



	<b>Experiment title:</b> HCV RNA dependent RNA polymerase	<b>Experiment number:</b> LS-1664
<b>Beamline</b> ID14-1	<b>Date of experiment:</b> from: 16-6-00 to: 19-6-00	<b>Date of report:</b> 02.08.00
<b>Shifts to BAG: 9</b>	<b>Local contact(s):</b> B. Rasmussen	<i>Received at ESRF:</i>
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## Report:

*Background:* Hepatitis C Virus (HCV) is a member of the *Flaviviridae* family and is a major human pathogen that has infected 3% of the world's population. The virus is capable of establishing a persistent infection, which in the majority of cases leads to chronic hepatitis. There is no vaccine against HCV, thus there is an urgent need to develop HCV specific antiviral agents to counteract the disease. We have crystallized the RNA dependent RNA polymerase (RdRp) of HCV and a related *Flaviviridae* virus GB virus B (GBV-B) RdRp in order to develop antivirals using this key enzyme as a target for inhibition.

### *Results:*

## Hepatitis C virus (HCV) RNA-dependent RNA polymerase (RdRp)

A number of data sets were collected from crystals of RdRp soaked with small molecule inhibitors in the presence of metal. Different soaking times and variation of the soaking buffer were tested in order to achieve successful binding. A summary of the data sets is presented in the following table. In addition to these data sets a significant part of the beam time was used for the screening of well diffracting crystals.

Two structures, after soaking with the compound and the metal were solved by molecular replacement and rigid body refinement. The fully refined structures were carefully examined. Only one metal ion coordinated to Asp220, Thr221 and water molecules, is present in the structure. Other soaking conditions will be investigated. We also have one big crystal of a mutant of which we plan to solve the structure.

## Summary of data collection

Data Set	RdRp + metal + Inhibitor-1	RdRp + metal+ Inhibitor-2	RdRp + metal + Inhibitor-2
Space group	P212121	P212121	P212121
Resolution	30 - 2.45	30 - 2.45	30-2.3
Rmerge (%)	4.8 (11.9)*	5.1 (21.8)*	5.2 (17.0)*
No. Observations	281,207	118,339	36,132
No. Unique	46,913	38,918	30,973
Completeness (%)	97.3	80.7	53.5
Inhibitor bound	No	No	No
Metal bound	Yes	Yes	Yes

\* highest resolution shell