



Abstract

CD73 predicts recurrence in patients with *CTNNB1* mutant endometrial tumors

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CLINICAL LIMITATION for improving outcomes

- ~10-15% of women diagnosed with surgically 'curable' disease, which are low grade, early stage endometrioid-type endometrial tumors, will recur and do poorly.
- CTNNB1* (β -catenin) mutations identify patients at high risk for recurrence, however, its clinical utility is limited. **Of patients with *CTNNB1* mutant tumors, ~50% do not recur.**
- There is an **urgent need to identify biomarkers that predict recurrence** in these patients, which may benefit from more aggressive clinical management.
- Surgery without adjuvant therapy is the current standard of care.

QUESTION: IS CD73 A PREDICTIVE BIOMARKER?

- We previously identified CD73, a cell surface enzyme, to promote membrane localization of wild-type β -catenin.
- In The Cancer Genome Atlas (TCGA) data set for uterine cancer, **~85% of *CTNNB1* mutations occur in exon 3, which is outside the domain necessary for β -catenin membrane localization.**
- In this study, we assessed whether CD73 regulates mutant β -catenin localization and is a predictive biomarker of recurrence.

HYPOTHESIS & APPROACH

- CD73 sequesters mutant β -catenin to the membrane whereby its loss is predictive of recurrence.
- qRT-PCR (**Fig. 1.**) for *CD73* was performed on $n=29$ EC tissues and immunohistochemistry (**Fig. 2. C**) for CD73 and β -catenin on $n=11$ tumors validated to have *CTNNB1* mutation by next generation sequencing. siRNA knockdown of CD73 and expression of mutant β -catenin were performed in HEC-1-A cells (**Fig. 2. A, B**)

RESULTS & CONCLUSION

- CD73 independently predicts disease recurrence in *CTNNB1* mutant tumors (**Fig. 1.**). **Loss of *CD73* is associated with recurrence.**
- Mechanistically, CD73 sequesters mutant β -catenin to the membrane (which limits disease progression and aggressiveness) (**Fig. 2.**).
- CD73 identifies women at high risk of recurrence which may benefit from adjuvant therapy.**

Fig. 1

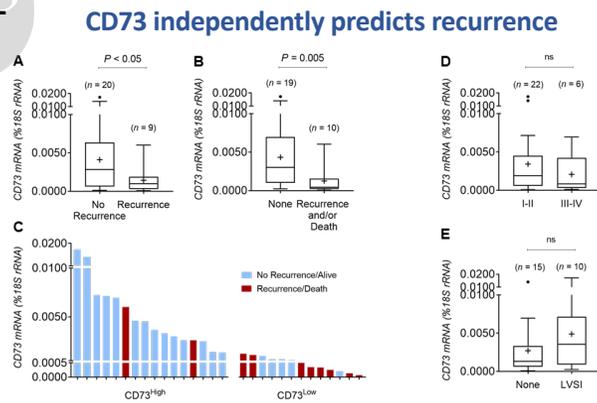
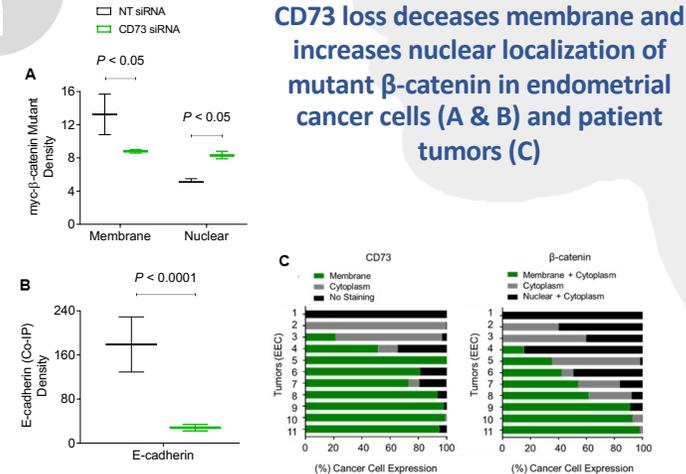


Fig. 2



Summary

