Structure and Recognition in the BARS/CtBP-dependent Transcription Regulation

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BARS/CtBP3 is a dual function protein acting as acyl-transferase in the Golgi apparatus (supporting membrane reshaping and vesicle traffic) [1], and as transcription co-repressor, in the nucleus, through the interaction with several enzymatic partners (e.g. histone deacetylases, HDACs). BARS/CtBP3 is based on a 3-domain structure, hosting a classical dehydrogenase fold [2]. Regulation of the two activities is achieved through competitive binding of NAD(H)/acyl-CoA, association equilibria, SUMO-ylation, and eventually through recognition of specific sequence motifs in the interacting partners. Binding of specific transcription factors to each subunit in the dimeric BARS/CtBP3, through a PXDLS sequence motif, is considered one of the basic mechanisms to recruit HDACs, and modify the chromatin structure, with ensuing transcription repression [2]. Structural considerations and mutant analyses indicate that different recognition sites are present on BARS/CtBP3 surface, in keeping with its pivotal role within a nuclear protein complex hosting more than twenty different proteins.

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Keywords: biomolecular recognition, enzyme function, transcription regulation