



THE UNIVERSITY OF TEXAS  
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# Sex Pheromone Biomimetics for Pest Control and Mechanistic Probing of OfurPBP2

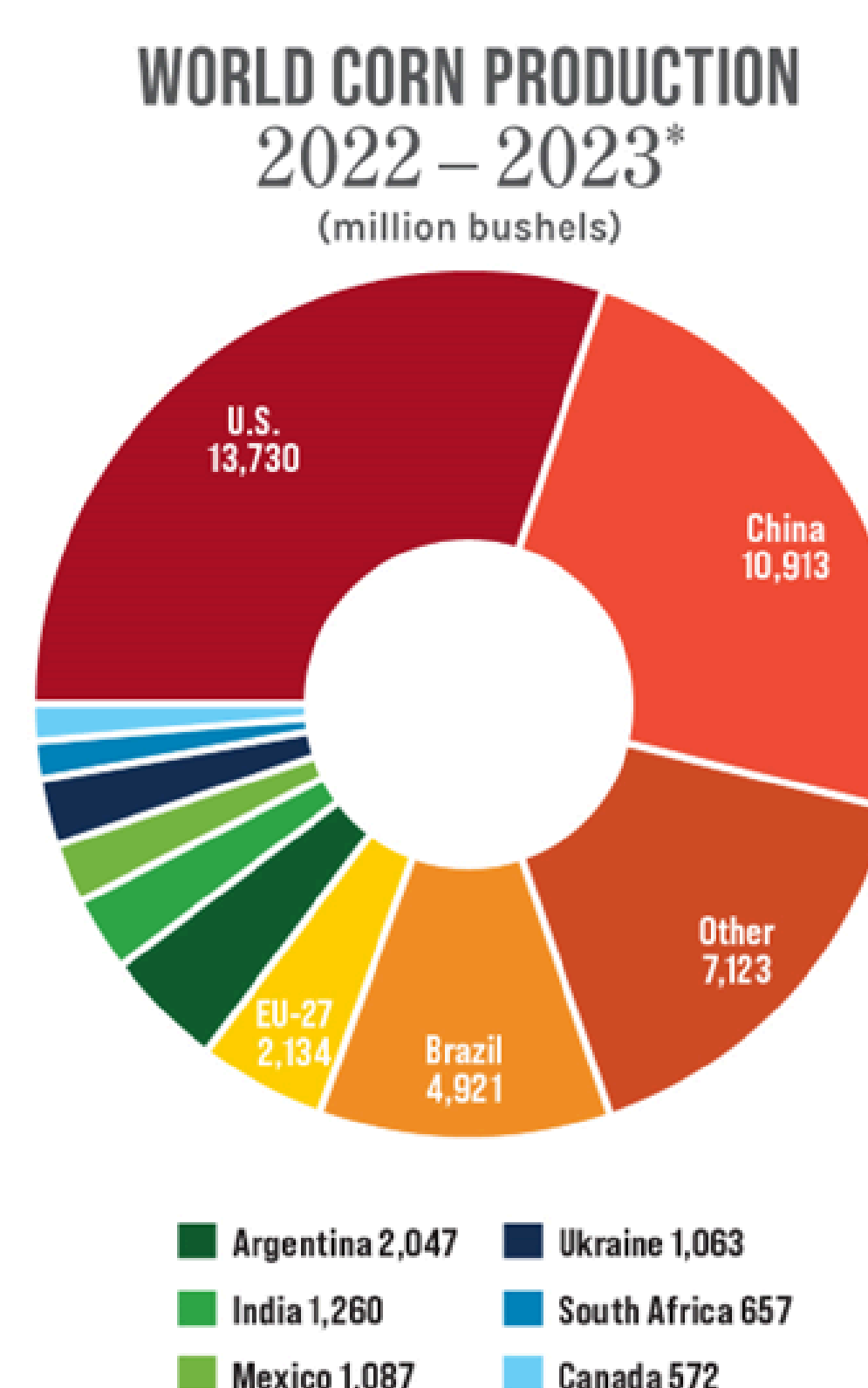
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Functional  
Organic  
Reactions &  
Materials



## ASIAN CORN BORER: AGRICULTURAL PEST

- Ostrinia furnacalis* (Asian Corn Borer) is native to Asia and the Pacific Islands
- Major agricultural pest targeting staple crops such as corn, cotton, millet, and hops
- Responsible for crop losses estimated at 6-9 million tons per year



Source: USDA, FAS Grain: World Markets and Trade, Jan. 12, 2023

\*projected for marketing year Oct. 1, 2022 – Sept. 30, 2023

## TARGET DESIGN

### Lipophilic tail

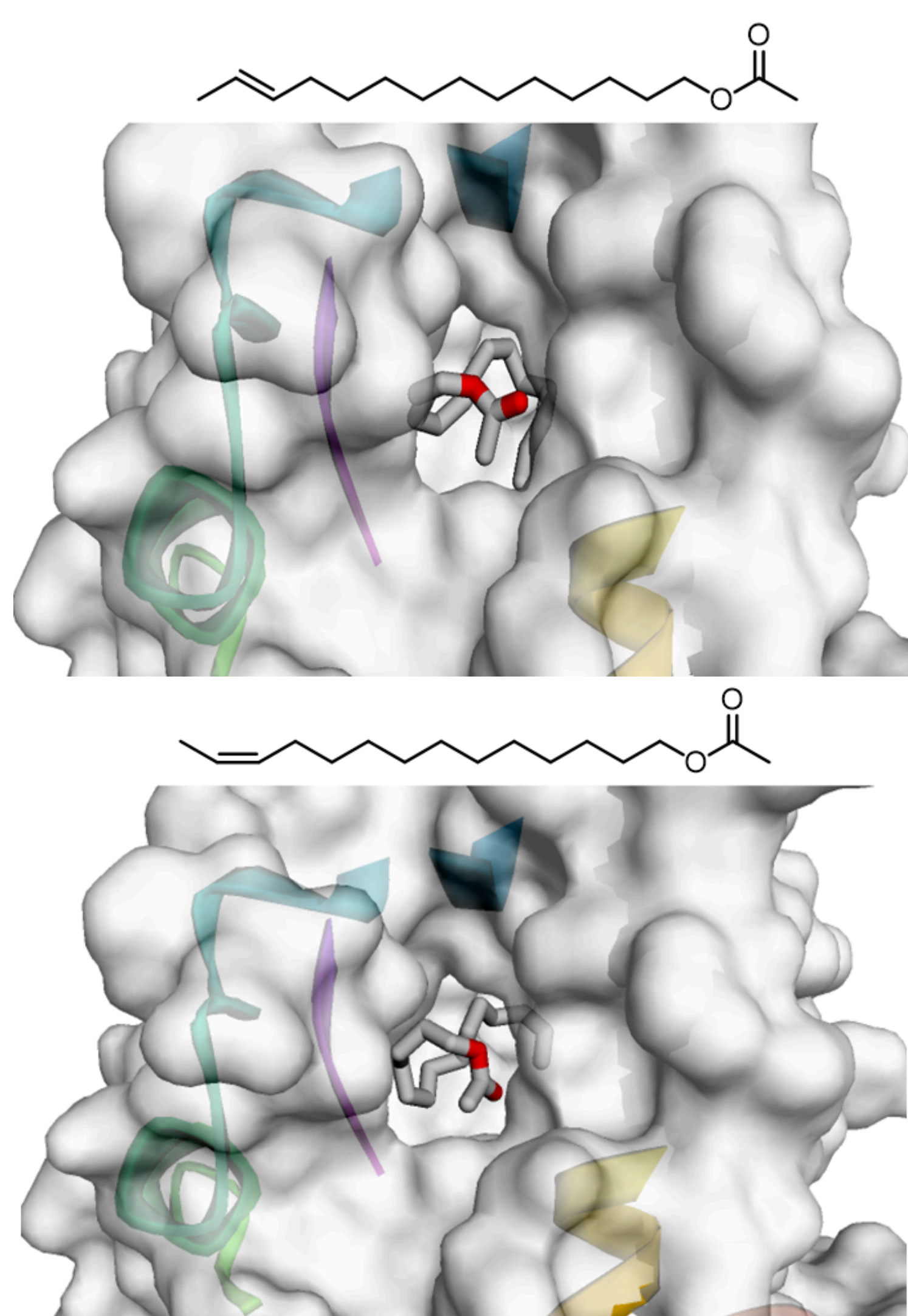
- Size
- Branching
- Electronic nature

### Polar head group

- 2°/3° amides
- 1,2,3-triazole
- 1,2,4-oxadiazole

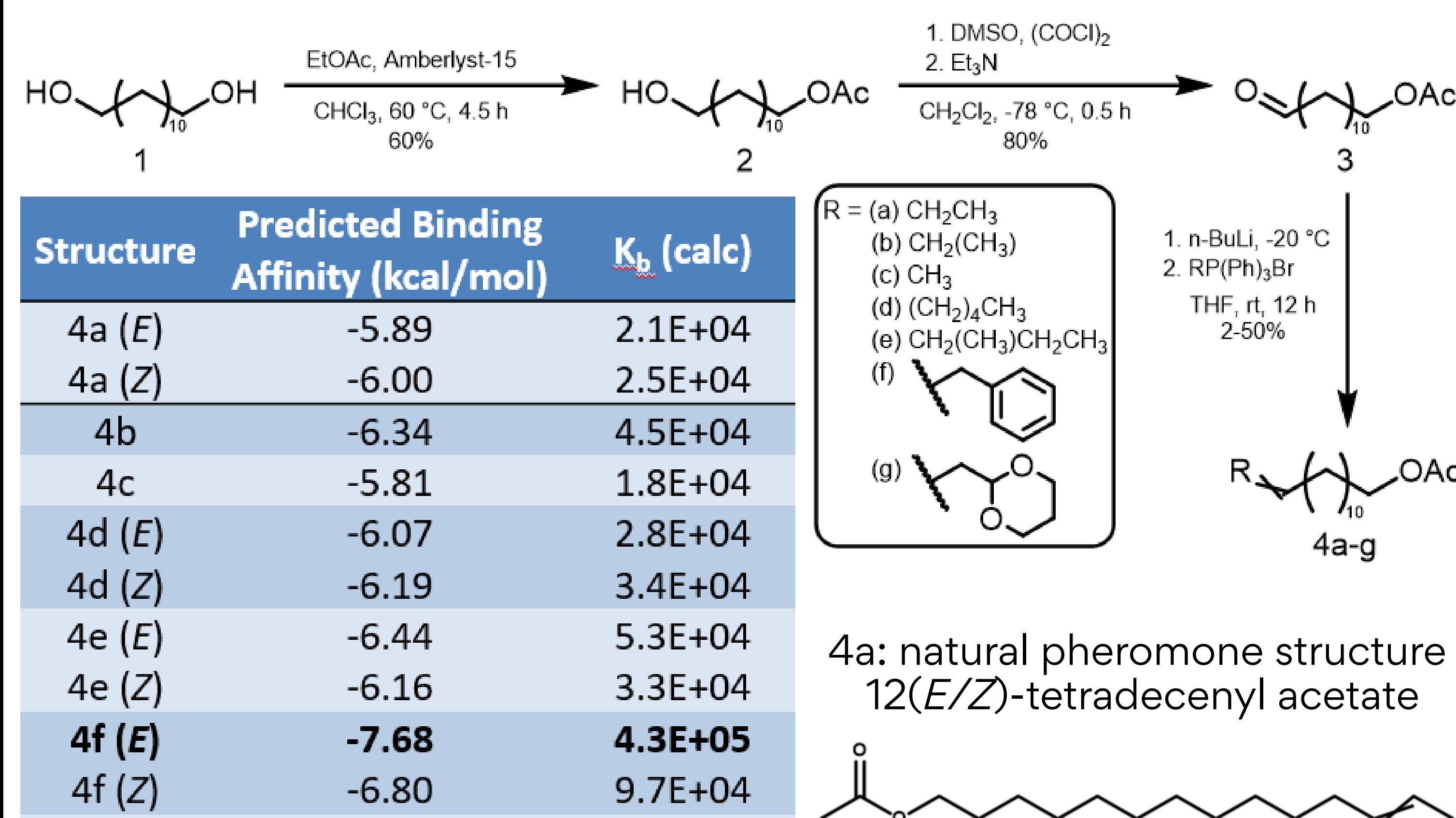
### U-shaped center

- Benzene
- Bicyclo[3.1.1]heptane



Targets docked using Webina, pH set to 6.5  
Eberhardt, J.; Santos-Martins, D.; Tillack, A. F.; Forli, S. *J. Chem. Inf. Model.* **2021**, 61 (8), 3891–3898. <https://doi.org/10.1021/acs.jcim.1c00203>

## LIPOPHILIC TAIL DERIVATIVES



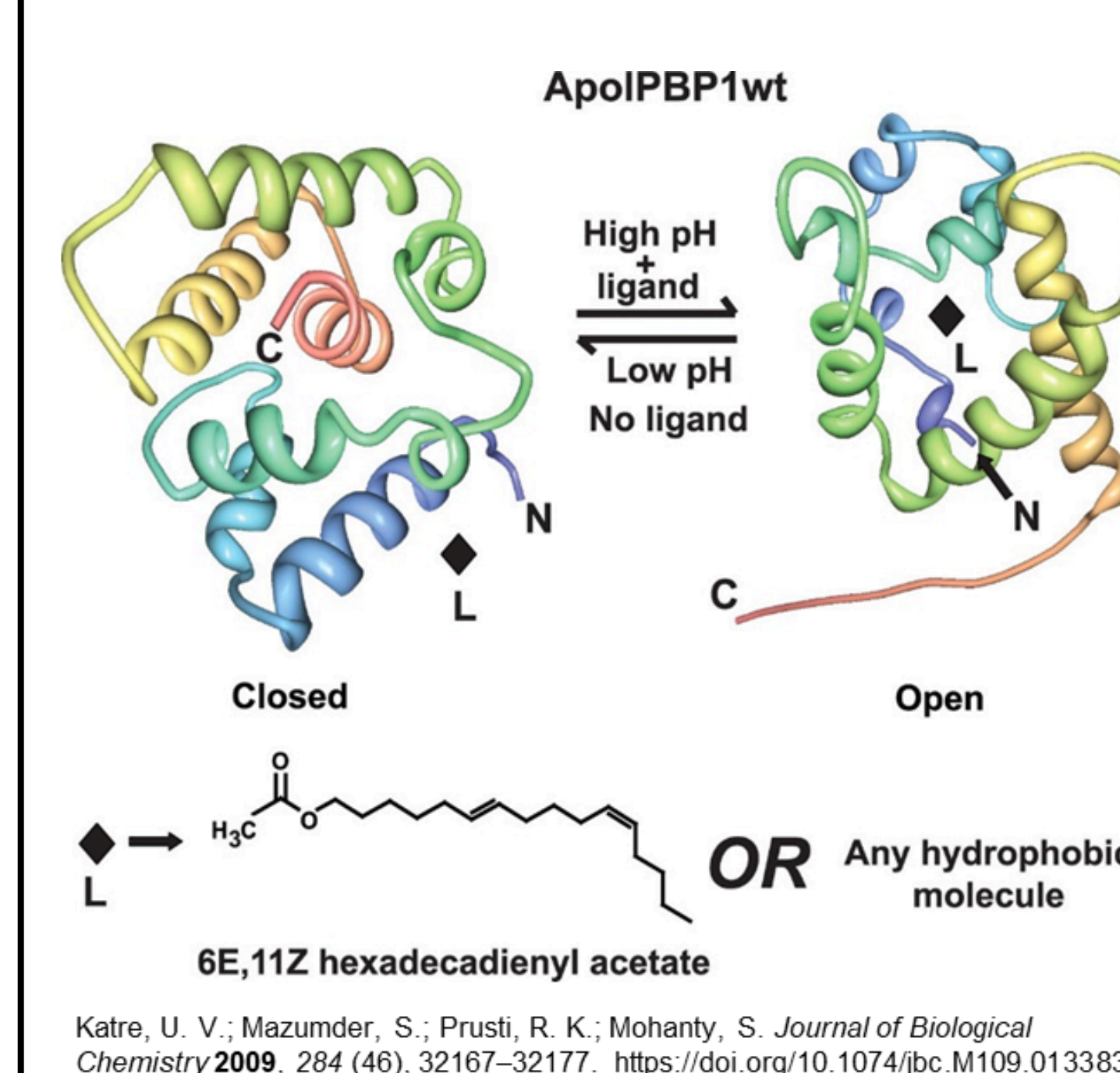
## POLAR HEAD DERIVATIVES

Structure	Predicted Binding Affinity (kcal/mol)	K <sub>b</sub> (calc)
4a (E)	-5.89	2.1E+04
4a (Z)	-6.00	2.5E+04
8 (E)	-6.72	8.5E+04
8 (Z)	-6.46	5.4E+04
11 (E)	-5.60	1.3E+04
11 (Z)	-5.77	1.7E+04
13 (E)	-6.05	2.7E+04
13 (Z)	-6.38	4.8E+04
15 (E)	-6.41	5.1E+04
15 (Z)	-5.87	2.0E+04
18 (E)	-6.54	6.2E+04
18 (Z)	-6.26	3.9E+04

## OPTIMIZED TARGETS

Structure	Predicted Binding Affinity (kcal/mol)	K <sub>b</sub> (calc)
4a (E)	-5.89	2.1E+04
4a (Z)	-6.00	2.5E+04
18a	-9.05	4.4E+06
18b	-8.51	1.7E+06
18c	-8.98	3.8E+06
18d	-9.24	5.9E+06
20a	-7.05	1.5E+05
20b	-7.12	1.7E+05
20c	-7.86	5.8E+05
20d	-7.72	4.6E+05

## MECHANISTIC PROBING



PBP mechanism known for several other Lepidopteran species including *Antheraea polyphemus*, *Bombyx mori*, and *Amyelois transitella*

### At pH 4.5:

- Helical C-terminus competes for the binding pocket
- N-terminal histidine gate open

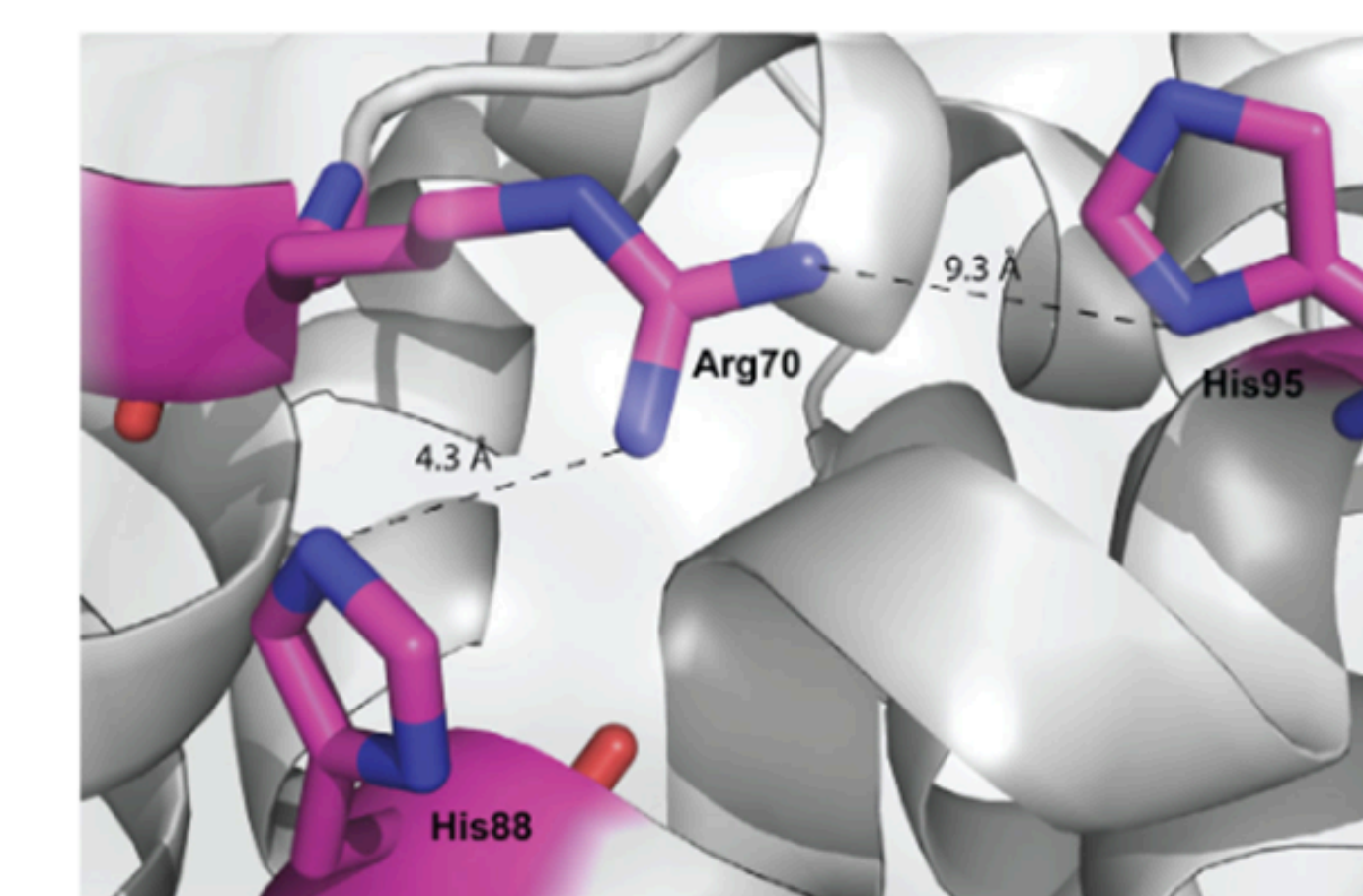
### At pH 6.5:

- Unstructured C-terminus leaves binding pocket open for ligand
- N-terminal histidine gate closed

### Unique features of OfurPBP2:

- C-terminal has four additional charged residues at pH 4.5
- C-terminal observed as a helix at pH 6.5, but overall protein exhibits flexible structure at pH 4.5
- N-terminal gate His70 substituted with Arg, additional His88

OfurPBP2 TEIHKLNWAPDHELLEEMMAEMKQ 144  
ApolPBP1 KEIHKLNWVPMDLVIGEVLAEV-- 142  
BmorPBP AEIHKLNWAPSMDEVAVGEILA EV-- 142  
AtrapBP1 KEIHNKWA PMDEVVVG EVLA EV-- 142



Dahal, S. R.; Lewellen, J. L.; Ayyappan, S.; Chaudhary, B. P.; Nukala, V.; Mohanty, S.

### Hypotheses:

- C-terminal does not occupy hydrophobic pocket in the ligand-free form
- C-terminal gate does not play a role in binding/release
- N-terminal gate (Arg70-His95) does not play a role in binding/release

## FUNDING AND COLLABORATION



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