



<b>Experiment title:</b> BAG Barcelona – Leader Protease	<b>Experiment number:</b> LS-1377/78	
<b>Beamline:</b> ID027B	<b>Date of experiment:</b> from: 11-6-99 to: 14-6-99	<b>Date of report:</b> 31-8-99
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**Report:**

Leader protease from Foot-and-Mouth Disease Virus (FMDV) cleaves itself from the growing polyprotein and inhibits the translation of the host cell RNA capped messengers by the cleavage of the eucaryotic initiation factor (eIF4G). We have recently elucidated the three-dimensional structure of the leader protease (Guarné et al, 1998). Leader protease structure allows to establish the molecular basis of substrate binding recognition and the P' requirements for the eIF4G cleavage. In order to find out the ability of the leader protease to recognize two different substrate sequences (KLK□GAG, at the polyprotein, and NLG□RTT, at the eIF4G), inactive variants of the leader protease including the two complete cleavage sequences have been constructed.

We have crystallized one of these variants and collected a 99.3% complete data set at the ID02B. Crystals diffract to 3.2 Å resolution and belong to P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>. Crystals contain eight molecules into the asymmetric unit and cell parameters are a=65.4 Å, b=100.1 Å and c=277 Å.

This variant has allowed to study the interactions of the first substrate of the leader protease (the viral polyprotein) with its active groove. Our aim now is solve the structure of the variant that include the cleavage sequence of the eIF4G.