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Crystal Structure of the BTB Domains from LRF and Kaiso: Implications for the Protein-protein Interaction properties of BTB transcription factors. P.J. Stogios¹, L. Chen², G.G. Privé^{1,2}, ¹Dept. of Medical Biophysics, Univ. of Toronto, Toronto, Canada. ²Ontario Cancer Inst., Toronto, Canada.

The BTB domain is a eukaryotic protein-protein interaction domain found in a variety of biological functions and contexts. There are many transcription factors (TF's) that contain the BTB domain and C2H2 zinc finger motifs, such as BCL6, PLZF, LRF, Kaiso and Miz1, each of which has been implicated in regulation of genes involved in cancer biology. In TF's that contain BTB domains, this domain's role is to mediate dimerization and in some cases, recruit enzyme complexes involved in chromatin remodeling and transcription regulation. Here we present recently solved structures of the BTB domains from the TF's LRF and Kaiso and progress towards the crystallization of the BTB domain from Miz1. In LRF-BTB, a protein-protein interaction groove that is utilized by some BTB domains to recruit transcription corepressors is lined with amino acids that are not compatible with corepressor binding. The BTB domain of Kaiso forms a double chain of oligomers in the crystal. This may reflect the tendency for BTB TF's to oligomerize on their DNA recognition sequences. Miz1-BTB crystals are currently being refined and improved to obtain well-diffracting crystals. These structures aid in our understanding of the mechanism of transcription regulation by BTB-zinc finger TF's and will be useful for future protein-protein interaction interference studies.