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LRP-1 a key modulator of TNBC progression

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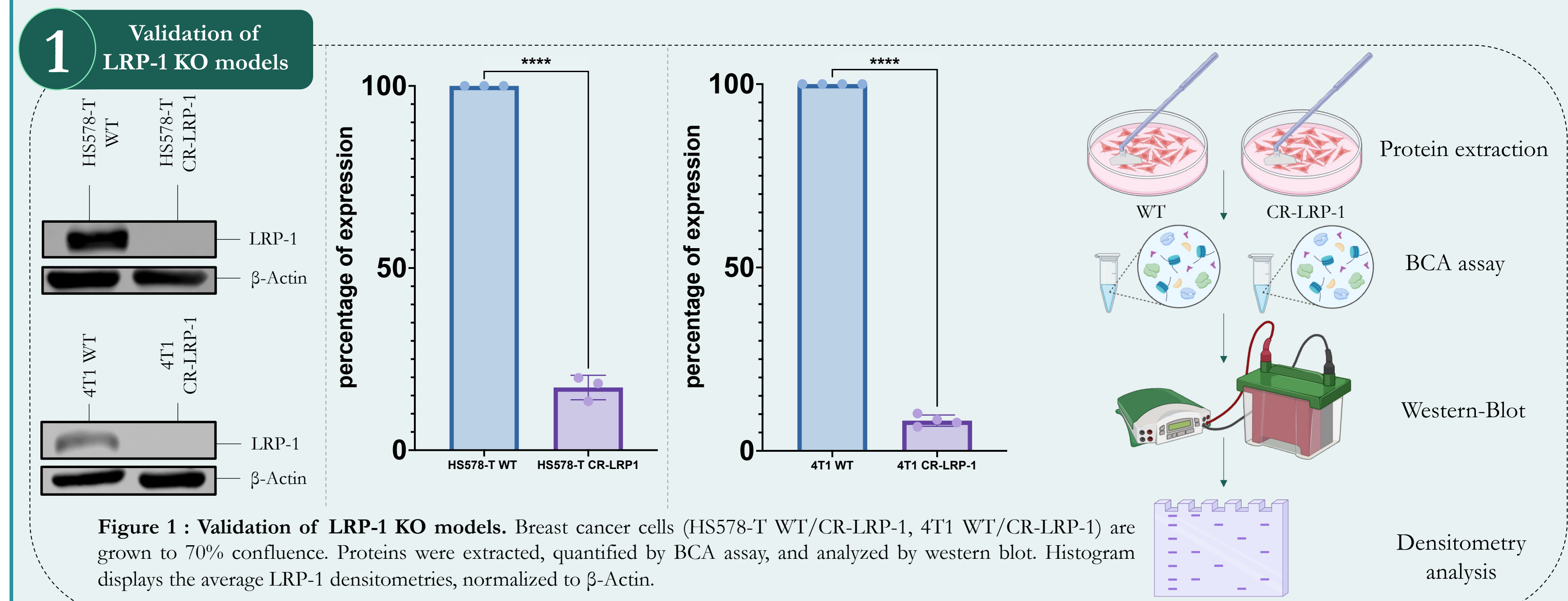
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Authors have equally contributed to this work*

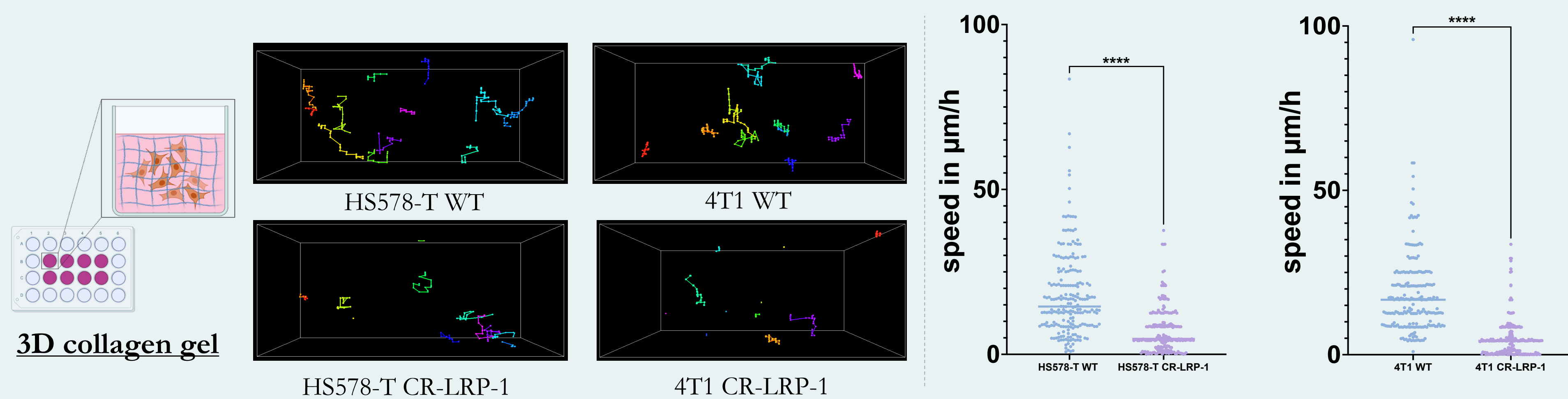
Introduction

Triple-negative breast cancers (TNBC) are a very aggressive subtype of breast cancer with high metastatic potential; they do not respond to hormone therapy and few targeted therapies are available. During metastatic dissemination, tumor cells undergo a cascade of events including invasion of surrounding tissues, followed by blood vessels intravasation and extravasation mechanisms. We focused on molecular deciphering mediated by the LRP-1 receptor (Low Density Lipoprotein Receptor-related Protein 1) in breast tumor progression using two cell lines of TNBC (HS578-T and 4T1) on which we performed a Knock-Out (KO) of the LRP-1 gene. These cell models have enabled us to study precisely the effect of LRP-1 on numerous key stages of carcinogenesis.

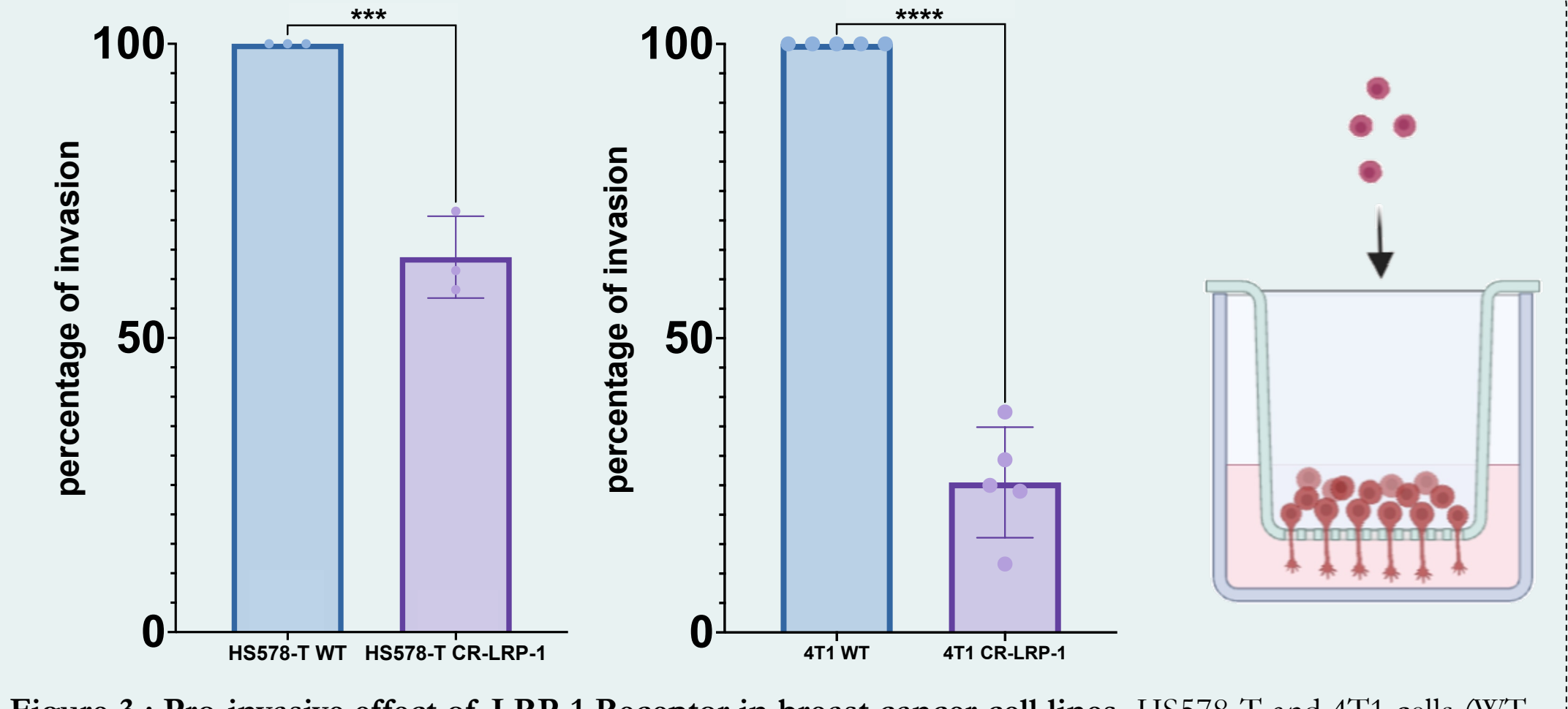
Results



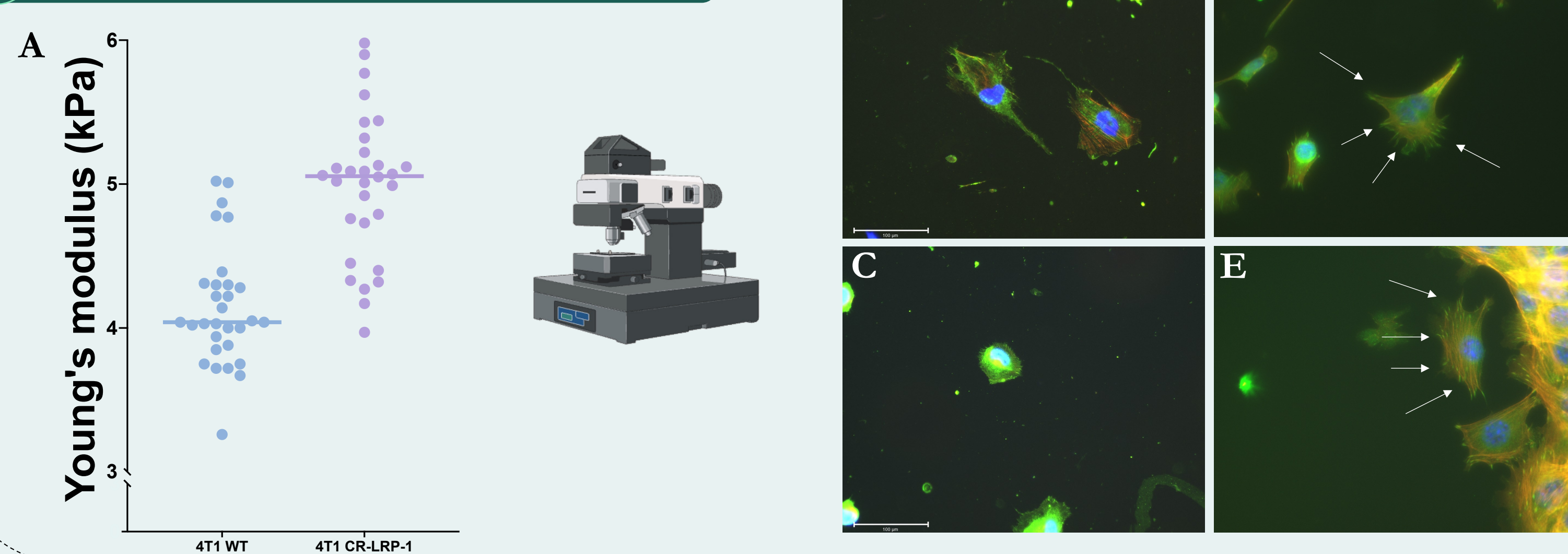
2 LRP-1 KO promotes the inhibition of cellular migration



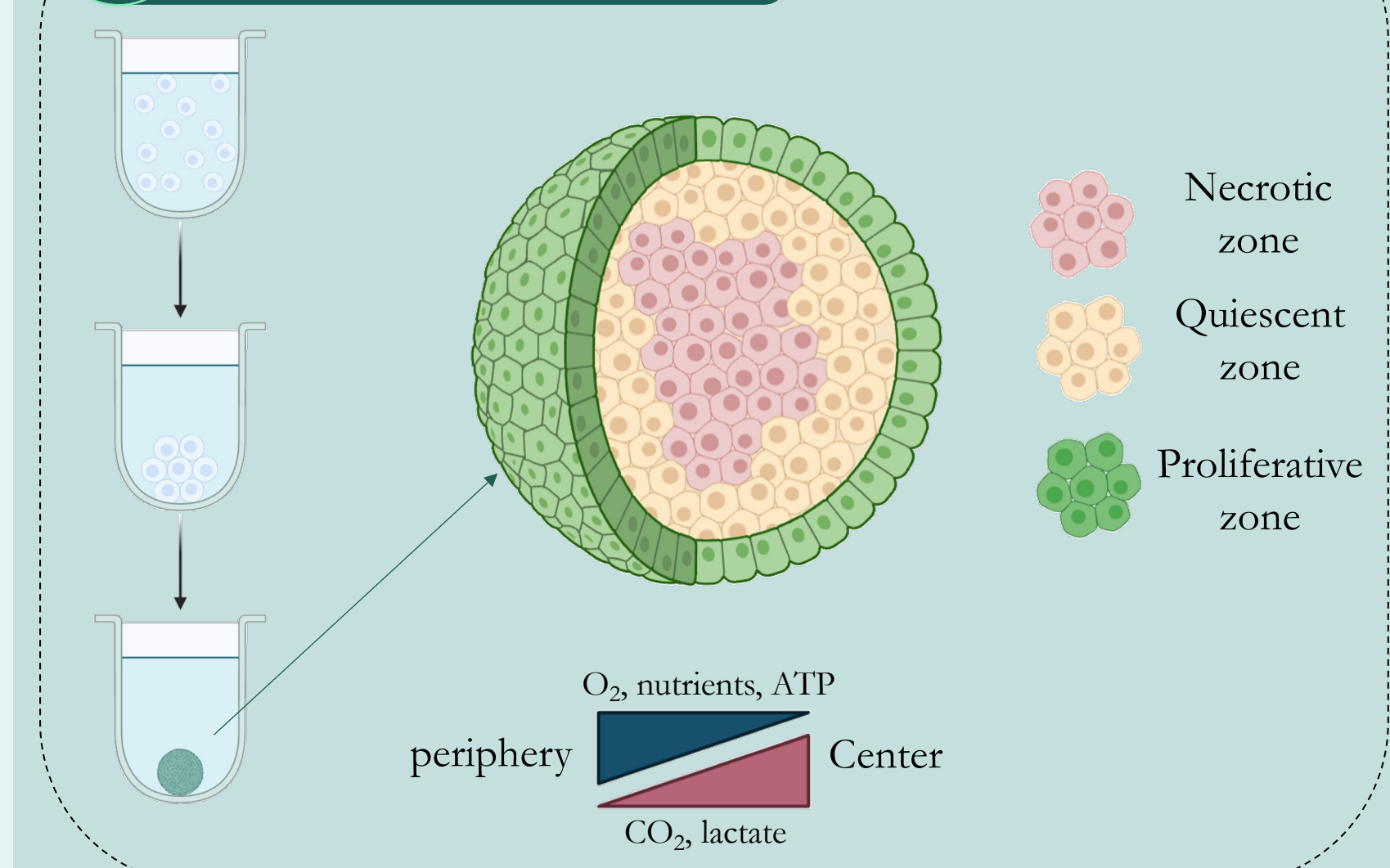
3 LRP-1 KO promotes the inhibition of cellular invasion



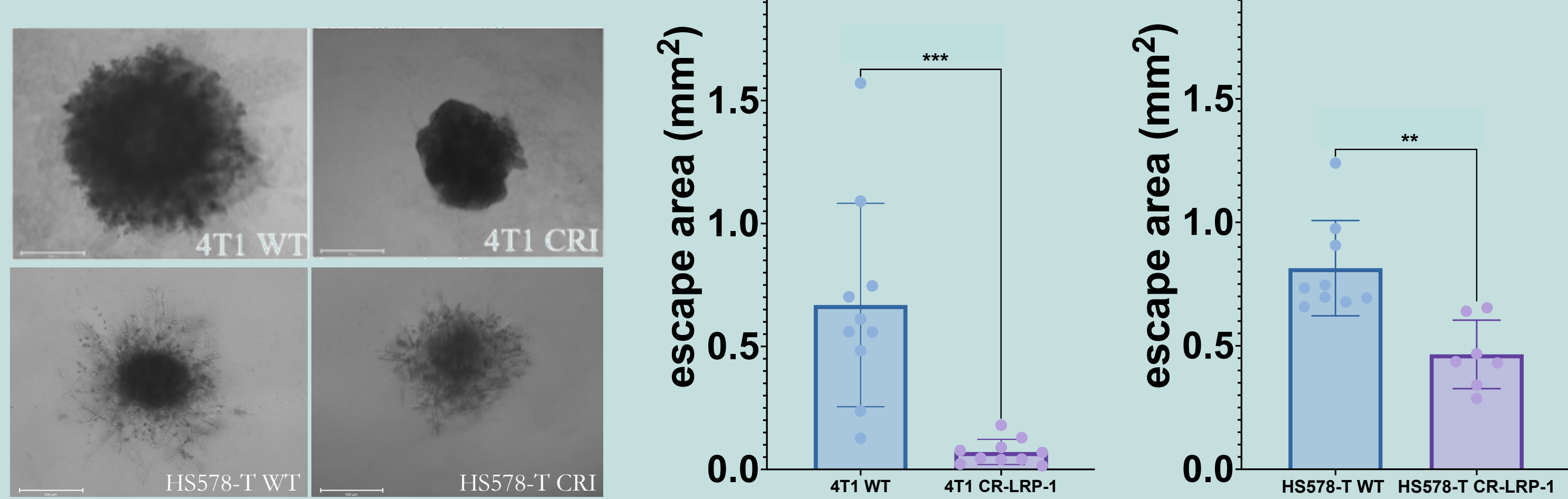
4 LRP-1 KO induces morphological cellular modifications



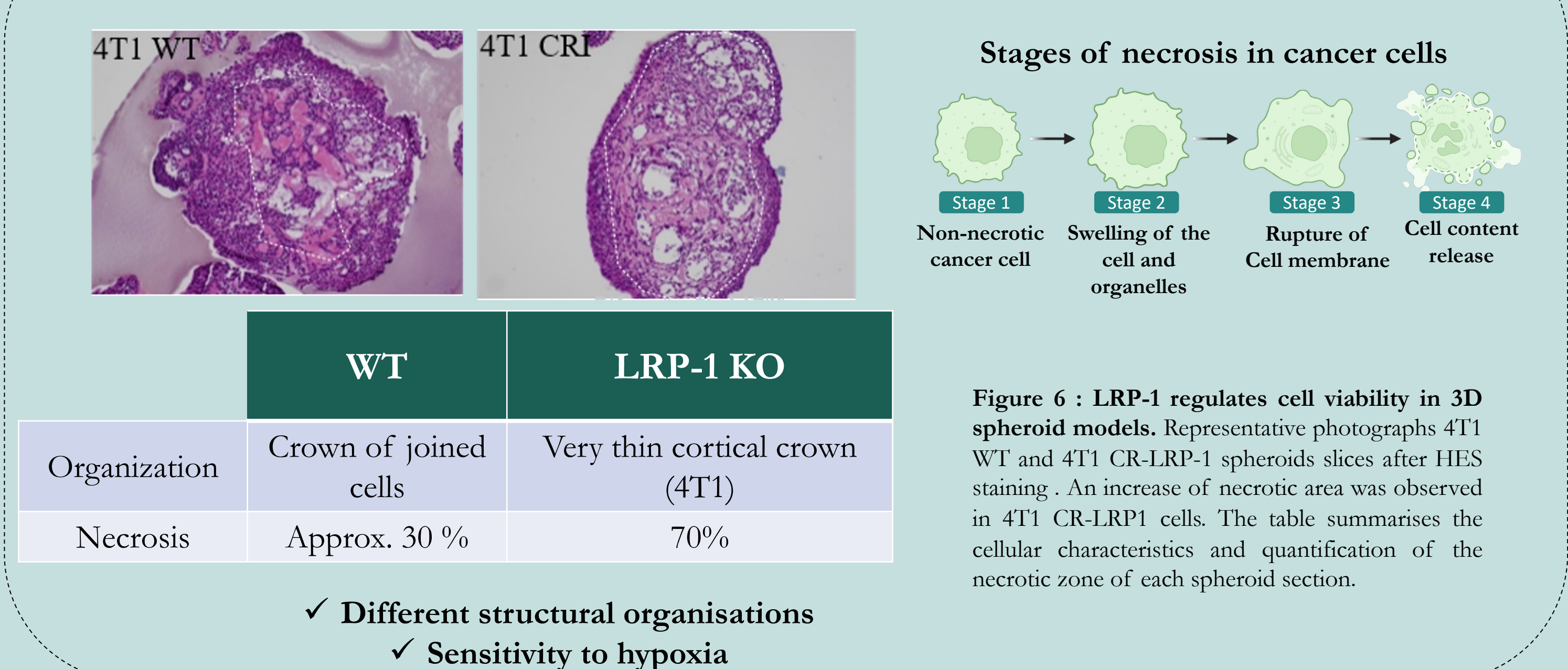
5 Spheroid formation model



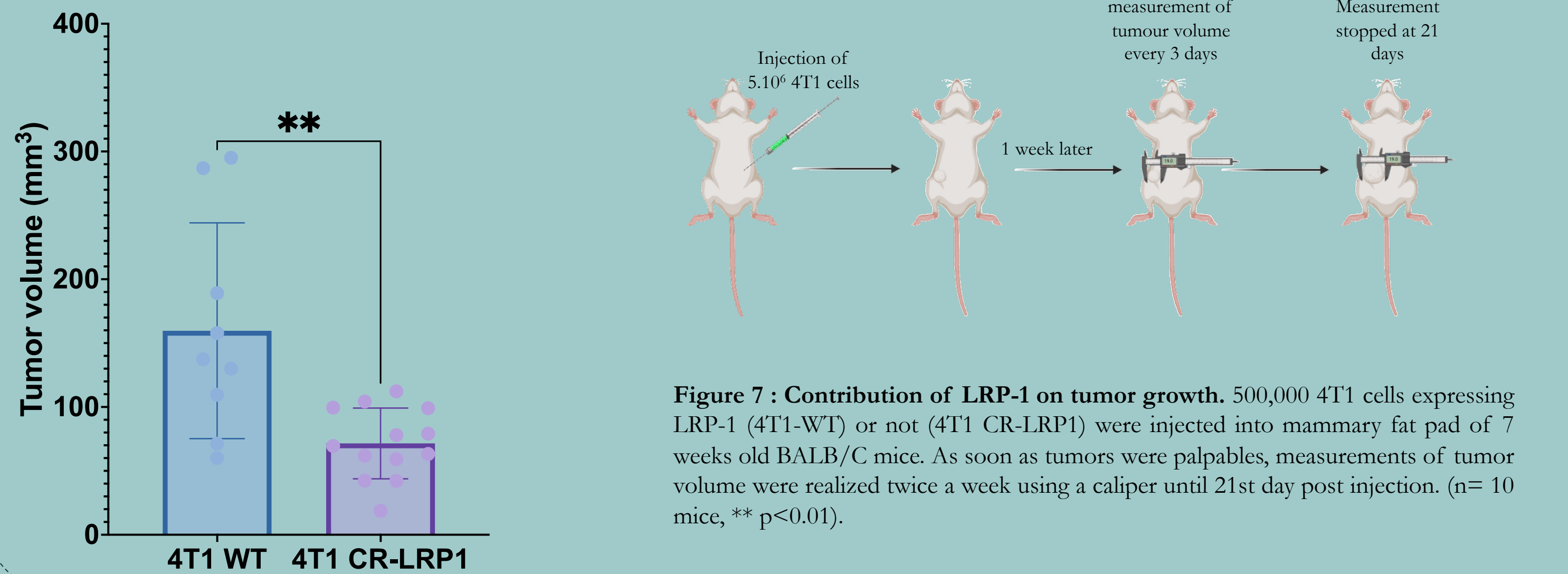
6 LRP-1 KO promotes the inhibition of cellular evasion in 3D model



7 LRP-1 KO promotes necrosis in a 3D spheroid model



8 LRP-1 promotes tumor growth in a syngeneic model



Conclusion

Taken together, our results highlight the role of LRP-1 in TNBC models via the regulation of migratory and invasive capacities as well as cell viability of tumor cells. These results were reinforced by in vivo experiments which demonstrate the pro-tumoral role of LRP-1. Proteomic analyses are ongoing to decipher the molecular pathways regulated by LRP-1.

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