# rnafold.com

RNA druggability assessment

## Job summary

| | |
|---|---|
| **Job ID:** | 2gis-demo |
| **Date:** | 2026-05-11 21:13 UTC |
| **Sequence length:** | 94 nt |
| **Conformers:** | 5 |
| **Pockets detected:** | 25 (across all frames) |
| **Clusters:** | 11 (5 passing persistence floor) |
| **Top-3 surfaced:** | 3 |
| **RhoFold pLDDT (mean):** | 82.151 |

**Sequence:**

GGCUUAUCAAGAGAGGUGGAGGGACUGGCCCGAUGAAACCCGGCAACCAGAAAUGGUGCCAAUUCCUGCAGCGGAAACGU
UGAAAGAUGAGCCA

# Top-3 candidate druggable pockets

## #1 Cluster 4 (geometric rank #1)

NEAR (38%)

**Persistence:**
1.00 (5 of 5 frames)
**Geometric score (ranking):**
9.000 = persistence × n_residues_intersected (1.00 × 9)
**Mean druggability (metadata, not ranking):**
0.029 -- fpocket protein-trained score, see Methods
**Median druggability:**
0.001
**Max druggability:**
0.096
**Centroid (A):**
-7.05 -0.50 -0.33
**Residues (union):**
7, 8, 9, 10, 11, 12, 59, 60, 61, 62, 63, 64
**Residues (intersection):**
9, 10, 11, 12, 60, 61, 62, 63, 64
**Binding-site overlap (benchmark):**
6/16 residues (38%) - near (>=30% of binding-site residues)

## #2 Cluster 0 (geometric rank #2)

NONE (6%)

**Persistence:**
0.80 (4 of 5 frames)
**Geometric score (ranking):**
8.800 = persistence × n_residues_intersected (0.80 × 11)
**Mean druggability (metadata, not ranking):**
0.009 -- fpocket protein-trained score, see Methods
**Median druggability:**
0.002
**Max druggability:**
0.031
**Centroid (A):**
3.00 10.19 -6.32
**Residues (union):**
23, 24, 25, 26, 27, 28, 29, 64, 65, 66, 67, 68, 85, 86, 87
**Residues (intersection):**
23, 24, 25, 26, 27, 28, 64, 65, 66, 67, 85
**Binding-site overlap (benchmark):**
1/16 residues (6%) - neither strict nor near

## #3 Cluster 2 (geometric rank #3)

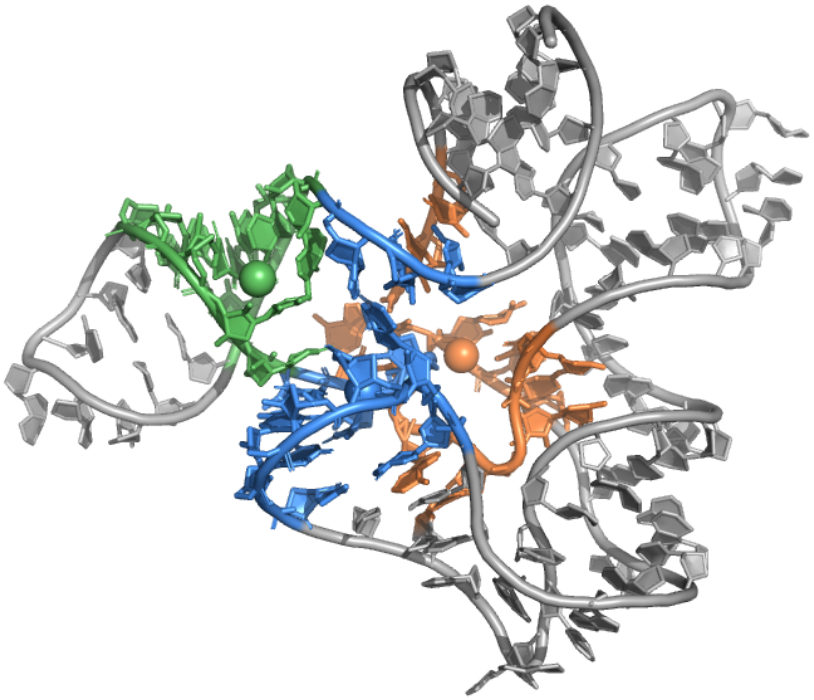
NONE (0%)

**Persistence:**
1.00 (5 of 5 frames)
**Geometric score (ranking):**
4.000 = persistence × n_residues_intersected (1.00 × 4)
**Mean druggability (metadata, not ranking):**
0.026 -- fpocket protein-trained score, see Methods
**Median druggability:**
0.001
**Max druggability:**
0.128

**Centroid (A):**
4.37  4.66  -17.39
**Residues (union):**
67, 68, 69, 70, 71, 80, 81, 82, 83, 84
**Residues (intersection):**
68, 69, 83, 84
**Binding-site overlap (benchmark):**
0/16 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 4; #2 = cluster 0; #3 = cluster 2.



## 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 A, max 5.7 A, min alpha-spheres 35, clustering distance 1.65 A). 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.