Background
Glutamine is the most abundant, free amino acid in plasma, utilized by cancer cells for survival and rapid reproduction. Cancer cells employ glutamine through a transporter (ASCT2) and metabolizing it through a catalyzing enzyme. During glutaminolysis, the amino acid transporter, SLC1A5 (ASCT2), metabolizes glutamine with a catalyzing enzyme.

Hypothesis
Mouse using the developed inhibitor of the ASCT2 amino acid transporter, V-9302, malignant tumors will be unable to metabolize glutamine leading to difficulties in proliferation and an imbalance of metabolites in the microenvironment.

Materials and methods
Mouse selection by genotyping

V-9302 treatment in-vivo
- Mice with 
  - Mice with Cre;+/; Kras+; Smad4f/f are the only ones that will grow tumor with only a 25% chance of occurring. B. Genotyping through gel electrophoresis allows for the identification of the groups in the study.

Results

Glutamine
- Decreases in Lactate
- Decreases in Glutamine/ Glutamate
- Decreases in Choline/ Acetate

Glutamate
- Decreases in Lactate
- Decreases in Glutaminolysis

Total Choline
- Decreases in Lactate
- Decreases in Glutaminolysis

Lactate
- Decreases in Lactate

Acetate
- Decreases in Lactate

Fig. 4 Measurement of Metabolites by Nuclear Magnetic Resonance (NMR). A. Glutamine, B. Glutamate, C. Total Choline, D. Lactate, E. Acetate from all three groups in the study.

Results (cont.)
- After treatment, the metabolism profile changed.
- NMR showed lower levels of glutamine, glutamate, and total choline in treated mice compared to the control group.
- Lactate was lower at elevated doses of V9302.
- Acetate displayed lower levels in group 3 while group 1 saw no change.

Histology
- Histologically, chronic exposure of V9302 led to tumors that were less advanced than tumors from the acute dose control groups.

Conclusions
- This investigation attempted to treat malignant cancer cells with V-9302 in different ways and found some changes in metabolic profile.
- It is possible that interference with inhibiting glutamine transporter changes cancer characteristics.
- However, it is essential to gain a better understanding of glutaminolysis as well as other cancer metabolisms before determining the most effective usage of V9302 and what manipulations can improve its benefits in treating cancer.

References