Novel Enzyme in CoQ10 Biosynthesis Pathway as a Novel Target to Treat Pancreatic Ductal Adenocarcinoma

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Technology

Metabolome studies of radioactively-labeled O2 in the Pacold lab have led to the discovery of a new enzyme in the Coenzyme Q10 (CoQ10) biosynthesis pathway and identified the enzyme involved as HPDL, and its product as 4-hydroxymandelic acid (4-HMA). Because CoQ10 is important for tumor growth, the Pacold lab tested whether HPDL and the 4-HMA-dependent CoQ10 biosynthesis pathway were needed for pancreatic ductal adenocarcinoma (PDAC) growth in vivo. They have shown that deleting HPDL in PDAC cells and mice attenuates tumor growth. Furthermore, patients with PDAC tumors that have high HPDL expression show poor overall survival. Based on the findings from the Pacold lab, we believe that there is a clear benefit from therapies targeting HPDL or CoQ10 biosynthesis in treating PDAC.

Background

PDAC is one of the most aggressive tumors, killing over 90% of patients, partly because it does not present with obvious symptoms until it is in advanced, unresectable and untreatable stages. The global burden of PDAC has doubled in the last quarter century and is projected to be the second leading cause of cancer deaths in the USA in the next 20–30 year.

Very few targets have been identified against PDAC and most PDAC patients grow resistant to current therapies. The current state of PDAC presents an unmet clinical need to identify new targets in hopes of extending patient survival and improving quality of life.

Applications

- HPDL levels can be used as a biomarker for survival in PDAC patients
- Targeting HPDL or CoQ10 biosynthesis can be used as treatment for PDAC

Advantages

- HPDL represents a novel target for treating PDAC, a disease with an extremely poor prognosis
- Deleting HPDL in PDAC cells and mice attenuates tumor growth. In addition, high HPDL expression correlates with overall survival

IP Status

Provisional patent application pending

References

1. Banh, R.S., Kim, E.S., Spillier, Q. et al. , The polar oxy-metabolome reveals the 4-hydroxymandelate CoQ10 synthesis pathway