EUROPEAN SYNCHROTRON RADIATION FACILITY
ESRF User Office
BP 220, F-38043 GRENOBLE CEDEX, France
Delivery address: 6 rue Jules Horowitz, 38043 GRENOBLE, France
Tel: +33 (0)4 7688 2552; fax: +33 (0)4 7688 2020; email: useroff@esrf.fr; web: http://www.esrf.fr

BAG Beam time Progress Report

This represents a summary of the BAG progress in the reporting period, and is **in addition to** the standard ESRF report sheet for each project which will be used for the Review of the BAG.

BAG Title	**BAG Barcelona Human Pancreatic Ribonuclease 1**
Allocation Period	**ID14-EH2 Feb-23-2000 to Feb-24-2000 LS-1666**

List of publications resulting from ESRF beam time

Three-dimensional Structure of the Human Pancreatic Ribonuclease 1 (in preparation)

Global Summary

Human ribonuclease enzymes (RNases) constitute a group of proteins with ribonucleolytic activity differing in their specific activity, substrate preferences and optimal conditions of the enzymatic reaction (4). In addition to their catalytic activity, some members of the human RNase family show other biological capabilities, like neurotoxicity (1) or angiogenic activity (5). mRNA expression studies have shown characteristic distribution patterns for the different human RNase enzymes in several body tissues and fluids (3).

The amino acid sequences of human RNase enzymes show different degrees of similarity, ranging from that found between RNase 2 (eosinophil-derived neurotoxin, EDN) and 3 (eosinophil cationic protein, ECP) with 70% identity to 47% identity between RNase 1 and angiogenin (Ang), the member that is less related to the others (3,7).

Human pancreatic ribonuclease 1 (rhRNase 1), which is considered to be a counterpart of bovine pancreatic RNase A, has been isolated and characterized first by Weickmann *et al.* in 1981. hRNase 1 is classified into the secretory-type RNases, prefers poly (C) over poly (U) strongly and has different glycosylation patterns.

Truncation of 7 amino acid residues in the amino-terminal sequence resulted in much reduction in ribonucleolytic activity and in affinity to human placental RNase inhibitor (PRI). In addition, the reduced affinity to PRI enhances the cytotoxic activity For this reason, the amino-terminally truncated rhRNase 1 (des.1-7 hRNase 1) could be effective as an anti-cancer drug. (2)

Mature form of recombinant des.1-7 hRNase 1 was produced in *E.coli* using T7 expression system, purified and crystallized. Crystals were grown by the vapour diffusion method at room temperature from hanging drops. These crystals have a laminar shape, belong to space group $P2_12_12_1$ with unit cell parameters a=32.691,b=42.733,c=79.894, and diffract beyond 1.8 Å resolution.

REFERENCES:
(1) Durack, D. T., Ackerman, S. J., Loegering, D. A. & Gleich, G. J. (1981). *Proc. Natl Acad. Sci. USA,* **78**, 5165-5169.
(2) Futami, J., Seno, M., Kosaka, M., Tada, H., Seno, S. & Yamada, H. (1995). *Biochemical and Biophysical research communications.* **216**, 406-413.
(3) Futami, J., Tsushima, Y., Murato, Y., Tada, H., Sasaki, J., Seno, M. & Yamada, H. (1997). *DNA Cell Biol.* **16**, 413-419.
(4) Sorrentino, S. & Libonati, M. (1997).*FEBS Letters,* **404**, 1-5.
(5) Strydom, D. J. Fett, J. W., Lobb, R. R., Alderman, E. M., Bethune, J. L., Riordan, J. F. & Vallee, B. L. (1985). *Biochemistry,* **24**, 5486-5494.
(6) 4Weickmann, J. L., Elson, M., & Glitz, D. G. (1981). *Biochemistry,* **20**, 1272-1278.
(7) Zhou, H-M. & Strydom, D. J. (1993) *Eur. J. Biochem.* **217**, 401-410.

Visits made to the ESRF

Date(s) of visits	Beamline	No. of Shifts	Short Summary of each Visit
1. 23 to 24-Feb-2000	ID14-EH2	3	One dataset was collected at 1.8 Å.The structure was processed and solved *in situ*.