EUROPEAN **S**YNCHROTRON **R**ADIATION **F**ACILITY

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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:** Structure of the E. Coli expressed C. Term domain of the ovine prion protein	**Experiment number**: 30-01-552
Beamline: BM30a	**Date of experiment**: from: 5/12/02 to: 6/12/02	**Date of report**:
Shifts: 3	**Local contact(s)**: J.-L. Ferrer	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

F. Eghiaian*, **B. Gigant**, **and M. Knossow* LEBS, CNRS, Gif sur Yvette**

Report:

2 shifts used

Structural studies of recombinant ovine prion protein

PrPc is an ubiquituous cell surface glycoprotein of unknown function expressed in various mammal species. Conversion of this protein from its cellular form (PrPc) to insoluble amyloïd fibrils (PrPSc) is the main event of prion diseases, a group of fatal neurodegenerative disorders that appear sporadically as well as after hereditary or infectious transmission.

Prion infectious agent is mainly composed of PrPSc and seems devoid of nucleic acid, a feature that makes this group of diseases exceptional. Spreading of prion into challenged organisms requires expression of cell host PrPc, and is modulated by several mutations in the PrP gene. Transmission of prion across mammal species is apparently facilitated by sequence identity between PrPc and PrPSc. The latter observations suggest that at one point, prion pathogenesis includes recognition of PrPc by the infectious agent or by another unknown *factor X*, this interaction leading afterward to conversion of PrPc to PrPSc. On the basis of this hypothesis, structural changes leading to stability changes or alteration of ligand binding are expected from disease-related sequence variations of PrP. To idenify the structural changes associated to disease-related sequence variations of PrP, we have undertaken to determine its structure by X-ray crystallography.

During our visit, we tested crystals constituted of sheep recombinant PrP(114-231) in complex with VRQ14 Fab fragment. Space group is $P2_12_12$ (a=91Å, b=145Å, c=43Å), with one complex molecule per unit cell. Data were measured to 2,5 Å resolution (Rmerge 3,3%,). Structure was solved by molecular replacement using Fab and prion models. Examination of the structure gives insight into the role of disease related positions in prion structure and stability. Our observations are now being prepared for publication.