

# Peptide Design

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Article

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## Accurate de novo design of high-affinity protein-binding macrocycles using deep learning

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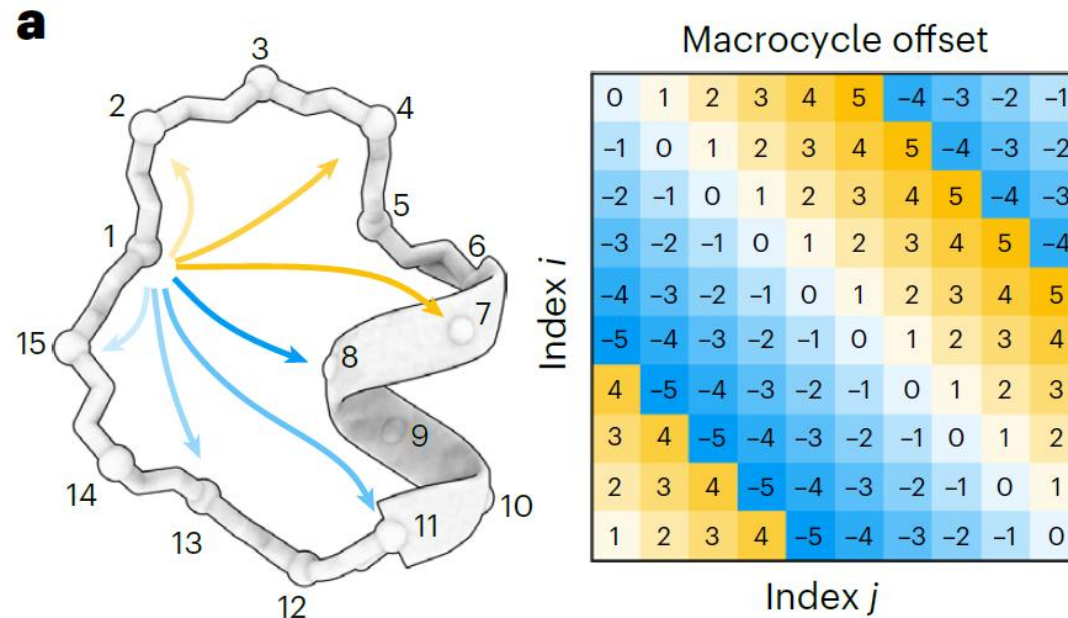
Check for updates

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Developing macrocyclic binders to therapeutic proteins typically relies on large-scale screening methods that are resource intensive and provide

Relevant for exam: Figures 1 (excluding 1c, 1d), 2, 3 and 4

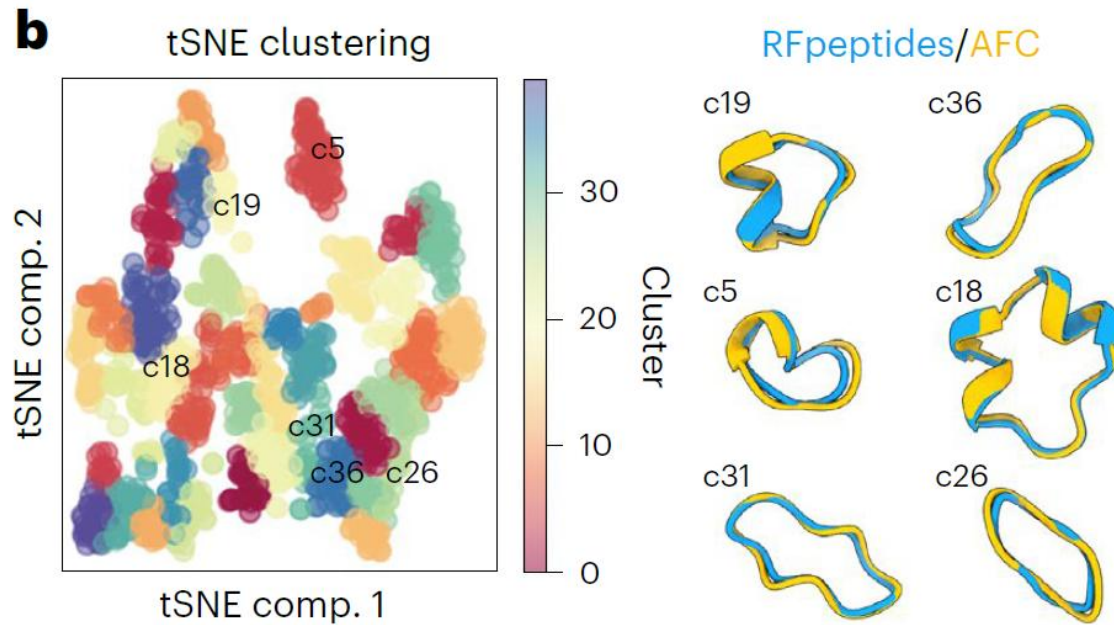
# Figure 1a



“... implemented a modified cyclic relative position encoding for RF2 ...”

- What is RF2?
- What is «cyclic positional encoding scheme»

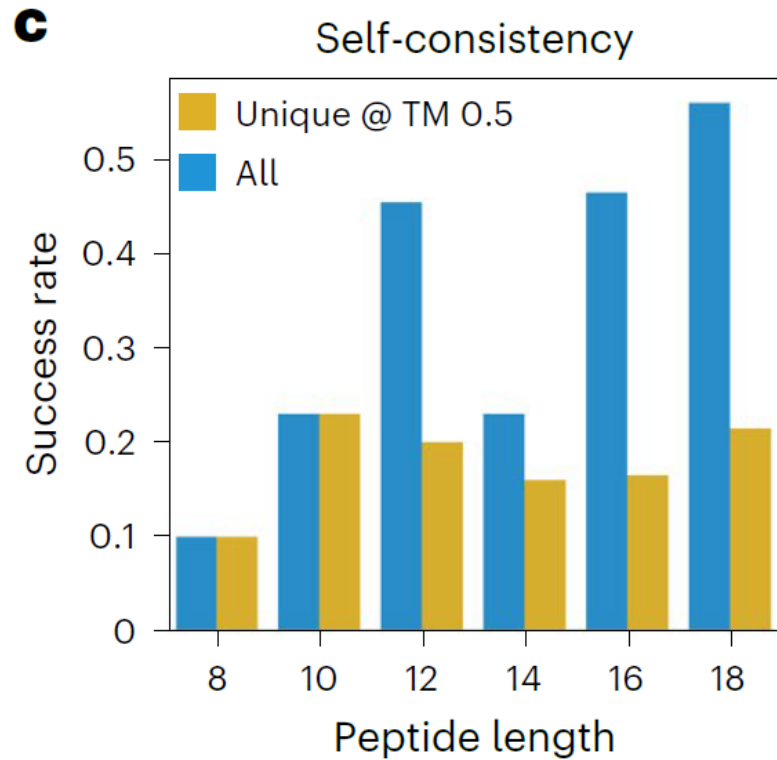
# Figure 1b



“... applied RF2 diffusion to generate 48'000 macrocyclic peptide backbones ...”

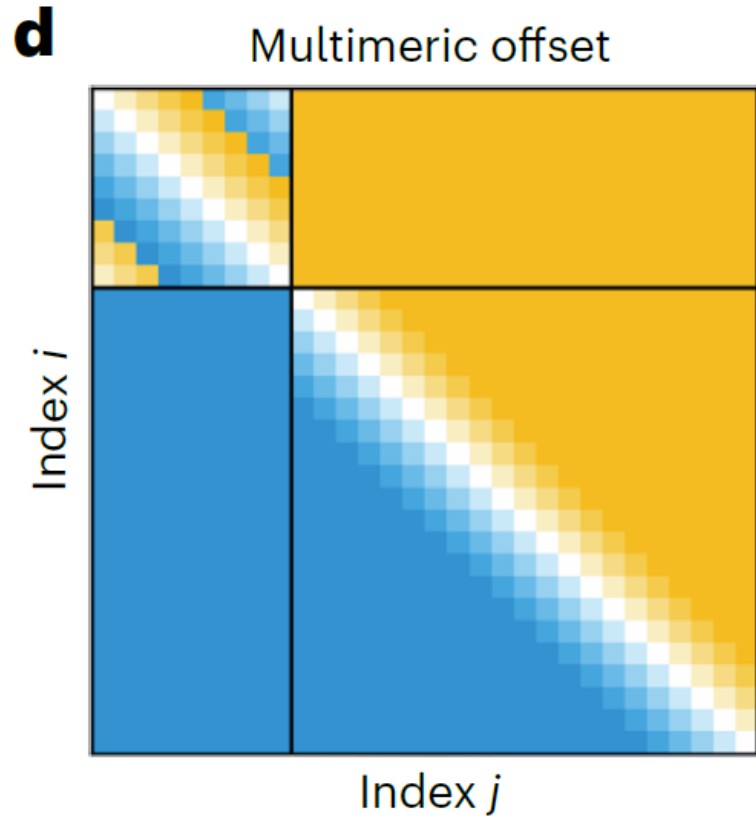
- How long were cyclic peptides?
- How many backbones were found?
- What are the «color patches» (left)?
- What are blue/yellow structures (right)?

# Figure 1c



- What is this graph showing?

# Figure 1d

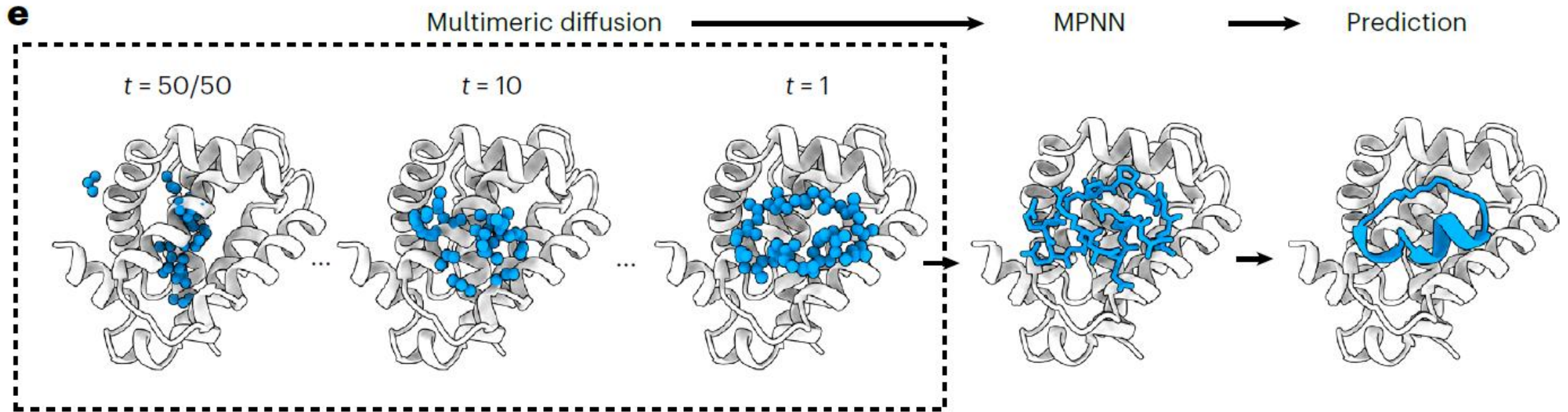


“... cyclic relative position  
encoding for peptide chain ...”

“... standard positional encoding  
for target ...”

- What is this figure showing?

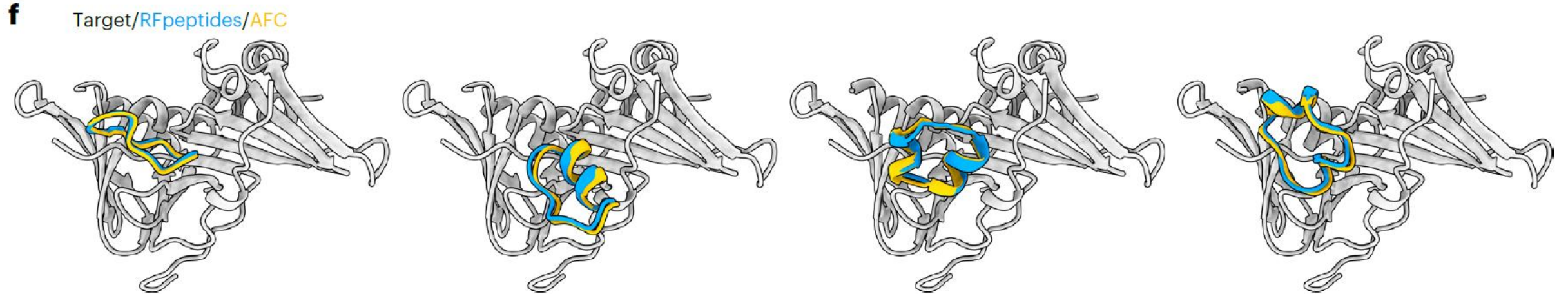
# Figure 1e



What are the following steps in this workflow:

- Multimeric diffusion?
- MPNN?
- Prediction?

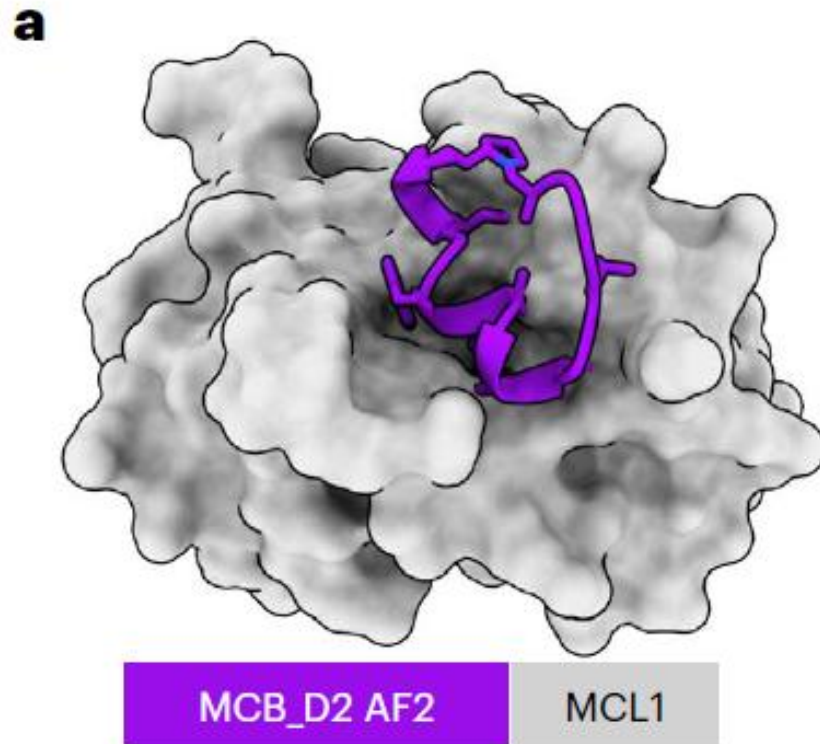
# Figure 1e



What do these four figures/structures represent?

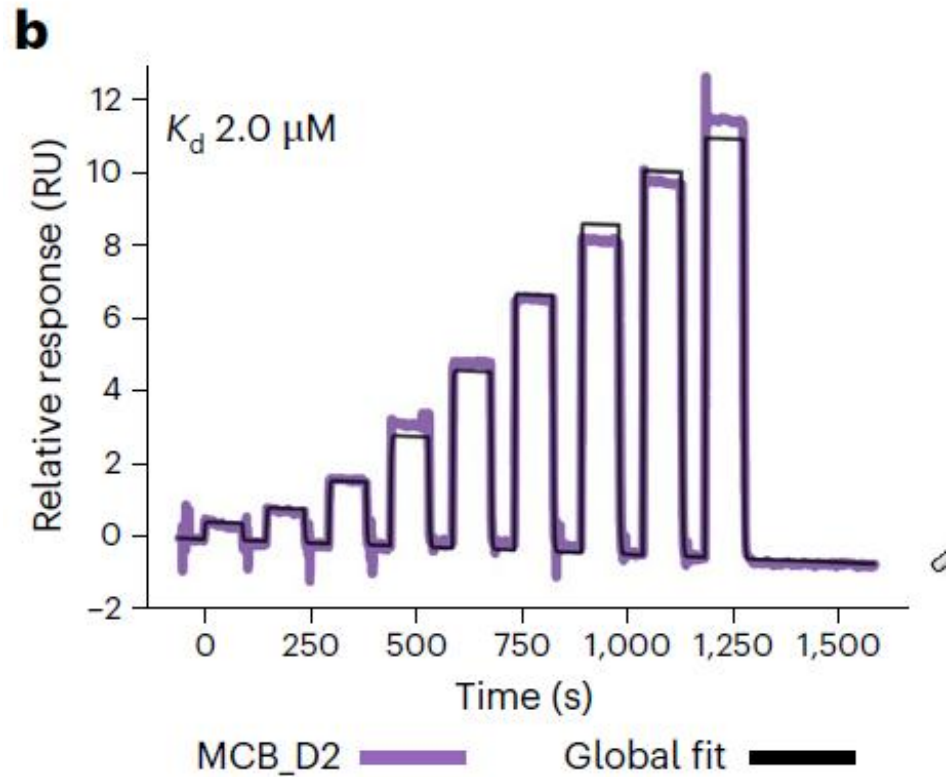
- White/grey: target?
- Blue: RF peptides?
- Yellow: AFC?

## Figure 2a



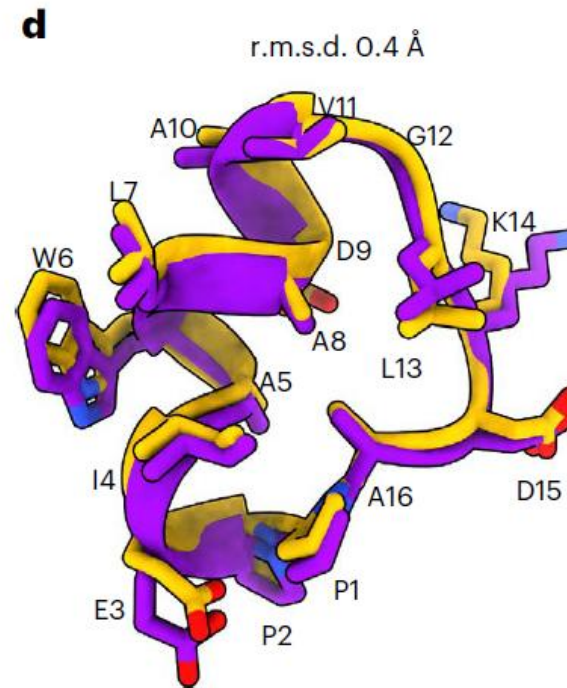
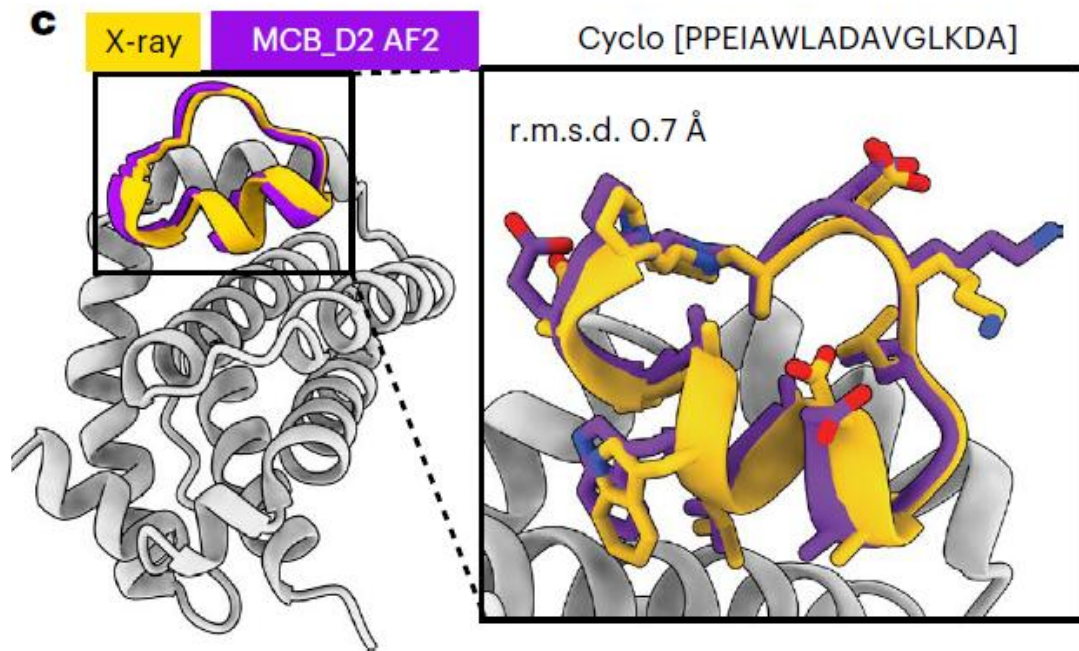
- Target?
- 1984 designs were found: How were they downselected?
- How many were synthesized / obtained?

# Figure 2b



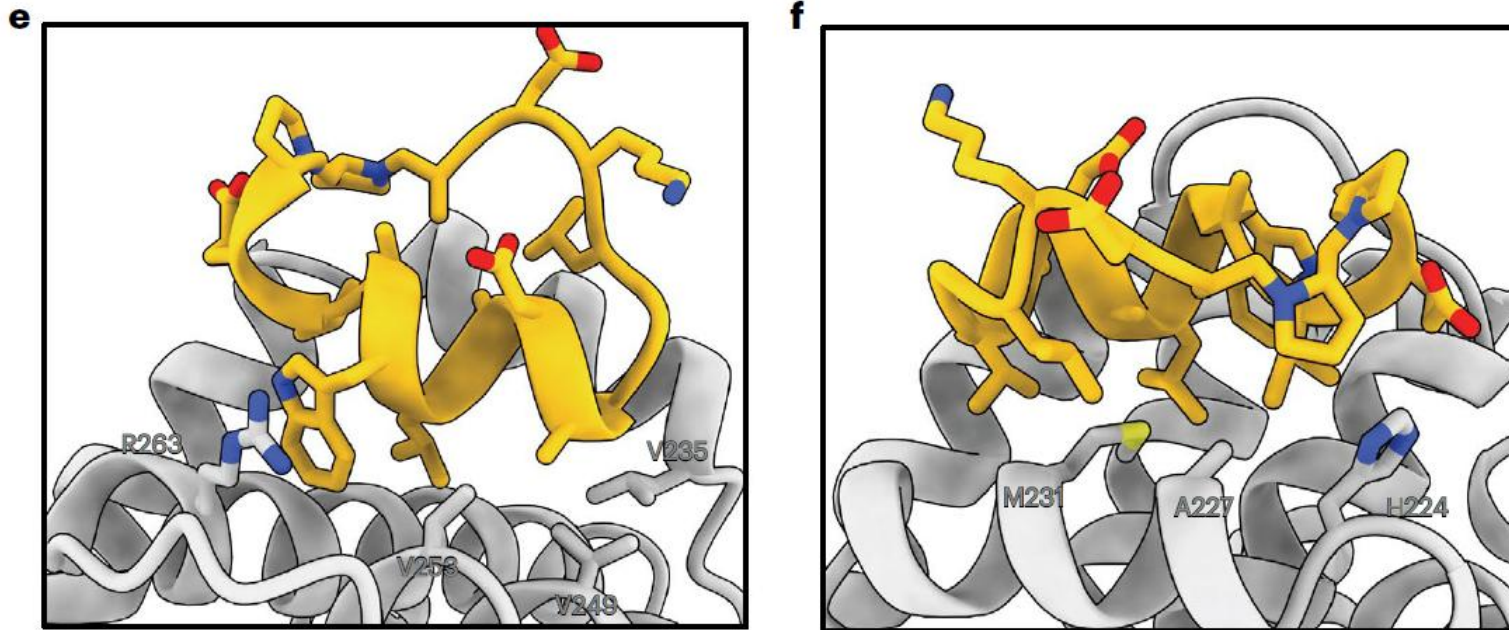
- What is this graph showing?
- X-axis? Y-axis?
- Grey color? Purple color?
- Binding affinity?

# Figure 2c



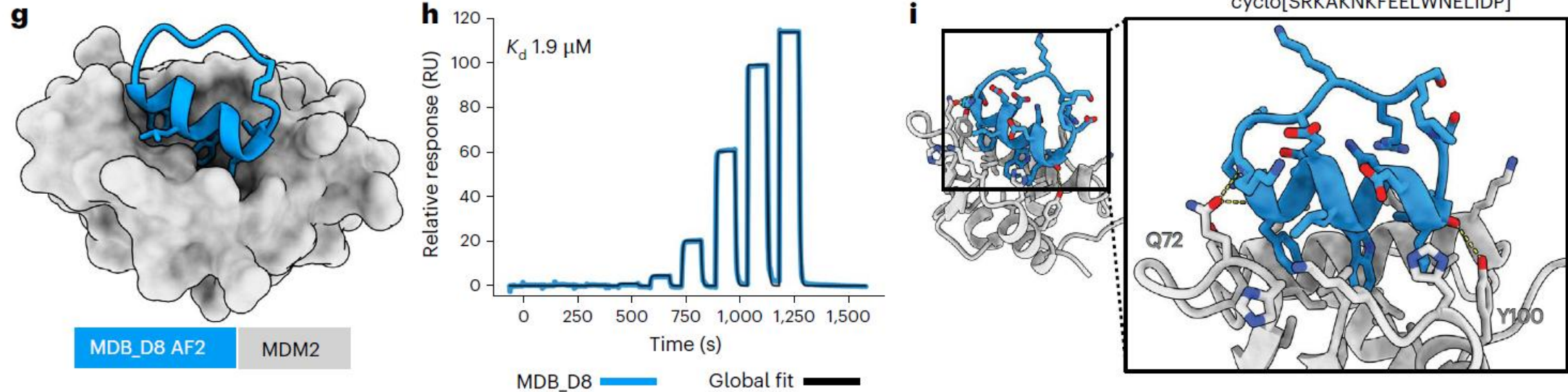
- What is this structure showing?
- Yellow?
- Purple?

## Figures 2e and 2f



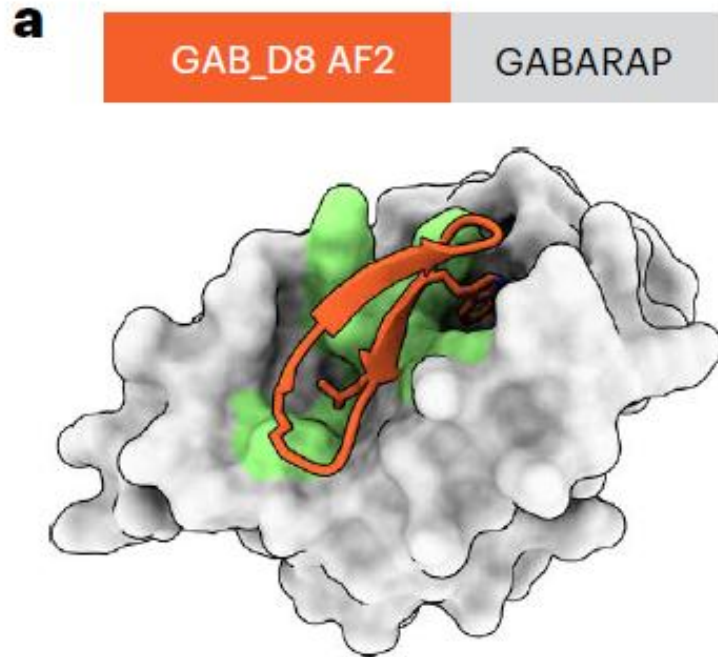
What do they want to show with these two structures?

# Figure 2g-i



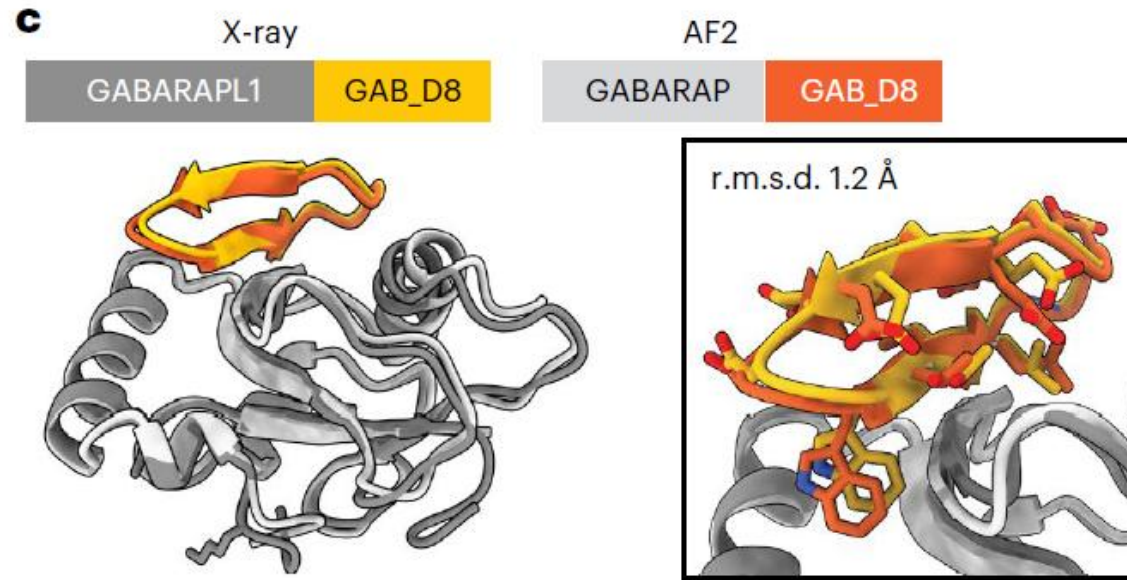
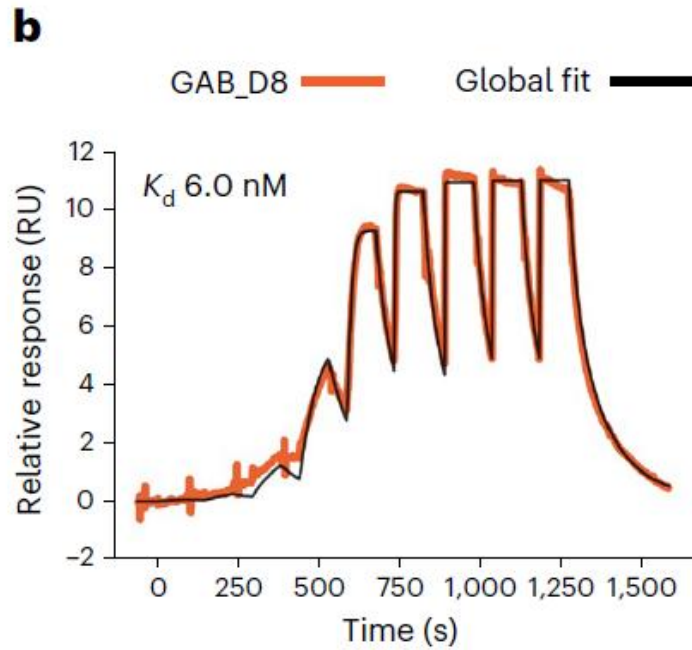
- Target?
- How many backbones designed?
- Length of cyclic peptides?
- How were the designs ranked?
- How many were synthesized/obtained?
- Best affinity?
- Are the structures in (g) and (i) models or based on experimental data?

# Figure 3a



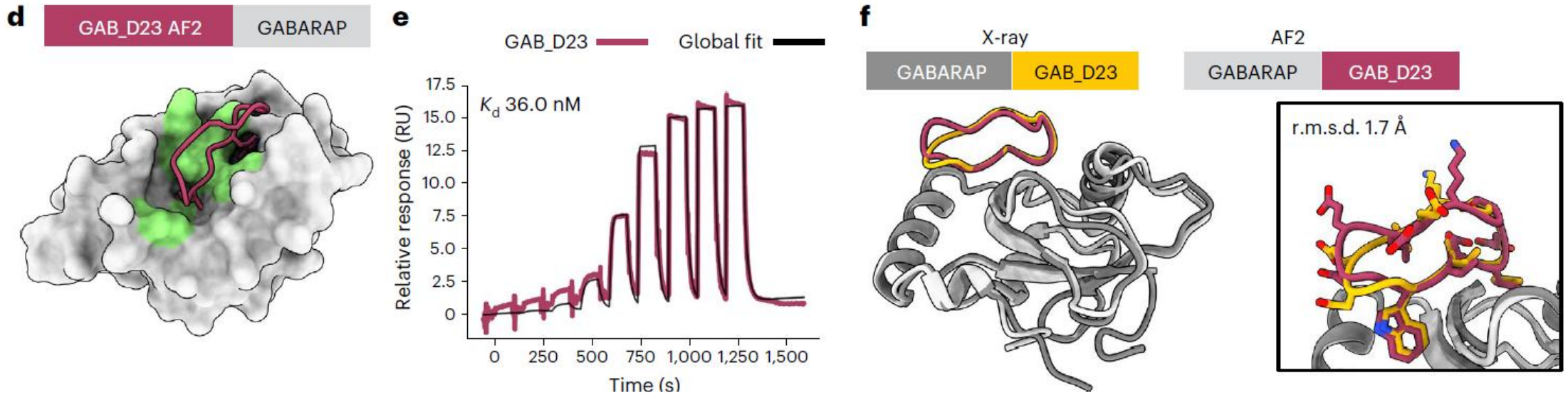
- Target?
- Binders designed to a random site?
- How many backbones designed?
- How many peptide sequences designed?
- Length of cyclic peptides?
- How were the designs ranked?

# Figure 3b-c



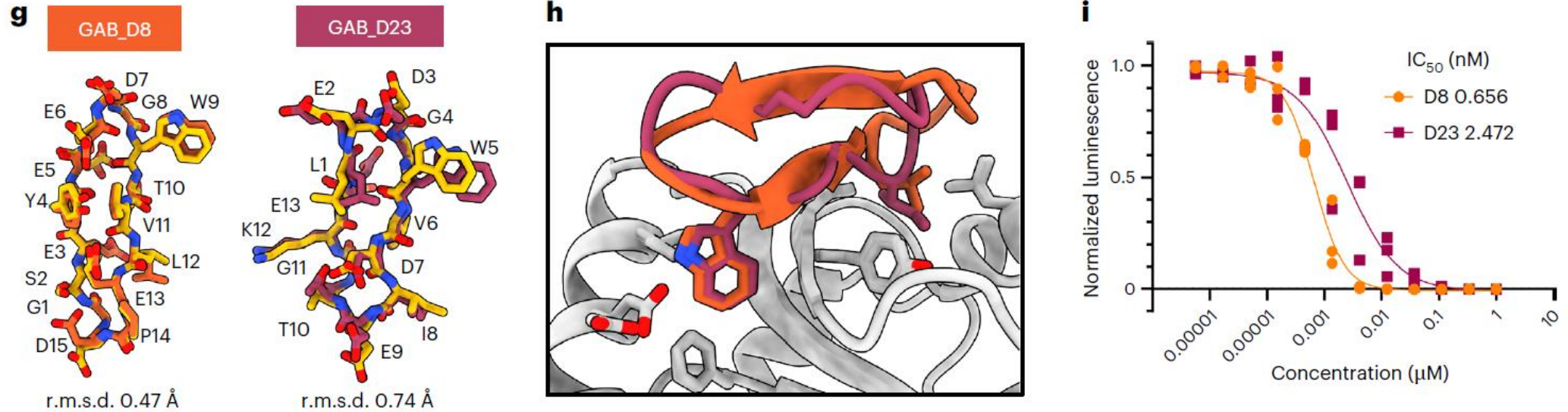
- Affintiy? Method?
- Structures:
  - Orange?
  - Yellow?

# Figure 3d-f



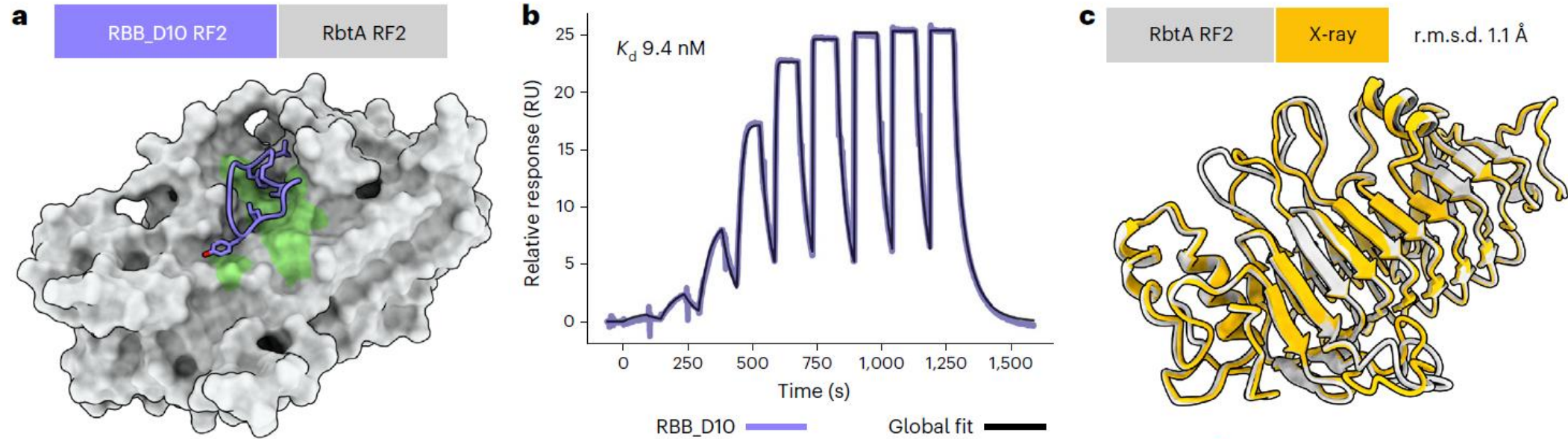
- Difference to Figures 3a-c?

# Figure 3g-i



- What are these panels showing?
- Were peptides binding GABARAP previously known?

# Figure 4a-c



- Target?
- What was new/particularly challenging with this target?
- Binders directed to hotspot region?
- Number of designed backbones?
- Number of designed sequences?
- How many were chosen and how?
- How many were tested?

# Figure 4d-h

