

Job summary

Job ID:	hcv-ires-ia-demo
Date:	2026-07-03 10:15 UTC
Sequence length:	55 nt
Conformers:	5
Pockets detected:	15 (across all frames)
Clusters:	6 (3 passing persistence floor)
Top-3 surfaced:	3
RhoFold pLDDT (mean):	0.812

Sequence:

GGCUGUGAGGAACUACUGUCUUCACGCCUUCGGGAGUGUCGUGCAGCCUCCAGCC

Top-3 candidate druggable pockets

#1 Cluster 1 (geometric rank #1)

STRICT (80%)

Persistence:

1.00 (5 of 5 frames)

Geometric score (ranking):

7.000 = persistence × n_residues_intersected (1.00 × 7)

Mean druggability (metadata, not ranking):

0.005 -- fpocket protein-trained score, see Methods

Median druggability:

0.001

Max druggability:

0.018

Centroid (A):

9.02 -4.85 -1.45

Residues (union):

10, 11, 12, 13, 15, 16, 43, 45, 46, 47

Residues (intersection):

10, 11, 12, 15, 43, 46, 47

Binding-site overlap (benchmark):

8/10 residues (80%) - strict ($\geq 50\%$ of binding-site residues)

#2 Cluster 0 (geometric rank #2)

STRICT (70%)

Persistence:

1.00 (5 of 5 frames)

Geometric score (ranking):

6.000 = persistence × n_residues_intersected (1.00 × 6)

Mean druggability (metadata, not ranking):

0.103 -- fpocket protein-trained score, see Methods

Median druggability:

0.075

Max druggability:

0.255

Centroid (A):

8.17 -13.09 1.77

Residues (union):

13, 14, 15, 16, 17, 18, 41, 42, 43, 44, 45, 46

Residues (intersection):

13, 14, 16, 42, 43, 44

Binding-site overlap (benchmark):

7/10 residues (70%) - strict ($\geq 50\%$ of binding-site residues)

#3 Cluster 4 (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):

0.254 -- fpocket protein-trained score, see Methods

Median druggability:

0.254

Max druggability:

0.480

Centroid (A):

-8.94 -20.01 34.26

Residues (union):

29, 30, 31, 32, 33

Residues (intersection):

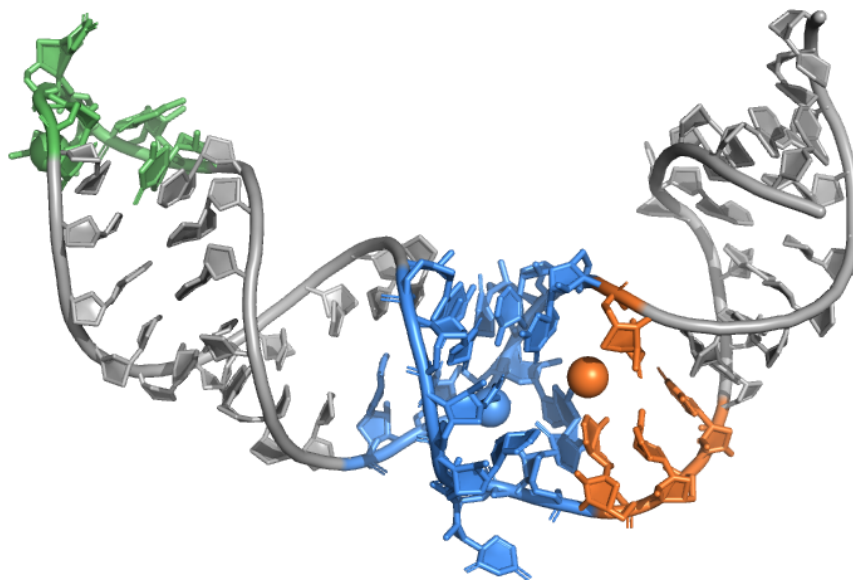
29, 30, 31, 32

Binding-site overlap (benchmark):

0/10 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 1; #2 = cluster 0; #3 = cluster 4.



Methods

v0.2 ranks candidate pockets by structural persistence across the conformational ensemble, weighted by binding-residue stability (score = persistence x n_residues_intersected). The cross-frame ensemble ranker is the load-bearing architectural contribution of v0.2. On a seven-target cleft-binder benchmark, RNA-tuned cavity detection alone (whether ours or the published fpocketR parameters, Veenbaas et al. 2025) recovers 0 of 7 at strict@1 and 2 of 7 at near@1; adding the 5-frame ANM ensemble + cross-frame geometric ranker on top lifts recovery to 3 of 7 strict@1 (overlap >= 50%) and 6 of 7 near@1 (overlap >= 30%). fpocket's protein-trained 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 are 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). These parameters are consistent with the published fpocketR approach (Veenbaas et al., PNAS 2025), which formalised the same RNA tuning the field has converged on for fpocket on RNA targets. 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.

References. Shen T. et al. (2024). RhoFold+: accurate RNA 3D structure prediction using a language model-based deep learning approach. Nature Methods. Bakan A., Meireles L.M., Bahar I. (2011). ProDy: Protein Dynamics Inferred from Theory and Experiment. Bioinformatics 27, 1575-1577. Le Guilloux V., Schmidtke P., Tuffery P. (2009). Fpocket: An open source platform for ligand pocket detection. BMC Bioinformatics 10, 168. Veenbaas S.D., Koehn J.T., Irving P.S., Lama N.N., Weeks K.M. (2025). Ligand-binding pockets in RNA and where to find them. PNAS 122(17):e2422346122.

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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