# A newly crystallized structure of human formylglycine-generating enzyme

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## Abstract

The formylglycine-generating enzyme (FGE) plays a key role in the posttranslational modification of the active site of all known human sulfatases. Several mutations in the SUMF1 gene encoding FGE are known, that lead to severely decreased activity or instability of the enzyme. The resulting lack of sulfatase modification leads to a disease known as multiple sulfatase deficiency (MSD). Previously crystallized structures of FGE are missing a surface loop that had to be cleaved off by treatment with elastase prior to crystallization [1]. Here, we report the first crystallization of human FGE without the necessity for elastase treatment. Crystals of untreated FGE are isomorphous to those of the elastase-treated protein. The loop participates in a crystal contact and is well defined in the electron density. Comparison with previous structures of elastase-treated FGE co-crystallized with substrate peptides revealed that this loop partly covers the substrate-binding groove of the active site. A clash of one sidechain with the substrate indicates that the loop needs to undergo a conformational change upon substrate binding. This assumption is supported by the occasional occurrence of crystals with a shorter *b*-axis, in which the loop becomes disordered.

[1] Thomas Dierks, Achim Dickmanns, Andrea Preusser-Kunze, Bernhard Schmidt, Malaiyalam Mariappan, Kurt von Figura, Ralf Ficner, and Markus Georg Rudolph. Molecular Basis for Multiple Sulfatase Deficiency and Mechanism for Formylglycine Generation of the Human Formylglycine-Generating Enzyme. Cell, Vol. 121, 541-552 (2005)