

# Structure and Replication of Hepatitis Delta Virus RNA

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<b>1</b>	<b>Introduction</b>	<b>2</b>
<b>2</b>	<b>RNAs and Ribonucleoproteins</b>	<b>2</b>
2.1	Genome and Antigenome	2
2.2	mRNA	3
2.3	Other HDV RNAs	4
2.4	RNA Structure	5
2.5	Ribonucleoproteins	6
<b>3</b>	<b>RNA Replication</b>	<b>7</b>
3.1	Roles of Delta Proteins	7
3.1.1	The Essential Small Delta Protein	7
3.1.2	Other Forms of Delta Protein	7
3.1.3	Replication with an Unchanging Separate Source of Small Delta Protein	8
3.2	Enzymology of RNA-Directed Transcription	8
3.3	Initiation of Replication	9
3.4	Double Rolling-Circle Model	11
3.5	Template-Switching, Reconstitution, and Recombination	12
3.6	Inhibition of Replication	14
3.6.1	Resistance to Interferons	14
3.6.2	Sensitivity to Ribavirin	14
3.6.3	Sensitivity to siRNA	15
3.6.4	Resistance to Dicer	15
3.7	Cytopathic Effect of Replication	15
<b>4</b>	<b>Evolution of the RNA Sequence</b>	<b>16</b>
4.1	Accumulation of Changes	16
4.2	ADAR-Editing	17
4.3	Origin	17
<b>5</b>	<b>Outlook</b>	<b>18</b>
	<b>References</b>	<b>18</b>

**Abstract** While this volume covers many different aspects of hepatitis delta virus (HDV) replication, the focus in this chapter is on studies of the structure and replication of the HDV RNA genome. An evaluation of such studies is not only an integral part of our understanding of HDV infections but it also sheds new light on some

important aspects of cell biology, such as the fidelity of RNA transcription by a host RNA polymerase and on various forms of post-transcriptional RNA processing. Representations of the replication of the RNA genome are frequently simplified to a form of rolling-circle model, analogous to what have been described for plant viroids. One theme of this review is that such models, even after some revision, deceptively simplify the complexity of HDV replication and can fail to make clear major questions yet to be solved.

## 1

### Introduction

Other reviews on the topic of hepatitis delta virus (HDV) RNA structure and replication have been previously published (Cunha et al. 2003; Gerin et al. 2001; Taylor 2003, 2004). Moreover this volume contains current reviews on other aspects of HDV infection, in addition to one chapter on HDV replication (see chapter by T.B. Macnaughton and M.M.C. Lai, this volume). The objective of this chapter therefore will be to not only review information regarding HDV genome structure and replication, but also to consider what might be new insights and to point to questions yet to be solved.

Over the years HDV has provoked interest because of the many unique features associated with its replication including RNA-directed transcription by a host enzyme, ribozyme domains, and essential RNA editing. It has also been associated with a deceptive simplicity: a very small genome encoding only one or two viral proteins to account for, and a rolling-circle model of replication that seems plausible. However, as described in this chapter, we are becoming aware of a greater complexity associated with the replication of this apparently simple virus.

## 2

### RNAs and Ribonucleoproteins

#### 2.1

##### Genome and Antigenome

The genome of HDV is a small RNA of about 1,700 nucleotides in length with a circular conformation. We often refer to this RNA as single-stranded; however, based on predictions from the nucleotide sequence and certain experimental studies, we are convinced that this RNA can fold on itself via intra-molecular base pairing to form an unbranched rod-like structure. In this way, about 74% of all the nucleotides are involved in base pairing (Sect. 2.4).