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A structural overview of Pontin, Reptin and their complex(es)

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Pontin, also known as RuvBL1 and Reptin, also known as RuvBL2 are highly conserved eukaryotic proteins belonging to the AAA+ family of ATPases, and closely related to the bacterial DNA helicase RuvB. They are ubiquitously expressed and have been associated with many cellular functions. In addition, a link was established between Pontin, Reptin and cancer [1].

The crystal structure of human Pontin was determined in our lab in 2006 [2]. It is hexameric, formed by ADP-bound monomers. Each monomer contains 3 domains: domains I and III are involved in ATP binding and hydrolysis and are structurally similar to equivalent domains in the bacterial homolog RuvB; a sequence insertion intercalated into domain I folds into domain II, unique among AAA+ proteins.

3D structures of Pontin/Reptin complexes were determined by other groups using electron microscopy [3-4]. In the human and yeast complexes, Pontin and Reptin form a dodecamer with two structurally distinct hexameric rings. It was suggested that both rings interact via domain II, but neither study settled the issue of whether the rings are homo- or hetero-oligomeric. However, a third EM study reported a single hetero-hexameric ring structure for the yeast Pontin/Reptin complex [5].

The first crystal structure of a Pontin/Reptin complex with a truncated domain II was published in 2011 by our lab [6]. The structure of a SeMet derivative revealed a dodecamer formed by two heterohexameric rings composed of alternating Pontin and Reptin monomers that interact via the retained part of domain II. More recently, the crystal structure of a full-length homologue from the thermophilic fungus *Chaetomium thermophilum* was published [7] and structures of larger complexes integrating Pontin/Reptin heterohexamers were obtained by EM [8-9].

The crystal structure of truncated Reptin was published in 2012 [10]. We have been working towards the crystal structure of full-length Reptin. To date, the best diffraction data were measured to 3.4 Å at ALBA XALOC and a preliminary structure obtained by MR. However, the location of domain II could not be ascertained and the search for better-diffracting crystals continues.

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