ESRF

ESRF	**Experiment title:** Structure of a Nitric Oxide Sensor protein	**Experiment number**: MX 277
Beamline: ID29	**Date of experiment**: from: 02 feb 2004 to: 03 feb 2004	**Date of report**: 08 oct 2004
Shifts: 2	**Local contact(s)**: Bill Shepard	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Pierre Nioche & C. S. Raman

University of Texas Houston – Medical School

6431 Fannin, MSB 6.504

Houston TX 77054

USA

Report:

The article related to this work on the structure determination of a Nitric Oxide Sensor is actually in print at Science and has been released online on the 7th of October 2004. The abstract is copied on the next page.

The experiments performed at ESRF were the first tries to solve the $SONO_{HD}$ (Sensor Of Nitric Oxide heme domain) structure. At that time, no synchrotron beamtime was available for us in the USA and these experiments have only been possible by a "rapid access" to the ESRF facility. They provided us with 4Å resolution full MAD dataset and 3.5Å single wavelength dataset. Those data were very crucial because they allowed us to calculate a first map and gave us critical hints to increase the resolution of our crystal.

Now, we wish to continue this work by studying the mechanism by which $SONO_{HD}$ activates its partners. To do so we will co-crystallize $SONO_{HD}$ with:
1) Small molecules such as nitric oxide and carbon monoxide in order to get insights on the subtile changes in the active sites of $SONO_{HD}$.
2) Protein domains from different partners such as MCP (Methyl Accepting Chemotaxis Proteins), HK (Histidine Kinase) and GC (Guanylate cyclase). These structures will provide a molecular basis to explain why $SONO_{HD}$ acts as a ubiquitous molecular switch and also understand how sGC (soluble Guanylyl Cyclase) gets activated and regulates cGMP production.
Once again, the results are expected to be published in a high profile journal.

In order to complete our goals, we therefore request in 2005, two blocks of synchrotron access for MAD experiments with three shifts each.

Sincerely,

Pierre

Abstrat:

Nitric oxide (NO) is extremely toxic to *Clostridium botulinum*, but its molecular targets are unknown. Here, we identify a heme protein sensor (SONO) that displays femtomolar affinity for NO. The crystal structure of the SONO heme domain reveals a novel fold and a strategically placed tyrosine residue that modulates heme-nitrosyl coordination. Furthermore, the domain architecture of a SONO ortholog cloned from *Chlamydomonas reinhardtii* indicates that NO signaling through cyclic guanosine monophosphate arose before the origin of multicellular eukaryotes. Our findings have broad implications for understanding bacterial responses to NO, as well as for the activation of mammalian NO-sensitive guanylyl cyclase.