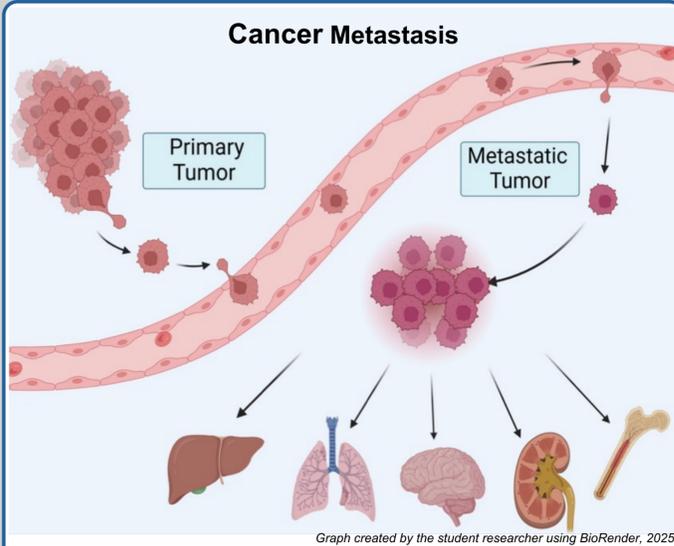


# Bioinformatic analysis of metastasis-associated metabolic landscape reveals an oncogenic role for the transsulfuration pathway

## Introduction/Background

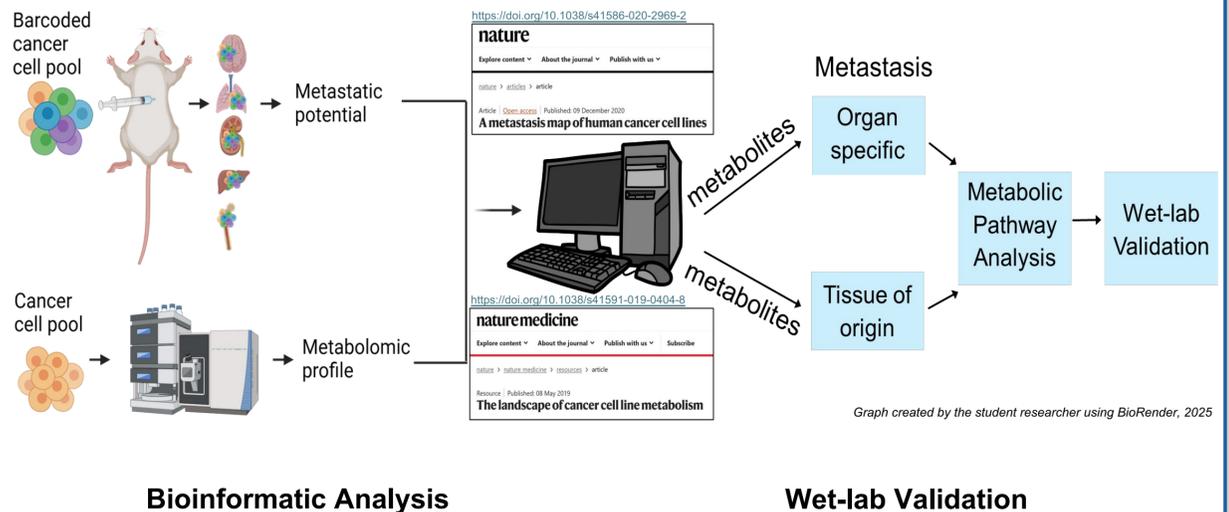


- Cancer is a leading cause of death worldwide [1], with cancer metastasis accounting for the majority of cancer-related deaths [2].
- Cancer metastasis is the process by which cancer cells break off from the primary tumor, overcome a series of hurdles, enter the circulatory system, and spread to other parts of the body where they don't belong [3-5].
- Therapies targeting metastatic cancer cells are very limited.

## Question

How do metastatic cancer cells (“seeds”) adapt their metabolism to thrive in foreign microenvironments they have traveled to (new “soil”)?

## Methods

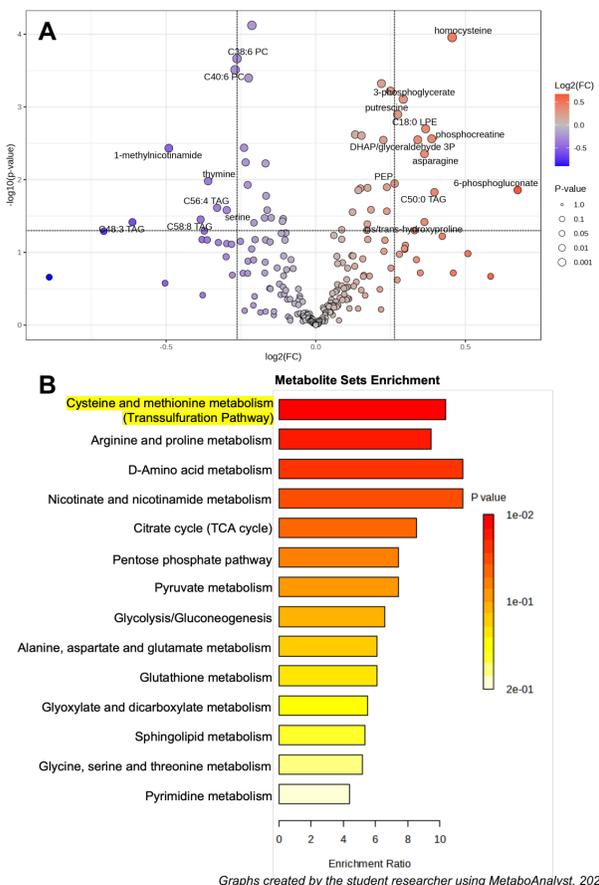


This study systematically examined the association between cancer metabolism and metastasis by integrating two complementary datasets, both derived from the Cancer Cell Line Encyclopedia (CCLE): the Metastasis Map (MetMap) [6] and large-scale metabolomic profiling [7].

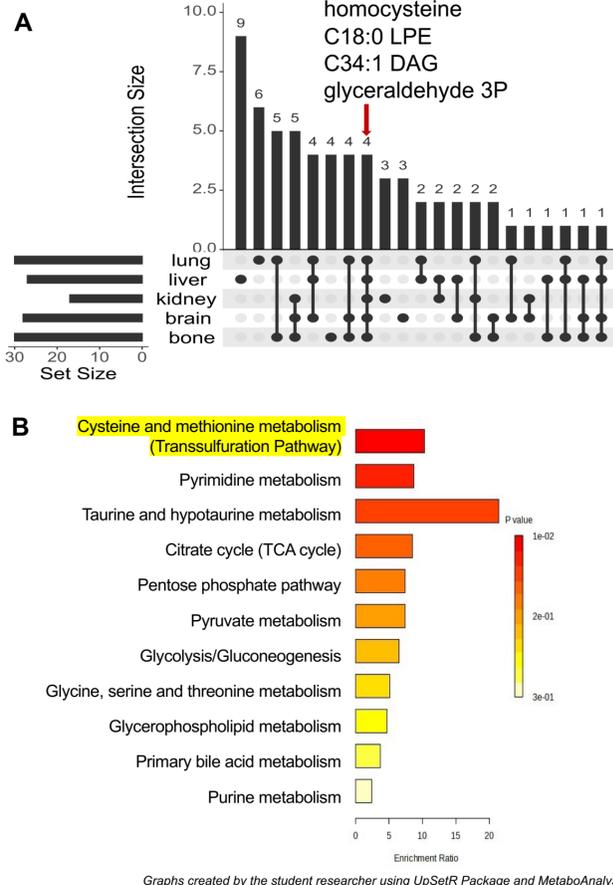
Wound healing assays and a transwell invasion assay were used with methionine deprivation and cystathionine  $\beta$ -synthase (CBS) inhibition to validate the computational findings and prove causation.

## Results

### 1. The transsulfuration pathway is strongly enriched in cancer cells with high metastatic potential

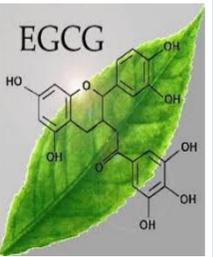


### 2. Analysis of shared metabolites and metabolic pathways across different organ-specific metastases



## Application

Epigallocatechin Gallate (EGCG) is an over-the-counter dietary supplement extracted from green tea that may help with weight management and anti-inflammation [8]. This study suggests that EGCG may hold the potential to treat or prevent pancreatic cancer metastasis.



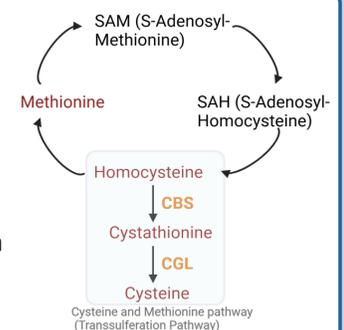
Dietary methionine restriction is sufficient to reduce circulating methionine in most human and animal studies within just days of consuming such diets [9]. Dietary methionine restriction represents a strategy with potential to limit metastatic progression.



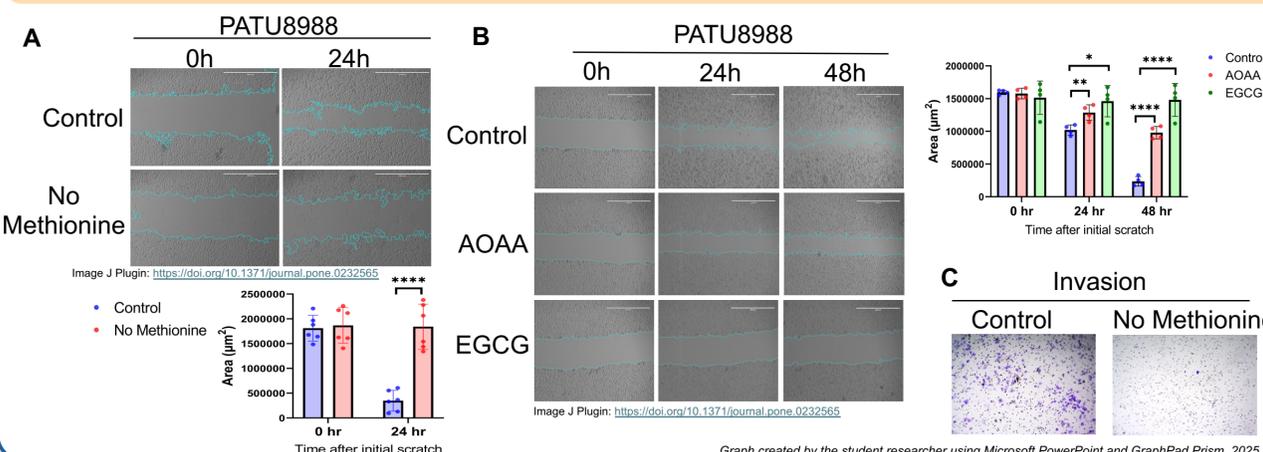
Jansen, M. (2014). The Low Methionine Recipe Book. Jr Press. <https://www.amazon.com/Low-Methionine-Recipe-Book-methionine/dp/0993633420>

## Conclusions

- The transsulfuration pathway plays a key role in cancer metastasis.
- Both distant organs and tissue of origin play crucial roles in reshaping metabolism to promote metastasis.
- Wet-lab validation demonstrated that targeting this pathway, either through methionine withdrawal or CBS inhibition, significantly reduces cancer cell migration and invasion.



### 3. Blocking the transsulfuration pathway by methionine withdrawal or CBS inhibitors inhibits metastatic pancreatic cancer cell migration and invasion



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