X	**Experiment title:** Ebola virus matrix protein VP40	**Experiment number:** LS1535
Beamline: various	**Date of experiment:** from: various to:	**Date of report:** 1/3/00
Shifts:	**Local contact(s):** Gordon Leonard, Marc van Raaij, Wim Burmeister	*Received at ESRF:* - 2 MAR. 2000

Names and affiliations of applicants (* indicates experimentalists):

Winfried Weissenhorn*, EMBL

Report:

Background:

Ebola virus maturation occurs at the plasma membrane of infected cells and involves the clustering of the viral matrix protein VP40 at the assembly site as well as its interaction with the lipid bilayer. Here we report the X-ray crystal structure of VP40 from Ebola virus at 2.0 Å resolution and the membrane-associative form of the matrix protein by electron microscopy. The crystal structure reveals that Ebola virus VP40 is distinct from all other known viral matrix protein structures, consisting of two domains with unique folds, connected by a flexible linker. The C-terminal domain, which is absolutely required for membrane binding, contains large hydrophobic patches that may be involved in the interaction with lipid bilayers. Likewise, a highly basic region is shared between the two domains. We further show that VP40 oligomerizes upon membrane interaction, probably based on the hexameric unit observed for two C-terminal truncated molecules. The crystal structure reveals how the molecule may be able to switch from a monomeric conformation to a hexameric form, as observed *in vitro*. The observation of a membrane-induced conformational change to achieve lattice formation may be a first step in the assembly process, common to many enveloped viruses.

(i) A native data set of monomeric VP40 was collected at EH3. Crystals belonging to space group C2 diffracted to 2.3 Å resolution. In addition, a platinum derivative with a single site was collected with data to 2.7 Å.
(ii) A MAD experiment of a VP40 platinum derivatized crystal was performed on BM-14; three datasets around the platinum absorption edge were collected with diffraction to 3.0 Å. The phases obtained from this experiment were of insufficient quality to build the model.
(ii) A second MAD experiment was performed with selenomethione derivatized VP40. Three datasets were collected at BM-14 with diffraction data to 2.0 Å resolution. These datasets were used to solve the structure, which has been refined to 2.0 Å resolution.

(iv) A native dataset of the hexameric crystal form was collected at EH3 with diffraction data to 3.8 Å resolution.
(v) Another native dataset of hexameric VP40 was collected at EH4 with diffraction to 2.5 Å resolution.