

## Job summary

<b>Job ID:</b>	5c45-demo
<b>Date:</b>	2026-05-11 21:05 UTC
<b>Sequence length:</b>	54 nt
<b>Conformers:</b>	5
<b>Pockets detected:</b>	12 (across all frames)
<b>Clusters:</b>	6 (3 passing persistence floor)
<b>Top-3 surfaced:</b>	3
<b>RhoFold pLDDT (mean):</b>	75.369

## Sequence:

GGAUUUUCGGGGCAGGGUGAAAUUCCCGACCGGUGGUAUAGUCCACGAAAAGCUU

# Top-3 candidate druggable pockets

## #1 Cluster 0 (geometric rank #1)

NEAR (40%)

**Persistence:**

1.00 (5 of 5 frames)

**Geometric score (ranking):**

5.000 = persistence × n\_residues\_intersected (1.00 × 5)

**Mean druggability (metadata, not ranking):**

0.025 -- fpocket protein-trained score, see Methods

**Median druggability:**

0.008

**Max druggability:**

0.098

**Centroid (A):**

5.17 -0.80 4.15

**Residues (union):**

9, 10, 11, 31, 32, 33, 34, 35, 41, 42

**Residues (intersection):**

9, 10, 32, 33, 41

**Binding-site overlap (benchmark):**

2/5 residues (40%) - near ( $\geq 30\%$  of binding-site residues)

## #2 Cluster 2 (geometric rank #2)

NEAR (40%)

**Persistence:**

0.40 (2 of 5 frames)

**Geometric score (ranking):**

2.000 = persistence × n\_residues\_intersected (0.40 × 5)

**Mean druggability (metadata, not ranking):**

0.006 -- fpocket protein-trained score, see Methods

**Median druggability:**

0.006

**Max druggability:**

0.013

**Centroid (A):**

-1.72 4.88 2.26

**Residues (union):**

10, 11, 12, 29, 30, 31

**Residues (intersection):**

10, 11, 12, 30, 31

**Binding-site overlap (benchmark):**

2/5 residues (40%) - near ( $\geq 30\%$  of binding-site residues)

## #3 Cluster 1 (geometric rank #3)

NONE (0%)

**Persistence:**

0.40 (2 of 5 frames)

**Geometric score (ranking):**

1.600 = persistence × n\_residues\_intersected (0.40 × 4)

**Mean druggability (metadata, not ranking):**

0.277 -- fpocket protein-trained score, see Methods

**Median druggability:**

0.277

**Max druggability:**

0.302

**Centroid (A):**

-11.88 19.67 -11.99

**Residues (union):**

18, 19, 21, 22, 24

**Residues (intersection):**

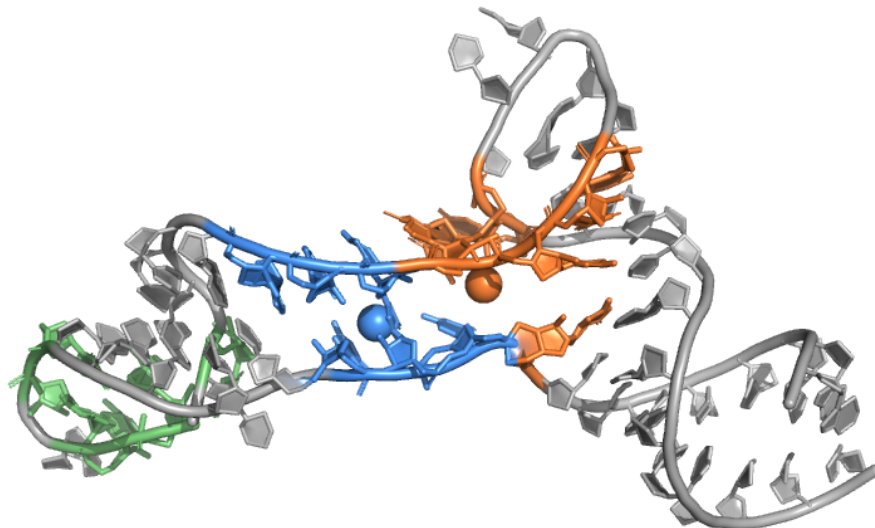
18, 21, 22, 24

**Binding-site overlap (benchmark):**

0/5 residues (0%) - neither strict nor near

## Predicted structure with top-3 pockets

Cartoon backbone, gray. Top-3 pocket residues highlighted (orange / azure / green = ranks 1 / 2 / 3). Centroid spheres shown at the geometric centre of each cluster's Kabsch-aligned member centres. Legend: #1 = cluster 0; #2 = cluster 2; #3 = cluster 1.



## Methods

v0.2 ranks candidate pockets by structural persistence across the conformational ensemble, weighted by binding-residue stability (score = persistence x n\_residues\_intersected). This replaces the v0.1 ranker, which used fpocket's druggability score as the primary ranking signal. fpocket's druggability score is the output of a logistic regression trained on protein druggable-vs-non-druggable cavities; its dominant feature is normalised against a protein hydrophobic-density range that does not transfer to RNA cavities. On validated RNA benchmark targets the protein-trained classifier consistently scored the actual binding-site cluster near zero while assigning non-binding cavities scores in the 0.1-0.7 range. The geometric ranker recovers the binding-site cluster at rank-1 on 3 of 4 v0.1 retro benchmark targets vs 0 of 4 with the previous ranker. fpocket's druggability score is still computed and reported per cluster as metadata; druggability assessment itself is left to the customer's medicinal chemistry workflow.

Structures are predicted using RhoFold+ (Apache 2.0). Conformational ensemble generated by anisotropic network model (ANM) normal-mode sampling on the C3' backbone, perturbing along the 10 lowest-frequency collective modes (ProDy, BSD-3). Pockets detected per conformer using fpocket (MIT) with RNA-tuned alpha-sphere and clustering parameters (min radius 3.0 Å, max 5.7 Å, min alpha-spheres 35, clustering distance 1.65 Å). Pockets are clustered across the ensemble after Kabsch-aligning frames to the reference. Persistence is the fraction of frames a cluster is detected in; binding-residue stability is the count of residues contacted by the cluster in every member frame. Clusters with persistence below the configured floor are excluded from the customer-visible top-3.

For targets with diverse-tail evolutionary representation (sequences with at least one homolog at <77% identity, or a non-trivial fraction of homologs in the 70-80% identity band), an MSA-aware structure prediction path is available as an opt-in mode. This empirical screening criterion is calibrated on a benchmark of seven RNA targets and will be refined as more targets accumulate. Single-sequence prediction is the default for all other targets.

Results are computational predictions. Experimental validation is required before use in drug development or clinical applications.

## Binding-mode caveat

Pipeline detects cleft-shaped binding pockets. Groove-binding modes and shallow surface-deformation binding may be missed. Contact us if your target's binding mode is groove-mediated.

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