ESRF	**Experiment title:** Crystal structure of Dog Gastric Lipase in its open form	**Experiment number:** LS1657
Beamline: BM14	**Date of experiment:** from: 25/7/00 to: 26/7/00	**Date of report:** Aug00
Shifts: 2	**Local contact(s):** Gordon LEONARD	*Received at ESRF:*

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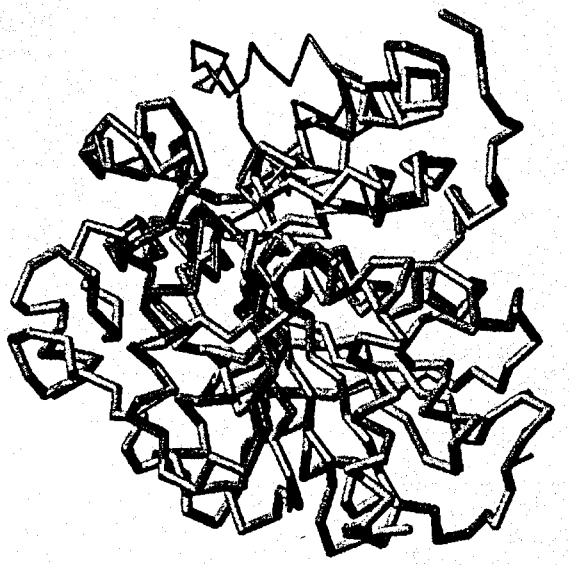
Report:

Fat digestion in humans requires not only the classical pancreatic lipase but also gastric lipase, which is stable and active despite highly acidic stomach environment. The crystal structure of human gastric lipase has been solved last year in the laboratory at 3.0 Å resolution. This globular enzyme consist of a core domain belonging to the α/β hydrolase-fold family and a "cap" domain, which is analogous to that present in serine carboxypeptidase. It possesses a classical catalytic triad (Ser 153, His 353, Asp 324). The catalytic serine is deeply buried under a segment consisting of 30 residues, which can be defined as a lid. The displacement of the lid is necessary for the substrates to have access to the active site. Crystals of dog gastric lipase complexed with a covalently bound inhibitor have been obtained. They belong to the space group $C222_1$ (A=61.2, B=164.5, C=177.1) with two molecules per asymmetric unit and diffract to 2.7 Å resolution. A complete data set (24389 reflections, 97.9 % completness) has been collected on the ESRF beam line BM 14 on july the 25th. After processing with the program DENZO and scaling with the program SCALA, the statistics for the data set were as follow : R-merge 6.7 % (19.6 % in the last shell), multiplicity 3.0 (2.2), $I/\sigma(I)$ 6.6. (1.8). The structure was solved with the molecular replacement method using the program AmoRe. The human gastric lipase structure, without the lid, was used as the search model. The rotation function yielded only one significant solution (correlation 12.4). The translation function gave clearly the position of the two molecules (correlation 45.0, R-factor 44.2). The refinement using the program CNS is in progress (R-factor 25.2 %, R-free 30.7 %). The structure of the lid in the open form has been built in the difference fourrier density map using the program Turbo-Frodo.



Superposition of dog gastric lipase in the open form (in yellow) and human gastric lipase in the closed form (in blue). The movement of the lid (residues 213 to 249) makes the active serine (in red) accessible to the substrate.