ESRF	**Experiment title:** SH3BGRL3, glutaredoxin like protein	**Experiment number**: MX129
Beamline: ID14-1	**Date of experiment**: from: 09/02/2004 to: 09/02/2004	**Date of report**: 02/07/2004
Shifts: 1	**Local contact(s)**:	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Nardini Marco,

Dept. of Physics-INFM, University of Genova

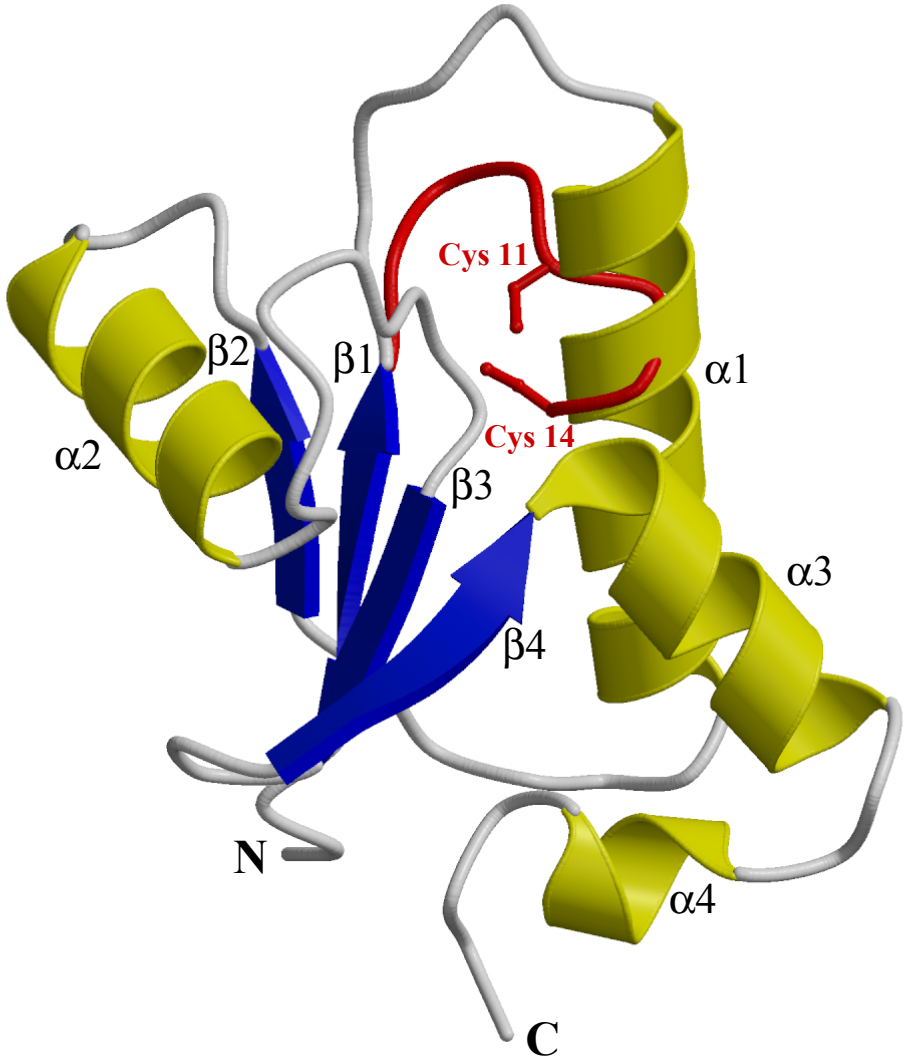
c/o X-ray Structural Biology Lab, Advanced Biotechnology Center,

Largo Rosanna Benzi, 10, 16132 Genova, Italy

Report:

Abstract of the article: M. Nardini, M. Mazzocco, A. Massaro, M. Maffei, A. Vergano, A. Donadini, P. Scartezzini and M. Bolognesi (2004) Crystal structure of the glutaredoxin-like protein SH3BGRL3 at 1.6 Å resolution. *Biochem. Biophys. Res. Comm.* **318,** 470-476.

We report the 1.6 Å resolution crystal structure of SH3BGRL3, a member of a new mammalian protein family of unknown function. The observed "thioredoxin fold" of SH3BGRL3 matches the tertiary structure of glutaredoxins, even in the N-terminal region where the sequence similarity between the two protein families is negligible. In particular, SH3BGRL3 displays structural modifications at the N-terminal Cys-x-x-Cys loop, responsible for glutathione binding and catalysis in glutaredoxins. The loop hosts a six residue insertion, yielding an extra N-terminal capped helical turn, firstly observed here for the thioredoxin fold. This, together with deletion of both Cys residues, results in a substantial reshaping of the neighbouring cleft, where glutathione is hosted in glutaredoxins. While not active in redox reaction and glutathione binding, SH3BGRL3 may act as an endogenous modulator of glutaredoxin activities by competing, with its fully conserved thioredoxin fold, for binding to yet unknown target proteins.



Schematic drawing of the crystal structure of mouse SH3BGRL3 glutaredoxin-like protein. The loop between strand β1 and helix α1 is structurally compared with a corresponding loop of active *E. coli* Grx3 (red color, PDB-code 1FOV), where the Cys residues of the CxxC motif are highlighted.