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.
- 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.

HYPOTHESIS & APPROACH

- CD73 sequestrates 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 sequestrates 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.

Summary

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