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Crystal structures of human secretory proteins ZG16p and ZG16b

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Introduction

ZG16p is a secretory lectin that mediates condensation-sorting of pancreatic enzymes to the zymogen granule membrane in pancreatic acinar cells. ZG16p are shown to interact with glycosaminoglycans and the binding is considered to be important for condensation sorting of pancreatic enzymes. ZG16b is known to a homolog of ZG16p. ZG16b/PAUF, a paralog of ZG16p, is highly expressed in human pancreatic cancer and plays a role in gene regulation and cancer metastasis. In order to obtain insights into structure-function relationships, we conducted crystallographic studies of human ZG16p lectin as well as ZG16b [1].

Experimental Procedure

The $(His)_6$-MBP-fused human ZG16p and ZG16b proteins were purified with a Ni-Sepharose column and then digested with TEV protease. The MBP tag was removed by chromatography through a Ni Sepharose column. The proteins were further purified by size exclusion chromatography. ZG16p and ZG16b crystals were obtained by the sitting drop vapor diffusion method and data sets were collected at PF-AR NW12A and NE3A beamlines. The crystal structures were solved by molecular replacement method using the program Molrep. The refined structure of ZG16p has a crystallographic *R*-factor of 20.4% (R_{free} = 22.8%) in the 20.00-1.65 Å resolution range. The structure of ZG16b has a crystallographic *R*-factor of 22.0% (R_{free} = 28.3%) in the 40.00-2.75 Å resolution range. (Fig. 1).

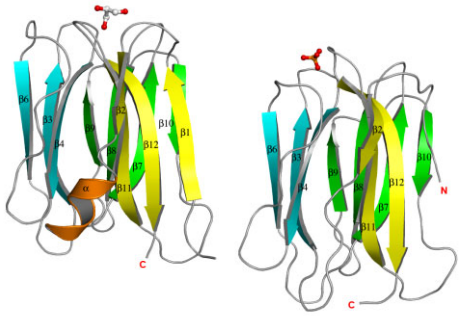

Fig. 1 Crystal structures of ZG16p (left) and ZG16b (right).

Results and Discussion

ZG16p assumes a Jacalin-related β-prism fold, the first to be reported among mammalian lectins. The putative sugar-binding site of ZG16p is occupied by a glycerol molecule, mimicking the mannose bound to plant lectins such as Banlec. ZG16b also has a β-prism fold, but some amino acid residues of the putative sugar-binding site differ from those of the mannose-type binding site suggesting altered preference. A positively charged patch, which may bind sulfated glycosaminoglycans, is located around the putative sugar-binding site of ZG16p and ZG16b. Taken together, we suggest that the sugar-binding site and the adjacent basic patch of ZG16p and ZG16b cooperatively form a functional glycosaminoglycan-binding site.

Reference

[1] M. Kanagawa et al., *Biochem. Biophys. Res. Commun.* **404**, 201 (2011).

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