for both prokaryotic and eukaryotic enzymes is largely conserved. However there are several structural differences between prokaryotic UGM and eukaryotic AfUGM mainly because of five additional inserts in AfUGM, two of with play an important role in tetramerization. Comparing the un-complexed, native AfUGM structure and the ligand-bound AfUGM structure (both oxidized and reduced FAD) allowed us to address structural changes (loop movements) that play an important role in substrate binding and redox state. Structural binding studies on AfUGM revealed a unique substrate binding mechanism significantly different from proUGMs. This has helped us in identifying important conserved residues in AfUGM substrate binding and recognition. Based on the crystal structure we have made mutants of important active site residues.

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Keywords: crystallography, eukUGM, mutagenesis

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Solution of the structure of the TNF-TNFR2 complex

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Tumor necrosis factor (TNF) is an inflammatory cytokine that has important roles in various immune responses, which are mediated through its two receptors, TNF receptor 1 (TNFR1) and TNFR2. Antibody-based therapy against TNF is used clinically to treat several chronic autoimmune diseases; however, such treatment sometimes results in serious side effects, which are thought to be caused by the blocking of signals from both TNFRs. Therefore, knowledge of the structural basis for the recognition of TNF by each receptor would be invaluable in designing TNFR-selective drugs. Here, we solved the 3.0 angstrom resolution structure of the TNF-TNFR2 complex, which provided insight into the molecular recognition of TNF by TNFR2. Comparison to the known TNFR1 structure highlighted several differences between the ligand-binding interfaces of the two receptors. Additionally, we also demonstrated that TNF-TNFR2 formed aggregates on the surface of cells, which may be required for signal initiation. These results may contribute to the design of therapeutics for autoimmune diseases.

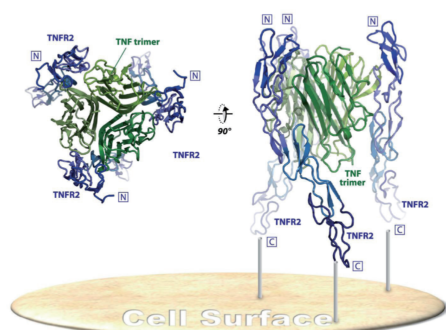

Fig. The structure of the TNF-TNFR2 complex (PDB:3ALQ)

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Keywords: cytokine, receptor, complex

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The structure of BRMS1 nuclear export signal reveals a hexamer of coiled coils

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We present here the first structural report of Breast Cancer Metastasis Suppressor 1 (BRMS1), a member of the metastasis suppressor proteins group, which during recent years have drawn much attention since they suppress metastasis without affecting the growth of the primary tumour [1]. The relevance of the predicted N-terminal coiled coil on the molecular recognition of some of the BRMS1 partners [2, 3], on its cellular localization [4] and on the role of BRMS1 biological functions such as transcriptional repression [3], prompted us to characterize its three-dimensional structure by X-Ray crystallography.

The structure of BRMS1 N-terminal region, reveals that residues 51 to 98 form an antiparallel coiled coil motif, and also that it has the capability of homo-oligomerizing in a hexameric conformation, by forming a trimer of coiled coil dimers. We have also performed hydrodynamic experiments that strongly supported the prevalence in solution of this quaternary structure for $BRMS1_{51-98}$.

This work explores the structural features of BRMS1 N-terminal region to help clarifying the role of this area in the context of the full-length protein. Our crystallographic and biophysical results suggest that the biological function of BRMS1 may be affected by its ability to promote molecular clustering through its N-terminal coiled coil region.

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Keywords: BRMS1, coiled coil domain, X-Ray Structure.

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The role of glutathione transferases in herbicide resistant black grass weeds

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