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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:** Crystal structure of the Lactococcus lactis formamidopyrimidine-DNA glycosylase bound to a substrat analogue-containing DNA	**Experiment number:** **TC-173**
Beamline: ID14-2	**Date of experiment:** from: 11/12/2003 to: 12/12/2003	**Date of report:** 20/09/2004
Shifts: 3	**Local contact(s):** Gordon LEONARD	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Franck COSTE* (CNRS, CBM Orléans, IR2)

Report:

In our lab, we solved the crystal structure of a complex between the Lactococcus lactis FPG protein and a cFapydG-containing DNA but the resolution (2.8Å) was not sufficient to be sure of the damaged base conformation. So, we applied to the ESRF to get some powerful synchrotron beam time.

During the 3 allocated shifts, 16 crystals were tested and 9 x-ray diffraction datasets were collected. One of these datasets was good enough to solve the structure of our Protein/DNA complex at 1.8Å resolution. This is the first time that the Fapy lesion is observed in a complex with a DNA repair enzyme (figure 1).

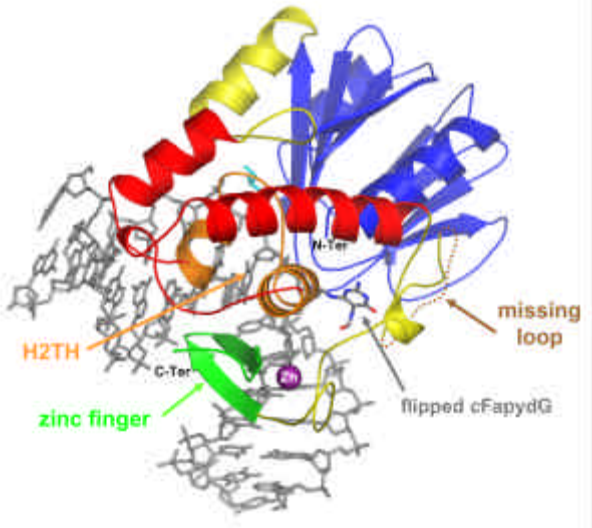

Figure 1
Overall structure of the Fpg/DNA complex showing the DNA torsion centred on the damaged nucleobase and the extrahelical conformation adopted by the *c*FapydG inside the Fpg substrate binding pocket. Secondary structures are color-coded according to the definition of Sugahara *et al.* (2000).

The results are described in the following publication :

Coste F, Ober M, Carell T, Boiteux S, Zelwer C & Castaing B.
"Structural basis for the recognition of the FapydG lesion (2,6-diamino-4-hydroxy-5-formamidopyrimidine) by the Fpg DNA glycosylase"
J Biol Chem. 2004 Jul 10 [Epub ahead of print]

Abstract:

Formamidopyrimidine-DNA glycosylase (Fpg) is a DNA repair enzyme which excises oxidized purines such as 7,8-dihydro-8-oxoguanine (8-oxoG) and 2,6-diamino-4-hydroxy-5-formamidopyrimidine (FapyG) from damaged DNA. Here, we report the crystal structure of the Fpg protein from Lactococcus lactis (LlFpg) bound to a cFapydG-containing DNA. The structure reveals that Fpg stabilizes the cFapydG nucleoside into an extrahelical conformation inside its substrate binding pocket. In contrast to the recognition of the 8-oxodG lesion which is bound with the glycosidic bond in a syn conformation, the cFapydG lesion displays in the complex an anti conformation. Furthermore, Fpg establishes interactions with all the functional groups of the FapyG base-lesion which can be classified in two categories: (i) those specifying a purine derived lesion (here a guanine), involved in the Watson-Crick face recognition of the lesion and probably contributing to an optimal orientation of the pyrimidine-ring moiety in the binding pocket and (ii) those specifying the imidazole-ring opened moiety of FapyG and probably participating also in the rotameric selection of the FapydG nucleobase. These interactions involve strictly conserved Fpg residues and structural water molecules mediated interactions. The significant differences between the Fpg recognition modes of 8-oxodG and FapydG provide new insights into the Fpg substrate specificity.