Poster Presentation

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Crystal Structure of BRP39 protein expressed during Mammary Gland Apoptosis

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Breast regression protein (BRP39) from mice is a 39 kDa protein which is a member of chitolectin class of GH18 family. High levels of expression of BRP39 have been detected in breast carcinoma. It has been proposed that this may act as a protecting signalling factor and also help in proliferation of cells during breast cancer. It can act as a potential candidate for rational structure based drug design against breast cancer. Here, we report the crystal structure of recombinant BRP39 in a deglycosylated form which was expressed in a heterologous system i.e E.Coli. To understand the role of sugar moiety, crystal structure of a deglycosylated chitolectin is an essential requirement. The structure was solved by molecular replacement method of phase determination and refined to a 2.6 A° resolution. The overall structure of BRP39 consists of two globular domains: a large (β/α)8 TIM barrel domain and a small (α+β) domain. The most striking observation from BRP39 structure is the conformation of critical Trp 100 residue into the β-barrel of carbohydrate binding groove of BRP39. The structure reveals that the glycan moiety plays an important role in the orientation of critical Trp100 in the β-barrel. In deglycosylated BRP39, it orients away from the barrel and resembles the conformation as seen in non-glycosylated chitinases. In contrast to this, the corresponding Trp is oriented into the barrel in case of other glycosylated homologues of BRP39 which may have its implications in sugar binding. Furthermore, in MGP-40, the altered conformation of loop is stabilized by H-bonding and stacking interactions whereas in BRP39, no hydrogen bond was observed between any of the residues of this loop except for Trp100 which interacts with a water molecule may be to stabilize its conformation. Another important observation in the sugar binding groove of BRP39 structure is the mutation of two important residues, one in TIM barrel domain and another in a part of α+β domain which is also involved in sugar binding. Asn100 and Arg263 in Hcgp39 and other chitinase- like proteins (SPX-40 structures) are replaced by Lys101 and Lys264 in BRP39. Both of these residues i.e. Asn100 and Arg 263 in HCgp39 have been reported to be involved in stabilizing the binding of GlcNAc inside the groove. Possibly, there is a significant distortion in the shape of sugar binding groove due to these mutations in BRP39.

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