We use molecular features and metric learning to predict gene expression

Cheminformatics deciphers stress response and virulence pathways in infection

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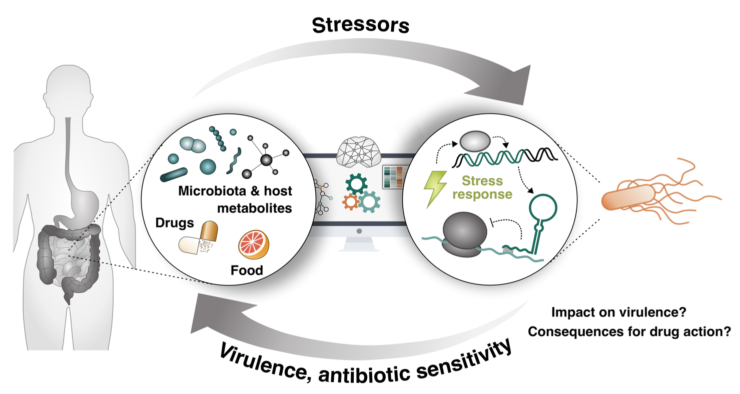
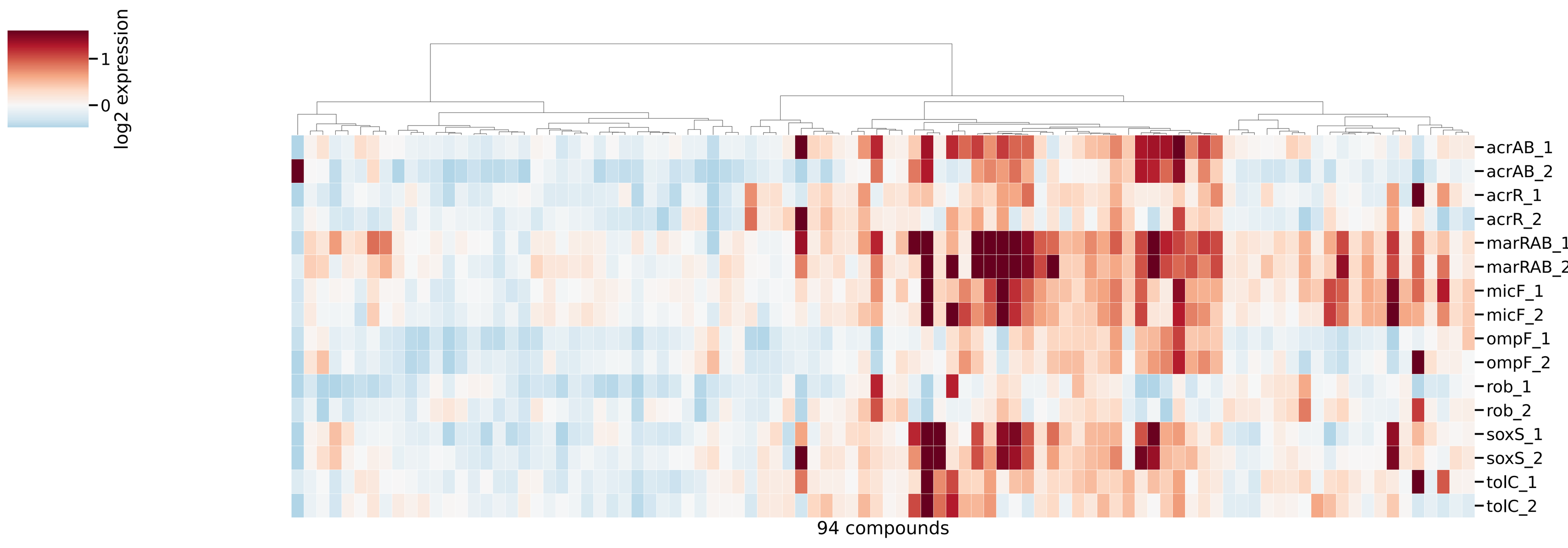
Small compounds and their effect on microbes

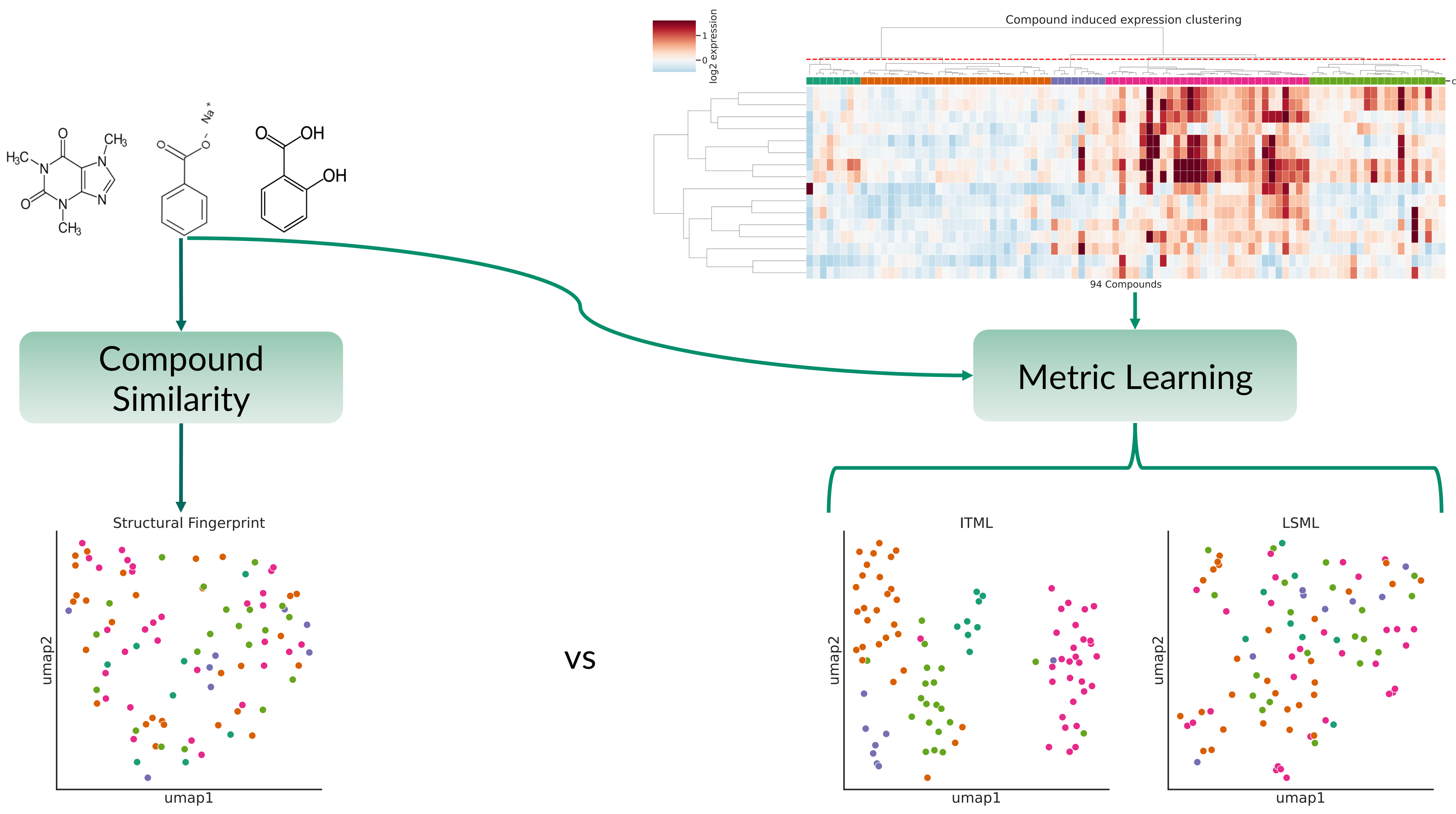
Much is unknown about which chemical signals trigger different stress responses in bacterial pathogens. Reporter assay experiments are time-consuming and expensive. **Compounds must be prioritized for further study.**





Structural fingerprints and metric learning

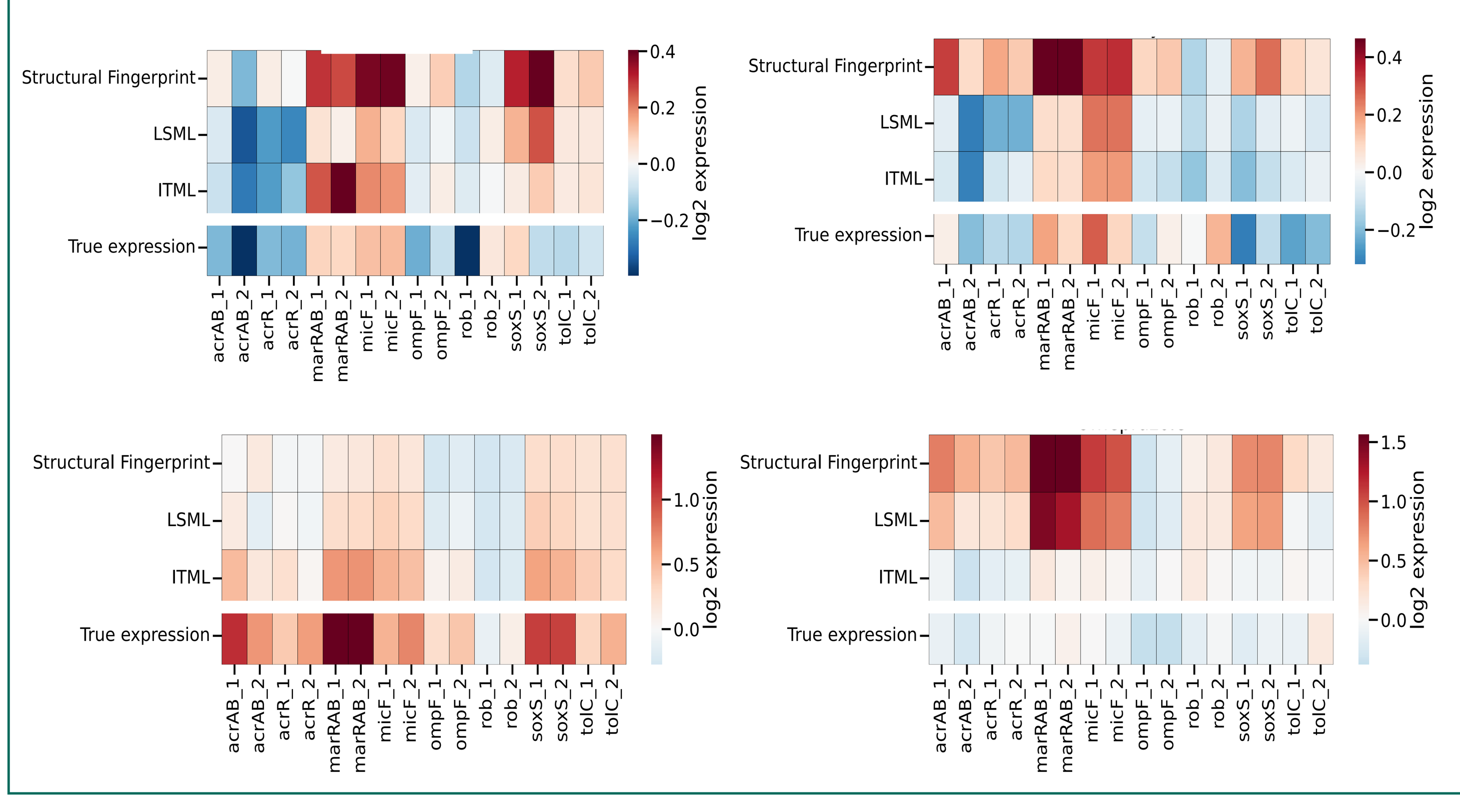
Structural fingerprints alone are partially predictive of the expression pattern they induce. We use metric learning to **learn a molecular representation that is more predictive of gene expression.**



Predicting the effect of new compounds

Using the learned molecular representation, we **predict the expression patterns induced by *unseen* compounds.**

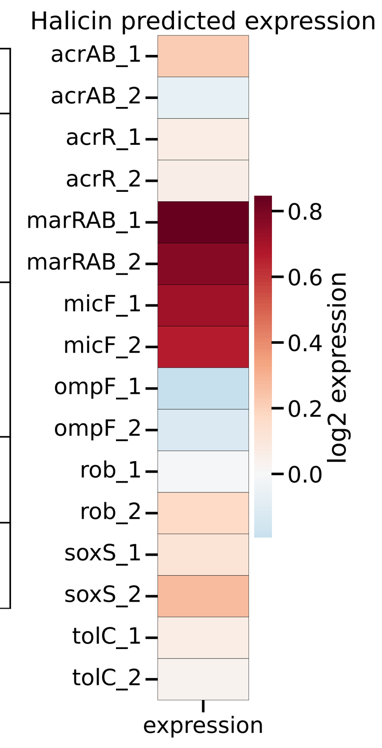
This can **enable the characterization of novel antibiotics and adjuvants**, such as Halicin.



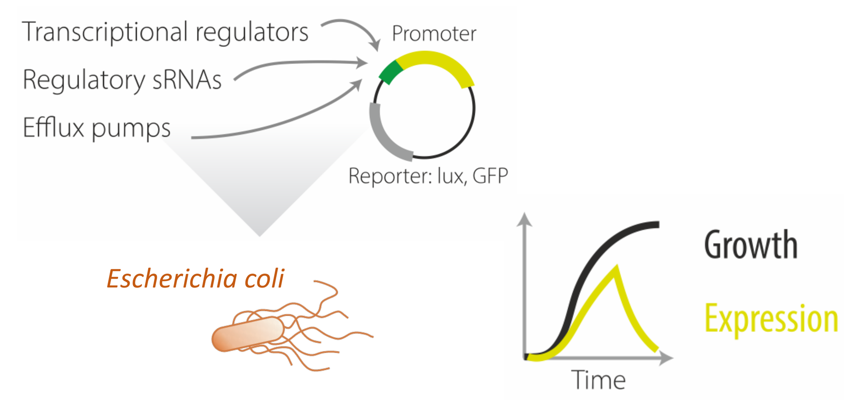
Halicin Nearest Neighbours

Name	Class
4-aminosalicylic acid	Antibiotic
Sodium benzoate	Antifungal
Metronidazole	Antibiotic
Trimethoprim	Antibiotic

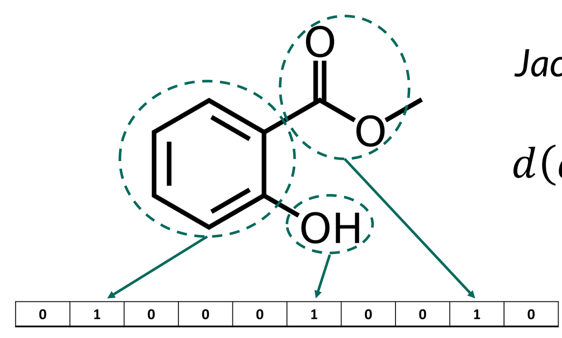
Halicin predicted expression



Reporter assay experiments

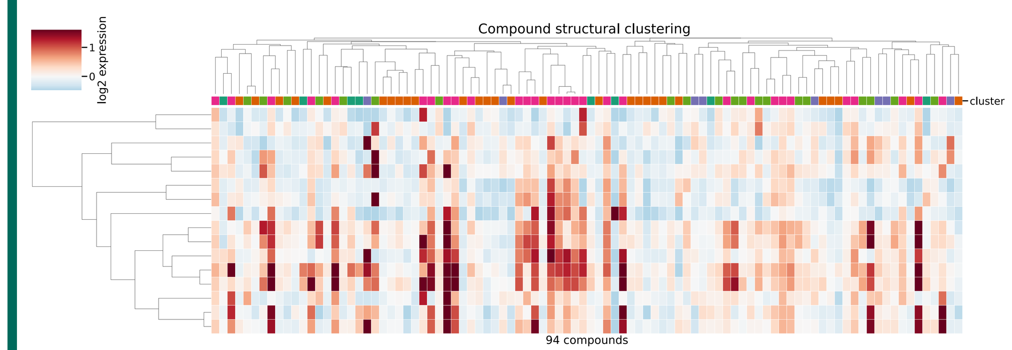


Structural fingerprints



Jaccard distance

$$d(a,b) = \frac{|a \cup b| - |a \cap b|}{|a \cup b|}$$



Metric Learning

Information Theoretic Metric Learning:

$$\min_{A} KL(p(\boldsymbol{x};A_0)||p(\boldsymbol{x};A))$$

$$s.t. \quad d_A(\boldsymbol{x}_i,\boldsymbol{x}_j) \le u \quad (i,j) \in S$$

$$d_A(\boldsymbol{x}_i,\boldsymbol{x}_j) \ge l \quad (i,j) \in D$$

Model selection

Makine a new prediction

$$u(\boldsymbol{x}) = \frac{\sum_{i=1}^{N} w_i(\boldsymbol{x}) u_i}{\sum_{i=1}^{N} w_i(\boldsymbol{x})}$$

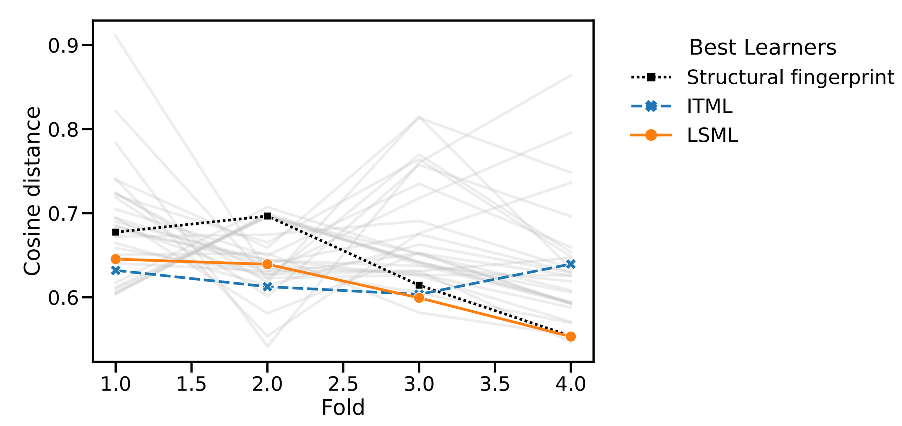
Inverse distance weighting

$$w_i(\boldsymbol{x}) = \frac{1}{d(\boldsymbol{x}, xi)}$$

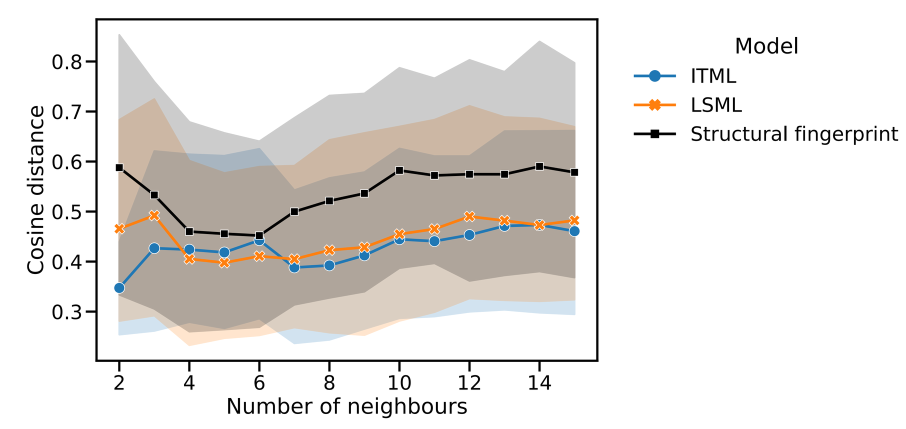
Evaluating a new prediction

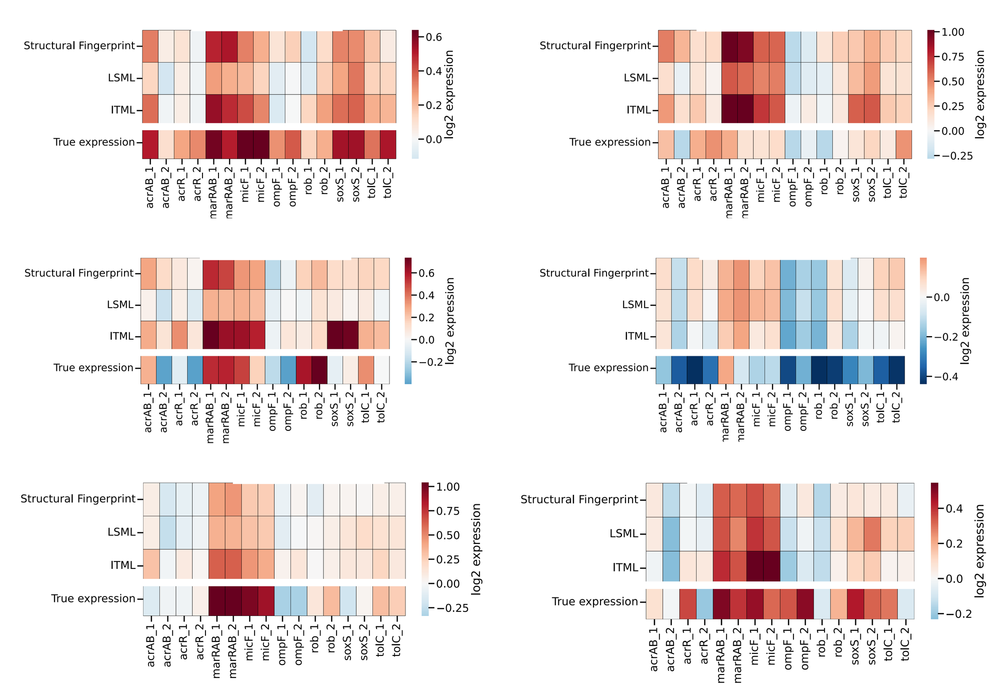
$$d(u,v) = 1 - \frac{u \cdot v}{||u||_2 ||v||_2}$$

Cosine distance



Out of bag predictions





Literature:

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