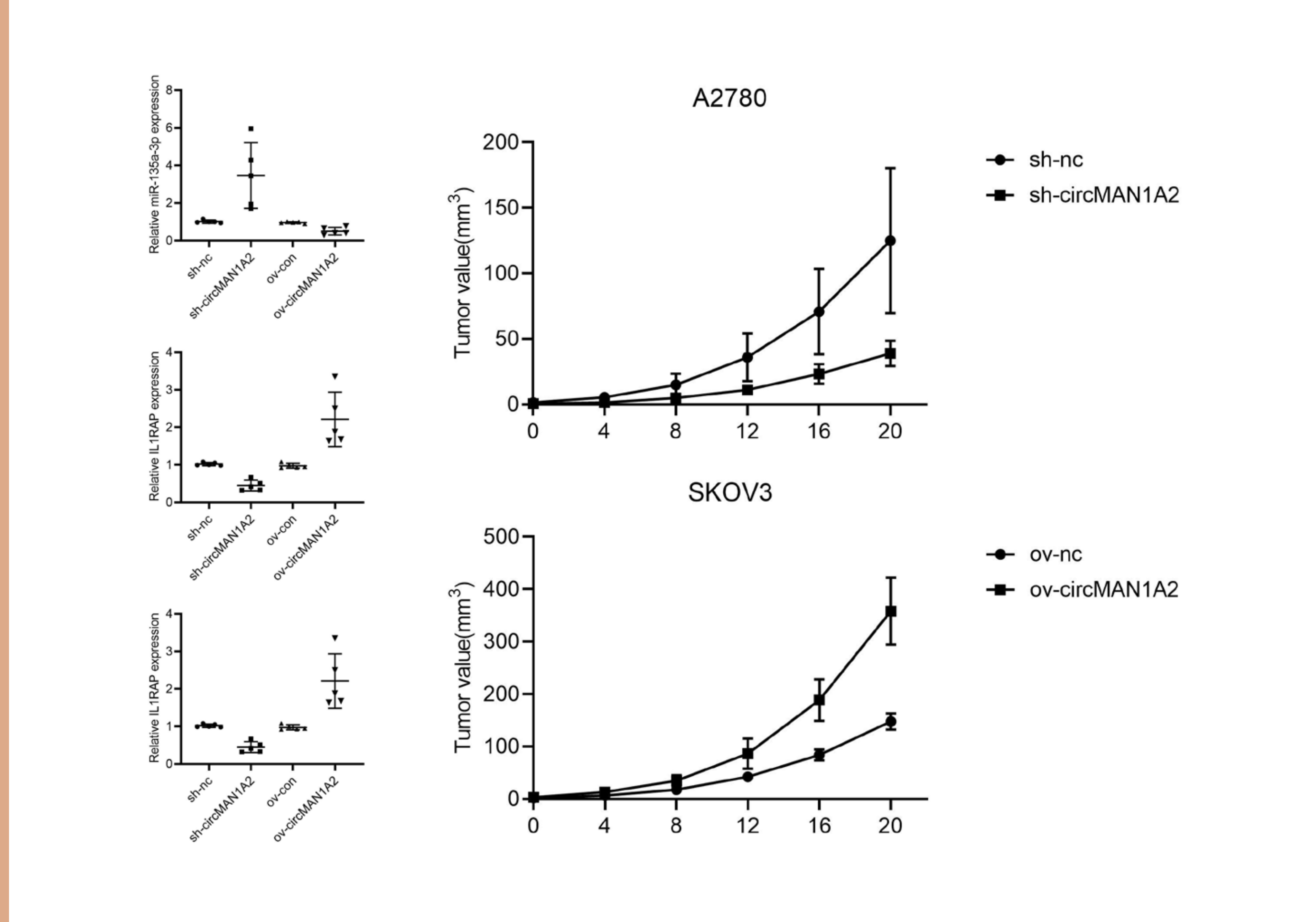


Schematic diagram of circMAN1A2 overexpression and knockdown sites.



## CONCLUSION

Our study found that a circular RNA molecule called circMAN1A2 is elevated in ovarian cancer and drives cancer progression. It does this by acting as a sponge to inhibit the microRNA, miR-135a-3p. This allows higher expression of the IL1RAP protein, activating the TAK1 signaling pathway and promoting ovarian cancer cell proliferation and tumor growth.



## KEY TAKEAWAYS

- CircMAN1A2 is a novel driver of ovarian cancer progression
- CircMAN1A2 acts as a microRNA sponge to inhibit miR-135a-3p
- CircMAN1A2 upregulates IL1RAP and activates TAK1 signaling by sponging miR-135a-3p
- Targeting the circMAN1A2/miR-135a-3p/IL1RAP/TAK1 axis provides a potential new therapeutic strategy for ovarian cancer