

PHOSPHOGLYCERATE DEHYDROGENASE PLAYS A VITAL ROLE IN ER-STRESS-RELATED INTESTINAL INFLAMMATION

Björn Konukiewitz

UEG Week Copenhagen 2023

Poster

IBD

October 15, 2023

Serine metabolism enzyme PHGDH is elevated in IBD patients and linked to inflammation, with experimental models showing that disrupted serine synthesis impairs mitochondrial function and drives proinflammatory cytokine production in intestinal epithelial cells.

KEY POINTS

- PHGDH expression was significantly increased in both ulcerative colitis and Crohn's disease patients compared to healthy controls in two cohorts (N=67 and N=212), and correlated with degree of inflammation and ER stress marker HSP90B1
- Chemical induction of ER stress strongly increased expression of serine synthesis enzymes Phgdh, Psat1, and Psph in murine intestinal epithelial cells and organoids
- Inhibition of PHGDH with BI-4916 in serine/glycine-deprived conditions resulted in significantly disrupted mitochondrial function (basal, ATP-linked, and maximum respiration) and strong induction of proinflammatory cytokines Cxcl1 and Il6 following LPS or tunicamycin treatment
- Co-treatment with glycine and formate rescued mitochondrial dysfunction and inhibited Cxcl1 overactivation in intestinal epithelial cells, suggesting serine feeds into one-carbon metabolism to provide mitochondrial-derived formate
- The authors conclude the data suggest a previously underappreciated role of cellular serine metabolism in IBD pathophysiology through epithelial-derived proinflammatory mechanisms

VIEW THIS CONTENT ON GUTFLIX

<https://gutflix.eu/search/d/408665ba-743c-11ee-9bed-0242ac140004>



AI-generated summary

This summary was generated by an AI large language model based on the content transcript. It is for informational purposes only and should not be considered a substitute for clinical judgment. Always rely on your professional expertise and the full clinical context when making clinical decisions.