



	Experiment title: RNA fragment (SS29) of the mammalian signal recognition particle (SRP)	Experiment number: LS-1386
Beamline: BM14	Date of experiment: from: 1/3/99 to: 2/3/99	Date of report: 31/8/99
Shifts: 3	Local contact(s): Gordon A. Leonard	<i>Received at ESRF:</i>
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Report:

Background: The mammalian Signal Recognition Particle (SRP) is an essential cytoplasmic ribonucleoprotein complex involved in targeting signal peptide containing proteins to the endoplasmic reticulum. Assembly of SRP requires that protein SRP19 binds first to helix 6 of the SRP-RNA before the signal-peptide recognizing protein, SRP54, can bind to helix 8 of the RNA. Helix 6 is closed by a GGAG tetraloop which has been shown to form part of the SRP19 binding site.

Results: The high resolution (2.0 Å) structure of a fragment of human SRP-RNA comprising 29 nucleotides of helix 6 has been determined by the MAD method using bromine-labeled RNA (Table 1). In the crystal the molecule forms 28-mer duplexes rather than the native monomeric hairpin structure, although two chemically equivalent 11 bp stretches of the duplex represent the presumed native structure. The duplex has highly distorted A-RNA geometry due to the occurrence of several non-Watson Crick base-pairs.

adenine bases, adopts a different conformation in the two native-like parts of the structure. The structure also shows the 2'3'-cyclic phosphate reaction product of the hammerhead ribozyme cleavage reaction.

Conclusions: The 29-mer RNA is the first RNA structure of the human SRP and provides some insight into the binding mode of SRP19. The observed strong irregularities of the RNA helix make the major groove wide and flat enough to possibly accommodate an α -helix of SRP19. The variety of non-canonical base pairs observed enlarges the limited repertoire of irregular RNA folds known to date and the observed conformation of the 2'3'-cyclic phosphate containing Ade-29 is consistent with the current understanding of the hammerhead ribozyme reaction mechanism.

Reference:

Wild, K., Weichenrieder, O., Leonard, G.A. & Cusack, S. (1999). The 2 Å structure of helix 6 of the human Signal Recognition Particle RNA. *Structure*, in press.

Table 1. Summary of the diffraction data[†]

Three wavelength Br MAD at BM14	inflection	peak	hard remote
Wavelength (Å)	0.9200	0.9197	0.9170
Resolution (Å)	28-3.0	28-3.0	28-3.0
Completeness (%)	92.5 (95.1)	92.5 (95.3)	93.2 (95.9)
Unique reflections	4,859	4,857	4,894
Multiplicity	5.3	5.0	5.0
R _{sym} [‡] (%)	7.1 (30.1)	7.4 (29.7)	7.3 (28.9)
Dispersive and anomalous differences [*]			
Br MAD inflection	5.7	4.8	5.8
Br MAD peak		6.3	5.5
Br MAD hard remote			6.7
Phasing statistics [#]			
R _{cullis} (%)	63.9	67.2	73.1
Phasing power	1.80	1.66	1.43
FOM		0.60	

[†]Native data at 2.0 Å had previously been collected at ESRF beamline ID14-EH4. Numbers in parenthesis correspond to the values of the highest resolution bin. Friedel pairs are

[‡] [#] ^{*}