



# Leveraging core enzyme structures for microbiota targeted functional regulation: Urease as an example

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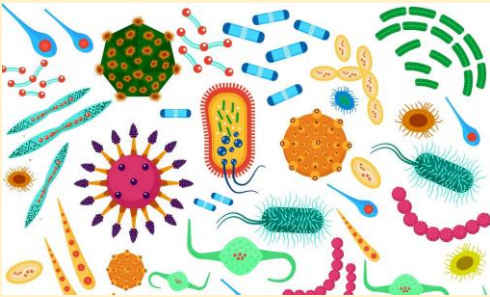
Shengguo Zhao, Huiyue Zhong, Yue He, Xiaojiao Li, Li Zhu, Zhanbo Xiong, Xiaoyin Zhang, et al. 2025. Leveraging core enzyme structures for microbiota targeted functional regulation: Urease as an example. *iMeta* 4: e70032.

<https://doi.org/10.1002/imt2.70032>



# Research Background

## Functional Regulation of Microbiome



### Traditional Regulation Methods:

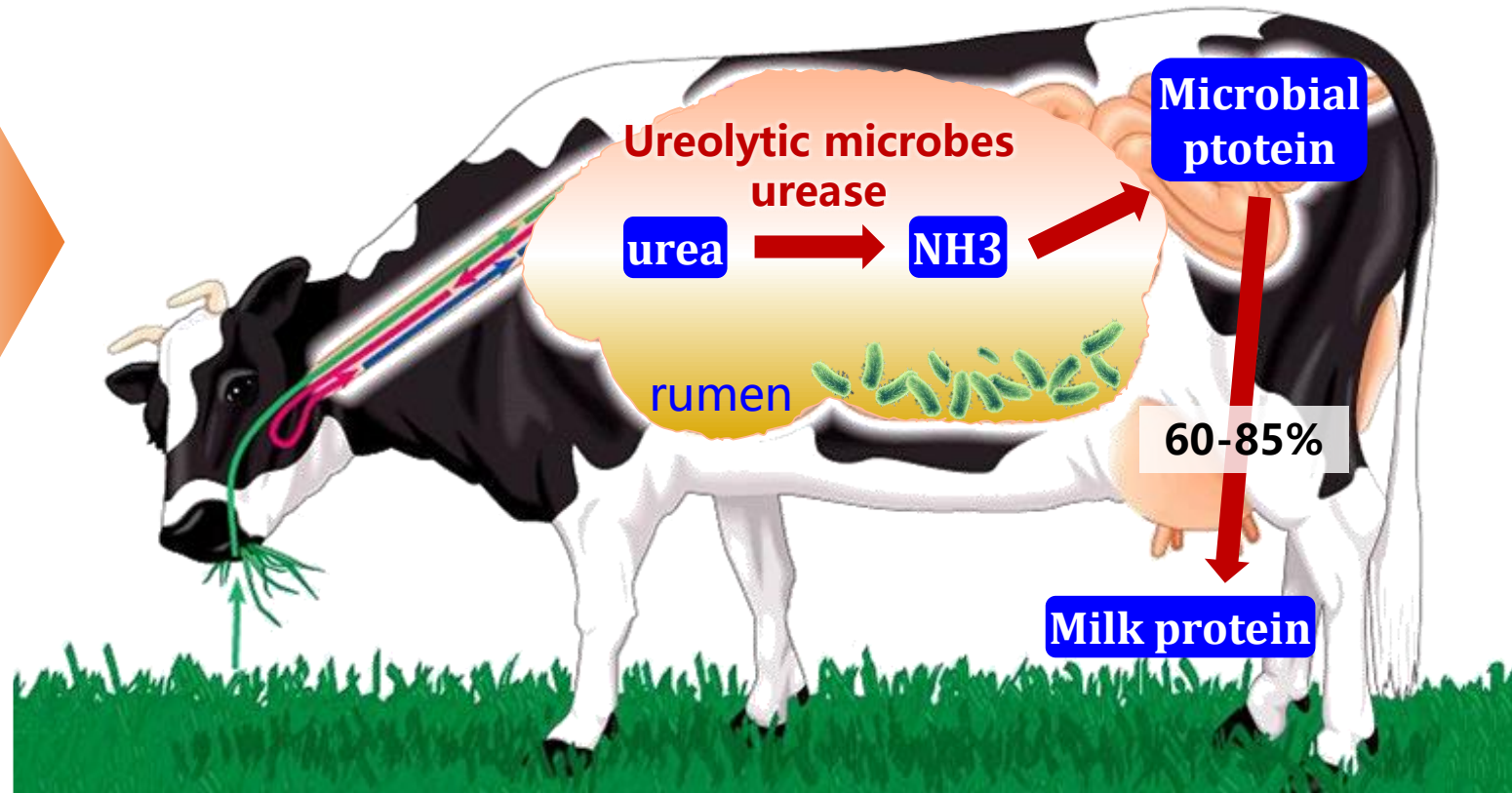
- Broad-spectrum antibiotics
- Probiotics
- Dietary interventions

### Limitations:

- Low targeting specificity
- Non-targeted perturbations

## Regulation of Urea Degradation by Rumen Microbiota:

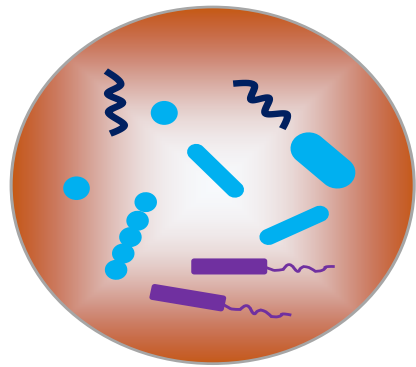
- Excessive urease activity leads to low nitrogen utilization efficiency



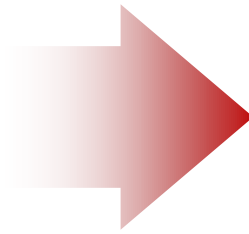


# Highlights

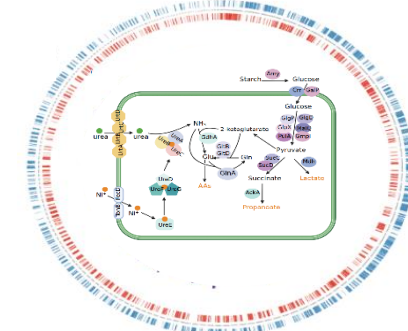
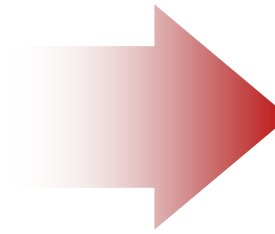
## Leveraging Core Enzyme Structures for Microbiota Targeted Functional Regulation



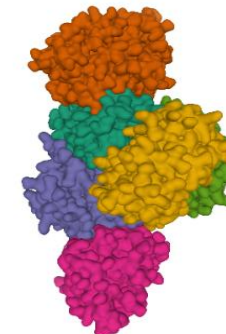
Microbiota



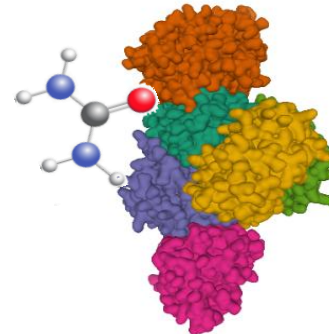
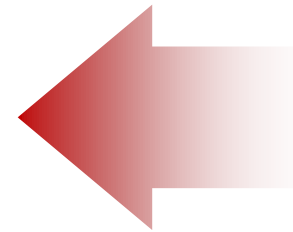
Core enzyme identification



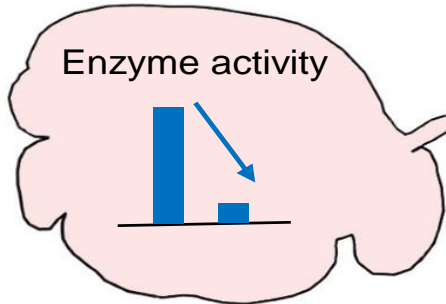
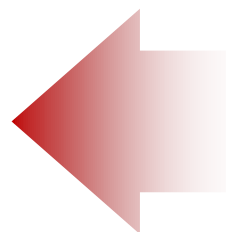
Genome and pathway



Enzyme protein structure

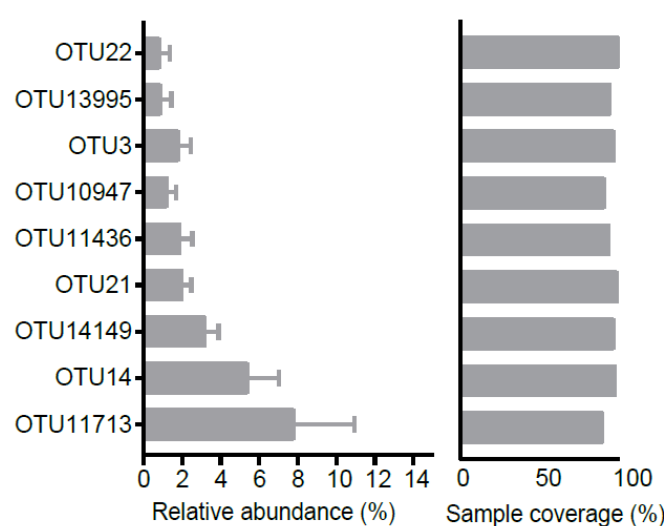
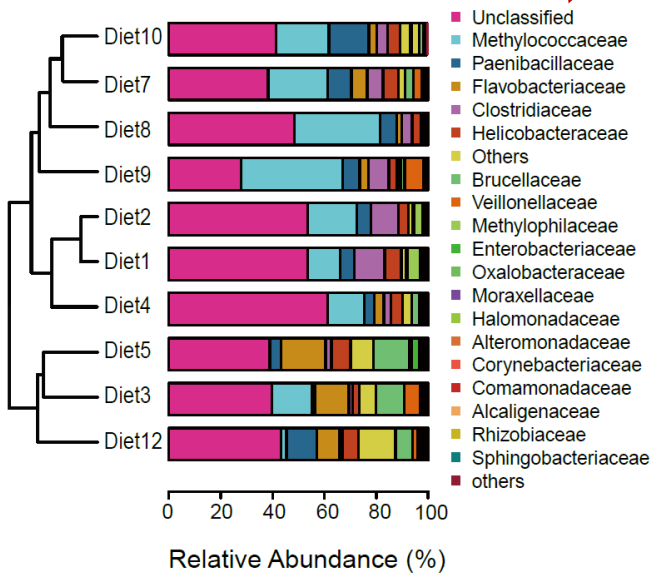
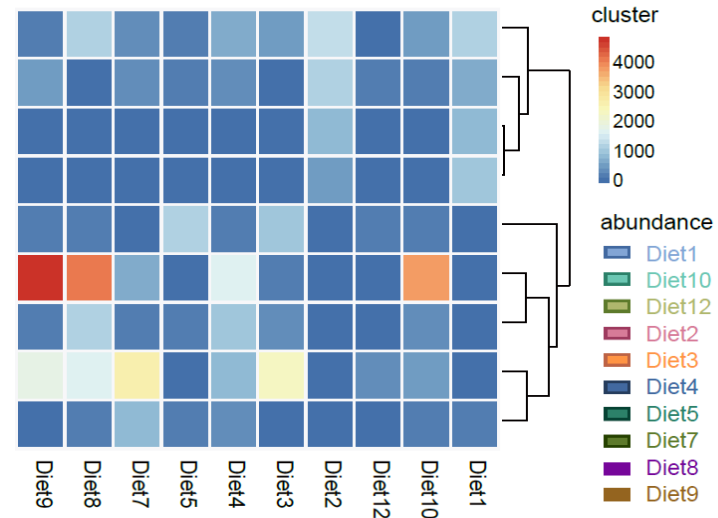
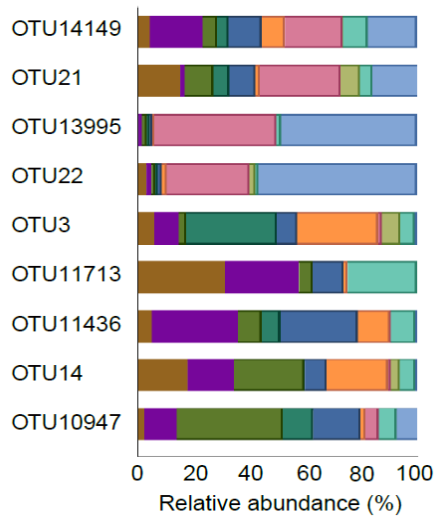
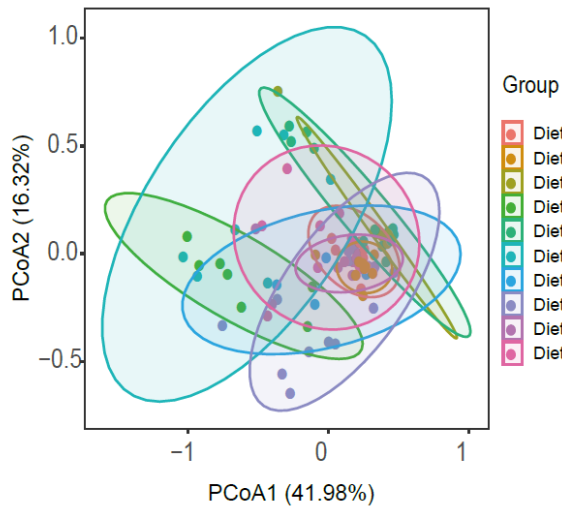


Docking screening

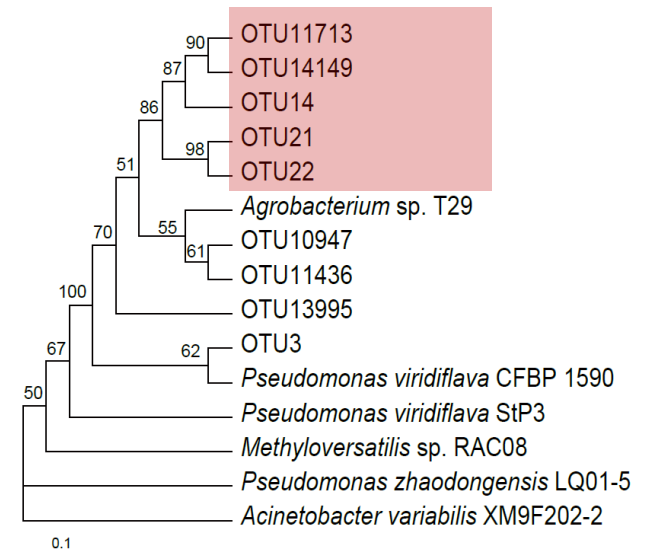


Function validation

# Identification of Dominant Ureasases in Rumen Microbes

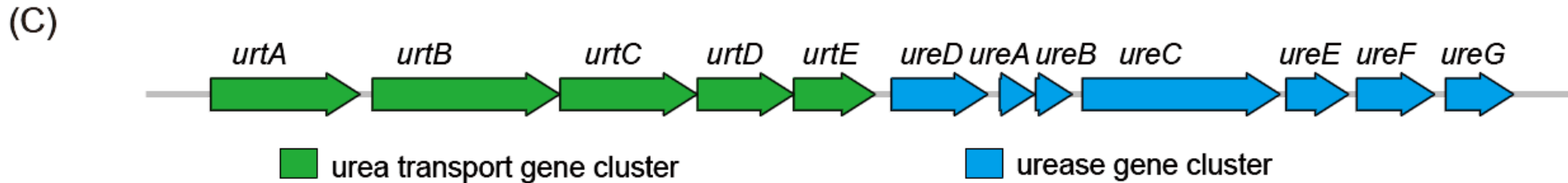
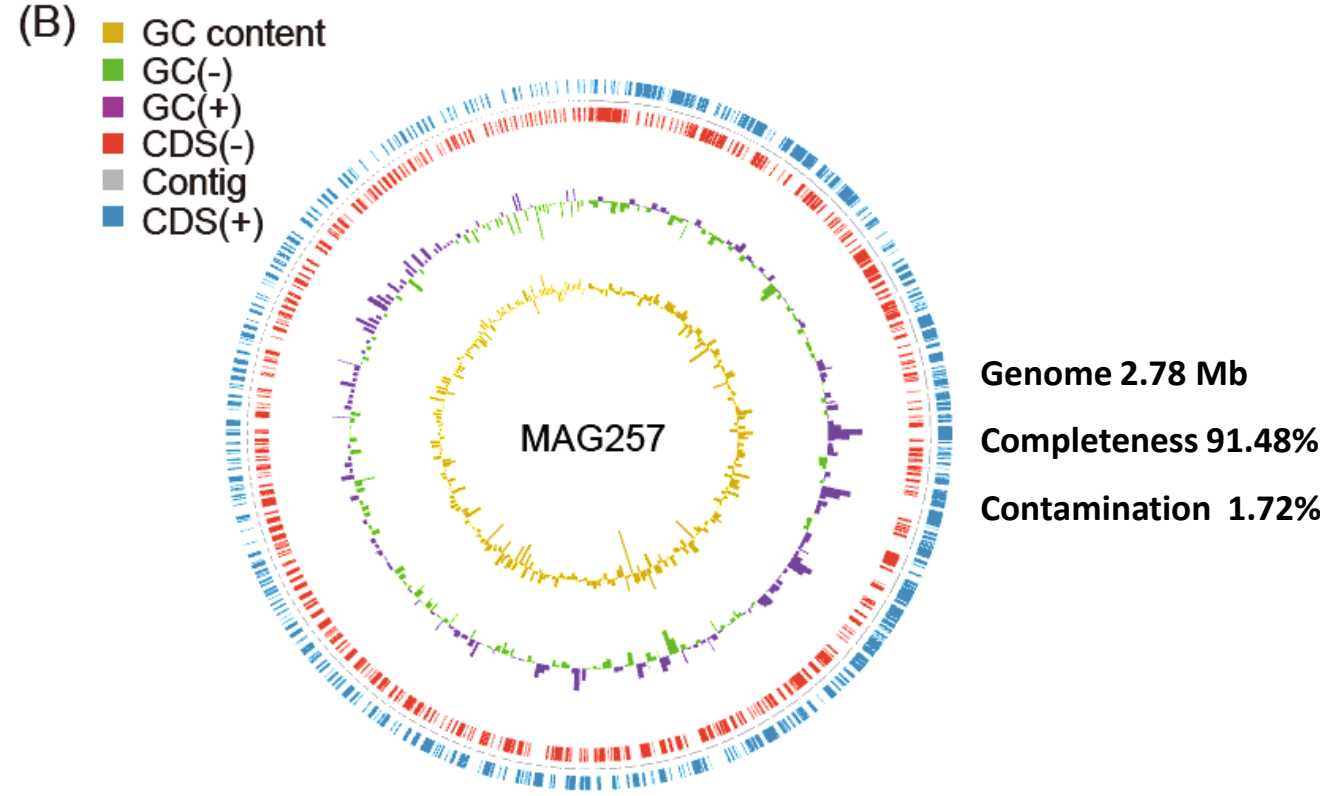
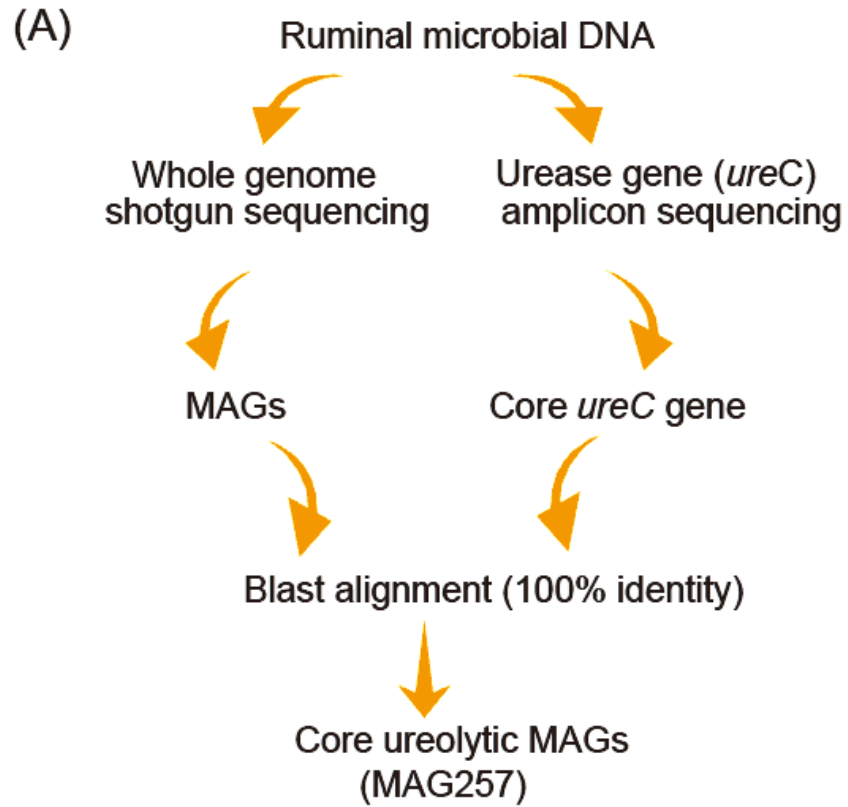


**Abundance >1%, coverage >85%**



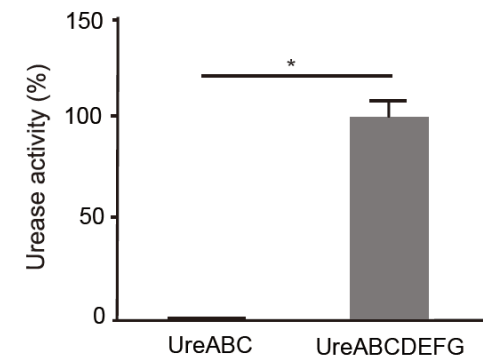
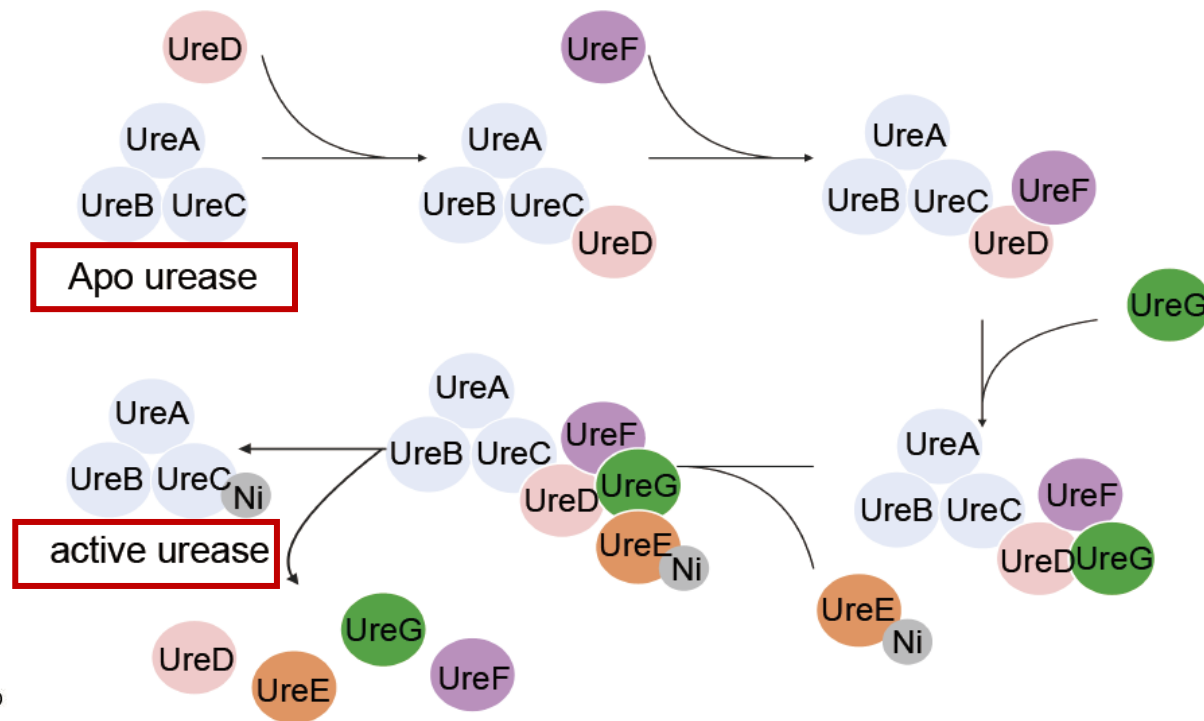
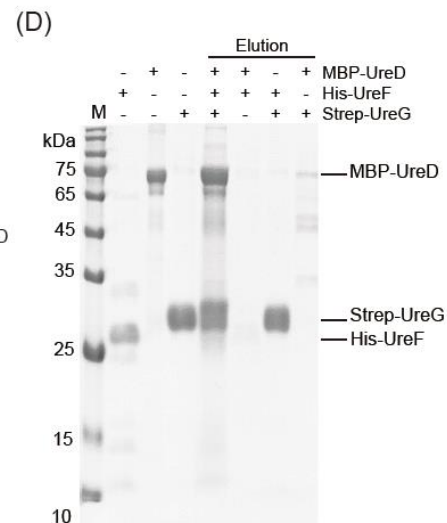
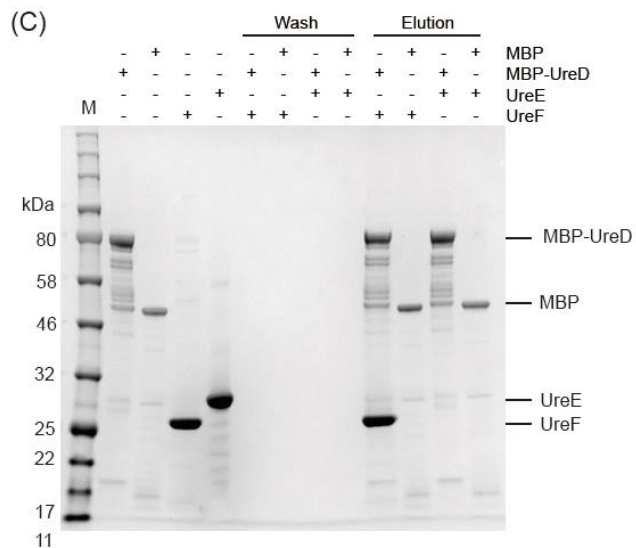
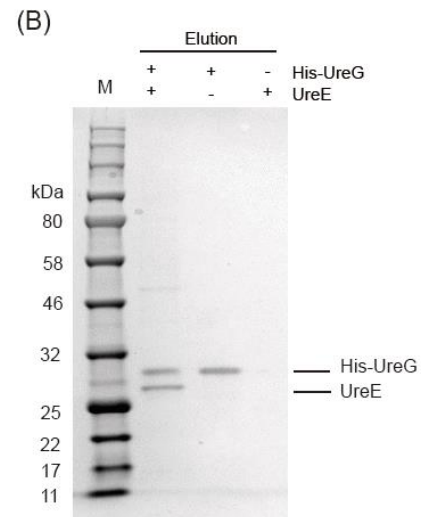
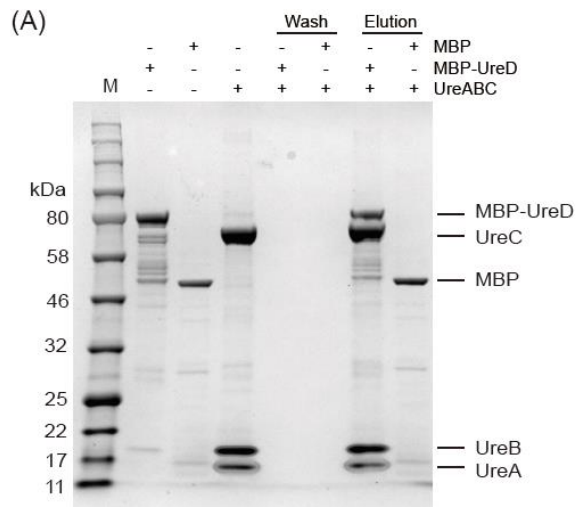


# Identification of Genomes Harboring Dominant Ureasases



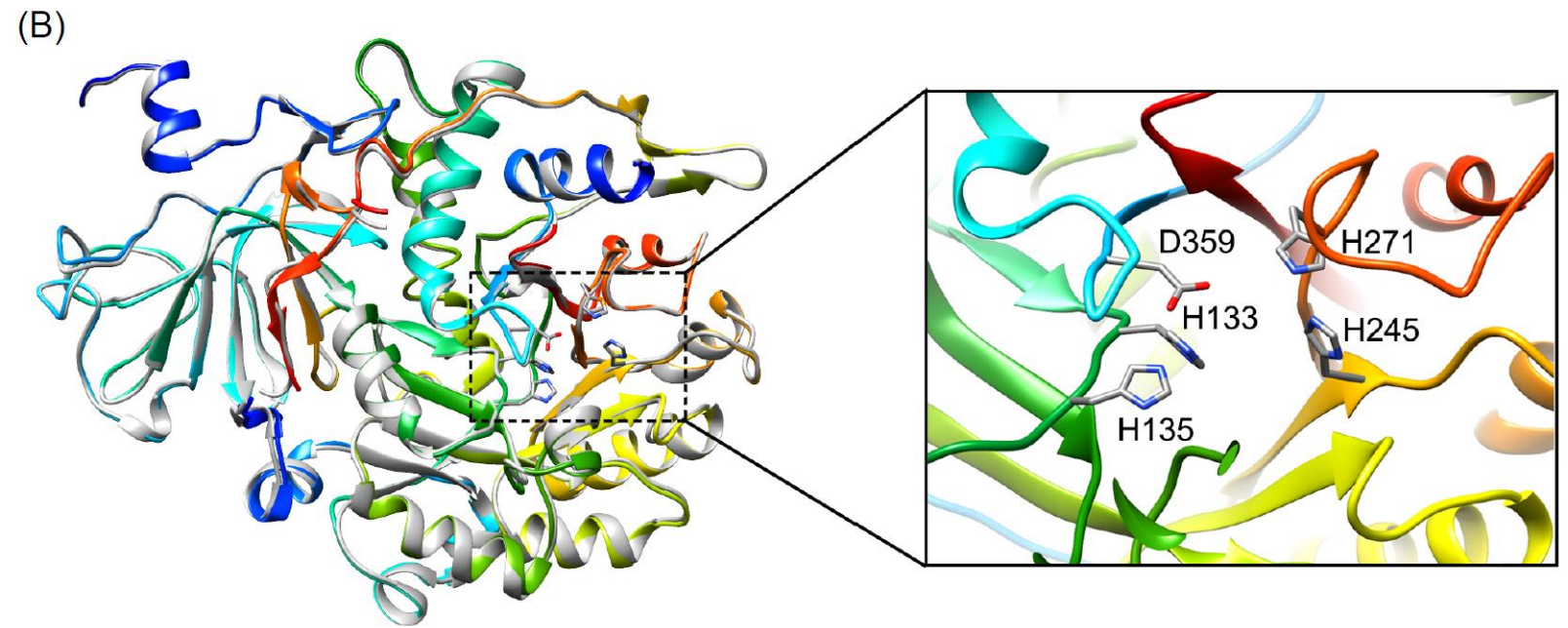
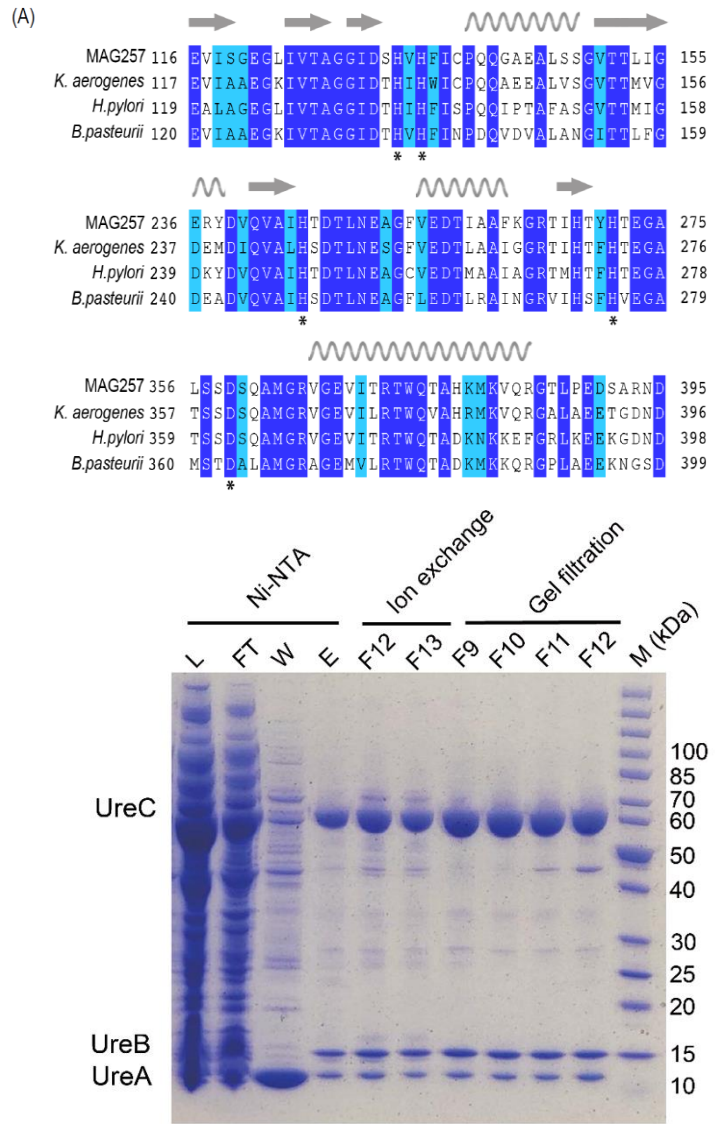


# Protein-Protein Interactions of Dominant Ureasases





# Protein-Protein Interactions of Dominant Ureases

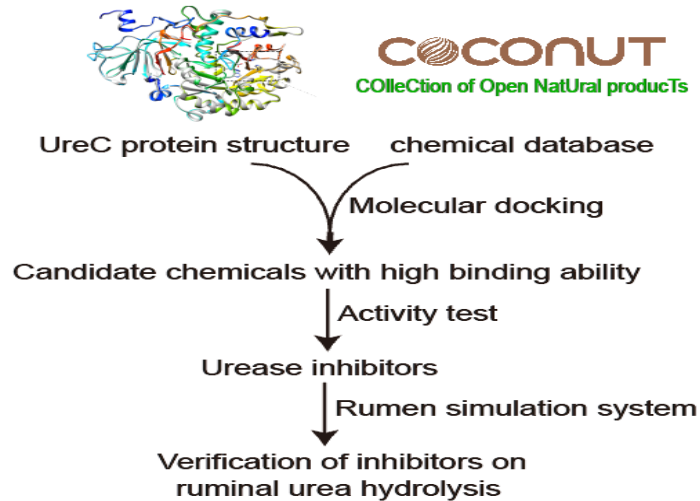


Cryo-EM structure of urease UreC protein (3.1 Å)

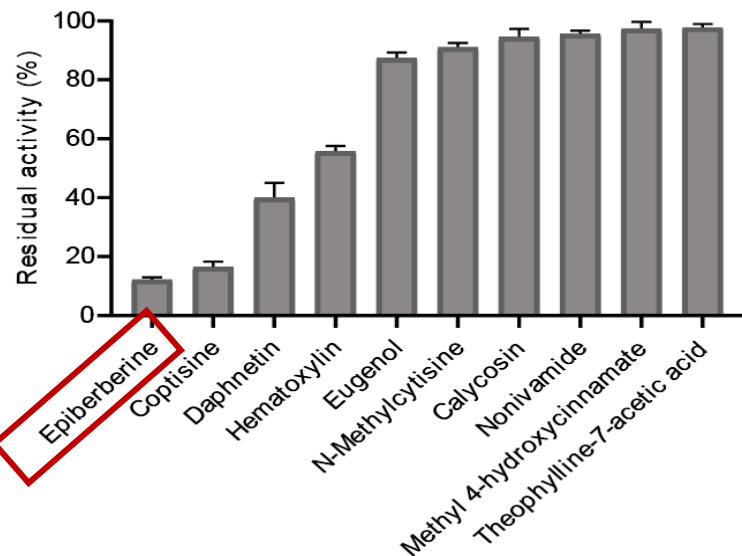


# Screening and Validation of Urease Inhibitors

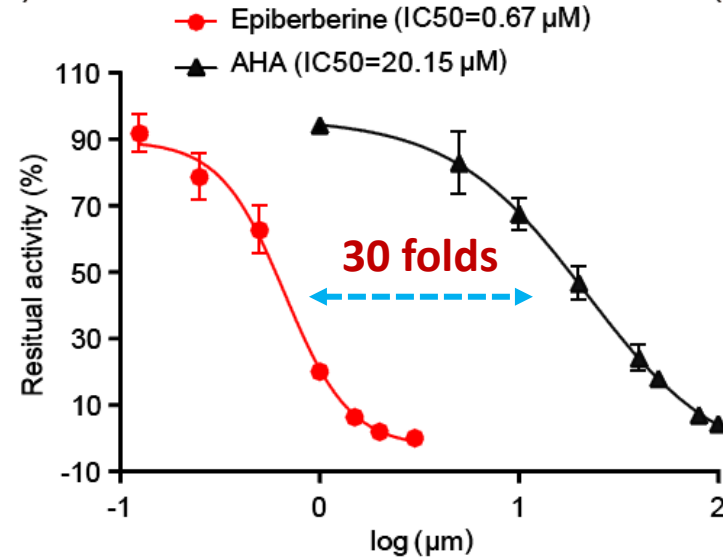
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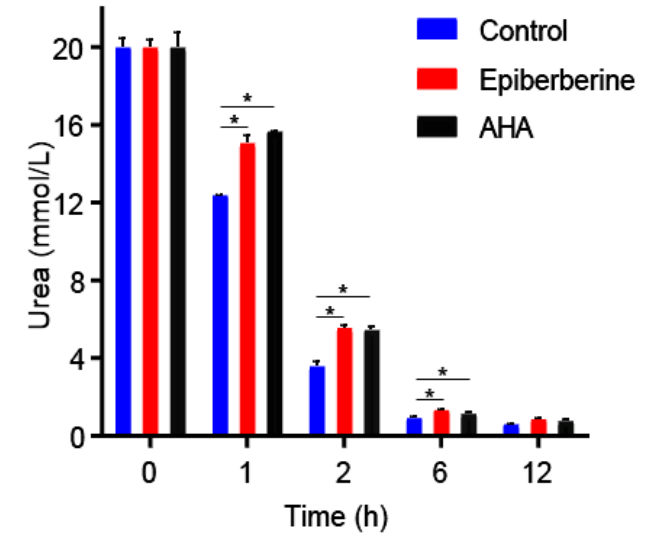
(B)



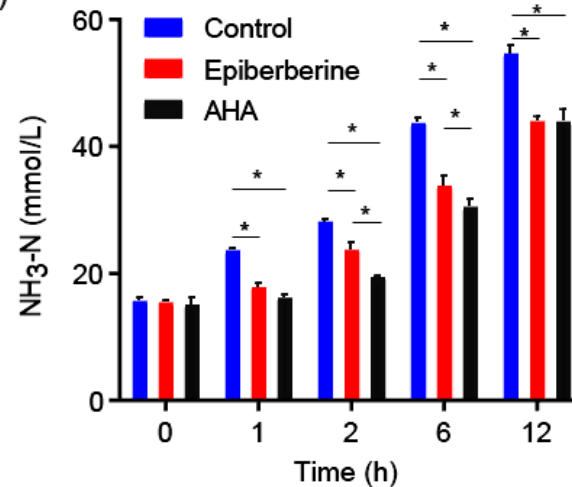
(C)



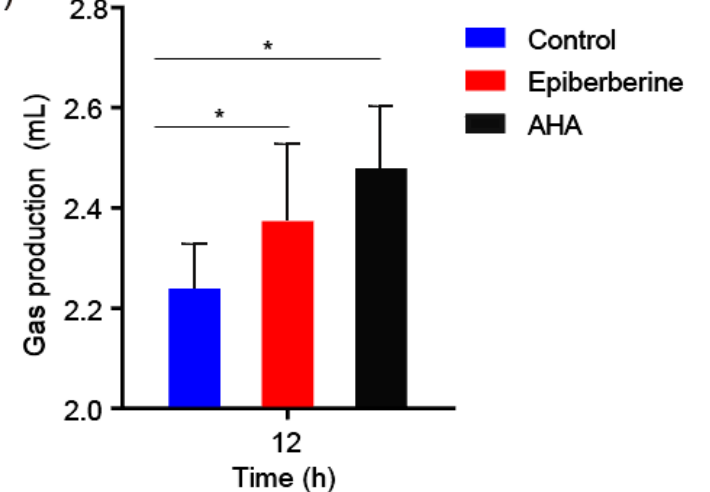
(D)



(E)

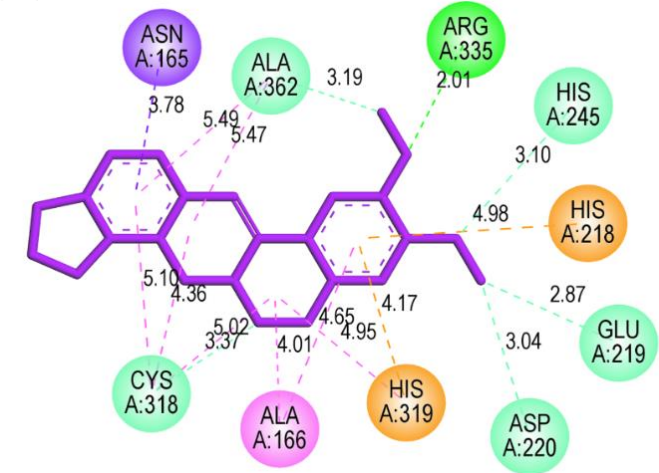
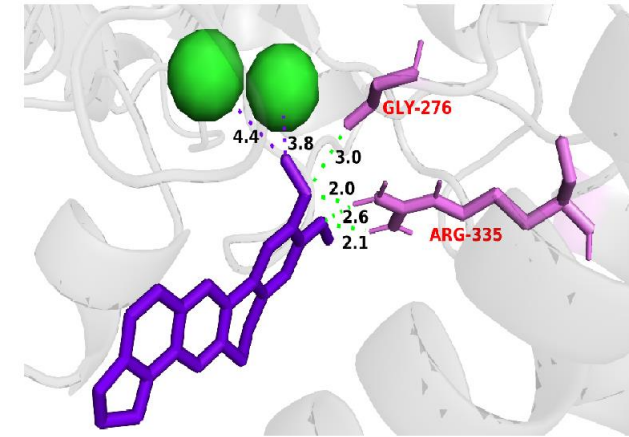
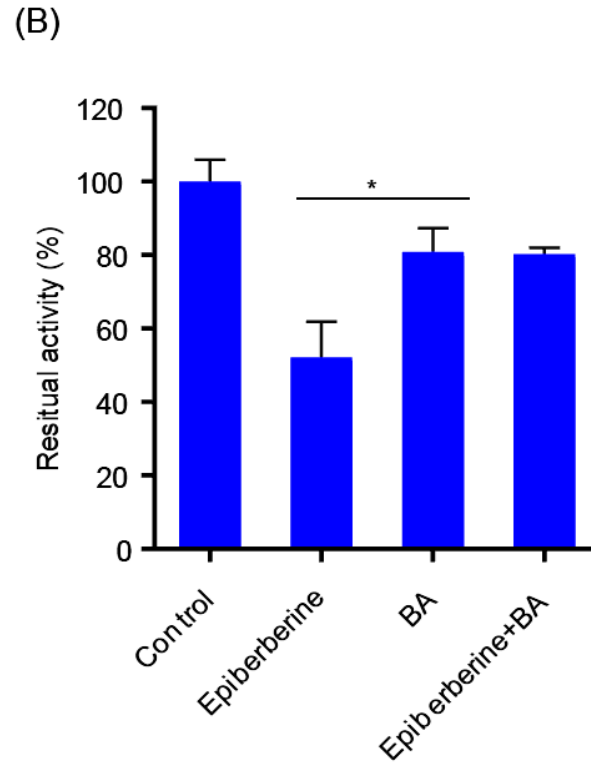
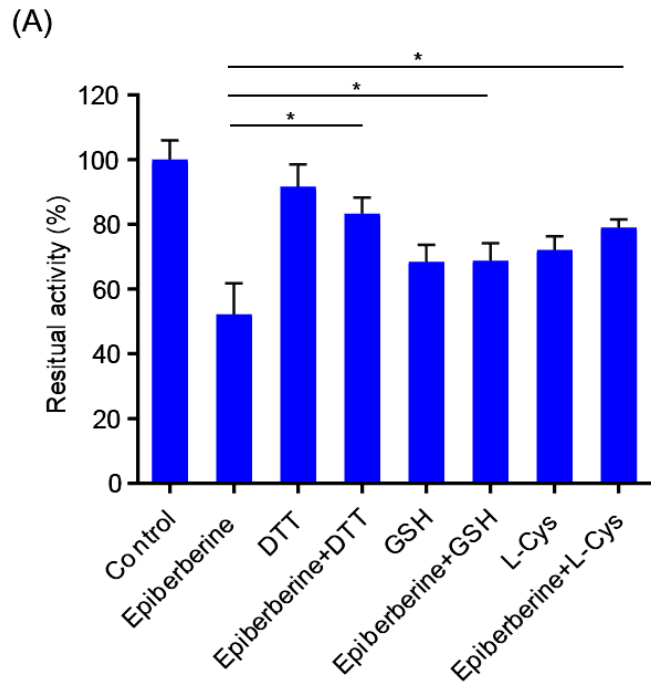


(F)





# Mechanism of Urease Inhibition by Epiberberine



## Interactions

- Coventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Sigma
- Pi-Alkyl
- Pi-Cation

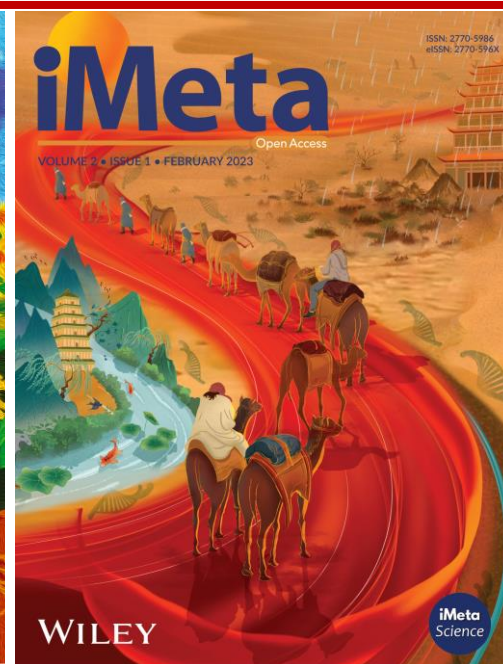


# Conclusion

- ❑ We have developed and experimentally validated an innovative methodology for targeted modulation of microbial community functions.
- ❑ We successfully identified the key microbial urease responsible for urea metabolism and demonstrated that the plant-derived epiberberine serves as a highly effective inhibitor of rumen microbial urease activity.


Shengguo Zhao, Huiyue Zhong, Yue He, Xiaojiao Li, Li Zhu, Zhanbo Xiong, Xiaoyin Zhang, et al. 2025. Leveraging core enzyme structures for microbiota targeted functional regulation: Urease as an example. *iMeta* 4: e70032.

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