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ESRF

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office using the **Electronic Report Submission Application:**

http://193.49.43.2:8080/smis/servlet/UserUtils?start

Reports supporting requests for additional beam time

Reports can now be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.

ESRF	**Experiment title:** Sttructure of HCV RdRp NS5B from genotype 2b	**Experiment number**: MX-267
Beamline: ID14-1	**Date of experiment**: from: October 30th to: November 1st	**Date of report**: July 25th 2005
Shifts: 2	**Local contact(s)**: Dr. Joanna Timmins	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

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Report:

Introduction

Hepatitis C is a global pandemic with 3-4% of the world's population infected. Currently the only treatment is interferon alpha as either a monotherapy or jointly administered with ribavirin, yet this treatment is only effective in 40-50% of patients with the most common strain, 1B. Six genotypes of the Hepatitis C virus (HCV) exist and each with several subtypes. In addition, the high mutation rate of the virus means that in any one infection, the virus is likely present as a complex pool of quasispecies. While genotype does not correlate with disease severity, it is a major determinant in treatment efficacy and several examples of genotype-specific drug resistances have been observed. In order to better understand the structural basis for the genotypic heterogeneity in NS5B inhibition, specifically with regard to the resistance to nonnucleoside inhibitors, we aimed to determine the three-dimensional structure of a C-terminally truncated (DC21) HCV 2b NS5B RNA dependent RNA polymerase.

Data collected

We have crystallized and solved the structure of the HCV 2b polymerase. Three data sets from native HCV 2b polymerase crystals were collected with the best one diffracting to 1.9Å resolution. Crystals belong to the monoclinic C2 space group with 2 molecules per asymmetric unit. We have also collected data from crystals soaked either in presence of GTP or of an allosteric indole based NNI and a combination of the two molecules. The structure of the 2b enzyme has been refined to 1.9 Å resolution.However, neither GTP or inhibitors were bound to the enzyme.

A manuscript describing the structure is now in perparation.