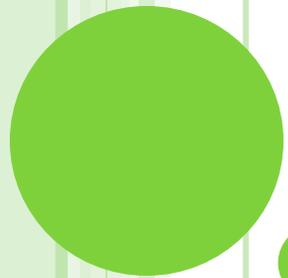


Investigate the Role That MBNL3 Plays in the Ovarian Cancer

Speaker: 吳佩蓁

Advisor: 潘惠錦 教授

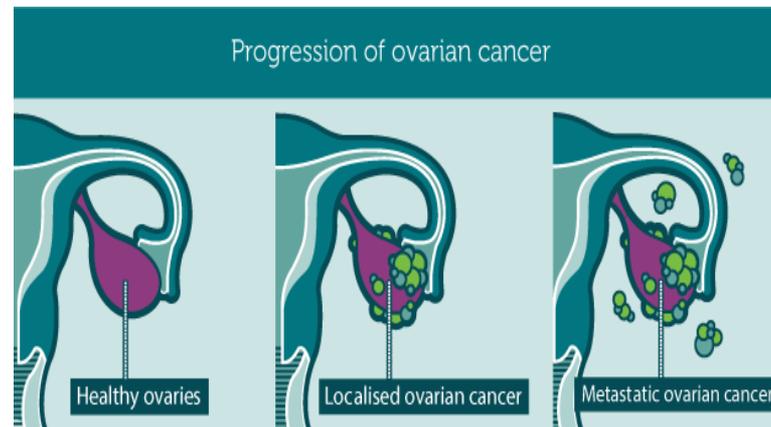


INTRODUCTION



Ovarian Cancer

- no early symptoms
- diagnosed at a late stage
- the highest mortality rate in all gynecological cancers



Muscleblind-like protein (MBNL)

- MBNL1, MBNL2 and MBNL3 proteins are regulators of **alternative splicing** and have four Cys3His **zinc finger** domains that confer **RNA binding** activity.

(Teplova M. et al., Nat Struct Mol Biol, 2008; Pascual M. et al., Differentiation, 2006)



- MBNL1 and MBNL2 express in all tissues; MBNL3 expresses in **muscle precursor cells, liver, placenta** and **testis**.

(Kanadia RN. et al., Gene ExprPatterns, 2003; Fardaei et al., 2002; Miller et al., 2000; Lee et al., 2007)



MBNL3

- is abundant in **proliferating myoblasts**

(Squillace RM. et al., *Dev Biol.* 2002)

- an **inhibitor of myoblast differentiation**

(Lee KS. et al., *Differentiation* 2008)

- occurs during the **embryonic period** and during **muscle regeneration**

(Kanadia, R.N. et al., 2003; Lee, K.S et al., 2007; Liang, J. et al., 2008)



MBNL3 & Cancer

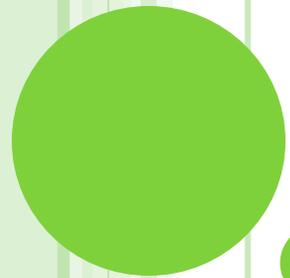
- Mbnl3 mainly expresses in the highly **proliferative tissues** of adult mammalian cells and is highly correlated with **cell proliferation**.
- MBNL3 affects the growth and migration in **prostate cancer** and **leukemia**.

(Lu, Z.X. et al., *Mol Cancer Res.* 2015; Holm, F. et al., *Proc Natl Acad Sci USA*, 2015)



→ **MBNL3 may also play an important role in ovarian cancer**

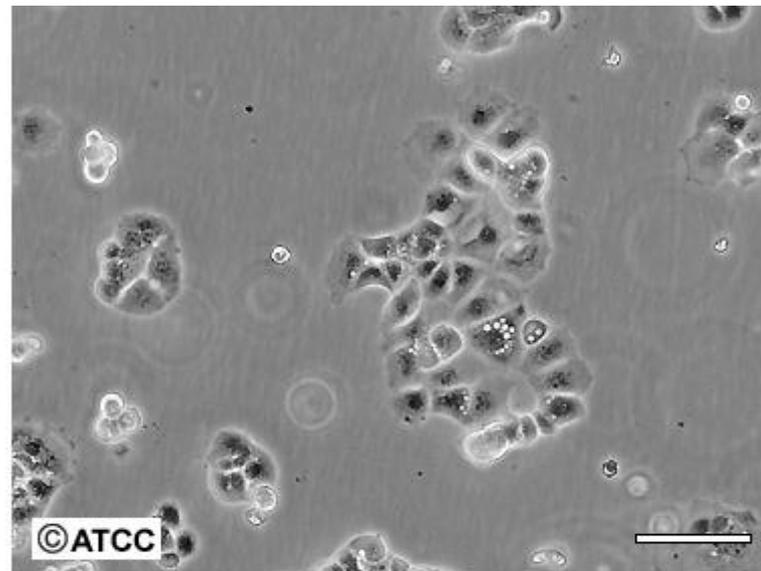




MATERIALS & METHODS

MATERIALS -- Ovarian Cell Lines

- **IOSE** : normal human ovarian surface epithelial
- **OVCAR-3** : High grade ovarian serous adenocarcinoma
- **HeyC2** : High grade ovarian serous adenocarcinoma

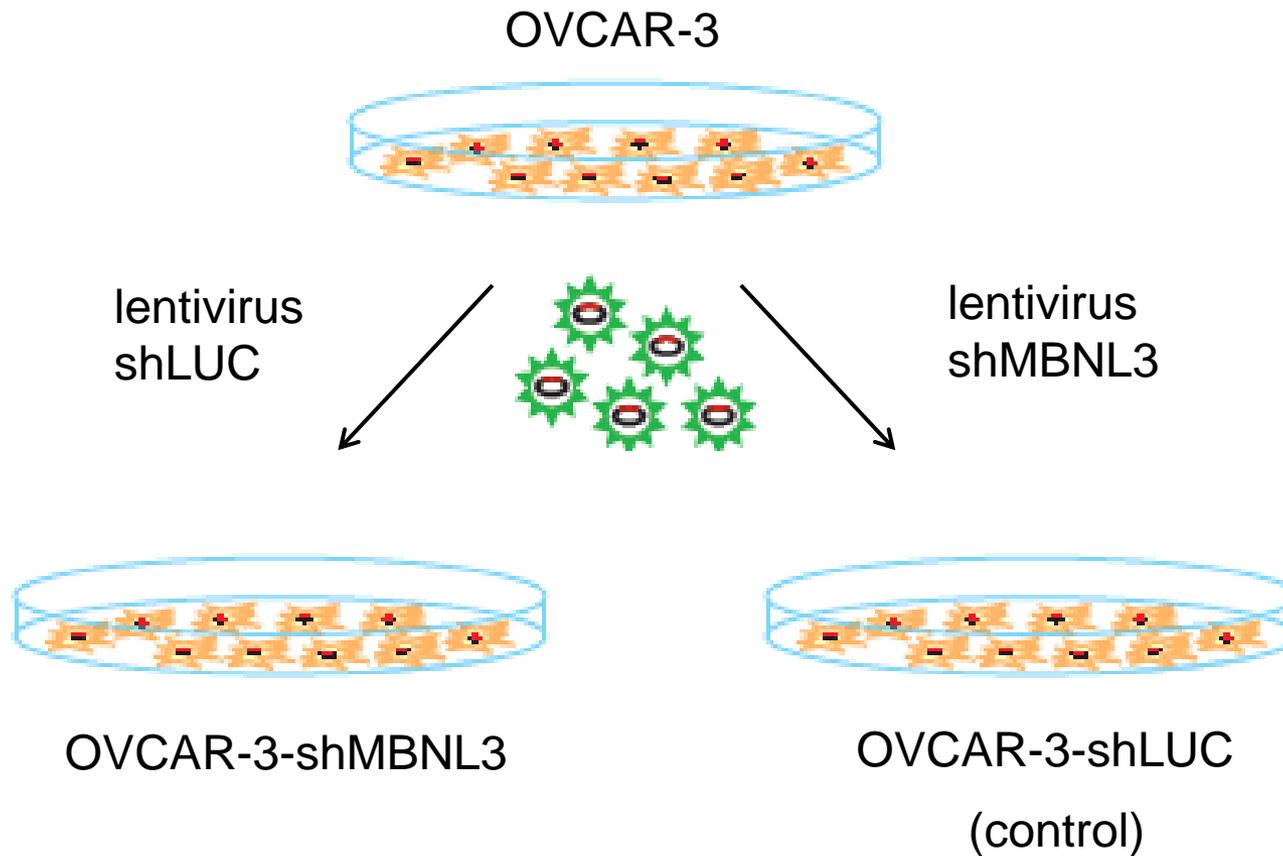


Low Density

Scale Bar = 100µm



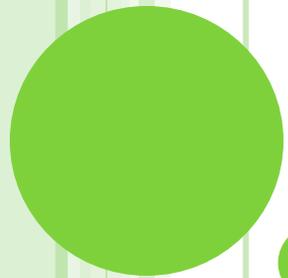
Ovarian Cancer Cell knockdown



MTT Assay

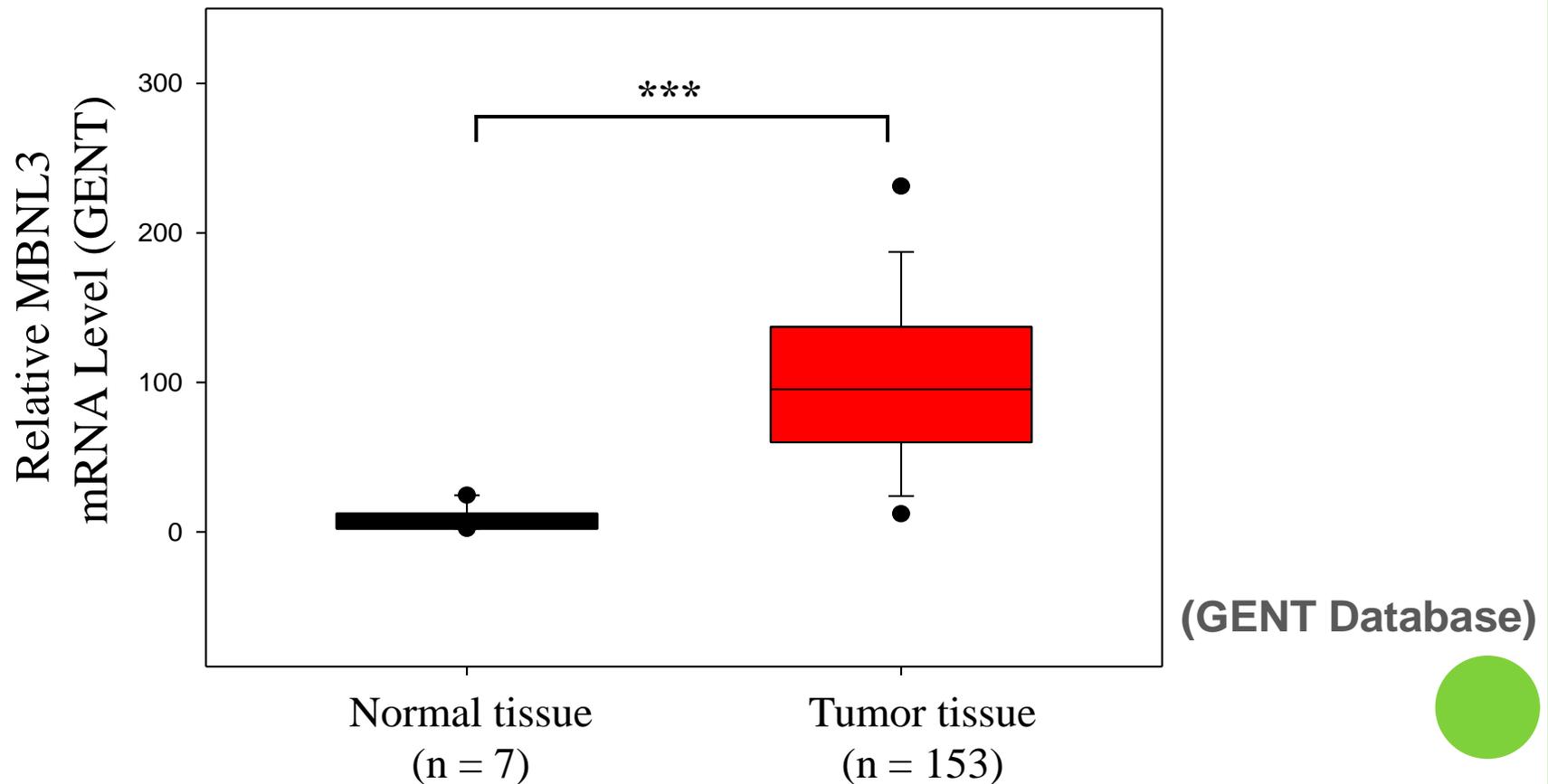
- cell growth rate



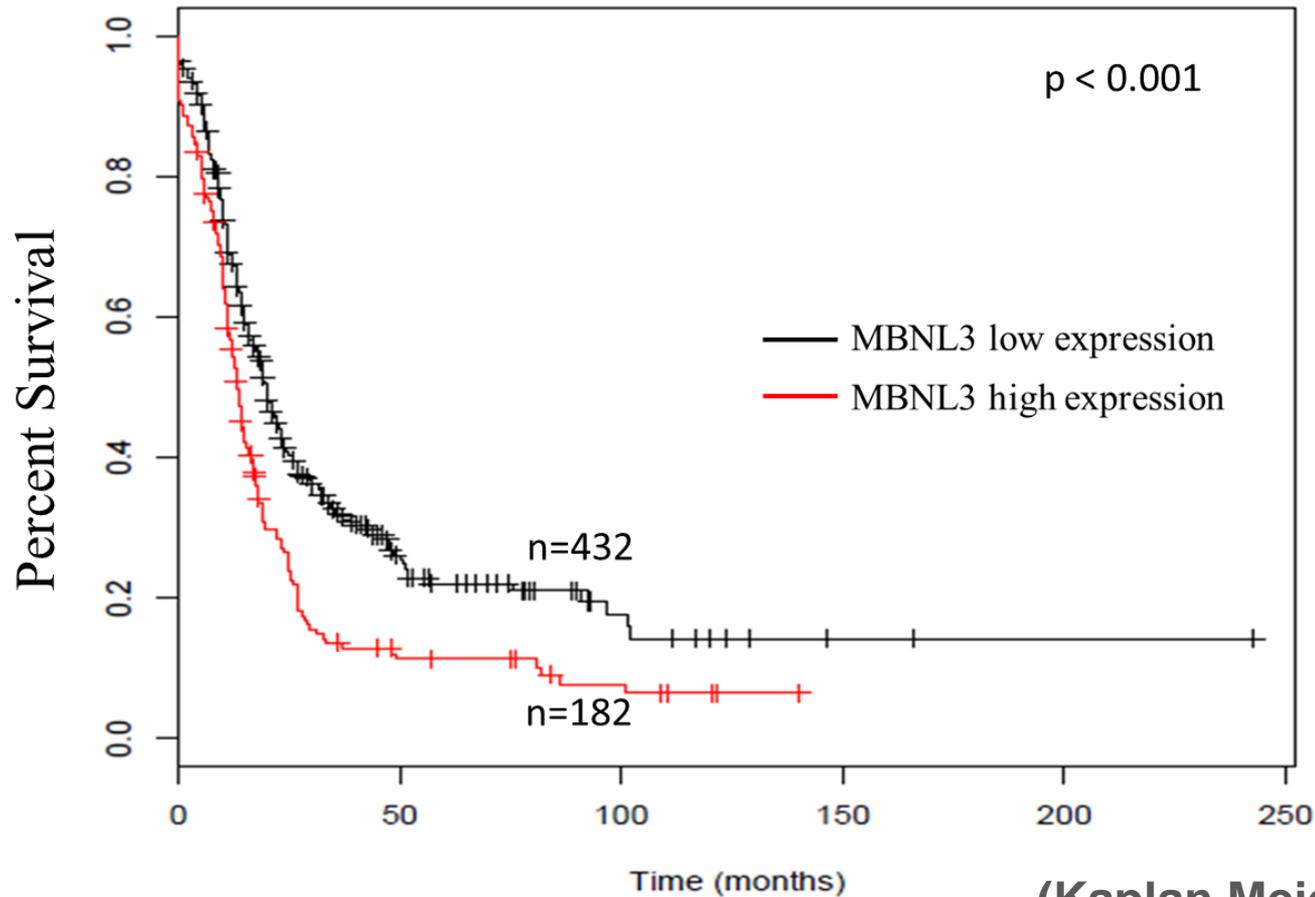


RESULTS

Higher MBNL3 mRNA Expression in Ovarian Tumor Tissue



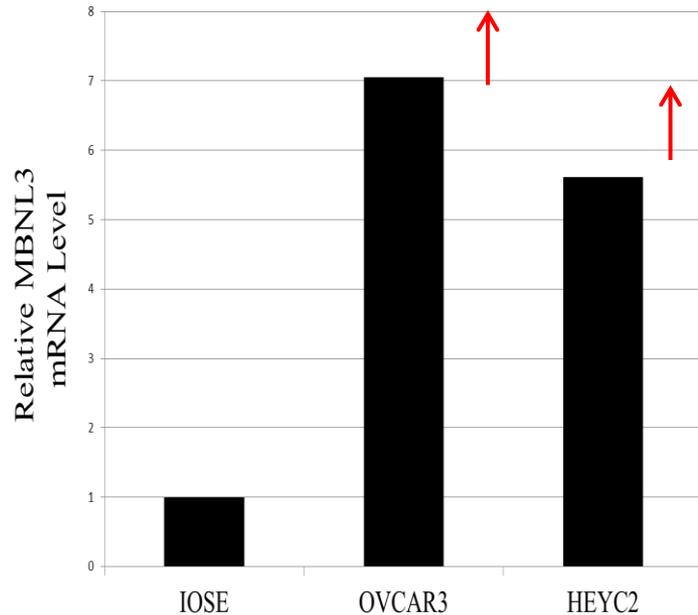
Higher MBNL3 Expression With Lower Survival Rate in Ovarian Cancer Patients



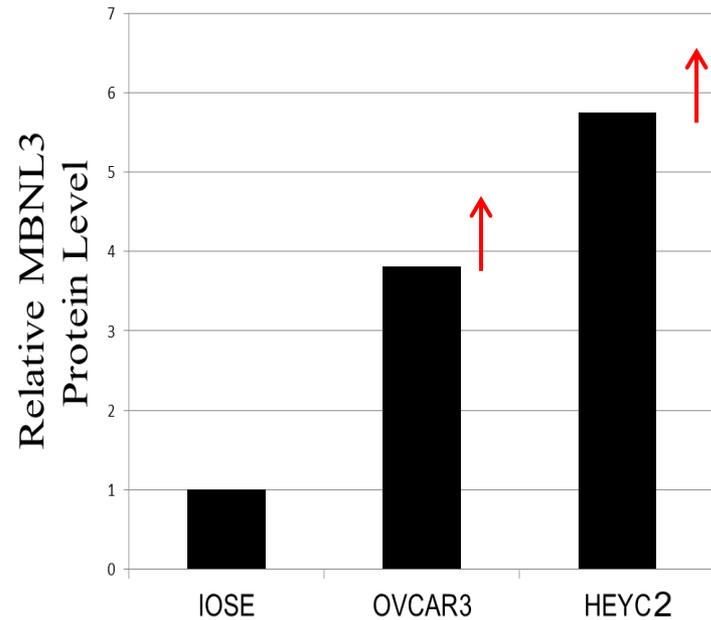
(Kaplan Meier plotter)

Endogenous MBNL3 mRNA / Protein Expression in OVCAR-3 AND HEYC2

A.

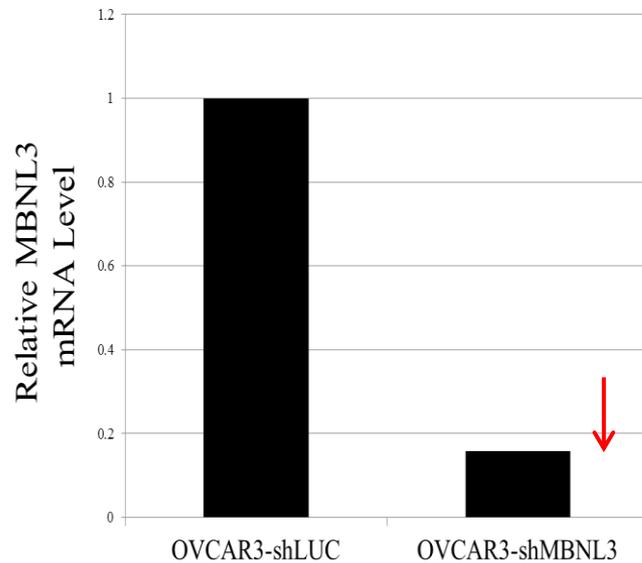


B.

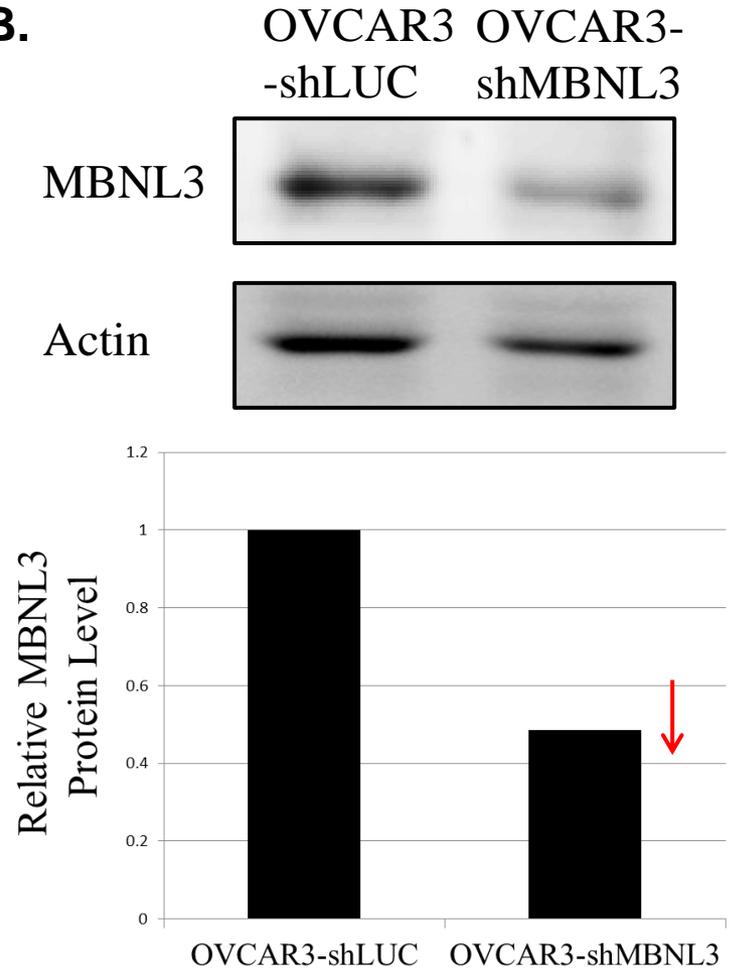


MBNL3 Knockdown Efficiency in OVCAR-3

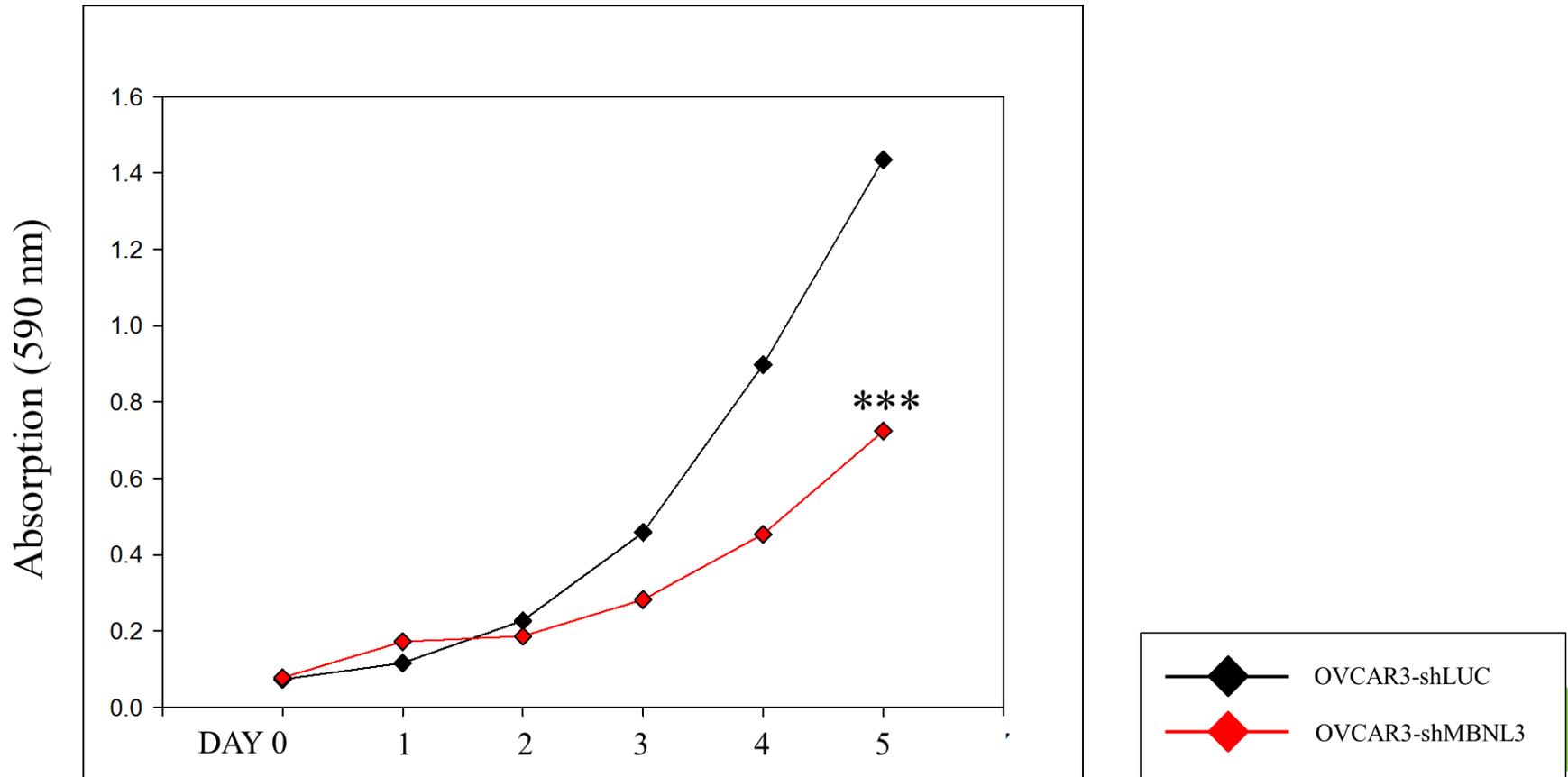
A.



B.



MBNL3 Knockdown Inhibited OVCAR-3 Growth

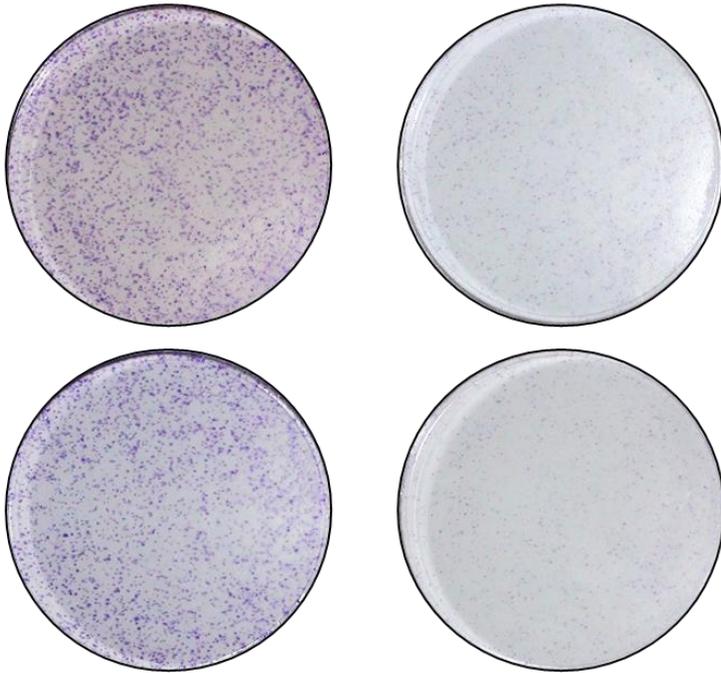


MBNL3 Knockdown Inhibited Proliferation Ability of OVCAR-3

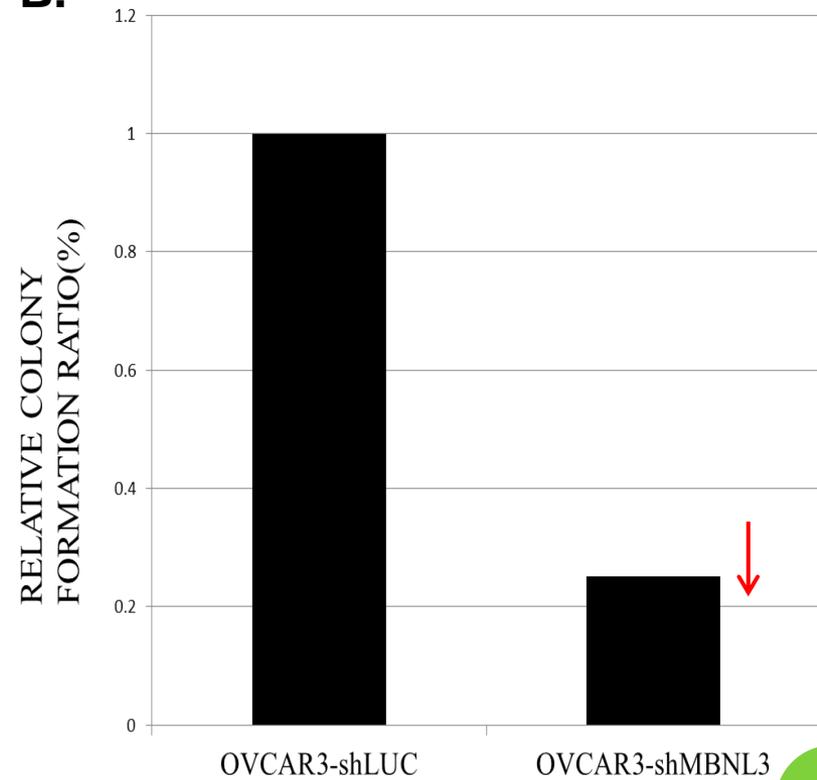
A.

OVCAR3-shLUC

OVCAR3-shMBNL3



B.

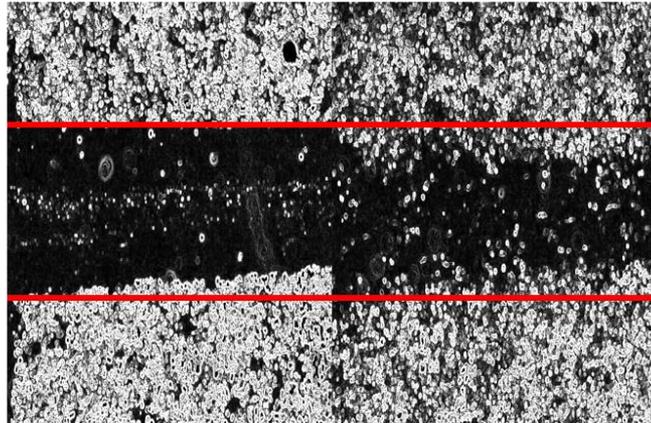


MBNL3 Knockdown Inhibited OVCAR-3 Motility

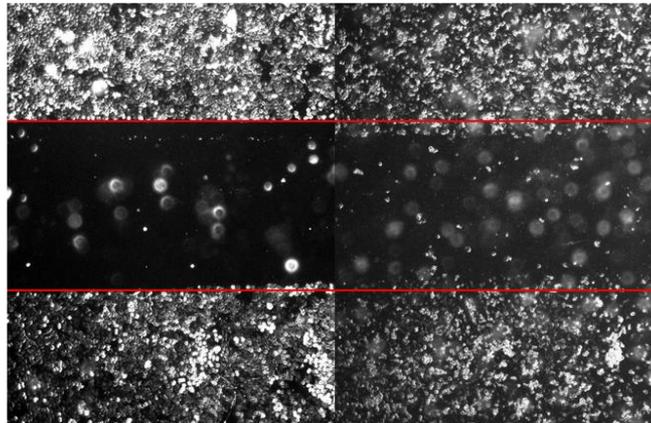
0 DAY

4 DAY

OVCAR3-shLUC

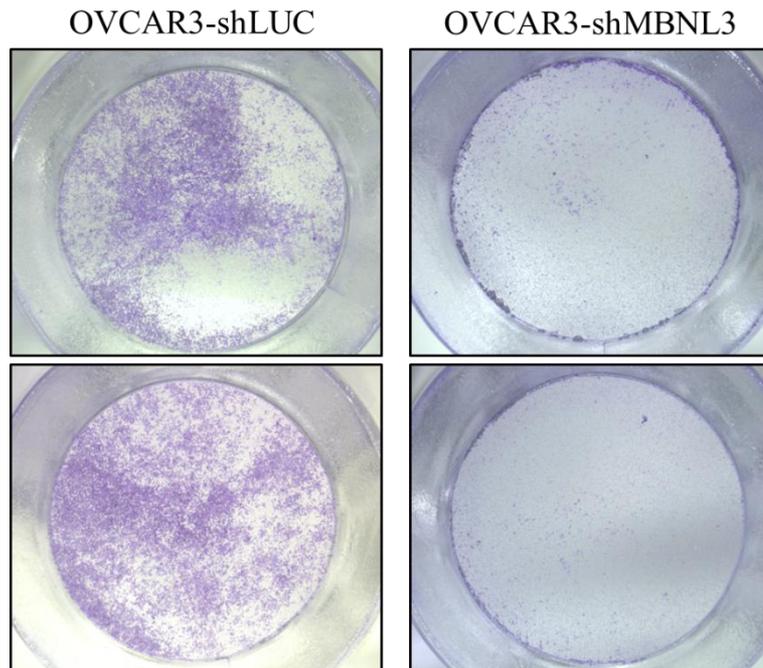


OVCAR3-shMBNL3

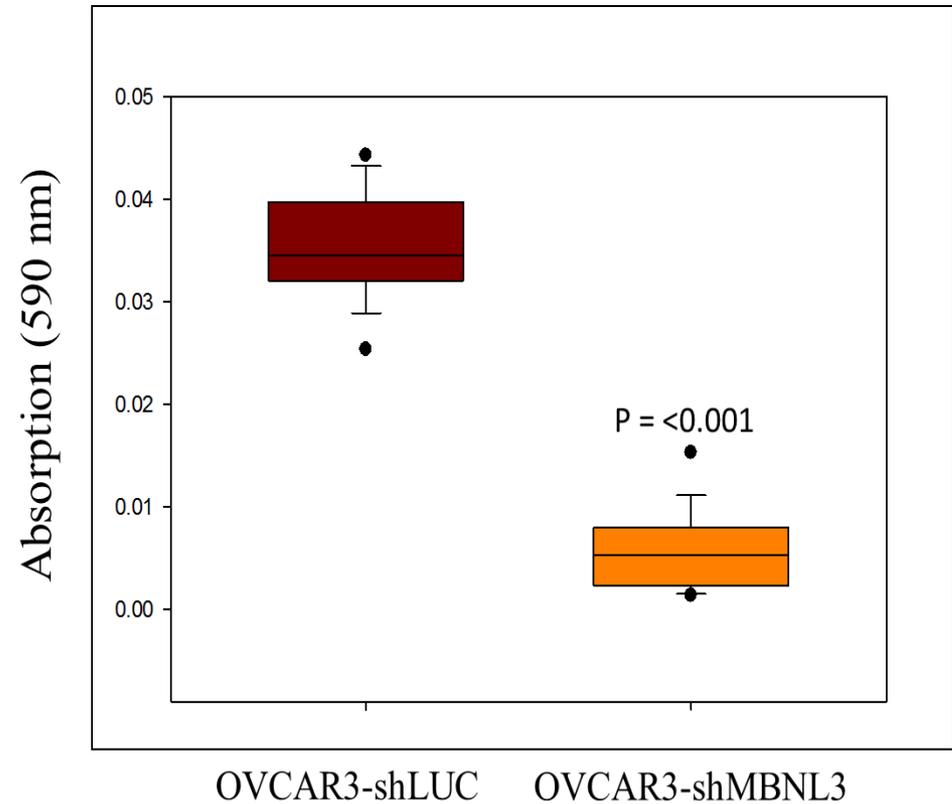


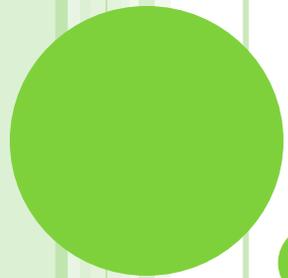
MBNL3 Knockdown Inhibited Migration Ability of OVCAR-3

A.



B.





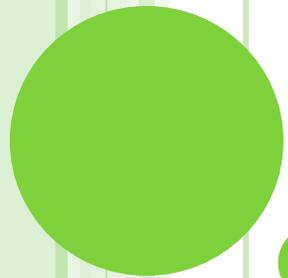
SUMMARY



- Higher MBNL3 expression in ovarian cancer cell
- Knockdown of MBNL3 in OVCAR-3 could significantly inhibit cancer cell growth/proliferation, and migration ability.

MBNL3 plays an important role in ovary cancer. It seems to be a quite promising target for ovarian cancer therapy.





FUTURE WORK



- to further confirm by using **HEYC2** cell lines
- in vivo experiments with NOD/SCID mice to investigate if MBNL3 would affect **tumor size** and **metastasis**





thank you!

