Annotated tertiary interactions in RNA structures reveal new interactions and composite motifs

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RNA folding is hierarchical

- Tertiary motifs serve as modular building blocks in the RNA architecture.
- To understand the role of RNA tertiary motifs in RNA folding will help to understand RNA 3D prediction.

TPP riboswitch (PDB: 2GDI)
RNA tertiary motifs

Kissing hairpin

Coaxial helix

Pseudoknot

HIV-1 fragment (PDB: 1ZCI)
JMB V.356 771 (2006)

Viral pseudoknot (PDB: 1L2X)
PNAS USA V.99 4302 (2002)
Annotating 3D RNA

• Selected seven key RNA tertiary motifs: coaxial helix, A-minor motif, ribose zipper, tetraloop-tetraloop receptor, pseudoknot, kissing hairpin, and tRNA D-loop:T-loop.
• Searched RNA tertiary motifs via different computer programs.
• Annotate tertiary interaction motifs.
• Perform analysis over the diagrams produced.
RNA dataset criteria

• High resolution (≤ 3.0 Å)
• Structure size (> 2 nt/strand)
• Representative sequences (1)
  (≤ 55% sequence identity)
• Structures should have at least one tertiary motif

Final dataset: 54 RNA crystal structures

• Use of RNAVIEW (2), FR3D (3), 3DNA (4) and RZparser (5) to annotate motifs

(1) Hobohm U. et al. Protein Science 1:409-17 (1992)
(2) Yang et al. NAR; 31(13), 3450-60 (2003)
(5) Tamura and Holbroook. JMB; 320(3), 455-74 (2002)
RNA junctions have a high probability (84%) to contain at least one coaxial helix.
23S rRNA

PDB: 1VQO
MOLL. CELL. V. 20 437 (2005)
Distribution of tertiary motifs

- For 54 high-resolution RNA structures, 601 RNA tertiary interactions were found. Most of them occur in the 16S and 23S rRNAs.
- Ribose zippers, coaxial helices and A-minor interactions are highly abundant (88%).
A-minor involved in long-range interactions

Structural context of the inserted A in A-minor

Structural context of the Watson-Crick pair in A-minor

- Helix (WC)
- Helix (non-WC)
- Internal
- Terminal
- Junction
- Other SS

- 1
- 2
- 3
- 4-5

A-minor motif
Ribose zipper
Pseudoknot
Helices joint by long-range interactions

23S rRNA (PDB: 1VQO)
MOL. CELL V.20 437 (2005)
Correlated motifs

- Many A-minor motifs (64%) are involved with coaxial helices.
- Coaxial helices (70%) interact with A-minor.
- Most ribose zippers (70%) contain an A-minor.
- Every loop-loop receptor contains a ribose zipper, which in turn contains one or more A-minor motif 87% of the time.
Summary and future work

• The correlations observed suggest that RNA tertiary motifs work in a cooperative way between motifs and can form composite motifs.
• To investigate the rules that allow prediction on interactions between motifs.
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Loop-loop receptor
A-minor and similar interactions

(a) A-minor type I  
PDB: 1FFK

(b) A-minor type II  
PDB: 1FFK

(c) A-minor type 0  
PDB: 1FFK

(d) PDB: 2J00

(e) PDB: 1VQO

(f) PDB: 1FFK

(g) PDB: 1U6B

(h) PDB: 2G1S

(i) PDB: 2GCV