

# Fighting food contamination with artificial intelligence: a general framework for identifying novel toxin-degrading enzymes

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## 1 Motivation & Method

**Mycotoxin contamination** of food and feed remains a continuing safety issue. Global investigations have revealed that mycotoxins were detected in ~70% of crop samples<sup>1</sup>. Enzyme-based mycotoxin elimination is a highly specific, safe, and environmentally friendly treatment solution; however, few specific mycotoxin-degrading enzymes have been reported<sup>2,3</sup>.

- **An enzyme promiscuity prediction model**, named PU-EPP, was developed based on positive-unlabeled deep learning and used for screening mycotoxin-degrading enzymes (Fig 1);
- **Two mycotoxins** with high contamination levels, zearalenone (ZEA) and ochratoxin A (OTA), were selected as case studies;
- **A cell-free protein expression system** was used to verify the enzymes' activities; ten enzymes for each toxin were selected according to the prediction of PU-EPP.

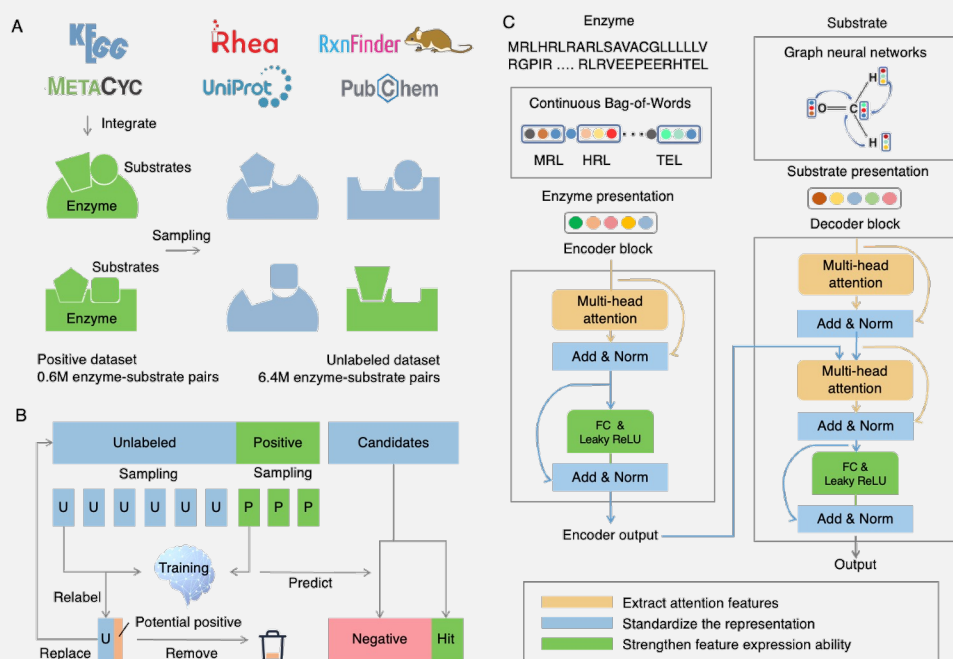


Fig 1. The framework of the positive unlabeled learning-based enzyme promiscuity prediction (PU-EPP) model. (A) Known enzyme-substrate pairs were collected from Rhea, KEGG, MetaCyc, and RxnFinder. (B) Framework of PU learning. (C) Detailed implementation of PU-EPP.

## 4 Contribution to Sustainable Food Systems

Mycotoxin contamination leads to significant losses in livestock production and human health risks. With climate change and new agricultural practices, the level of contamination has been estimated to increase in the future.

We expect that the PU-EPP proposed herein will become a useful tool for discovering specific enzymes to eliminate food contaminants efficiently, improving food quality and reducing food loss.

## 2 Results

- **PU-EPP achieved better performance** than previous models;
- **15 new ZEA and OTA degrading enzymes** were identified in 29d, of which six could degrade >90% mycotoxin content within 3 h. In food matrices, they still could degrade mycotoxins despite a certain decrease in activity (Fig 2);
- **A general framework was proposed** based on PU-EPP and cell-free expression to identify enzymes for other contaminants.

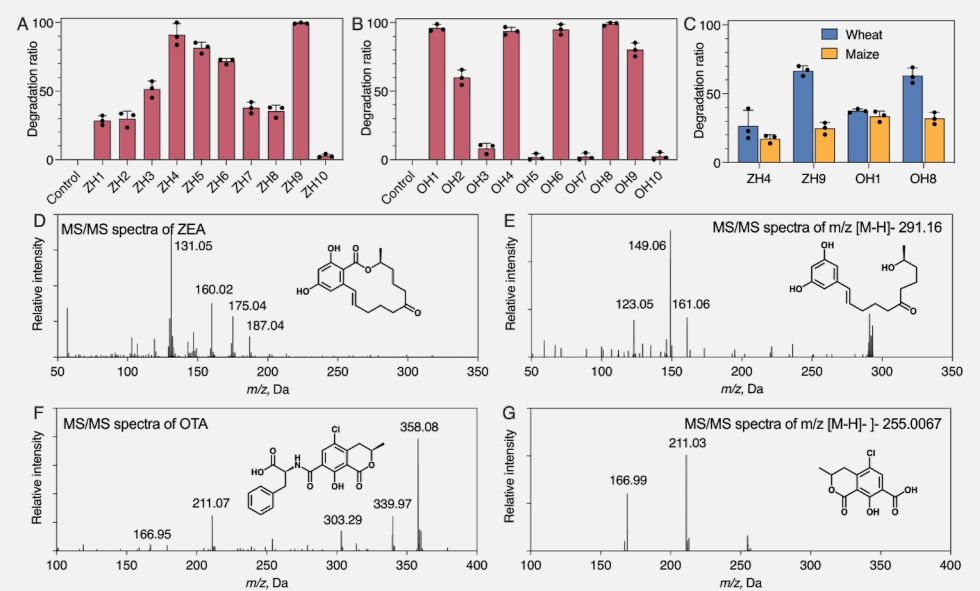


Fig 2. Experimental verification of the catalytic activity of candidate enzymes. (A, B) The degradation ratio of enzymes on mycotoxins ZEA and OTA. (C) The degradation ratio of enzymes for mycotoxin in wheat and maize flour. (D-G) The MS/MS spectra of ZEA and OTA and their degradation products. Error bars represent  $\pm$  s.d.

## 3 Conclusion

- A general framework is proposed, which shortens the time needed for new enzyme discovery from years to 29 days;
- It can better elucidate the biotransformation capacity of living organisms;
- It enables identifying important enzyme residues, which can assist in enzyme modification and ultimately promote the practical application of enzymes.

