

## Poster Presentation

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### Structural basis for the interaction of HSP90 with R2TP and TTT complexes

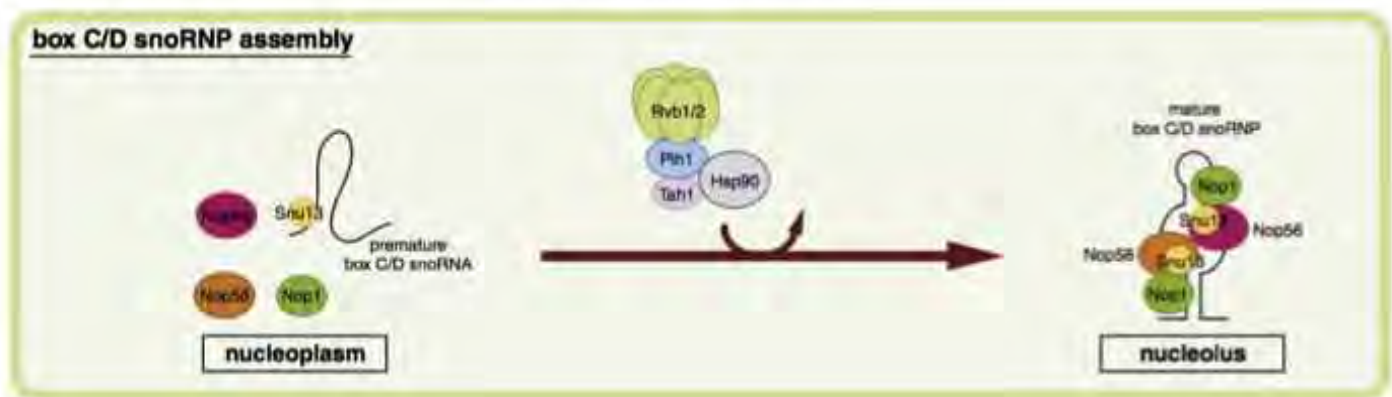
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Assembly and regulation of snoRNPs, RNA polymerases, PI3-kinase-like kinases and the chromatin remodelling complexes, depends on both the TTT complex (Tel2-Tti1-Tti2) and the R2TP complex (Rvb1-Rvb2-Tah1-Pih1p in yeast and RuvBL1-RuvBL2-RPAP3-Pih1D1 in metazoa), which provide the direct connection to Hsp90. Previous studies have shown that the R2TP complex recruits client proteins to Hsp90 for their folding and assembly. In this study, we have determined the crystal structures of three complexes: Hsp90-Tah1-Pih1p, Hsp90-Tah1, Hsp90-RPAP3 (TPR1 and TPR2 domains of RPAP3, each in complex with Hsp90). Tah1 was shown to have an unusual TPR domain, composed of only five  $\alpha$ -helices instead of the more usual six or seven. As expected, Tah1 TPR domain binds to the conserved MEEVD motif at the C-terminus of HSP90. In contrast, the C-terminal region of Tah1 is unstructured in the apo form but wraps around the CS domain of Pih1p, thus becoming ordered in the complex, and bridging the interaction between Hsp90 and Pih1p. We show a different modus operandii of Tah1-Hsp90 binding in yeast relative to RPAP3-Hsp90 interactions in metazoa. Finally, we present the crystal structure of the Pih domain of Pih1D1 bound to a phosphopeptide of Tel2 that reveals a novel phosphopeptide-binding domain specific for a subset of CK2 phosphorylation sites. Together these structures define the basis by which the R2TP complex connects the Hsp90 chaperone system to the TTT complex.

[1] Y. Kakiyama, W. Houry, *Biochimica et Biophysica Acta - Molecular Cell Research*, 2012, 1823, 101-107

### Function of R2TP Complex



**Keywords:** HSP90, R2TP, RPAP3