

Presenting Lei Zhang¹, Haoran E¹, Yue Zhao¹, Deping Zhao¹, Chang Chen¹

¹. Department of Thoracic Surgery, Shanghai Pulmonary Hospital, School of Medicine, Tongji University

Correspondence: Lei Zhang z11653045@163.com

INTRODUCTION

Thymic epithelial tumors (TETs) are rare and molecularly heterogeneous malignancies with poorly defined metabolic vulnerabilities. Arginine metabolism is increasingly recognized as an important regulator of tumor growth and immune suppression, yet its role in TETs remains largely unexplored. Here, we integrated LC–MS/MS-based metabolomic profiling of **98 TET specimens** with TCGA bioinformatic analyses to identify key metabolic drivers and investigate the functional roles of **AGMAT** and **ARG1** in TET progression.

METHODS

Design: Tumor specimens from **98 patients with thymic epithelial tumors (TETs)** were subjected to **LC–MS/MS-based metabolomic profiling** to characterize metabolic alterations across the cohort. Metabolomic data were integrated with **TCGA transcriptomic datasets** and **bioinformatic analyses** to identify dysregulated metabolic pathways and prioritize candidate enzymes associated with TET biology. **AGMAT** and **ARG1** emerged as key enzymes involved in amino acid and arginine-related metabolic reprogramming. Their biological functions were subsequently investigated using **cell-based functional assays** to evaluate effects on tumor-cell growth and malignant phenotypes, and further validated in **in vivo tumor models**. Mechanistic experiments were then performed to determine the downstream molecular pathways through which AGMAT and ARG1 promote TET initiation and progression.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- Our findings identify **AGMAT** and **ARG1** as **key metabolic regulators in TETs**, linking arginine-related metabolic reprogramming to tumor initiation and progression. These results suggest that the **AGMAT/ARG1 metabolic axis** may represent a **potential biomarker** and **therapeutic vulnerability** in TETs.

Future Direction for Research

- Future studies should validate these findings in **larger, independent TET cohorts** and further define the downstream metabolic and signaling mechanisms driven by AGMAT and ARG1. Exploring **targeted inhibition of this metabolic axis**, alone or in combination with immunotherapy, may provide new therapeutic opportunities for patients with TETs.

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RESULTS

