ESRF	Experiment title: **Structure-aided drug design.** *BAG: Uppsala (II)* 4 SEP 2000	**Experiment number:** LS-1520 a
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Shifts: 3	**Local contact(s):** Wim Burmeister	*Received at ESRF:*

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Report:

Data were collected of HIV-1 protease in complex with a new type of inhibitor with the name msl439. Totally 90 images of 1 degree rotation were collected from one single unfrozen crystal, which is a record. Normally only 30-40 deg can be obtained from one crystal. Data to 1.95 Å were obtained with a completeness of 93.1 %. The linear R-fac was for all reflexions 6.4%. The structure was refined to R value of 0.216 and Rfree of 0.247. The structure is used for the further development of these inhibitors. Publications have not yet been written. This project is in collaboration with scientists connected to Stockholm University and Medivir AB.

Data were also collected of HIV-1 reverse transcriptase, drug resistant mutant in complex with an inhibitor lead compound inhibitor called msc194. The drug resistant mutant K103N is common to most of the presently used drugs of the non-nucleoside type. Msc194 show however high activity and the structure of the complex indicates that the inhibitory activity

can increased with small modifications in inhibitor structure. Diffracation data to 2.7 Å resolution was collected in 0.5 deg steps. 250 images were collected using 8 unfrozen crystals. Data were scaled to an R-value = 11.4 % and 85 % of data to 2.9 Å resolution. Structure was refined to R= 21.3 % and Rfree= 27.1 %. This project is in collaboration with scientists connected to Uppsala University and Medivir AB. The work has led to patents by Medivir AB.

Different techniques were tried for cryo-cooling of these crystals, but without success, so data collection was performed at 4 °C.