EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

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 via the User Portal:
https://wwws.esrf.fr/misapps/SMISWebClient/protected/welcome.do

Deadlines for submission of Experimental Reports

Experimental reports must be submitted within the period of 3 months after the end of the experiment.

Experiment Report supporting a new proposal ("relevant report")

If you are submitting a proposal for a new project, or to continue a project for which you have previously been allocated beam time, you must submit a report on each of your previous measurement(s):

- even on those carried out close to the proposal submission deadline (it can be a *"preliminary report"),*
- even for experiments whose scientific area is different form the scientific area of the new proposal,
- carried out on CRG beamlines.

You must then register the report(s) as "relevant report(s)" in the new application form for beam time.

Deadlines for submitting a report supporting a new proposal

- 1st March Proposal Round - **5th March**
- 10th September Proposal Round - **13th September**

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.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report in English.
- include the experiment number 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:** Multi-organ investigation of early markers predictive of dementia in age-related frailty	**Experiment number**: MD1326
Beamline: ID17	**Date of experiment**: from: 15 November 2022 to: 18 November 2022	**Date of report**:
Shifts: 9	**Local contact(s)**: Herwig Requardt	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

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Report:

In the present experiment, we exploited X-ray phase contrast tomography to investigate the senescence-accelerated prone (SAMP8) mouse model, which reproduces the effects of the age-related human frailty, a syndrome characterized by cumulative decline at physical, cognitive, and psychological levels, resulting in vulnerability to minor stressors with higher risks of adverse outcomes. SAMP8 exhibits characteristic disorders that correspond to pathophysiological states found in aged humans: decreased motor coordination, cardiovascular alterations, age-related behavioral deterioration such as deficits in learning and memory and emotional disorders, and by pathological alterations in the brain that have been associated with dementia.

We investigated SAMP8 and control mice to assess the structural alterations in ileum and colon of mice in aging. In particular we intended to describe and quantify the alterations caused by aging in the intestinal barrier, which appears to be a potential site for inflammation in several neurodegenerative disease.
We imaged 12 samples of ileum from SAMP8 mice, and 6 samples from control mice. Then we imaged samples of colon: 5 samples from SAMP8 mice, and 2 samples from control mice. The samples were prepared at Neuroscience Department at "Mario Negri" Institute for Pharmacological Research IRCCS (Milan, Italy) in agreement with current national regulations. The samples will be fixed in 4% paraformaldehyde for 24h, then dehydrated through a graded ethanol series (70/95/100%), put in propylene oxide, and included in paraffin.

Data acquisition was carried out using monochromatic incident X-ray beam with an energy of 30 keV. The sample-detector distance was set at 23 cm. The detector had an effective pixel size of 0.7 micron. The tomography was produced by means of 2500 projections covering a total angle range of 180°. When required by the sample dimensions, we performed tomographic acquisition by using the extended field-of-view mode. The acquisition time for each angular position was 100 ms.

Data preprocessing, phase retrieval and tomographic reconstruction were performed in situ by using ID17rec and Tomwer software. The process was very time-consuming and often we faced problems, so we have exploited it limitedly to check the quality of the measurements and verify that the samples fitted the FOV.

Therefore, we have carried out the complete pre-processing, phase retrieval and tomographic reconstruction once we returned home by means of our software and optimized scripts.

By comparing SAMP8 and control mice we have been able to identify some alterations in the intestinal structure, in particular in the tunica muscolaris and in the Paneth cells, which are a prominent secretory epithelial cell type that resides at the base of intestinal crypts and releases antimicrobial peptides. We are still working on the interpretation of the data with our collaborators of Neuroscience Department at "Mario Negri" Institute for Pharmacological Research IRCCS (Milan, Italy), that are correlating our findings with MRI data acquired on the same mice. In addition, we are performing immuno-histological analysis on the XPCT-measured samples to unequivocally identify the structures and cells that we are able to see in the tomography images.

Given the special situation of ID17 at the time we performed the experiment, commissioning, alignment and setup preparation procedures (for which we received extra time) were carried out independently by the users of this beamtime. The results of the experiment appear very good and promising.